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Impact of the COVID-19 pandemic on patients with paediatric cancer in low-income, middle-income and high-income countries: a multicentre, international, observational cohort study

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ABSTRACT

Objectives Paediatric cancer is a leading cause of death for children. Children in low-income and middle-income countries (LMICs) were four times more likely to die than children in high-income countries (HICs). This study aimed to test the hypothesis that the COVID-19 pandemic had affected the delivery of healthcare services worldwide, and exacerbated the disparity in paediatric cancer outcomes between LMICs and HICs.

Design A multicentre, international, collaborative cohort study.

Setting 91 hospitals and cancer centres in 39 countries providing cancer treatment to paediatric patients between March and December 2020.

Participants Patients were included if they were under the age of 18 years, and newly diagnosed with or undergoing active cancer treatment for Acute lymphoblastic leukaemia, non-Hodgkin's lymphoma, Hodgkin lymphoma, Wilms' tumour, sarcoma, retinoblastoma, gliomas, medulloblastomas or neuroblastomas, in keeping with the WHO Global Initiative for Childhood Cancer.

Main outcome measure All-cause mortality at 30 days and 90 days.

Results 1660 patients were recruited. 219 children had changes to their treatment due to the pandemic. Patients in LMICs were primarily affected (n=182/219, 83.1%). Relative to patients with paediatric cancer in HICs, patients with paediatric cancer in LMICs had 12.1 (95% CI 2.93 to 50.3) and 7.9 (95% CI 3.2 to 19.7) times the odds of death at 30 days and 90 days, respectively, after presentation during the COVID-19 pandemic (p<0.001). After adjusting for confounders, patients with paediatric cancer in LMICs had 15.6 (95% CI 3.7 to 65.8) times the odds of death at 30 days (p<0.001).

Conclusions The COVID-19 pandemic has affected paediatric oncology service provision. It has disproportionately affected patients in LMICs, highlighting and compounding existing disparities in healthcare systems globally that need addressing urgently. However, many patients with paediatric cancer continued to receive their normal standard of care. This speaks to the adaptability and resilience of healthcare systems and healthcare workers globally.

Strengths and limitations of this study

- This is the first large-series, global, multicentre, international cohort study to explore the effect of the COVID-19 pandemic on paediatric oncology care, which includes data from 1660 patients in 39 countries.
- The collaborative approach for this study allowed a large series of high-quality data to be collected in a timely manner without overburdening centres, with 91 centres being involved in this study.
- A single study database was used, which allowed for data-analysis to occur to ascertain the short-term outcome for paediatric oncology patients while the study continued to collect follow-up data.
- This is an interim-report, and many centres involved in the wider study—including all centres in India—have not been able to gain ethical approval to share their data for this report; although approvals will be in place to share data after 12 month follow-up data has been collected in December 2021.
- This study has limited its focus to nine of the the most common paediatric cancers globally as identified by the WHO, and hence does not capture the effects of the pandemic on rarer cancers.

INTRODUCTION

Approximately 200 000–400 000 children are newly diagnosed with cancer annually.[1–4] Cancers in the paediatric population differ greatly from those in adults, particularly in the diagnoses seen and the availability of suitable healthcare.[5] Fewer than 20% of all paediatric cancers are found in high-income countries (HICs), where multimodal

care is more accessible.[2] Despite being ostensibly highly curable diseases, delays in diagnosis and paucity of care for many patients with paediatric cancer has resulted in paediatric cancer being the second leading cause of non-communicable disease deaths for children worldwide.[1–4] More than 90% of these deaths occur in low-income and middle-income countries (LMICs).[4] The inordinately high number of person-years of life lost make paediatric cancer care a global health priority.[2]

The COVID-19 pandemic may have exacerbated the imbalance of paediatric cancer outcomes between LMICs and HICs. There were reports globally on the cancellation of elective health services—including paediatric surgery and radiotherapy, essential outpatient services, shortage of essential medications, delays in diagnosis, hospital inpatient services being overwhelmed and healthcare staffing issues.[6–8] During the initial phase of the pandemic, the reorganisation of paediatric cancer services worldwide was partly driven by assumptions that patients with paediatric cancer were particularly vulnerable to COVID-19. This assumption has since been refuted[9] with the largest study to date on this topic identifying only 259 children with cancer suffering from severe COVID-19 infection worldwide.[10] The international paediatric cancer community swiftly adapted their guidance to emphasise the importance of continuing care for patients with paediatric cancer.[11] Despite this, three international cross-sectional studies conducted by different research teams at different timepoints reported that the majority of clinicians surveyed believed that their paediatric cancer centre had reduced their usual level of care either as a precaution, or due to a lack of resources or accessibility.[8 12 13] These reported delays or alterations to treatment—if accurate—could prove extremely detrimental to patients with paediatric cancer in both the short term and the long term.[8 14]

As all international analyses reported thus far have been cross-sectional studies focused on the perceptions of clinicians,[8 12 13] there remains a need to corroborate these findings and assess the impact of the pandemic on the outcomes of patients with paediatric cancer. Therefore, we conducted an international, multicentre, cohort study with the primary aim to ascertain the short-term outcome across 16 HICs and 25 LMICs during the COVID-19 pandemic by determining 30-day and 90-day all-cause mortality rates for paediatric oncology patients who underwent treatment. We also examined the factors that influenced these outcomes including tumour specific data, patient-specific demographics, and changes to health system frameworks. Secondary objectives of this study are to evaluate (1) the changes to paediatric cancer management during the COVID-19 pandemic, (2) the factors that influenced these changes from a health systems framework (eg, infrastructure, workforce, redeployment of staff, access to services) and (3) the number of patients with paediatric cancer who were placed under palliative care or who sought abandonment of treatment during the pandemic. The WHO Global Initiative for Childhood Cancer (GICC) has primarily used six common cancers as a benchmark for assessing global paediatric cancer care: acute lymphoblastic leukaemia (ALL), Burkitt lymphoma, Hodgkin lymphoma, retinoblastoma, Wilms' tumour and low-grade glioma.[15] Therefore, this study focuses on the GICC identified cancer benchmarks and four other paediatric cancer manifestations that had been identified to be common in both LMICs and HICs: sarcoma, high-grade glioma, medulloblastoma and neuroblastomas.

METHODS

Study design

This is a multicentre, international, mixed (retrospective and prospective), collaborative (online supplemental appendix S1) cohort study at 91 hospitals in 39 countries (online supplemental appendix S2). Only routine, anonymised data was collected, and no clinical care pathways were changed for the study as per the study protocol.[16] Participating collaborators gained local approvals in accordance with their institutional ethical regulations (online supplemental appendices S3–S5). Reporting has been conducted in line with the Strengthening the Reporting of Observational Studies in Epidemiology statement for observational studies[17] (online supplemental appendix S6).

Study setting

Hospitals or cancer centres in all continents providing cancer treatment to paediatric patients were eligible to participate in this study.[16] The World Bank classification of the fiscal year of 2021 was utilised to categorise centres as HIC or LMIC.[18] Local collaborators at all study sites were responsible for identifying eligible patients for inclusion and collecting data using the Research Electronic Data Capture (REDCap) web application.

Participants

Patients at participating centres were included if they were under the age of 18 years and newly diagnosed with or undergoing active treatment for an eligible cancer between 12 March 2020—the date that the WHO declared the start of the COVID-19 pandemic—and 12 December 2020. Eligible cancers were: ALL, non-Hodgkin's lymphoma, Hodgkin lymphoma, Wilms' tumour, sarcoma (osteosarcoma, Ewing sarcoma and rhabdomyosarcoma), retinoblastoma, glioma, medulloblastoma and neuroblastoma in keeping with the WHO GICC. Site investigators were provided with a range of written materials setting out possible strategies to capture consecutive eligible patients. In addition, investigators were invited to join social media groups and teleconferences for the purpose of troubleshooting site-specific recruitment issues and shared learning. The importance of working across paediatric oncological specialties was emphasised throughout to minimise bias that could be introduced by certain

patients not being included. Sample size was calculated as per the protocol.[16]

Outcome variables

The primary outcomes were all-cause mortality at 30 days and 90 days from initial anti-cancer treatment as of 12th March 2020. The key secondary outcomes were any alterations to paediatric cancer treatment decisions during the COVID-19 pandemic and changes to health system frameworks which led to these alterations, as reported by local collaborators. Additional secondary outcomes were any complications within 30 days of first anti-cancer treatment as of 12th March 2020 and the number of patients who abandoned treatment.

Other variables

Baseline patient variables included age, weight at admission, patient sex and American Society of Anesthesiologists (ASA) grade at the time of presentation. Baseline tumour variables included tumour type, staging and diagnosis date. Definitions for tumour types were provided for reference.[16] Treatment variables included initial multidisciplinary team (MDT) decision, date thereof and treatment type (chemotherapy, radiotherapy, immunological therapy, surgery, palliative treatment and/or no anticancer treatment). For patients receiving radiotherapy, radiation field and type was reported. For patients receiving surgery, hospital COVID-19 designation was reported; a cold hospital was defined as COVID-19-free zone and a hot hospital was defined as a zone with a confirmed COVID-19 case where active treatment for COVID-19 was administered. The National Confidential Enquiry into Patient Outcome and Death (NCEPOD) Classification of Intervention was used to define the urgency of surgery.[19] The reason for surgery—whether diagnostic, curative or palliative—and the time from admission to surgery were also reported. Specific data fields from the proforma can be found in online supplemental appendix S7.

Data validation

To validate the data and reduce the potential for bias due to incomplete case ascertainment, a three-stage process was performed at a randomly selected subset (10%) of participating centres. First, key processes used to recruit and follow-up eligible patients were self-reported by local leads. Second, an independent validator from the same centre quantitatively reported case ascertainment. Third, a local independent validator randomly sampled a section of the data for accuracy. The targets for validation were a secure and accurate record of patients entered onto REDCap with no case/data duplication and data accuracy >95%.

Statistical methods

All duplicates were removed post-data validation. Missing data for covariates were analysed to determine if they were related to the outcome and either complete-case analyses or multiple imputation techniques were used for the analyses accordingly. Baseline characteristics for LMIC and HIC countries are presented as proportions or mean (SD) or median (range) and statistical differences were determined using a chi-square test or Fisher's exact test. Statistical differences in 30-day and 90-day mortality between LMICs and HICs were determined using Fisher's exact test due to low event rates. A discrete time survival model was used to assess time to 30-day mortality adjusting for important prognostic factors and displayed using Kaplan-Meier plots. Multivariate logistic regression analyses were conducted between covariates and the primary outcome of 30-day mortality. The LASSO (Least Absolute Shrinkage and Selection Operator) method was utilised for variable selection, and to determine the final multilevel multivariable logistic model of covariates affecting outcomes. Results are presented as ORs or hazard ratios with corresponding 95% CIs. Data were analysed using Stata V.15.1 and SAS V.9.4.

Patient and public involvement

The steering committee met with the parents of 11 children from across North America, Europe, Asia and Africa during the planning of this study. Their children had a range of neoplasms including leukaemia, rhabdomyosarcoma, osteosarcoma and Wilm's tumour. It was found that 40% of the children represented in the group had been impacted by COVID-19 in one of three key-ways: follow-up clinics had become virtual; delays in treatment; and parents having to receive news from doctors without their partners. All parents agreed on the value and benefit of the study. Two parents (one from the UK and one from Nigeria) agreed to provide their input on the findings and dissemination of the results.

RESULTS

A total of 1660 patients were eligible for the study. They were recruited consecutively across the 91 hospitals (LMICs: 65/91, 71.4%) in 39 countries (figure 1, online supplemental appendices S1 and S2). A total of 1104 patients (66.5%) were from LMICs and 556 were from HICs (table 1 and online supplemental appendix S8). Patients with paediatric cancer in LMICs were typically

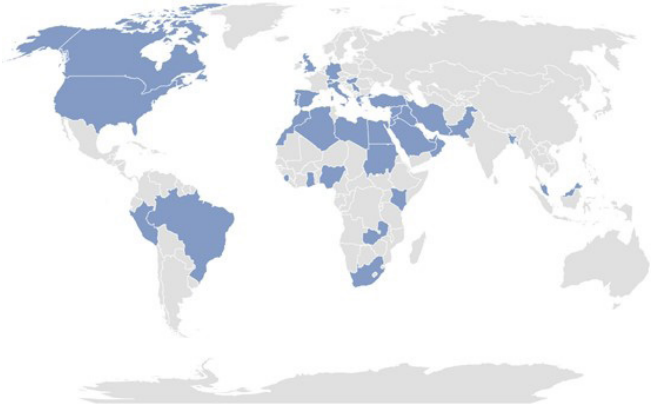

Figure 1 Location of the 39 countries that had centres participating in this study.

Table 1 Baseline characteristics

Variable		LMICs (N=1104) N (%)	HICs (N=556) N (%)	Total (N=1660) N (%)	P value
Age (years), median (range)		5.00 (2.0–10.0)	7.00 (3.0–13.0)	6.00 (3.0–11.0)	<0.001
Sex	Female	469 (42.5)	230 (41.4)	699 (42.1)	0.66
	Male	631 (57.2)	324 (58.3)	955 (57.5)	
	Missing	4 (0.4)	2 (0.4)	6 (0.4)	
Weight (kg), median (range)		18.0 (13.0–29.0)	27.1 (16.8–49.1)	20.0 (14.0–35.0)	<0.001
ASA grade	(1a) Normal healthy patient	344 (31.2)	101 (18.2)	445 (26.8)	<0.001
	(2a) Patient with mild systemic disease	423 (38.3)	206 (37.1)	629 (37.9)	
	(3a) Patient with severe systemic disease	149 (13.5)	220 (39.6)	369 (22.2)	
	(4a) Patient with severe systemic disease that is a constant threat to life	34 (3.1)	25 (4.5)	59 (3.6)	
	(5a) Moribund patient who is not expected to survive without the operation	8 (0.7)	0 (0.0)	8 (0.5)	
	Missing	146 (13.2)	4 (0.7)	150 (9.0)	
Tumour type	Non-Hodgkin's lymphoma	89 (8.1)	29 (5.2)	118 (7.1)	<0.001
	Acute lymphoblastic leukaemia	380 (34.4)	234 (42.1)	614 (37.0)	
	Ewing sarcoma	32 (2.9)	31 (5.6)	63 (3.8)	
	Glioma	73 (6.6)	69 (12.4)	142 (8.6)	
	Hodgkin lymphoma	63 (5.7)	38 (6.8)	101 (6.1)	
	Medulloblastoma	57 (5.2)	31 (5.6)	88 (5.3)	
	Neuroblastoma	80 (7.2)	48 (8.6)	128 (7.7)	
	Osteosarcoma	45 (4.1)	25 (4.5)	70 (4.2)	
	Retinoblastoma	87 (7.9)	4 (0.7)	91 (5.5)	
	Rhabdomyosarcoma	61 (5.5)	25 (4.5)	86 (5.2)	
	Wilms tumour	137 (12.4)	22 (4.0)	159 (9.6)	
Was patient tested for COVID-19?	No	631 (57.2)	148 (26.6)	779 (46.9)	<0.001
	Yes	367 (33.2)	366 (65.8)	733 (44.2)	
	Missing	106 (9.6)	42 (7.6)	148 (8.9)	
Was patient diagnosed with COVID-19?	No	943 (85.4)	519 (93.3)	1462 (88.1)	0.004
	Not applicable (no anti-cancer treatment given post March 11th 2020)	11 (1.0)	3 (0.)	14 (0.8)	
	Proven with laboratory test or CT Thorax	31 (2.8)	6 (1.1)	38 (2.2)	
	Probable—clinically suspected	5 (0.54)	3 (0.5)	8 (0.5)	
	Unknown	74 (6.7)	19 (3.4)	93 (5.6)	

Continued

Table 1 Continued

Variable	LMICs (N=1104) N (%)	HICs (N=556) N (%)	Total (N=1660) N (%)	P value
Missing	40 (3.6)	6 (1.1)	46 (2.8)	

ASA, American Society of Anesthesiologists; HICs, high-income countries; LMICs, low-income and middle-income countries.

younger, lighter in weight and had a lower ASA grade at presentation than the patients recruited in HICs (table 1). The most common paediatric cancer in both HICs and LMICs included in this study was ALL (n=614/1660, 37.0%). Retinoblastomas were more common among LMIC patients (n=87/1104, 7.9%) than HIC patients (n=4/556, 0.7%). A minority of patients with paediatric cancer in both LMICs and HICs were diagnosed with COVID-19.

Central nervous system (CNS) involvement data were available for 557 patients with ALL (LMICs: n=337/380, 88.7%; HICs: n=220/234, 94.0%). Most of these patients were negative for CNS involvement (LMICS: n=312/337, 92.6%; HICs: n=179/220, 81.4%). Ann Arbor staging data was available for most patients with Hodgkin lymphoma (LMICs: n=52/63, 82.5%; HICs: n=33/38, 86.8%). Among HIC patients, 17 were stage II (51.5%), 5 were stage III (15.2%), and 11 were stage IV (33.3%). Among LMIC patients, 5 were stage I (9.6%), 14 were stage II (26.9%), 14 were stage III (26.9%) and 19 were stage IV (36.5%). Similarly, Ann Arbor staging data were available for most patients with non-Hodgkin's lymphoma (LMICs: n=61/89, 68.5%; HICs: n=23/29, 79.3%). Among HIC patients, five were stage I (21.7%), five were stage II (21.7%), sevenwere stage III (30.4%) and six were stage IV (26.1%). Among LMIC patients, 7 were stage I (11.5%), 8 were stage II (13.1%), 31 were stage III (50.8%) and 15 were stage IV (24.6%). Staging data were available for 131 patients with glioma (LMICs: n=65/73, 89.0%; HICs: n=66/69, 95.7%). Most of these patients had a low-grade glioma (LMICS: n=40/65, 61.5%; HICs: n=53/66, 80.3%). For the remaining 499 patients in LMICs with a paediatric cancer, staging was known for 400 patients (80.2%): 208 had localised cancer (52.0%), 75 had regional cancer (18.8%), and 117 had metastatic cancer (29.3%). Similarly, for the remaining 186 patients in HICs with a paediatric cancer, 68 had localised cancer (36.6%), 21 had regional cancer (11.3%) and 64 had metastatic cancer (34.4%).

After 30 days postpresentation, 64 patients (3.9%) were lost to follow-up (figure 2 and table 2). Where data were available, the risk of death among patients with paediatric cancer in LMICs at 30 days after presentation was 4.3% (95% CI 3.1 to 5.5). The tumour types of the patients in LMICs that died at 30 days were ALL (n=8), non-Hodgkin's lymphoma (n=7), medulloblastoma (n=7), glioma (n=6), neuroblastoma (n=6), rhabdosarcoma (n=4), retinoblastoma (n=3), Wilms' tumour (n=3) and osteosarcoma (n=1). Of these deaths, 2 were in low-income countries (n=2/35, 5.7%), 16 were in lower-middle-income countries (n=16/488, 3.3%) and 27 were in upper-middle-income countries (n=27/528, 5.1%). The risk of death among patients with paediatric cancer in HICs at 30 days after presentation was 0.4% (95% CI 0.0 to 0.9). The tumour types of the patients in HICs that died at 30 days were ALL (n=1) and rhabdosarcoma (n=1). Relative to patients with paediatric cancer in HICs, patients with paediatric cancer in LMICs had 12.1 (95% CI 2.9 to 50.3) times the odds of death at 30 days after presentation during the COVID-19 pandemic (p<0.001). At 90 days, 187 patients (11.3%) overall had been lost to follow-up (figure 2 and table 2). The risk of death among patients with paediatric cancer in LMICs at 90 days after presentation was 7.0% (95% CI 5.4 to 8.6). The risk of death among patients with paediatric cancer in HICs at 90 days after presentation was 0.9% (95% CI 0.1 to 1.8). Relative to patients with paediatric cancer in HICs, patients with paediatric cancer in LMICs had 7.9 (95% CI 3.2 to 19.7) times the odds of death at 90 days after presentation during the COVID-19 pandemic (p<0.001). Among paediatric patients who survived to 30 days, relative to patients with paediatric cancer in HICs (0.6%), patients with paediatric cancer in LMICs (2.3%) had 4.2 (95% CI 1.2 to 14.1) times the odds of death at 90 days after presentation during the COVID-19 pandemic

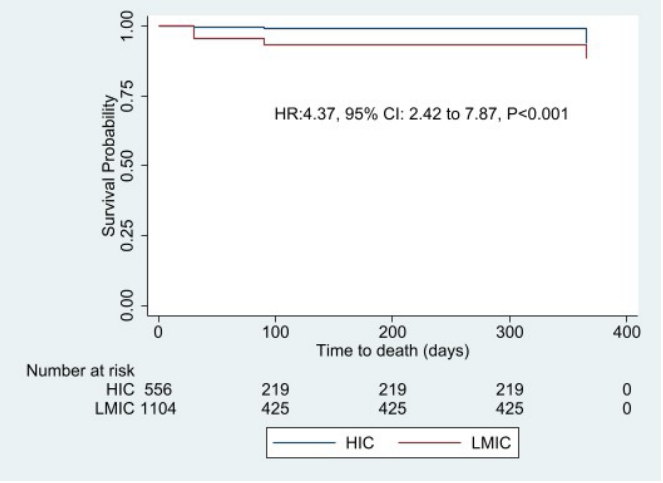

Figure 2 Kaplan-Meier survival curve of patients with paediatric cancer in high-income countries (HICs) and low-income and middle-income countries (LMICs) adjusted for COVID-19 test outcome, MDT decision: anti-cancer therapy and whether the first admission was planned. MDT, multidisciplinary team.

Table 2 Thirty-day and 90-day mortality

		LMICs (N=1104) N (%)	HICs (N=556) N (%)	P value
30-day mortality	Alive	1006 (91.1)	543 (97.7)	<0.0001
	Dead	45 (4.1)	2 (0.4)	
	Unknown	53 (4.8)	11 (2.0)	
90-day mortality	Alive	878 (79.5)	524 (94.2)	<0.0001
	Dead	66 (6.0)	5 (0.9)	
	Unknown	160 (14.5%)	27 (4.9%)	

HICs, high-income countries; LMICs, low-income and middle-income countries.

(p=0.0104). The tumour types of the patients in LMICs that died between 30 and 90 days were ALL (n=7), non-Hodgkin's lymphoma (n=1), medulloblastoma (n=2), glioma (n=1), neuroblastoma (n=5), rhabdosarcoma (n=1), Wilms' tumour (n=2), Ewing's sarcoma (n=1) and osteosarcoma (n=1). The tumour types of the patients in HICs that died between 30 and 90 days were ALL (n=2) and non-Hodgkin's lymphoma (n=1). All these deaths occurred in middle-income countries: 18 in lower-middle-income countries (n=18/427, 4.2%), and 3 were in upper-middle-income countries (n=3/442, 0.7%).

After adjusting for confounders, relative to patients with paediatric cancer in HICs, patients with paediatric cancer in LMICs had 15.6 times the odds of death at 30 days after presentation during the COVID-19 pandemic (p<0.001) (table 3). After adjusting for confounders, relative to patients with paediatric cancer who were not proven to be COVID-19 positive, patients with paediatric cancer who were COVID-19 positive postpresentation had 22.8 times the odds of death at 30 days after presentation (table 3 and figure 3).

A total of 219 children had delays or alterations to treatment. An initial MDT decision was made for 1435 of the included children (86.4%) to receive chemotherapy: 931 in LMICs and 504 in HICs. Secondary to the effects of the COVID-19 pandemic, 7 children in LMICs had their planned chemotherapy cancelled, 84 and 17 children in LMICs and HICs, respectively, had delayed delivery of their chemotherapy, 8 children in LMICs were given a reduced dose from the normal regimen that would have been given prior to the pandemic, 2 children in LMICs were given an increased dose compared with the normal regimen, 7 children in LMICs had fewer cycles of chemotherapy relative to the normal regimen, 6 children in LMICs and one child in an HIC had more cycles of chemotherapy relative to the normal regimen, 5 children in LMICs and 1 child in an HIC had a shorter duration of total treatment than would normally be given, 18 children

Table 3 Multivariable Generalised Linear Model analysis using Least Absolute Shrinkage and Selection Operator method for variable selection: 30-day mortality

		OR	95% CI	P value
World Bank Income Status (Reference: HIC)	LMIC	15.6	3.7 to 65.8	<0.001
COVID Status (Reference: COVID negative)	Not applicable (No anti-cancer treatment given post March 11th 2020)	0.62	0.08 to 4.73	0.642
	Proven with laboratory test or CT Thorax	22.8	3.75 to 4.73	0.013
	Probable – clinically suspected	0.001	0.001 to 999.99	–
	Unknown	0.30	0.04 to 2.31	0.250
MDT decision (Reference: no anticancer therapy)	Provide anticancer therapy	7.69	1.37 to 43.3	0.021
Was the first admission planned? (reference: Yes)	No	0.23	0.12 to 0.44	<0.001

HIC, high-income country; LMIC, low-income and middle-income country; MDT, multidisciplinary team.

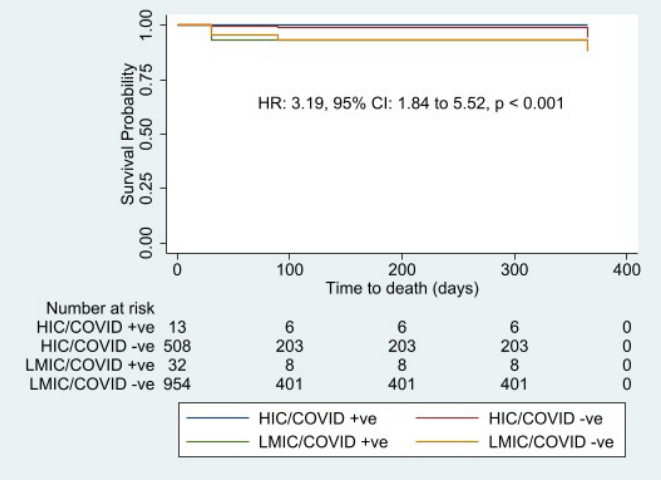

Figure 3 Kaplan-Meier survival curve of patients with paediatric cancer in high-income countries (HICs) and low-income and middle-income countries (LMICs) stratified by COVID-19 positivity.

in LMICs had a longer duration of treatment than would normally be given, 21 children in LMICs and one child in an HIC were given a different chemotherapy agent compared with the normal regimen, and 8 children in LMICs were given chemotherapy through an alternative route of administration. In addition, the families of 17 children in LMICs and 1 child in an HIC abandoned this treatment. The drivers behind these changes are listed in table 4.

Similarly, an initial MDT decision was made for 226 of the included children (13.6%) to receive radiotherapy: 131 in LMICs and 95 in HICs. Secondary to the effects of the COVID-19 pandemic, one child in an LMIC had their planned radiotherapy cancelled, eight and eight children in LMICs and HICs, respectively, had delayed delivery of their radiotherapy, and three children were given radiotherapy through a different modality than would normally be given. In addition, the family of one child in an HIC abandoned their treatment. An initial MDT decision was made for 48 of the included children (2.9%) to receive immunotherapy: 18 in LMICs and 30 in HICs. Secondary to the effects of the COVID-19 pandemic, 1 child in an LMIC had their planned immunotherapy cancelled, 2 and 3 children in LMICs and HICs, respectively, had delayed delivery of their immunotherapy. In addition, the family of one child in an HIC abandoned this treatment. An initial MDT decision was made for 518 patients (31.2%) to undergo surgery: 364 in LMICs and 154 in HICs. Secondary to the effects of the COVID-19 pandemic, one child in an LMIC had their planned surgery cancelled, 47 and 10 children in LMICs and HICs, respectively, had delayed surgery, 8 children in LMICs and one child in an HIC had a change in the choice of their operation, 8 children in LMICs and one child in an HIC had their operation performed in an alternative hospital (reported to have prevented a delay in surgery), once child in an LMIC underwent neoadjuvant therapy where this would not typically have been indicated, 3 children in LMICs and one child in an HIC underwent a longer course of neoadjuvant therapy, 1 child in an LMIC did not undergo a neoadjuvant therapy that would normally been indicated and 1 child was switch to palliative care. An additional 10 children in LMICs and 4 children in HICs were deemed to be for palliative care at the initial MDT. In addition, the families of three children in LMICs and one child in an HIC abandoned this treatment. The drivers behind these changes are listed in table 4.

DISCUSSION

Children with cancer have had their treatments delayed, interrupted, or modified due to the direct effects of COVID-19 and the measures imposed to minimise COVID-19 mortality and morbidity. These delays and alterations only affected a minority of patients with paediatric cancer. They primarily affected patients with paediatric cancer in LMICs. Relative to patients with paediatric cancer in HICs, patients with paediatric cancer in LMICs had 12.1 and 7.9 times the risk of death at 30 days and 90 days, respectively, after presentation during the COVID-19 pandemic. After adjusting for confounders—such as age, sex, weight, ASA grade, tumour type and tumour staging, relative to patients with paediatric cancer in HICs, patients with paediatric cancer in LMICs had 15.6 times the odds of all-cause mortality during the COVID-19 pandemic. This is substantially higher than prepandemic figures of children in LMICs being four times more likely to die[1 20] A minority of patients with paediatric cancer in both LMICs and HICs were diagnosed with COVID-19, with most of these cases being in LMICs. Being diagnosed with COVID-19 was associated with greater odds of death at 30 days after presentation. It should be noted that being diagnosed with COVID-19 was a reason for delays in seeking care and providing treatment as well as alterations to treatment.

While our analyses do corroborate the perceptions of clinicians globally:[8 12 13] the provision of paediatric oncology services have been adversely impacted by the COVID-19 pandemic, this has only affected a minority of patients receiving treatment. Most patients with paediatric cancer have continued to receive the standard of care that they would have received prior to the pandemic. This speaks to the adaptability and resilience of healthcare systems and healthcare workers globally. Creation of new legislation,[21] increasing utilisation of technology,[22] and optimising the allocation of resources[12] are some of the commendable efforts that have mitigated the impact of the pandemic on patients with paediatric cancer. The benefits of these interventions could persist beyond the pandemic. The probability of this occurring is dependent on individuals, organisations dedicated to paediatric cancer care, and governments continuing to work collectively, interprofessionally and globally.

It should be noted that the impact of the COVID-19 pandemic on paediatric oncology services highlights

Table 4 Reasons for the changes to the treatments

Reason for the change	Chemotherapy (N)	Radiotherapy (N)	Immunotherapy (N)	Surgery (N)
Decision making	85	10	3	35
Change in policy	47	5	2	26
Change in treatment plan by lead clinician	38	5	1	9
Infrastructure	78	9	2	53
Lockdown/travel restrictions	48	3	0	36
Lack of hospital beds	12	2	0	10
Lack of outpatient facilities for support	3	2	2	0
Lack of blood products	1	0	0	1
Lack of personal protective equipment	6	1	0	3
Lack of equipment to deliver the therapy	4	1	0	2
Lack of drugs	4	0	0	1
Workforce	13	1	0	5
Insufficient staff due to redeployment/restructuring	9	1	0	5
Insufficient staff due to sickness	4	0	0	0
Service delivery	12	3	0	15
Restructuring of services	3	1	0	4
Transfer to a different institution	9	2	0	11
Financing	3	3	0	3
Inability to pay	3	3	0	3
Patient factors	20	1	1	5
Patient/patient's family choose to avoid treatment due to the pandemic	18	1	1	4
Caregiver infected with COVID-19	2	0	0	1
Other	14	4	0	5
Patient has COVID-19	6	3	0	0

existing inequities in healthcare systems. Prior to the pandemic, children diagnosed with cancer in an HIC had a mean 5-year survival rate of 80%,[1 20] whereby children in LMICs had a mean 5-year survival rates of 20%.[1] The discrepancy is due to delays in diagnosis,[23 24] lack of access,[25] poor investment into services[26] and inadequate support for workforce development[27] in LMICs. Our results indicate the pandemic has exacerbated these issues: increasing delays, reducing access and diverting resources to other areas. While single centre studies have reported that the pandemic has caused delays to care in HICs,[28 29] our results show these issues are principally affecting children in LMICs. These delays could adversely impact short-term outcomes with children in LMICs at approximately 15 times the odds of dying, which is higher than figures reported prior to the pandemic.[1 30] This disparity in mortality needs urgent attention from policymakers and health advocates globally, especially given the lack of funding for childhood cancers in LMICs. In addition, our results suggest that the COVID-19 pandemic is contributing to the existing issue of treatment abandonment in LMICs.[31] All in all, the pandemic has exacerbated pre-existing disparities, and clearly demonstrated that children in the poorest nations are once again being disproportionately affected.

It is also important to critically appraise our finding that patients with paediatric cancer who were COVID-19 positive postpresentation had an increased risk of death

at 30 days after presentation. A recent systematic review reported that children with cancer and COVID-19 do not have significantly different outcomes from children with cancer given the same standard of care.[32] However, in this cohort study, the patients infected with COVID-19 were not provided the same standard of care as those who did not have the infection, as it was a reason for delaying treatment or changing treatment modalities. This was especially the case for surgical treatment, which may reflect the fact that guidance suggested delaying surgery if needed.[11] This underscores a problem unearthed by this study. The most common reason for children with cancer not being given their usual standard of care were changes in policy, lead clinician decision, and lockdown or travel restrictions. Changes may have been driven by the desire to reduce transmission of COVID-19 among patients with paediatric cancer, despite the fact that patients with paediatric cancer are not particularly vulnerable to COVID-19[9] nor is there sufficient evidence that concurrent COVID-19 infection worsens outcomes.[32] Given the response to the pandemic appears to have had a larger effect on care than direct effects of the pandemic itself, the impact of the pandemic on patients with paediatric cancer can be mitigated through policy changes occurring now.

This study did have limitations. As a cohort study, it only followed children through time who were diagnosed with cancer. However, there have been frequent reports that the pandemic has decreased the number of children being identified to have cancer.[12] Therefore, the impact of the COVID-19 pandemic may be greater than that outlined here, especially as the underdiagnosis of cancer is an established reason for the increased mortality of patients with paediatric cancer in LMICs.[1 3 24] Furthermore, given existing difficulties in providing care for patients with paediatric cancer in LMICs, there is the possibility that patients who had alterations to their treatment during the COVID-19 pandemic may have had similar alterations if the pandemic had not occurred. To mitigate against this bias, we requested that all data collectors attest they have only submitted new issues brought about by the pandemic. Therefore, although we are not aware of a bias towards baseline gaps in service delivery, we cannot confirm that pre-existing issues with service provision and supply chains did not contribute to the disparity in care showcased by this study. Similarly, although we are aware that children with cancer are four times more likely to die in LMICs than in HICs,[1 20] we do not have specific baseline data for the centres involved in our study as this is the first study of its kind for most participating LMIC centres. Furthermore, there was a disparity in the type of hospitals participating in this study between LMICs and HICs. Participating LMIC sites tended to be tertiary hospitals, while HIC sites included a larger mix of general hospitals, paediatric hospitals and paediatric oncology hospitals (online supplemental appendix S2). There is an inherent variability in capacity for cancer care between these hospital types.[33] The inclusion of hospitals in HICs that were not specialised for the care of children with cancer may have resulted in an underestimation of the effect of the COVID-19 pandemic on this population in LMICs relative to HICs. In addition, there was an 18% lost to follow-up at 90 days, and those individuals may have been different from those who were included. Ultimately, over 1400 patients across 39 countries were followed up over 90 days, suggesting we are able to provide a comprehensive report of the global effect of this pandemic on paediatric oncology care. It should be noted, however, that there was an inequitable distribution of participants from HICs and LMICs. Approximately two-thirds of all participants were based in LMICs. However, given the historical lack of presence of individuals from LMICs in international studies, these data points provide a novel opportunity to assess global surgery related knowledge and the quality of global surgery care being offered.

This is the first large-series, geographically comprehensive, multicentre, international cohort study to explore the management of childhood cancers in low, middle and HICs across the globe during the COVID-19 pandemic. It illustrates the stark disparities that continue to exist in children's cancer care, and the multiple impacts that COVID-19 pandemic has had on healthcare systems across the globe. Our results underscore the need for a renewed assessment of resource requirements during this pandemic and the sharing of approaches that have minimised the negative effects on paediatric cancer care. This pandemic has become the defining crisis of our generation, and its ramifications may stretch beyond the acute crisis and have far reaching consequences for the future. Understanding its true impact, taking on key lessons and identifying vulnerabilities within health systems helps us develop solutions, which will also prove critical on our path towards equitable global paediatric oncology care.

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Iran: Maryam Ghavami Adel
Iraq: Abdulrahman Omar Taha
Italy: Calogero Virgone, Francesco Pata, Gaetano Gallo
Jordan: Mohammad K. Abou Chaar, Faris Ayasra
Kenya: Eric Mwangi Irungu
Libya: Muhammed Elhadi
Malaysia: Shireen Anne Nah, Dayang Anita Abdul Aziz
Malta: Victor Calvagna
Morocco: Outani Oumaima, Zineb Bentounsi
Nigeria: Adesoji Ademuyiwa
Oman: Dhruv Nath Ghosh
Pakistan: Muhammad Arshad, Lubna Samad
Peru: Lily Saldana
Portugal: Jan Godzinsky
Saudi Arabia: Abdelbasit Ali, Ehab Alameer
Serbia: Dragana Janic
Sierra Leone: Mohamed Bella Jalloh, Nellie Bell
Singapore: Annette Jacobsen, Chan Hon Chui
South Africa: Milind Chitnis
Spain: Israel Fernandez Pineda, Lucas Krauel, Maricarmen Olivos
Sudan: Waha Rahama, Hazim Elfatih
Switzerland: Raphael N. Vuille-dit-Bille
Syria: Alaa Hamdan
Turkey: Arda Isik
United Arab Emirates: Asim Noor Rana
United Kingdom: Kokila Lakhoo, Kate Cross, Max Pachl
United States of America: Andrea Hayes-Jordan, Roshni Dasgupta
Zambia: Patricia Shinondo, Amon Ngongola
Middle-East and North Africa: Mohamedraed Elshami

Appendix S2: Participating Centres

LMIC

Centre Anti-Cancer, Algeria
Centre hospitalier universitaire de Batna, Algeria
CHU Saâdna Abdenour de Sétif, Algeria
Chittagong Medical College Hospital, Bangladesh
Dhaka Medical College Hospital, Bangladesh
Dhaka Shishu (Children) Hospital, Bangladesh
Brazilian National Cancer Institute (INCA), Brazil
GPACI - Grupo de Pesquisa e Assistência ao Câncer Infantil, Brazil
Pediatric Oncology Institute – GRAACC, Brazil
Ain Shams University Hospital, Egypt
Al-Hussein University Hospital, Egypt
Borg El-Arab University Hospital, Egypt
El Safa Hospital, Egypt
El Sheikh Zayed Specialized Hospital, Egypt
Helwan University Hospital, Egypt
Kasr Al Ainy Hospital, Egypt
Menoufia University Hospital, Egypt
MISR Cancer Centre, Egypt
Tanta University Hospital, Egypt
Wingat Royal Hospital, Egypt
Zagazig University Hospital, Egypt
Tamale Teaching Hospital, Ghana
Shahid Baghaei Hospital, Iran
Ibn Al-Atheer Hospital, Iraq
Raparin Pediatric Teaching Hospital, Iraq
Al Bashir Hospital, Jordan
King Abdullah University Hospital, Jordan
King Hussein Cancer Center, Jordan
AIC Kijabe Hospital, Kenya
Benghazi Pediatric Hospital, Libya
Sabha Medical Centre, Libya
Tobruk Medical Centre, Libya
Tripoli University Hospital, Libya
Universiti Kebangsaan Malaysia Medical Centre, Malaysia
University of Malaya Medical Centre, Malaysia
Centre Hospitalo-Universitaire Ibn Sina de Rabat (CHIS), Morocco
Hôpital des Spécialités ONO, Morocco
Abubakar Tafawa Balewa University Teaching Hospital, Nigeria
Ahmadu Bello University Teaching Hospital, Nigeria
Federal Medical Center, Abeokuta, Nigeria
Federal Medical Center, Lokoja, Nigeria
Federal Teaching Hospital Ido-Ekiti, Nigeria
Lagos University Teaching Hospital, Nigeria
National Hospital, Nigeria
Nnamdi Azikiwe University Teaching Hospital, Nigeria
Olabisi Onabanjo University Teaching Hospital, Nigeria
University College Hospital (UCH), Nigeria
University of Abuja Teaching Hospital, Nigeria
University of Ilorin Teaching Hospital, Nigeria
Usman Danfodiyo University Teaching Hospital, Nigeria
Aga Khan University Hospital, Pakistan
Lahore General Hospital, Pakistan
Liaquat National Hospital and Medical College, Pakistan
The Indus Hospital, Pakistan
Instituto Nacional de Enfermedades Neoplásicas, Peru
Clinic for Neurosurgery, Clinical Center of Serbia, Serbia

. *BMJ Open* 2022; 12:e054690. doi: 10.1136/bmjopen-2021-054690

Ola During Children's Hospital, Sierra Leone
Frere Hospital, South Africa
National Cancer Institute, Sudan
Tishreen University Hospital, Syria
Dr. Lutfi Kirdar Kartal Training and Research Hospital, Turkey
Kanuni Sultan Süleyman Research and Training Hospital, Turkey
Ministry of Health Marmara University Pendik Research and Application Hospital, Turkey
Ondokuz Mayıs Üniversitesinin, Turkey
University Teaching Hospital, Zambia

HIC

Salmaniya Medical Complex, Bahrain
Pantai Jerudong Specialist Centre, Brunei
The Hospital for Sick Children, Canada
University Medical Center Hamburg-Eppendorf, Germany
AHEPA University General Hospital, Greece
Medical University of Pecs, Department of Paediatrics, Hungary
Policlinico Umberto I, Sapienza University of Rome, Italy
Mater Dei Hospital, Sir Anthony Mamo Oncology Centre, Malta
Khoula Hospital, Oman
Centro Hospitalar Universitário de São João, Portugal
King Fahd Central Hospital, Saudi Arabia
King Salman Armed Forces Hospital, Saudi Arabia
Prince Mohammed bin Nasser Hospital, Jazan, Saudi Arabia
KK Women's and Children's Hospital, Singapore
Vall d'Hebron University Hospital, Spain
University Children's Hospital of Basel, Switzerland
Dubai Hospital, United Arab Emirates
Alder Hay Children's Hospital, United Kingdom
Birmingham Children's Hospital, United Kingdom
Gloucestershire Hospitals NHS Foundation Trust, United Kingdom
John Radcliffe Hospital, United Kingdom
Children's Hospital of Wisconsin, United States of America
Johns Hopkins Hospital Bloomberg Children's Hospital, United States of America
Mayo Clinic, United States of America
University of Texas Medical Branch, United States of America
Yale New Haven Hospital, United States of America

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Yale

Human Research Protection Program
Institutional Review Boards
FWA00002571
25 Science Park – 3rd Fl., 150 Munson St.
New Haven CT 06520-8327

Telephone: 203-785-4688
http://www.yale.edu/hrpp

September 1, 2020

APPROVAL OF SUBMISSION VIA EXPEDITED REVIEW

Approval Date: 9/1/2020

Investigator:	Emily Christison-Lagay
Type of Review:	Initial Study
Title of Study:	Pediatric tumor surgery during the COVID-19 pandemic: an international, multicenter observational cohort study (COVIDPaedCancerSurg) – Yale New Haven Hospital branch
IRB Protocol ID:	2000028852
Submission ID:	2000028852

Research activities associated with this submission are approved and may begin consistent with the terms of IRB approval.

The IRB has determined that this protocol presents minimal risk to subjects.

This approval is for medical record review only. This approval does not authorize patient contact.

Please be advised that Yale-New Haven Hospital and Yale Medical Group have implemented a new reporting request process. Requests for medical records should be made through JDAT as described at http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx.

YNHH and Yale University consider it a violation of patient privacy for research personnel to review medical records of patients who have opted out of research use of their records. All record review requests should therefore be through JDAT.

The IRB has determined that informed consent can be waived for this medical record review.

The IRB has granted a waiver of HIPAA authorization for access to and use of protected health information (PHI) as described in the approved protocol for this medical record review. This waiver does not authorize subject contact.

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HIPAA regulations require that accounting logs be maintained when researchers access patient records under a waiver of authorization including those approved for recruitment purposes. You are thereby reminded of your obligation to create the log. For further information on maintaining logs and on the accounting of disclosures, please see hipaa.yale.edu.

IRB approval of research or proposed changes to previously approved research does NOT constitute institutional approval for initiating or resuming in-person research during a pandemic. It is your responsibility to comply with institutional, federal, state, and local requirements (including Centers for Disease Control (CDC) and State of Connecticut guidelines), and other applicable policies. Please review the Yale requirements for research reactivation on the Yale website: https://research.yale.edu/phase-2-research-reactivation.

See the next pages for important reminders and the list of IRB approved documents.

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IMPORTANT REMINDERS:

- This research does not require IRB continuing review.
- You are obligated to submit the following to the IRB:
    - **Modifications**: Changes must be submitted with a modification and approved by the IRB prior to implementation except to eliminate immediate hazards to participants. This includes changes to study procedures, informed consent documents, recruitment activities or study personnel.
    - **Reportable New Information:** Information that requires prompt reporting to the IRB must be done so within 5 days of the PI becoming aware of the event (see Policy 710: Reporting Unanticipated Problems Involving Risks to Subjects or Others, including Adverse Events). This includes potential serious noncompliance, continuing noncompliance, and unanticipated problems to subjects or others.
    - **Closure request** (to end the IRB's oversight) when:
        i. The protocol is permanently closed to enrollment,
        ii. All subjects have completed all protocol related interventions and interactions, and
        iii. Analysis of private identifiable information is completed.
- In conducting this activity, you should refer to and follow the Investigator Manual (HRP-103) as applicable, which can be found in the IRB Library within the IRB system.

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IRB APROVED DOCUMENTATION:

• Main Data Collection Form, Category: Study questionnaires, measures, focus groups/interview questions;
• YNHH Specific Data Collection Form, Category: Study questionnaires, measures, focus groups/interview questions;
• Concept Approval, Category: Ancillary Committee Approval;
• Medical Record Review Protocol, Category: IRB Protocol;

Please keep this letter with your copy of the approved protocol documents.

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E-mail: mhrec@moh.gov.bn

MHREC Executive Screening Suite
Basement Carpark Level 1
Raja Isteri Pengiran Anak Saleha Hospital
Bandar Seri Begawan BA1710
Negara Brunei Darussalam

Our Ref : MHREC/MOH/2020/14(2)

25th November 2020
9 Rabiulakhir 1442

To:
Miss Janice Wong
Consultant Paediatric Surgeon
Department of General Surgery
RIPAS Hospital

Dear Miss Janice,

Re: "A global study looking at the Impact of the Coronavirus disease (COVID-19) on the care of childhood cancers (COVIDPaedsCancer)"

We are pleased to inform you that Medical and Health Research & Ethic Committee has given **full approval** to your research proposal entitled above.

Please also adhere to the conditions stated below:

- The study should comply to the Guidelines for Good Clinical Practice
- Any deviation to the study should have MHREC's written approval
- Please provide us a report of your research findings

This approval is valid for one year from the date of this letter or the proposed duration that you have applied for your study, whichever is shorter. If you wish to extend your research beyond this period, you are required to apply to MHREC at least one month before the end of your approval including a preliminary report of your research findings.

All the best with your research.

"BERSAMA KE ARAH WARGA SIHAT"
"Warga Sihat Negara Sejahtera"

Yours Sincerely,

[Dr Alice Yong Moi Ling]
Chairperson of Medical and Health Research & Ethics Committee

Hnphk

Cc 1. Deputy Permanent Secretary (Professional), MOH
2. Director General of Medical and Health Services, MOH.

MINIT

Yang Mulia
Miss Janice Wong
MBChB(Edin) MRCSEd FAMS(Paed Surgery)
Konsultan Pembedahan Pediatrik
Jabatan Pembedahan Umum
Hospital Raja Isteri Pengiran Anak Saleha

MEMOHON KEBENARAN MENJALANKAN AUDIT "A GLOBAL STUDY LOOKING AT THE IMPACT OF THE CORONAVIRUS DISEASE (COVID-19) ON THE CARE OF CHILDHOOD CANCERS (COVIDPAEDSCANCER)'

Dengan hormatnya merujuk permohonan Doktor bertarikh 20 Muharram 1442 bersamaan 10 Ogos 2020 mengenai perkara tersebut di atas.

Sehubungan dengan itu, Pejabat ini **tidak ada halangan** bagi Doktor menjalankan penyelidikan yang tersebut di atas. Walaubagaimanapun persetujuan atau keizinan dari *Medical and Research and Ethics Committe MHREC* perlu dipastikan dahulu sebelum membuat kajian.

Sekian disampaikan untuk makluman Doktor mengenainya.

'Bersama Ke Arah Warga Sihat'
'Sentiasa Berkhidmat Dengan Petunjuk Allah'

[ABDOL HAZIS BIN HAJI AHAD]
Pemangku Ketua Pegawai Eksekutif Tingkat Khas
Hospital Raja Isteri Pengiran Anak Saleha

Rujukan Kami:11/CEO/HRIPAS/4049/2002 Pt.2
Tarikh: 29 Muharram 1442H/ 17 September 2020

cc. Pejabat Ketua Pengarah Perkhidmatan dan Perubatan.
. *Medical and Health Research and Committee MHREC*
Penguasa Perubatan, Hospital Raja Isteri Pengiran Anak Saleha.

Dkn2012 / HA2

Tanta University
Faculty of Medicine
Research Ethics Committee
Federal Wide Assurance (FWA)
FWA00022834
IRB0010038

جامعـة طنطـا
كليـة الطـب
لجنة أخلاقيات البحث العلمي

Research Ethics Committee Review Report

Approval Code: 33965/7/20

Name of the PI محمد جمال البهنساوى

Position : مدرس

Name of the Department :طب الطوارىء و الاصابات

Type of the research: MSc ☐ MD ☐ Promotion research ☑

Project ☐

Paediatric tumour during the COVID-19 pandemic: an international, multicentre, observational cohort study

اورام الاطفال أثناء جائحة الكورونا المستجد: دراسة ملاحظية.جمعية من عدة مراكز دولية

Approved ☐ Disapproved ☐ Approved after modification ☑

This Research proposal conforms to the accepted ethical standard

Date: 19/7/2020

Chief of Ethics committee

Prof. Mona El-Gohary

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4-5
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5-6
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	6-10

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Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Baseline Information

Record ID

_____

The Global Health Research Group for Children's Non-Communicable Diseases (Global Children's NCDs) wishes to thank you for being a collaborator on our international multi-center study looking at the impact of the Coronavirus disease (COVID-19) on the care of childhood cancers: COVIDPaedsCancer

Are you able to provide a patient's date of birth?
◯ Yes
◯ No

In order to contribute to COVIDPaedsCancer you should first secure local study approval.

Has local study approval been secured?
◯ Yes
◯ No

Please secure local study approval before adding any patient data onto REDCap

Please select the option that is true for this patient
◯ Patient was undergoing active anti-cancer treatment on 12th March 2020
◯ Patient newly presented post 11th March 2020
◯ Neither of the above

Date of birth

_____
(Day-Month-Year)

_____

Age of patient (in years)

_____

Does this patient have a tumour?
◯ Yes
◯ No

This patient does not meet the inclusion criteria for COVIDPaedsCancer

Sex
◯ Female
◯ Male
◯ Ambiguous

Weight (kg)

_____
(First weight undertaken during admission)

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ASA Grade	◯ 1 - a normal healthy patient ◯ 2 - a patient with mild systemic disease ◯ 3 - a patient with severe systemic disease ◯ 4 - a patient with severe systemic disease that is a constant threat to life ◯ 5 - a moribund patient who is not expected to survive without the operation (ASA (American Society of Anesthesiologists) grade at the time of surgery)
Did this patient present to the hospital before July 12th 2020?	◯ Yes ◯ No

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Tumour Details

Diagnostic group/subgroup of tumour	◯ Acute lymphoblastic leukaemia ◯ Hodgkin lymphoma ◯ Non-Hodgkin lymphoma ◯ Neuroblastoma ◯ Wilms Tumour ◯ Rhabdomyosarcoma ◯ Osteosarcoma ◯ Ewings sarcoma ◯ Retinoblastoma ◯ Glioma ◯ Medulloblastoma
Grade of glioma	◯ Low grade (WHO grade I/II) ◯ High grade (WHO grade III/IV) ◯ Unknown
Staging	◯ CNS negative (CNS 1) ◯ CNS positive (CNS 2/3) ◯ Unknown (Central nervous system (CNS) disease: the presence of leukemia cells in the cerebral spinal fluid)
Staging	◯ Ann Arbor-stage IA/B ◯ Ann Arbor-stage IIA/B ◯ Ann Arbor-stage IIIA/B ◯ Ann Arbor-stage IVA/B ◯ Unknown
Staging	◯ Localised ◯ Regional ◯ Metastatic ◯ Unknown
Date of diagnosis	_____ (Day-Month-Year)
What was the initial MDT (tumour board) decision for managing this tumour? (select all that apply)	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ No anticancer therapy
Was a central venous catheter inserted in the patient?	◯ Yes ◯ No (Insertion of a central venous catheter does not count as surgery)
What type of central venous catheter was inserted?	◯ Peripherally inserted central catheter (PICC line) ◯ Portacaths ◯ Other
What type of central venous catheter was inserted? (other selected)	_____

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Date of treatment decision by the tumour board	_____ (Day-Month-Year)
Would this decision have been different prior to the COVID-19 pandemic?	◯ Yes ◯ No
What would the pre-COVID 19 decision for managing this tumour be?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ No anticancer therapy

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Chemotherapy

Did the patient have chemotherapy post March 11th 2020?	◯ Yes ◯ No
Did the patient have chemotherapy during their 30-day follow up period?	◯ Yes ◯ No
Did the patient have chemotherapy during their 90-day follow up period?	◯ Yes ◯ No
Is there still a plan for chemotherapy treatment?	◯ Yes ◯ No
Were there any changes to the chemotherapy treatment due to the COVID-19 pandemic?	☐ No change to chemotherapy care because of COVID-19 ☐ Chemotherapy treatment cancelled because of COVID-19 ☐ Chemotherapy treatment delayed because of COVID-19 ☐ Reduction from typical chemotherapy dose because of COVID-19 ☐ Increase from typical chemotherapy dose because of COVID-19 ☐ Reduction in the number of cycles of chemotherapy because of COVID-19 ☐ Increase in the number of cycles of chemotherapy because of COVID-19 ☐ Shorter duration of treatment because of COVID-19 ☐ Longer duration of treatment because of COVID-19 ☐ Change in choice of chemotherapy agent ☐ Change in route of administration of chemotherapy agent ☐ Change to/addition of an alternative anti-cancer treatment modality because of COVID-19

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What were the reasons for the change(s) to the treatment?	☐ Change in treatment as per local MDT / hospital policy (decision making) ☐ Change in treatment as per regional policy (decision making) ☐ Change in treatment as per national policy (decision making) ☐ Change in treatment plan by lead clinician (decision making) ☐ Lockdown/Travel restrictions prevent access to treatment (infrastructure) ☐ Lack of hospital inpatient beds (infrastructure) ☐ Lack of hospital intensive care beds (infrastructure) ☐ Lack of outpatient facilities for support post-discharge (infrastructure) ☐ Lack of blood products (infrastructure) ☐ Lack of personal protective equipment (infrastructure) ☐ Lack of equipment (infrastructure) ☐ Lack of drugs (infrastructure) ☐ Insufficient staff due to redeploymnent/restructuring (workforce) ☐ Insufficient staff due to sickness (workforce) ☐ No treatment available due to restructuring of services (service delivery) ☐ Transfer to a different institution for treatment (service delivery) ☐ Inability to pay for treatment (financing) ☐ Loss of employment by caregiver (financing) ☐ Patient/patient's family chooses to avoid treatment during the pandemic (patient factors) ☐ Treatment not possible as caregiver infected with Coronavirus and under mandatory isolation (patient factors) ☐ Other
What were the reasons for the change(s) to the treatment: other	_____

Confidential

Radiotherapy

Did the patient have radiotherapy post March 11th 2020?	◯ Yes ◯ No
Did the patient have radiotherapy during the 30-day follow up period?	◯ Yes ◯ No
Did the patient have radiotherapy during the 90-day follow up period?	◯ Yes ◯ No
Is there still a plan for radiotherapy treatment?	◯ Yes ◯ No
Were there any changes to the radiotherapy treatment due to the COVID-19 pandemic?	☐ No change to radiotherapy care because of COVID-19 ☐ Radiotherapy treatment cancelled because of COVID-19 ☐ Radiotherapy treatment delayed because of COVID-19 ☐ Decrease in typical radiotherapy dose per fraction because of COVID-19 ☐ Increase in typical radiotherapy dose per fraction because of COVID-19 ☐ Reduction in duration from typical radiotherapy length of treatment because of COVID-19 ☐ Increase in duration from typical radiotherapy length of treatment because of COVID-19 ☐ Change in radiotherapy modality because of COVID-19 ☐ Change to/addition of an alternative anti-cancer treatment modality because of COVID-19

Confidential

What were the reasons for the change(s) to the treatment?	☐ Change in treatment as per local MDT / hospital policy (decision making) ☐ Change in treatment as per regional policy (decision making) ☐ Change in treatment as per national policy (decision making) ☐ Change in treatment plan by lead clinician (decision making) ☐ Lockdown/Travel restrictions prevent access to treatment (infrastructure) ☐ Lack of hospital inpatient beds (infrastructure) ☐ Lack of hospital intensive care beds (infrastructure) ☐ Lack of outpatient facilities for support post-discharge (infrastructure) ☐ Lack of blood products (infrastructure) ☐ Lack of personal protective equipment (infrastructure) ☐ Lack of equipment (infrastructure) ☐ Lack of drugs (infrastructure) ☐ Insufficient staff due to redeploymnent/restructuring (workforce) ☐ Insufficient staff due to sickness (workforce) ☐ No treatment available due to restructuring of services (service delivery) ☐ Transfer to a different institution for treatment (service delivery) ☐ Inability to pay for treatment (financing) ☐ Loss of employment by caregiver (financing) ☐ Patient/patient's family chooses to avoid treatment during the pandemic (patient factors) ☐ Treatment not possible as caregiver infected with Coronavirus and under mandatory isolation (patient factors) ☐ Other
What were the reasons for the change(s) to the treatment: other	_____
What was the radiation field?	◯ Craniospinal ◯ Focal (brain)
What was the radiation field?	◯ Local ◯ Wide field
Radiotherapy approach	◯ Photon ◯ Proton beam
Did this represent a change to your typical radiotherapy approach in the pre-COVID-19 era?	◯ No change to radiotherapy approach ◯ Yes, chose to avoid photon radiotherapy related to COVID-19 ◯ Yes, chose to avoid proton beam radiotherapy related to COVID-19

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Immunological Therapy

Did the patient have immunotherapy post March 11th 2020?	◯ Yes ◯ No
Did the patient have immunotherapy during the 30-day follow up period?	◯ Yes ◯ No
Did the patient have immunotherapy during the 90-day follow up period?	◯ Yes ◯ No
Is there still a plan for immunotherapy treatment?	◯ Yes ◯ No
Were there any changes to the immunotherapy treatment due to the COVID-19 pandemic?	☐ No change to immunotherapy care because of COVID-19 ☐ Immunotherapy treatment cancelled because of COVID-19 ☐ Immunotherapy treatment delayed because of COVID-19 ☐ Change in typical immunotherapy dose because of COVID-19 ☐ Change in typical immunotherapy length of treatment because of COVID-19 ☐ Change to/addition of an alternative anti-cancer treatment modality because of COVID-19

Confidential

What were the reasons for the change(s) to the treatment?	☐ Change in treatment as per local MDT / hospital policy (decision making) ☐ Change in treatment as per regional policy (decision making) ☐ Change in treatment as per national policy (decision making) ☐ Change in treatment plan by lead clinician (decision making) ☐ Lockdown/Travel restrictions prevent access to treatment (infrastructure) ☐ Lack of hospital inpatient beds (infrastructure) ☐ Lack of hospital intensive care beds (infrastructure) ☐ Lack of outpatient facilities for support post-discharge (infrastructure) ☐ Lack of blood products (infrastructure) ☐ Lack of personal protective equipment (infrastructure) ☐ Lack of equipment (infrastructure) ☐ Lack of drugs (infrastructure) ☐ Insufficient staff due to redeploymnent/restructuring (workforce) ☐ Insufficient staff due to sickness (workforce) ☐ No treatment available due to restructuring of services (service delivery) ☐ Transfer to a different institution for treatment (service delivery) ☐ Inability to pay for treatment (financing) ☐ Loss of employment by caregiver (financing) ☐ Patient/patient's family chooses to avoid treatment during the pandemic (patient factors) ☐ Treatment not possible as caregiver infected with Coronavirus and under mandatory isolation (patient factors) ☐ Other
What were the reasons for the change(s) to the treatment: other	_____

Confidential

Surgery

Did the patient have surgery post March 11th 2020?	◯ Yes ◯ No
Did the patient have surgery during the 30-day follow up period?	◯ Yes ◯ No
Did the patient have surgery during the 90-day follow up period?	◯ Yes ◯ No
Date of first surgery post March 11th 2020	_____ (Day-Month-Year)
Is there still a plan for surgical treatment?	◯ Yes ◯ No
Were there any changes to the surgical treatment due to the COVID-19 pandemic?	☐ No change to operative care because of COVID-19 ☐ Operation not offered because of COVID-19 ☐ Operation abandoned because of COVID-19 ☐ Operation delayed because of COVID-19 ☐ Change in choice of operation ☐ Operation performed in an alternative hospital (e.g. designated COVID-free) ☐ Interventional radiology procedure performed before surgery where this would not typically have been indicated ☐ Underwent neoadjuvant therapy where this would not typically have been indicated ☐ No neoadjuvant therapy given, where this would typically have been indicated ☐ Underwent a longer or more intensive course of neoadjuvant therapy that would have typically been indicated ☐ Underwent a shorter or less intensive course of neoadjuvant therapy that would have typically been indicated ☐ Underwent adjuvant therapy where this would not typically have been indicated ☐ No adjuvant therapy, where this would typically have been indicated ☐ Not recruited to a clinical trial, where this would typically have been offered ☐ Recruited to a clinical trial, where this would not have previously been offered ☐ Changed to active palliative care instead of operative care

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What were the reasons for the change(s) to the treatment?	☐ Change in treatment as per local MDT / hospital policy (decision making) ☐ Change in treatment as per regional policy (decision making) ☐ Change in treatment as per national policy (decision making) ☐ Change in treatment plan by lead clinician (decision making) ☐ Lockdown/Travel restrictions prevent access to treatment (infrastructure) ☐ Lack of hospital inpatient beds (infrastructure) ☐ Lack of hospital intensive care beds (infrastructure) ☐ Lack of outpatient facilities for support post-discharge (infrastructure) ☐ Lack of blood products (infrastructure) ☐ Lack of personal protective equipment (infrastructure) ☐ Lack of equipment (infrastructure) ☐ Lack of drugs (infrastructure) ☐ Insufficient staff due to redeploymnent/restructuring (workforce) ☐ Insufficient staff due to sickness (workforce) ☐ No treatment available due to restructuring of services (service delivery) ☐ Transfer to a different institution for treatment (service delivery) ☐ Inability to pay for treatment (financing) ☐ Loss of employment by caregiver (financing) ☐ Patient/patient's family chooses to avoid treatment during the pandemic (patient factors) ☐ Treatment not possible as caregiver infected with Coronavirus and under mandatory isolation (patient factors) ☐ Other
What were the reasons for the change(s) to the treatment: other	_____
What type of hospital was the operation performed in?	◯ Designated COVID-free 'cold' hospital ◯ Designated COVID-treatment 'hot' hospital ◯ Undesignated hospital type with emergency department ◯ Undesignated hospital type without emergency department
Time from admission to operation (preoperative delay)	◯ < 6 hours ◯ 6-23 hours ◯ 24-47 hours ◯ 48-71 hours ◯ 72+ hours

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Urgency of surgery	◯ IMMEDIATE - life, limb or organ-saving intervention - within minutes of decision to operate ◯ URGENT - within hours of decision to operate ◯ EXPEDITED - patient requiring early treatment but no immediate threat to life, limb or organ - within days of decision to operate ◯ ELECTIVE - Intervention planned or booked in advance of routine admission to hospital (Full definitions available at: https://www.ncepod.org.uk/classification.html)
What was the reason urgent or emergency cancer surgery was required?	◯ Gastro-intestinal obstruction ◯ Bleeding ◯ Sepsis ◯ Tumour progression ◯ Organ perforation ◯ Functional compromise ◯ Other
Other reason for why urgent or emergency cancer surgery was required	_____
Did the patient have a mandatory self-isolation period before elective surgery?	◯ Yes, two weeks or more ◯ Yes, less than two weeks ◯ No
Was screening for COVID-19 performed within the 72 hours before surgery?	◯ No ◯ Yes - Laboratory test ◯ Yes - CT thorax ◯ Yes - Symptomatic screening or questionnaire only ◯ Yes - Other
Screening: Other	_____
Was the patient known to have COVID-19 infection before the time of surgery?	◯ Yes - proven with laboratory test or CT Thorax ◯ Probable - clinically suspected ◯ No ◯ Unknown
Had the COVID-19 infection resolved?	◯ Yes ◯ No
How long before the date of surgery was COVID-19 diagnosed?	◯ Less than 1 week ◯ 2 to 4 weeks ◯ 5 to 8 weeks ◯ Greater than 8 weeks
What was the primary purpose of the surgery?	◯ Diagnostic ◯ Curative ◯ Palliative
Type of anaesthesia used?	◯ Local ◯ Regional ◯ General

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Operative approach	◯ Open ◯ Minimally-invasive ◯ Minimally-invasive converted to open
Did this represent a change to your typical operative approach in the pre-COVID-19 era?	◯ No change to operative approach ◯ Yes, chose to avoid minimally invasive surgery related to COVID-19 ◯ Yes, chose to avoid open surgery related to COVID-19
Designation of the operating theatre	◯ Designated COVID treatment area (only COVID patients treated there) ◯ Designated non-COVID treatment area (only non-COVID patients treated there) ◯ No designation for this area (either COVID or non-COVID patients can be treated there) ◯ Not applicable
Designation of the intensive care unit	◯ Designated COVID treatment area (only COVID patients treated there) ◯ Designated non-COVID treatment area (only non-COVID patients treated there) ◯ No designation for this area (either COVID or non-COVID patients can be treated there) ◯ Not applicable
Would a post-operative intensive care unit stay have been planned in a pre-COVID-19 era?	◯ Yes ◯ No
Designation of the postoperative ward	◯ Designated COVID treatment area (only COVID patients treated there) ◯ Designated non-COVID treatment area (only non-COVID patients treated there) ◯ No designation for this area (either COVID or non-COVID patients can be treated there) ◯ Not applicable
Was a post-operative CT head performed?	◯ Yes ◯ No
Did any of the operating surgeons contract COVID-19 within 30-days of the date of surgery?	◯ Yes ◯ No
Did the patient undergo more than one surgery post March 11th 2020?	◯ Yes ◯ No

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No Anticancer Treatment

Did the patient or their family choose to avoid treatment during the pandemic before the initial MDT (tumour board) meeting?	◯ Yes ◯ No
Was the patient given palliative treatment post March 11th 2020??	◯ Yes ◯ No
Were there any changes to the palliative care treatment due to the COVID-19 pandemic?	☐ No change to palliative care because of COVID-19 ☐ Palliative treatment *not* provided because of COVID-19 ☐ Palliative treatment provided because of COVID-19 ☐ Palliative treatment delayed because of COVID-19 ☐ Change from typical palliative care plan because of COVID-19
What were the reasons for the change to palliative care treatment?	☐ Change in treatment as per local MDT / hospital policy (decision making) ☐ Change in treatment as per regional policy (decision making) ☐ Change in treatment as per national policy (decision making) ☐ Change in treatment plan by lead clinician (decision making) ☐ Lockdown/Travel restrictions prevent access to treatment (infrastructure) ☐ Lack of hospital inpatient beds (infrastructure) ☐ Lack of hospital intensive care beds (infrastructure) ☐ Lack of outpatient facilities for support post-discharge (infrastructure) ☐ Lack of blood products (infrastructure) ☐ Lack of personal protective equipment (infrastructure) ☐ Lack of equipment (infrastructure) ☐ Lack of drugs (infrastructure) ☐ Insufficient staff due to redeploymnent/restructuring (workforce) ☐ Insufficient staff due to sickness (workforce) ☐ No treatment available due to restructuring of services (service delivery) ☐ Transfer to a different institution for treatment (service delivery) ☐ Inability to pay for treatment (financing) ☐ Loss of employment by caregiver (financing) ☐ Patient/patient's family chooses to avoid treatment during the pandemic (patient factors) ☐ Treatment not possible as caregiver infected with Coronavirus and under mandatory isolation (patient factors) ☐ Other
What were the reasons for the change to palliative care treatment: other	_____

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Outcomes

Was screening for COVID-19 performed within 30 days from their first anti-cancer treatment post March 11th 2020?	◯ No ◯ Yes - Laboratory test ◯ Yes - CT thorax ◯ Yes - Symptomatic screening or questionnaire only ◯ Yes - Other ◯ Not applicable (no anti-cancer treatment given post March 11th 2020)
Was screening for COVID-19 performed within 30 days from their first anti-cancer treatment post March 11th 2020: other	_____
Was the patient diagnosed with COVID-19 within 30 days from their first anti-cancer treatment post March 11th 2020?	◯ Yes - proven with laboratory test or CT Thorax ◯ Probable - clinically suspected ◯ No ◯ Unknown ◯ Not applicable (no anti-cancer treatment given post March 11th 2020)
Complications within 30 days from their first surgical treatment post March 11th 2020?	☐ Anaesthetic complications ☐ Anastomotic leak ☐ Blood transfusion ☐ Cardiac arrest ☐ Pneumonia ☐ Sepsis ☐ Wound dehiscence ☐ Line Infection ☐ Neurological injury ☐ Vascular injury ☐ Altered bowel and bladder function ☐ Hepatic injury ☐ Other loss of function ☐ Early recurrence / Incomplete clearance ☐ No complications ☐ Not applicable (no anti-cancer treatment given post March 11th 2020)
Complications within 30 days from their first chemotherapy treatment post March 11th 2020?	☐ Anaesthetic complications ☐ Anastomotic leak ☐ Blood transfusion ☐ Cardiac arrest ☐ Pneumonia ☐ Sepsis ☐ Wound dehiscence ☐ Line Infection ☐ Neurological injury ☐ Vascular injury ☐ Altered bowel and bladder function ☐ Hepatic injury ☐ Other loss of function ☐ Early recurrence / Incomplete clearance ☐ No complications ☐ Not applicable (no anti-cancer treatment given post March 11th 2020)

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Complications within 30 days from their first radiotherapy treatment post March 11th 2020?	☐ Anaesthetic complications ☐ Anastomotic leak ☐ Blood transfusion ☐ Cardiac arrest ☐ Pneumonia ☐ Sepsis ☐ Wound dehiscence ☐ Line Infection ☐ Neurological injury ☐ Vascular injury ☐ Altered bowel and bladder function ☐ Hepatic injury ☐ Other loss of function ☐ Early recurrence / Incomplete clearance ☐ No complications ☐ Not applicable (no anti-cancer treatment given post March 11th 2020)
Complications within 30 days from their first immunotherapy treatment post March 11th 2020?	☐ Anaesthetic complications ☐ Anastomotic leak ☐ Blood transfusion ☐ Cardiac arrest ☐ Pneumonia ☐ Sepsis ☐ Wound dehiscence ☐ Line Infection ☐ Neurological injury ☐ Vascular injury ☐ Altered bowel and bladder function ☐ Hepatic injury ☐ Other loss of function ☐ Early recurrence / Incomplete clearance ☐ No complications ☐ Not applicable (no anti-cancer treatment given post March 11th 2020)
Outcomes at 30-day follow up?	◯ Died - did not receive anti-cancer treatment ◯ Died - during anti-cancer treatment ◯ Died - on days 0-7 after anti-cancer treatment ◯ Died - on days 8-30 after anti-cancer treatment ◯ Alive - remains admitted in hospital ◯ Alive - transferred to another hospital ◯ Alive - discharged to a rehabilitation centre ◯ Alive - discharged home
Mortality at 90-day follow up?	◯ Alive ◯ Dead ◯ Unknown
Total length of hospital stay (days) within the 90-day follow up period	_____

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How many admissions did the patient have within their 90-day follow up period?	◯ 1 ◯ 2 ◯ 3 ◯ 4 ◯ 5 ◯ 6 ◯ 7 ◯ 8 ◯ 9 ◯ 10 ◯ > 10
Was the 1st admission a planned admission?	◯ Yes ◯ No
Length of stay during 1st admission	_____
What treatments were provided during the 1st admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 2nd admission a planned admission?	◯ Yes ◯ No
Length of stay during 2nd admission	_____
What treatments were provided during the 2nd admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 3rd admission a planned admission?	◯ Yes ◯ No
Length of stay during 3rd admission	_____
What treatments were provided during the 3rd admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 4th admission a planned admission?	◯ Yes ◯ No
Length of stay during 4th admission	_____

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What treatments were provided during the 4th admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 5th admission a planned admission?	◯ Yes ◯ No
Length of stay during 5th admission	_____
What treatments were provided during the 5th admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 6th admission a planned admission?	◯ Yes ◯ No
Length of stay during 6th admission	_____
What treatments were provided during the 6th admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 7th admission a planned admission?	◯ Yes ◯ No
Length of stay during 7th admission	_____
What treatments were provided during the 7th admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 8th admission a planned admission?	◯ Yes ◯ No
Length of stay during 8th admission	_____
What treatments were provided during the 8th admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above

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Was the 9th admission a planned admission?	◯ Yes ◯ No
Length of stay during 9th admission	_____
What treatments were provided during the 9th admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Was the 10th admission a planned admission?	◯ Yes ◯ No
Length of stay during 10th admission	_____
What treatments were provided during the 10th admission?	☐ Chemotherapy ☐ Radiotherapy ☐ Immunological therapy ☐ Surgery ☐ Complication management ☐ None of the above
Mortality at 12-month follow-up?	◯ Alive ◯ Dead ◯ Unknown

Appendix S8 – Baseline Characteristics of low-and-middle-income countries sub-divided into low and middle income countries.

Variable		Low-income countries (N=36) N (%)	Lower-middle income countries (N=520) N (%)	Upper-middle income countries (N=548) N (%)
Age (years), median (range)		5.0 (3.5, 9)	5.0 (2, 10)	5.0 (3, 10)
Sex	Female	16 (44.4)	226 (43.5%)	227 (41.4)
	Male	20 (55.6)	290 (55.8%)	321 (58.6)
	Missing	0 (0.0)	4 (0.8%)	0 (0.0)
Weight (kg), median (range)		-	19 (14, 31)	18 (13, 27)
ASA grade	1 - a normal healthy patient	24 (66.7)	158 (30.4)	162 (29.6)
	2 - a patient with mild systemic disease	1 (2.8)	316 (60.8)	106 (19.3)
	3 - a patient with severe systemic disease	0 (0.0)	28 (5.4)	121 (22.1)
	4 - a patient with severe systemic disease that is a constant threat to life	0 (0.0)	9 (1.7)	25 (4.6)
	5 - a moribund patient who is not expected to survive without the operation	0 (0.0)	5 (1.0)	3 (0.5)
	Missing	11 (30.6)	4 (0.8)	131 (23.9)
Tumour Type	Non-Hodgkin lymphoma	6 (16.7)	46 (8.9)	37 (6.8)
	Acute lymphoblastic leukaemia	10 (27.8)	192 (36.9)	178 (32.5)
	Ewing sarcoma	5 (13.9)	19 (3.7)	8 (40.7)
	Glioma	0 (0.0)	21 (4.0)	52 (50.2)
	Hodgkin lymphoma	5 (13.9)	19 (3.7)	39 (57.3)
	Medulloblastoma	1 (2.8)	36 (6.9)	20 (61.0)
	Neuroblastoma	3 (8.3)	43 (8.3)	34 (67.2)
	Osteosarcoma	2 (5.6)	29 (5.6)	14 (69.7)
	Retinoblastoma	0 (0.0)	39 (7.5)	48 (78.5)
	Rhabdomyosarcoma	0 (0.0)	22 (4.2)	39 (7.1)
	Wilms Tumour	4 (11.1)	54 (10.3)	79 (14.4)
Was patient tested for covid within 30 days from their first anti-cancer treatment?	No	32 (91.4)	242 (46.5)	355 (64.8)
	Symptomatic screening only	3 (8.6)	113 (21.7)	69 (12.6)
	Yes – by CT Thorax	0 (0.0)	6 (1.2)	1 (0.2)
	Yes – by laboratory test	0 (0.0)	113 (21.7)	49 (8.9)
	Not applicable (No anti-cancer treatment given post March 11th 2020)	0 (0.0)	8 (1.5)	5 (0.9)
	Missing	0 (0.0)	38 (0.7)	68 (12.4)

Was patient diagnosed with covid?	No	10 (28.6)	452 (86.9)	452 (82.5)
	Not applicable (no anti-cancer treatment given post March 11th 2020)	0 (0.0)	7 (1.3)	7 (1.3)
	Proven with laboratory test or CT Thorax	0 (0.0)	21 (4.0)	21 (3.8)
	Probable - clinically suspected	0 (0.0)	5 (1.0)	5 (0.9)
	Unknown	25 (71.4)	8 (1.5)	8 (1.5)
	Missing	0 (0.0)	27 (5.2)	55 (10.0)