Unequal impact of the COVID-19 pandemic on paediatric cancer care: a population-based cohort study in China

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Summary

Background The COVID-19 pandemic has had widespread adverse collateral effects on health care delivery for non-COVID-19 disease conditions. Paediatric oncology care is reliant on prompt testing and diagnosis and on timely and coordinated multimodal treatment, all of which have been impacted by the pandemic. This study aimed to quantify the initial and enduring effects of the COVID-19 pandemic on the utilization of paediatric cancer care and to examine whether the pandemic differentially impacted specific demographic groups.

Method We performed an interrupted time series analysis using negative binomial regression to estimate the change in the monthly admissions for paediatric cancer patients (Age 0-17) associated with the COVID-19 pandemic and subsequent lockdown policies. We obtained data from deidentified individual electronic medical records of paediatric cancer inpatients admitted between January 1, 2015 and May 31, 2021 to a tertiary hospital that provides general and specialized healthcare services to an estimated population of 8.4 million in Jining China. Relative risk (RR) estimates representing monthly admissions compared with expected admissions had the pandemic not occurred were derived. The number of inpatient admissions lost due to the pandemic were estimated.

Findings The overall denominator for the paediatric population was 1 858 209 individuals in January 2015, which increased to 2 043 803 by May 2021. In total, there were 4 901 admissions for paediatric cancer during the study period, including 1 479 (30%) since February 2020 when the lockdown was implemented. A 33% reduction (95% CI: -43% to -22%) in admissions was observed in February 2020, with the largest relative reduction (-48%, 95% CI: -64% to -24%) among first-time admissions and admissions for patients from rural districts (-46%, 95% CI: -55% to -36%). Admissions quickly rebounded in March 2020 when many government-imposed mobility restrictions were lifted, and continued to resume gradually over time since April 2020, leading to a full recovery as of November 2020. However, the recovery for first-time admissions, and among female patients, younger patients (<5 years) and patients from rural districts was slower over time and incomplete (first-time admissions and rural patients) as of January 2021.

Interpretation The COVID-19 pandemic has had substantial impact on the timely utilization of paediatric oncology services in China, particularly in the early stage of the first wave. Importantly, some population groups were disproportionately affected and the recovery of admissions among those subgroups has been slow and incomplete, warranting targeted approaches to address potentially exacerbated gender and socio-economic inequalities in access to healthcare resources.

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Research in context

Evidence before this study

Previous studies have estimated the impact of the COVID-19 pandemic on healthcare delivery in various settings, finding sharp decreases in the treatment of non-COVID conditions. We searched PubMed and Google Scholar with the search terms "COVID-19, "SARS-COV-2", or "pandemic", combined with "health", "services", "cancer" or "oncology" in both English and Chinese for studies published between Jan 1, 2020 and Sep 5, 2021. We also searched the reference lists of identified studies to further identify other relevant publications. We found studies from both developed and developing countries reporting on the collateral impact of the pandemic on healthcare for patients with cancer. However, evidence of the effect of the pandemic on cancer diagnosis and service has been mainly limited to cross-sectional surveys. Most existing population-based studies had small sample sizes, focused only on an early and relatively short post-pandemic period, or relied on data collected at single time points before or during the pandemic. Moreover, these studies either included all patients or exclusively focused on adult patients with cancer; none specifically focused on paediatric cancer care. Studies have shown substantial pandemic associated reductions in outpatient visits and hospital admissions in China, particularly for stroke, respiratory disease, and non-emergency preventive care. However, we have found no published evidence specifically investigating longitudinal changes in paediatric cancer care, or that examined potential differential effects of the pandemic across subgroups of paediatric cancer patients.

Added value of this study

To our knowledge, this is the first study to explore the collateral effects of the COVID-19 pandemic on oncology care in China and the largest longitudinal cohort study to date that specifically assesses the impact of COVID-19 on paediatric oncology care. This study covered a large population and spanned a long follow-up period including 15 months since the outbreak in Wuhan in December 2019, which enabled us to quantify both the initial and enduring effects of COVID-19 pandemic over time. Additionally, this is the first study, to the best of our knowledge, that examined access to healthcare by sex, age and place of residence for patients in China during the COVID-19 pandemic.

Implication of all the available evidence

Data from routine health information systems could be used to monitor and evaluate the trend of people's access to health care, quality of care, health outcomes and their interactions with shock pandemic events.

This study demonstrates that the COVID-19 pandemic has had substantial impact on the timely utilization of paediatric oncology services in China, particularly in the early stage of the first wave. Importantly, female, younger children and those living in rural districts were disproportionately affected and the recovery of admissions among those subgroups has been slow and incomplete. In our view, our findings may serve notice to policy makers about the necessity to integrate an equity perspective into the disease outbreak preparedness and response. The COVID-19 pandemic's negative impact on health care of non-COVID-19 conditions may last even when the lockdown measures are removed and few or no more cases are reported at the local level. People-centered services and sufficient communications through multiple channels, both between patients and health service providers and among health-system actors, will be crucially important for addressing the likely negative consequences for diagnosis and treatment of cancer amidst the COVID-19 pandemic.

Introduction

The COVID-19 pandemic has disrupted health systems globally and has had widespread adverse collateral effects on health care delivery for non-COVID-19 diseases and conditions. In addition to being considered at higher risk for complications and worse outcomes from COVID-19,[1-3] patients with cancer require more hospital visits than patients with other chronic diseases.[4,5] Due to the nature of the disease and its treatment, paediatric oncology care is reliant on prompt testing and diagnosis, timely and coordinated multimodal treatment, and the involvement of multidisciplinary subspecialized teams throughout the disease trajectory.[4-8]

The prioritization of resources for patients infected with COVID-19 has generated a shortage of medical supplies and personal protective equipment. This factor — alongside lockdown measures and restricted public transportation — have contributed to deferred or forgone diagnoses and treatments for cancer, and even to the delay and suspension of the conduct of cancer clinical trials.[9-16] A cross-sectional survey conducted in 79 countries from all WHO regions in 2020 showed that 42% of institutions reported a decrease in newly diagnosed paediatric cancer cases, with 2% of institutions reporting complete suspension of evaluations for new suspected cancer cases and 7% of institutions reporting complete closure of paediatric hematology-oncology services. Additionally, 34% of institutions reported increased treatment abandonment.[6] Reduced surgical care, chemotherapy modifications, blood product shortages, and interruptions to radiotherapy were observed in a considerably high proportion of institutions.[1,6,10,12,17] Moreover, low- and middle-income countries with limited resources and less resilient health systems were disproportionately impacted.[1,6,12] However, evidence of the collateral effect of the pandemic on cancer diagnosis and service has been mainly limited to cross-sectional surveys of oncology centers.

These studies reflected the opinions and knowledge of respondents at a specific time point during an evolving pandemic and were unable to characterize the longitudinal effect on individual cancer service utilization.[1,6,12,18,19] Existing population-based studies conducted in the United States, England, New Zealand, Chile and India only focused on an early and relatively short post-pandemic period or relied on data collected at single time points before or during the pandemic.[9,11,12,20,21] In addition, these studies either included all patients or exclusively focused on adult patients with cancer, and none of them specifically assessed the effect on paediatric cancer care.

In February 2020, when the first wave of the pandemic in China reached its apex, and the widest and most stringent lockdown policies and mobility restrictions were enforced, both outpatient and inpatient visits declined precipitously in health facilities of all varieties and in all regions regardless of local variations in pandemic severity.[15] The effects were more profound in hospitals providing more specialized care than in primary care facilities, and greater in developed regions than in underdeveloped regions.[15] Healthcare resource utilization gradually rebounded soon after the outbreak peaked, but utilization patterns have not yet returned to their pre-COVID levels as of September 2020, the latest time point in existing investigations.[15,22,23] Due to the lack of data at the individual level, the heterogeneity of effects across therapeutic categories or demographic groups have not been investigated. Our study aims to assess the initial and enduring effects of the COVID-19 pandemic on the delivery and utilization of paediatric cancer care. Specifically, we quantify the reduction in the utilization of paediatric cancer care associated with the pandemic, and examine whether healthcare utilization recovered to pre-pandemic levels. We additionally aim to examine whether the pandemic differentially impacted specific demographic groups.

Methods

Study settings and data
The data are from Jining, a prefecture-level city with a population of 8·4 million in southwestern Shandong province. Since the first confirmed COVID-19 case diagnosed on Jan 23, 2020, 260 cases had been reported as of Aug 17, 2021 in Jining. The outcome measure was monthly inpatient admissions due to cancer. Data on paediatric inpatients (ages 0-17, the age range used by most hospitals in China to define paediatric care) admitted between Jan 1, 2015, and May 31, 2021 were obtained from the Affiliated Hospital of Jining Medical Hospital, one of the two tertiary hospitals providing cancer care service for the whole population in Jining. The database contains deidentified individual electronic medical records that include admission and discharge dates,

principal diagnosis at discharge, as well as demographic information of patients including sex, year of birth and district of residence. Single-year population estimates by age, sex and residence (rural or urban) were taken from the household registration system of the Public Security Bureau. Ethical approval was not required because data were de-identified and results are presented at the aggregate (group) level.

Study design and statistical analysis
To examine trends in paediatric cancer care utilization and to quantify changes associated with the COVID-19 pandemic, we employed an interrupted time series (ITS) analysis, a quasi-experimental design for causal inference widely used in the evaluation of healthcare interventions that are introduced at a distinct point in time.[24,25] Given a disperse variation structure in monthly counts of admissions, we used segmented negative binomial regression model, separating the time series into three periods: a pre-COVID-19 period (January 2015 to January 2020), a lockdown period (February 2020) and a post-lockdown period (March 2020 to May 2021). As our initial explorations of the form of the long-term trend suggested the appropriateness of the linear assumption, we included a linear effect of time to capture the long-term secular trend. We also included fixed-effect calendar month indicators as covariates to account for observed seasonal effects. The negative binomial model equation was expressed as follows.

$$\ln(E(Y_t)) = \beta_0 + \beta_1 T + \beta_{Feb} \text{ Feb} + \beta_{Mar} \text{ Mar}$$
$$+ \beta_{rec} (T - T_0) + \sum_{m=2}^{12} \beta_m \text{ M}$$
$$+ offset(\log(P_t))$$

where Y_t is the independent variable representing monthly admission for cancer inpatients at time (month) t. T and $T\text{-}T_0$ represent the time since the start of the study (January 2015) and the time since the lifting of lockdown conditions (T_0: March 2020). Feb is a binary indicator variable which is coded as "1" for admissions occurring during the lockdown period (February 2020), and "0" otherwise. Mar is an indicator variable for admissions occurring between January 2015 and February 2020, and is coded as "0", whereas admissions occurring during the period since the lifting of lockdown (March 2020 - May 2021) is coded as "1". M is the calendar month indicator accounting for the seasonal effect and P_t represents the catchment population at month t. Newey-West standard errors with autocorrelations of up to three lags were used. We repeated the regression model stratified by age group, sex, residence (rural vs. urban) and episode of care (first-time vs. all admissions). We also examined the interaction of the main effect terms with each subgroup to assess whether

patterns of utilization over time differed between key demographic patient groups.

We reported the level change (compared with the pre-pandemic forecasted level) for February and March 2020 (represented by the coefficients β_{Feb} and β_{Mar}, respectively), and the recovery slope change since April, represented by β_{rec}. Secondarily, we estimated the overall impact, calculated as the difference between the sum of fitted monthly outcomes in the presence of the COVID-19 pandemic (i.e., factual estimate) and that in the absence of the pandemic (i.e., counterfactual estimate), over the entire pandemic period (February 2020 to May 2021) and in the first three months of the pandemic (February through April, 2020). We simulated 10,000 predictions per month under each scenario (factual estimate and counterfactual estimate) using the estimated coefficients and their variance-covariance matrix of multivariate normal distribution derived from the model.[15,26] The 2·5 and 97·5 percentiles of the simulated values represented the 95% confidence interval of the difference. P-values were calculated as the smaller of the proportion of simulated values falling above or below zero (depending on the direction of the comparison), multiplied by two to present a 2-sided p-value. Given the evidence of comparable patterns in the change of health care utilization across China during the COVID-19 pandemic,[15] we also provided estimates of the potential overall national impact by assuming similar hospitalization rate for paediatric cancer and average impacts of the pandemic across the entirety of China.

All analyses were conducted in R-Version-4.0.2 (R-Project for Statistical Computing). A two-sided p<0·05 indicated statistical significance. This study is reported as per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.

Role of funding source
The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.
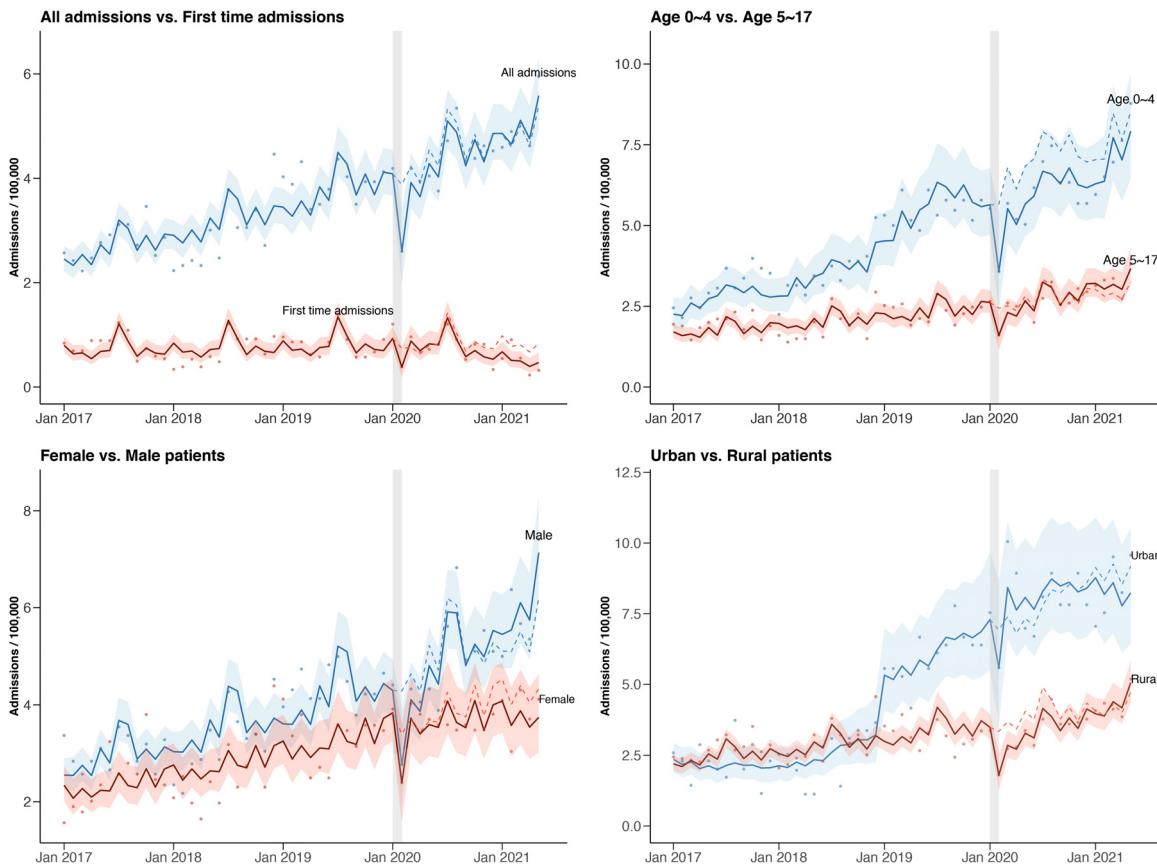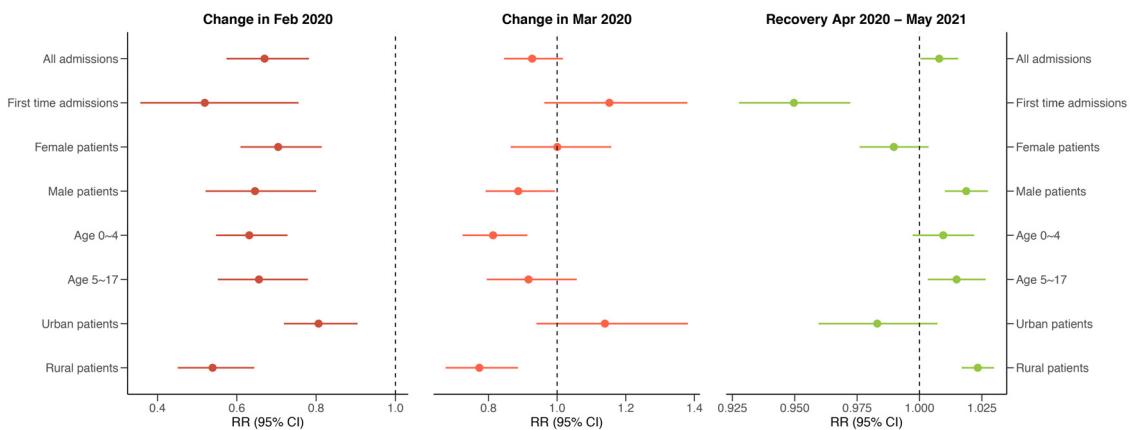
Results
The overall catchment population (ages 0-17) increased from 1 858 209 in January 2015 to 2 043 803 in May 2021. In total, there were 4 901 admissions for paediatric cancer in the study period, including 3 050 (62·2%) admissions for male patients, 1 905 (38·9%) for patients aged 0-4, 1 144 (23·3%) for patients from urban districts, 3 886 (79·3%: 78·2% for male and 81·0% for female; 77·0% for younger children and 80·7% for older ones) for patients with leukemia, 1,114 for (22·7%) first-time

admissions, and 1 479 (30·2%) admissions since the lockdown in February 2020. There was an overall increasing trend in the admissions rate for both male and female, urban and rural patients, and patients aged 0~4 and 5~17 (Figure 1). All of the 260 confirmed COVID-19 cases in the prefecture during the study period were diagnosed before March 2, 2020. No COVID-19 death had been reported as of May 31, 2021.

As is shown in Figure 1, the lockdown policies following the initial wave of COVID-19 were associated with a substantial immediate decrease in monthly admissions for paediatric cancer patients. In February 2020, a 33% (relative risk (RR)=0·67, 95% CI: 0·57-0·78, P<.0001) reduction in all admissions was observed (Figure 1A). The admissions rebounded in March 2020 (RR=0·93, 95% CI: 0·85-1·02, P=0·11) after intracity public transportation resumed and interdistrict travel restrictions were lifted, followed by an excess 1% increase per month (RR=1·01, 95% CI: 1·00-1·02, P=0·042) incrementally from April 2020 to May 2021 compared with the pre-pandemic period (Table 1). A 48% relative reduction in first-time admissions (RR=0·52, 95% CI: 0·36-0·76, P=0·0006) was detected in February 2020, which was 45% higher than the relative reduction in all inpatient admissions (48% vs. 33%, P=0·0008). After a rebound in March 2020 (RR=0·95, 95% CI: 0·93-0·97, P<·0001), first-time admissions continued to decrease by 5% per month compared with the expected (counterfactual) trend had the pandemic not occurred. By May 2021, the compounding effects per month resulted in an overall 43·5% decrease (95% CI: -59·1% to -24·2%, P=0·0002) from 17 (95% CI: 13-22) counterfactually estimated admissions down to 10 (95% CI: 7-13).

The immediate decrease in Feb 2020 was statistically significant and comparable among female (RR=0·70, 95% CI: 0·61-0·81, P<·0001) and male (RR=0·65, 95% CI: 0·52-0·80, P<·0001) inpatient admissions. After a quick rebound in March 2020, admissions for male patients continued to increase by 2% (95% CI: 1% -3%, P=0·0005) per month incrementally compared with pre-pandemic trend and surpassed the expected level in October 2020. In contrast, the recovery for admissions of female patients was incomplete, represented by a 1% decrease per month after an initial rebound in March 2020 (Figure 1, Table 1). Similarly, the decreases in the admissions for younger patients and patients from rural districts were more profound and recovery was slower compared with older patients and patients from urban districts, respectively.

Table 2 shows the number of admissions lost due to the COVID-19 pandemic during the lockdown month (February 2020), the first three months (February through April 2020), and the whole pandemic period (February 2020 to May 2021) respectively. Twenty-four (95% CI: 15 - 38) and 38 (95% CI: 14 - 64) admissions were lost during February 2020 and the first three

Figure 1. Interrupted time series analysis of changes in admissions for inpatients with cancer. (A) Dots represented observed admission rate (1/ 100, 000), solid lines indicate model-based factual estimate and dashed lines indicate counterfactual estimate assuming the pandemic did not occur. Shaded areas (light red/blue) indicated the 95% CI of the estimate. Grey rectangles indicate the period when the strictest lockdown policies were enforced. Results since January 2017 are show here. (B) 95% CIs or RRs for the estimated relative reduction in inpatient admissions in February 2020 (C) 95% CIs or RRs for the estimated relative reduction in inpatient admissions in March 2020 (D) 95% CIs of RRs for the estimated monthly relative change (in monthly multiplicative increments) in inpatient admissions from April 2020 to May 2021. See Table 1 for full relative change and 95% CIs, and testing for interactions. RR= relative risk.

	Change in Feb 2020				Change in Mar 2020				Monthly change Apr 2020- May 2021			
	RR (95% CI)	p-value	Ratio of RR (95% CI)	p-value	RR (95% CI)	p-value	Ratio of RR (95% CI)	p-value	RR (95% CI)[1]	p-value	Ratio of RR (95% CI)	p-value
All vs. First-time												
All	0·67 (0·57, 0·78)	<·0001	Ref		0·93 (0·85, 1·02)	·11	Ref		1·01 (1·00, 1·02)	·042	Ref	
First-time	0·52 (0·36, 0·76)	·0006	0·75 (0·63, 0·89)	·0008	1·15 (0·96, 1·38)	·12	1·25 (0·98, 1·60)	·071	0·95 (0·93, 0·97)	<·0001	0·94 (0·91, 0·96)	<·0001
Female vs. Male												
Female	0·70 (0·61, 0·81)	<·0001	Ref		1·00 (0·86, 1·16)	·99	Ref		0·99 (0·98, 1·00)	·15	Ref	
Male	0·65 (0·52, 0·80)	<·0001	0·92 (0·71, 1·19)	·51	0·89 (0·79, 0·99)	·038	0·89 (0·74, 1·07)	·20	1·02 (1·01, 1·03)	<·0001	1·03 (1·01, 1·05)	·0005
Young vs. Old												
Age 5-17	0·66 (0·55, 0·78)	<·0001	Ref		0·92 (0·79, 1·06)	·23	Ref		1·01 (1·00, 1·03)	·011	Ref	
Age 0-4	0·63 (0·55, 0·73)	<·0001	0·96 (0·77, 1·20)	·74	0·81 (0·72, 0·91)	<·0001	0·89 (0·74, 1·06)	·19	1·01 (1·00, 1·02)	·13	0·99 (0·98, 1·01)	·54
Urban vs. Rural												
Urban[2]	0·81 (0·72, 0·90)	·0002	Ref		1·14 (0·94, 1·38)	·18	Ref		0·98 (0·96, 1·01)	·17	Ref	
Rural	0·54 (0·45, 0·64)	<·0001	0·67 (0·54, 0·83)	·0002	0·77 (0·68, 0·89)	<·0001	0·68 (0·54, 0·85)	·0008	1·02 (1·02, 1·03)	<·0001	1·04 (1·02, 1·07)	·0017

Table 1: **Model based estimates for relative change.**
[1] RR (95% CI) for the estimated relative monthly (multiplicatively incremental) change in inpatient admissions.
[2] Index variable for time after 2018 was included in the regression model to adjust for non-linear trend in the pre-pandemic period.

	Change in Feb 2020			Change through Apr 2020			Change through May 2021			Calendar date at which admissions surpass the pre-pandemic level¹ for 3 consecutive months	Calendar date at which admissions surpass pre-pandemic forecasted trend for 3 consecutive months
	With COVID-19 and restrictions	Without COVID-19 and restrictions	diff	With COVID-19 and restrictions	Without COVID-19 and restrictions	diff	With COVID-19 and restrictions	Without COVID-19 and restrictions	diff		
All vs. First-time											
All	54 (41, 71)	80 (68, 93)	-26 (-39, -15)	208 (194, 222)	246 (216, 278)	-38 (-64, -14)	1464 (1432, 1496)	1517 (1369, 1677)	-54 (-220, 99)	Jul-20	Feb-21
First-time	8 (4, 16)	15 (10, 22)	-7 (-14, -3)	40 (36, 45)	44 (34, 56)	-4 (-14, 4)	221 (206, 238)	275 (229, 328)	-54 (-107, -7)	Jul-20	NA
Female vs. Male											
Female	32 (23, 45)	49 (39, 60)	-17 (-29, -8)	122 (115, 131)	151 (129, 175)	-28 (-48, -10)	938 (912, 966)	942 (830, 1074)	-5 (-130, 112)	Jul-20	Dec-20
Male	22 (14, 33)	31 (27, 35)	-9 (-14, -5)	86 (78, 96)	96 (84, 109)	-9 (-21, 2)	528 (503, 554)	576 (514, 643)	-48 (-119, 18)	NA	NA
Young vs. Old											
Age 5-17	22 (14, 33)	30 (26, 34)	-11 (-15, -7)	74 (70, 78)	97 (86, 110)	-23 (-35, -13)	523 (502, 546)	610 (528, 700)	-86 (-181, -1)	Aug-20	NA
Age 0-4	32 (23, 45)	49 (41, 58)	-17 (-26, -9)	122 (110, 135)	146 (129, 166)	-24 (-43, -7)	896 (863, 931)	897 (798, 1008)	-1 (-115, 107)	Sep-20	Nov-20
Urban vs. Rural											
Urban	20 (13, 31)	25 (22, 28)	-5 (-8, -2)	77 (66, 89)	75 (64, 88)	2 (-9, 13)	461 (435, 489)	466 (367, 587)	-5 (-128, 95)	May-20	May-20
Rural	31 (22, 44)	57 (47, 67)	-26 (-37, -17)	125 (118, 132)	177 (153, 204)	-53 (-78, -30)	982 (962, 1003)	1098 (943, 1270)	-115 (-290, 40)	Mar-21	May-21

Table 2: **Estimated change in number of inpatient admissions.**

¹ The pre-pandemic level indicates the mean monthly admissions during the three months (Nov 2019- Jan 2020) prior the lockdown.

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months from February 2020 respectively. Assuming similar average impacts of the pandemic across the entirety of China, these estimates would translate to 6 606 and 11 060 admissions lost, respectively, in the country overall. The loss in the first three months was statistically significant for all subgroups except for first-time admissions and admissions for females. We saw evidence of recovery in admissions for most subgroups over time. By May 2021, admissions had surpassed their pre-pandemic level except for female patients and new patients. Statistically significant reductions over the entire pandemic period were only evident in children aged 0~4 and for first-time admissions.

Discussion

Our study illustrates the considerable reductions in hospital admissions for paediatric cancer patients following the onset of the COVID-19 pandemic. Reductions were highest in Feb 2020 when lockdown measures and mobility restrictions were most stringent. A rebound was observed in March 2020, corresponding to the lifting of strict lockdown measures in Jining and the successful mitigation of COVID-19 transmission nationwide. The overall relative reduction was larger and the recovery was slower and incomplete for first-time patients admissions, admissions for female patients, infants and younger children (<5 years) and patients from rural districts.

To our knowledge, this is the first study to explore the collateral effects of the COVID-19 pandemic on oncology care in China and the largest longitudinal cohort study to date that specifically assesses the impact of COVID-19 on paediatric oncology care. A previous study using aggregate provincial level data demonstrated findings that were consistent with our own, indicating a remarkable reduction in outpatient and inpatient visits in every province of China in February 2020 irrespective of regional disparities in socioeconomic development and outbreak severity.[6,15,18] A comprehensive survey conducted in 213 institutions from the four continents confirmed the temporal complete closure of diagnosing new suspected paediatric cases, and the delay or failure in initiating cancer therapy.[6] Although outpatient services were temporally suspended in elective settings such as department of otorhinolaryngology and department of stomatology, there has been no evidence that tertiary hospitals in Jining proactively de-escalated the intensity of care provided in paediatric or oncology department.[27−29] The reduction in the utilization of paediatric cancer care is most likely attributable to massive mobility restrictions and the fear of getting infected with COVID-19 within health facilities.[15,23,30] A survey conducted in China indicated that over 40% of respondents feared in-hospital antenatal visits and over 50% considered or decided to defer or forgo their appointments.[31] Additionally, evidence

suggests that diagnostic and treatment pathways were modified or altered to minimize exposure to and poorer outcomes from COVID-19 infection.[16] For instance, experts at National Cancer Center of China have recommended that injectable chemotherapy may be substituted by oral drugs for patients in deep remission who are receiving maintenance therapy.[32,33] It has also been reported that the role of radiotherapy has expanded with COVID-19 as short course radiation therapy has often been used to replace or to delay other treatment modalities with higher infection risk for patients with rapidly proliferating tumors.[16,34]

Taken alongside findings of similar patterns of reduction in hospital admission for inpatients, our findings suggest that utilization patterns for paediatric cancer patients rebounded in Mar 2020 due to the lifting of lockdown in Jining and the control of rapid transmission within China, but recovery slowed thereafter. The recovery, although incomplete for some population groups, was quicker than the recovery of cancer services reported in other countries. This may be explained by the rapid, compressed nature of the outbreak in China,[35] where over 92% of its COVID-19 cases in 2020 were compressed in the first two months of the year. Nevertheless, since the control of the first wave of the pandemic in early 2020, China has been taking a "zero tolerance" COVID-19 policy that requires massive joint efforts from the entire society to stop local cases from turning into wider outbreaks.[36] Although no COVID-19 deaths and only a few positive COVID-19 cases were reported within a year preceding May 2021 in Jining, local government and the public were sensitive to internationally imported cases, and local outbreaks in neighbouring prefectures and provinces. The health QR (quick response) code system has been widely used since the lifting of massive lockdown measures. This approach relies on containing the transmission by tracking cases and close contacts. It has also been regarded as a tool that limits people's access to public spaces, especially those who have poor digital skills or have no smartphones or internet access, and those who have travel history.[37,38] The incremental delayed or missed visits and diagnosis in outpatient departments may further lead to the lag in the full recovery of treatment of cancer in the inpatient settings.

Previous studies showed that relative reductions in patient visits and hospital admissions were higher in larger metropolitan cities than in small cities, and higher in developed regions than in underdeveloped regions.[10,15] COVID-19 outbreaks in larger cities were longer, with higher incidence rates; correspondingly, stricter and longer mobility restrictions were implemented than for smaller, less populated cities.[15,35] Our study was able to disaggregate findings by place of residence (rural vs. urban) of patients rather than by the types or locations of health facilities in previous studies. We were therefore able to identify that the overall

relative reduction in admissions was larger and the recovery was slower for patients living in rural districts. Given that media coverage about COVID-19 prevention focused predominantly on large urban cities, urban residents reported more positive attitudes toward the effectiveness of community mitigation measures, and therefore were more likely to engage in preventive behaviors such as staying at home as much as possible and avoiding gatherings and public transportations.[39] However, interdistrict and intercity travel restrictions likely had large, adverse impacts on patients in rural districts as these measures prevented them from traveling to and seeking cancer care in hospitals in urban districts. The findings indicate the need to address capacity shortfalls of rural county hospitals in meeting residents' timely need of high quality primary and specialty care, both in response to the COVID-19 pandemic and for the long run.[40] Additionally, the financial and social security of low-income and low-skilled groups, especially for the large number of rural-hukou migrant workers, were disproportionately affected by the pandemic.[41−45] This is different from some other countries where the COVID-19 pandemic has had more severe labor-force impacts on urban adults than their rural counterparts.[8,46] Lower savings and the drop of income and employer-based health insurance coverage due to the sudden and unexpected furlough or job loss of parents likely further hindered rural children's access to healthcare services. Moreover, the differences in health insurance coverage levels between the rural residents and the urban employer are even starker. Although healthcare is generally less expensive in rural areas, the cost of treatment is disproportionately high for the rural population since rural residents seeking high quality care and/or specialty care travel to visit physicians at urban hospitals.[40]

Our study provides further evidence that female children and adolescent girls' access to health care for time-sensitive conditions have been disproportionately affected by the COVID-19 pandemic. Aside from notably larger reduction in female adults' access to health care likely due to their higher job loss and/or increased family responsibility caring for children during the pandemic,[11,13,47-50] disproportionate negative health consequences for girls, especially girls with disabilities or medical conditions have been reported, potentially reflecting a gender bias.[49,51] A comprehensive survey conducted in 46 countries indicated that about two-thirds (63%) of girls reported increased household chores, and over half (52%) of girls reported increased caring duties for siblings and others since the start of the COVID-19 pandemic, higher than 43% and 42% of boys respectively.[51,52] This multinational survey also indicated that girls were twice as likely as boys (20% vs. 10%) to claim that household chores were overwhelming and an obstacle to learning.[53] Although there has been no direct investigation about the underlying causes

of observed gender disparities in the adverse impact of the pandemic on paediatric health care in Jining and China, our findings may serve notice to policy makers about the necessity to integrate an equity perspective (e. g. gender, regional and social class inequity) into the disease outbreak preparedness and response.[54,55] The COVID-19 pandemic's negative impact on health care of non-COVID-19 conditions may last even when the lockdown measures are removed and few or no more cases are reported at the local level. Mitigation strategies may include promoting community outreach to and regular phone or Wechat (a multi-purpose messaging and social medial app) check-ins with girls in need of routine health care, or ensuring clear and sufficient communication to girls and their parents/care providers about alternative health services during the pandemic, including virtual care and in-home health care.[55,56]

Decreases in first-time admissions for paediatric cancer patients may reflect delays in diagnosis. Prompt diagnosis is critical as it allows the opportunity for the timely administration of treatment when the disease is still in its earliest stages, which can improve prognosis and better ensure positive treatment outcomes with minimal side or late effects.[57] The more profound decrease in younger children's access to health care may be explained by their parents' higher concern about hospital-acquired infections. The primary reason parents and caregivers claimed that they were not going out to get healthcare or medical supplies was due to worry about getting infected by COVID-19.[58] A significant association has been shown between a child's age and their guardian's awareness of the risk of infection and their corresponding uncertainty about being able to ensure the child's safety. The reported awareness was about 84% for parents of newborn and infant, 80% for parents of children aged 2-4, and 55% for those with the oldest children aged 15-17.[53] In many developing countries, there are no clear pathways of care for most cancers that patients can rely on or are aware of, which usually leads to confusion and delays.[56] Therefore, people-centered services and communications, both between patients and health service providers and among health-system actors, will be crucially important for reducing delays in diagnosis, treatment, and loss to follow-ups.[56,59]

The strength of our study is that the data covered a considerably large population and spanned a long period of follow-up, which enabled us to control for seasonal patterns, secular trends and potential unobserved time-varying confounding factors. Moreover, this is the first study, to the best of our knowledge, that examined access to healthcare by sex, age and place of residence for paediatric cancer patients in China during the COVID-19 pandemic, and is also the largest population-based cohort study specifically evaluating the impact of the pandemic on paediatric oncology care. However, the study had limitations. The data were from a single healthcare institution, so their generalizability may be

limited. Also, the adverse impact of the pandemic on paediatric cancer admissions may have been underestimated, since delays in utilization of health care resources among patients who had been treated in the provincial capital was not captured, especially in the early stage of the first wave of the pandemic. Additionally, analyses stratified by cancer type or stage were not conducted due to limited number of monthly admissions, missingness in stage or severity classification, and the predominance of leukemia admissions (about 80% overall). Moreover, our assessment of cancer care utilization only focused on care received in inpatient treatment settings, and did not reflect trends in outpatient visits or alternative telehealth visits and consultations. Lastly, we were not able to compare the quality of care before and during the COVID-19 outbreak, nor were we able to quantify changes in health outcomes of patients associated with the pandemic.

In summary, this study demonstrates that the COVID-19 pandemic has had substantial impact on the timely utilization of paediatric oncology services in China, particularly in the early stage of the first wave. Importantly, female, younger children and those living in rural districts were disproportionately affected and the recovery of admissions among those subgroups has been slow and incomplete, indicating the need to integrate a health equity perspective into the disease outbreak preparedness and response.

Contributors
Hong Xiao and Zhenhui Liu had full access to, verified all the data in the study, and take responsibility for the integrity of the data and the accuracy of data analysis.

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Data sharing statement
The datasets generated and analyzed during the current study are available from Dr Hong Xiao upon reasonable request.

Declaration of interests

The authors declare no competing interests related to the study.

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