



Early advice on managing children with cancer during the COVID-19 pandemic and a call for sharing experiences

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We are living very difficult times. The pandemic caused by SARS-CoV-2 (COVID-19) is rapidly affecting the delivery of care for children with cancer around the world. We have written this commentary to facilitate the dissemination of helpful information and useful links, and to place in perspective what we do and don't know about the COVID-19 pandemic and its impact in the practice of pediatric oncology.

Generally speaking, the impact that this virus may have on the paediatric population, and the management of children with cancer, remains unclear and poorly documented. The two sections below outline what has been published or communicated via academic websites, both in children and adults with cancer.

COVID-19 in the paediatric population

So far, very few reports describe the impact of COVID-19 in the paediatric population. Dong *et al* described the epidemiology of the infection in 2,143 suspected or confirmed cases in Chinese children aged up to 18yrs (median age 7yrs)¹. In this publication, only 4.4% were asymptomatic, while the majority (89.7%) presented with mild or moderate symptoms. Children under one year of age were more likely to develop severe or critical forms (10.1%). One child died from the infection. This report does not mention any relationship with underlying conditions, including cancer. A recent systematic literature review suggests that children account for less than 5% of diagnosed COVID-19 cases, and that they often have milder disease than adults².

Only one report has described the clinical course of COVID-19 in children with cancer. Chen *et al* described the case of a child with high risk acute lymphoblastic leukemia on maintenance chemotherapy who developed a neutropenic fever and cough in late January 2020, eight days following a course of moderate dose cyclophosphamide and Cytarabine³. Chest CT showed bilateral pneumonia with mild pleural effusion. The patient tested positive for Influenza A and was treated with broad spectrum antibiotics and oseltamvir, without any evidence of improvement. The child remained febrile and a repeat chest CT scan 11 days after symptom onset showed progressive changes. At that time, 2019-nCoV was suspected and testing proved positive. The child was isolated and treated with umifenovir, ribavirin and recombinant interferon α -1b nebulized inhalations, with addition of methylprednisolone and immunoglobulins. Seven days later, the child's blood count had recovered and the 2019-nCoV test result became negative, however, his overall condition deteriorated. Four days later, the 2019-nCoV test was positive again and he required transfer to the intensive care unit for increasing hypoxia. The report did not further document this case.

To this date, there are few published reports of COVID-19 in children with malignancies, though this situation will no doubt change rapidly. A description of the Italian experience at a major childhood cancer centre in Lombardy has recently been accepted for publication⁴. This documents five positive cases in childhood cancer patients all of whom had a mild course and survived. Three were managed at home, two in hospital.

We would like to highlight the need to create a system for open case reporting and registration to help advance our knowledge on the disease course in children with cancer and to share experiences in its management. SIOP, St. Jude and other stakeholders are working on a multi-stakeholder initiative for the creation of a COVID-19 information resource centre that is planned to include an open registry and a platform for experience sharing.

COVID-19 in adult patients with cancer

So far, we have had a limited number of reports of cases of COVID-19 in adult cancer patients. Liang *et al* reported 18 patients in a cohort of 1,590 Chinese cases⁵. Only four of these patients had received chemotherapy or had had a surgical intervention in the preceding month; 12 were on follow-up. The report found that compared to the general population, patients with cancer were prone to more severe events (defined as admission to the intensive care unit requiring invasive ventilation or death). However, other factors such as age and current or former smoking habits may also explain this difference.

Recommendations for the prevention or management of COVID-19 in the pediatric oncology population

So far, no detailed recommendations have been issued regarding the management of children with cancer during this pandemic⁶. However, some principles are paramount and should be considered for all children with cancer:

- Apply physical isolation for all children with cancer who are currently undergoing treatment. This includes confinement at home between treatments and single room admission during hospital stay where possible. Outpatient visits should be limited and other means of communication (phone, digital, and video communication) should be prioritized.
- Screen patients who present symptoms suggestive of the infection. This screening must be done regardless of the structure – pediatric, general hospitals or oncology centers.
- Limit access to pediatric wards and clinic spaces to one parent only. In these areas, promote, respect and enforce social distancing rules; at least six feet between individuals, and no grouping.

- Where feasible, create a COVID-19 free site for delivery of scheduled cancer care that can only be done in the hospital setting and which cannot be unduly delayed without compromising the expected cancer outcome. Control who has access to this location.
- Transfer as many aspects of case management as feasible to remote monitoring in the home or in the child's community.
- Generally speaking, follow basic principles of infection control in order to avoid any risk of cross-contamination.
- The use of appropriate personal protection equipment (PPE) by healthcare personnel (HCPs) is essential for safe care of patients on paediatric oncology units and to reduce risks of transmission. Use of PPE by patients, family members, and hospital staff in general is still a matter of debate. Efforts should be made to identify the optimal use of PPE equipment in case of shortage.

As far as the general management of patients is concerned, there is no reason to discontinue daily activities in pediatric haematology/oncology units or to turn away children with suspected cancer during this pandemic. Whether patients undergoing treatment should have their treatment altered remains unknown though it seems prudent to postpone high intensity treatments where feasible and to prepare to triage according to prognosis. Based on their experience, Chen *et al* recommend avoiding intensive chemotherapy for children with leukemia in remission³. However, the rarity of cases reported precludes the development of clear chemotherapy guidelines. As more information is available it may be pertinent to create an international task force to provide evidence-based consensus recommendations.

Services should also anticipate staff shortages due to illness, the need to care for sick relatives or requirements to self-isolate if living with or in close contact with a person suspected of having COVID19. Experience from other sudden catastrophes, such as the 2011 earthquake in Christchurch, New Zealand, have emphasised the need to move rapidly to 'short staff' rotas that are already deployed for work over extended holiday periods^{7,8}. This can help continuity of care and conserve staff morale through reasonable scheduled 'down time'. Staff also need to be cared for in other ways, with good information and protocols, confidence in their PPE and regular communications with a dedicated COVID19 response team in their hospital. Clear information for parents and families is also essential and several sources are already available (Table 1).

Several governments and international agencies have provided information and/or recommendations regarding COVID-19 (Table 1). Due to the large amount of misinformation and potentially harmful advice available on the internet, we strongly recommend to consult guidance from established health authorities. We will be publishing further guidance in the coming weeks, describing clinical consensus on acceptable adaptations to treatment protocols during the COVID19 crisis. These guidelines will be stratified according to country resource levels.

Finally, our ability to continue our work is closely interdependent with our respective healthcare systems' ability to respond to this pandemic⁹. The recent stark warning from physicians in Bergamo, Italy, emphasises the need for the whole of society to be prepared¹⁰. Urging the people close to each of us to do their part to limit the virus' spread – through self-isolation, social distancing and avoiding all non-essential travel – is crucial, as is the coming together of communities to help equip and protect the most vulnerable (including the elderly, homeless, or those with underlying health conditions) through the coming months.

Conflict of interest statement:

The authors have no conflicts of interest to declare.

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Table 1: Summary of weblinks (URLs) for recommendation of pediatric and oncology agencies regarding COVID-19

World Health Organization (WHO)	Global pandemic information updated daily. Advice for public and technical guidance for health care services	https://www.who.int/emergencies/diseases/novel-coronavirus-2019
USA Centers for Disease Control	Resources for individuals, the community and healthcare professionals	https://www.cdc.gov/coronavirus
World Society for Pediatric Infectious Diseases (WSPID)	Website with links for clinical guidance and international resources	https://wspid.org/covid-19/
Pan American Health Organization (PAHO)	Coronavirus Disease (Covid-19); excellent clinical guidance and resources in English and Spanish	https://www.paho.org/en/topics/coronavirus-infections/coronavirus-disease-covid-19
American Society of Clinical Oncology (ASCO)	ASCO Coronavirus Resources for patient care and clinical practice	https://www.asco.org/asco-coronavirus-information
Children's Oncology Group (COG)	Advice for parents in multiple languages	www.childrensoncologygroup.org www.survivorshipguidelines.org
Children's Cancer and Leukaemia Group (CCLG)	Guidance for families, children and young people undergoing cancer treatment	https://www.cclg.org.uk/news
St Jude Cure4Kids	Online St Jude COVID 19 Resource Center	https://www.cure4kids.org/ums/home/ https://www.cure4kids.org/ums/home/groups/detail/documents.php?groups_id=338 (login required)
UK Royal College of Paediatrics and Child Health	COVID19 Guidance for Paediatric Services	https://www.rcpch.ac.uk/resources/covid-19-guidance-paediatric-services

National University of Singapore	Evidence- based report of COVID19 sScience, diagnostics and clinical management	https://sph.nus.edu.sg/covid-19/ (freely available download)
European Society of Paediatric and Neonatal Intensive Care	Statement and practical experience from frontline colleagues in Lombardy region, Italy	https://espnice-online.org/News/Latest-News/Practical-advice-from-the-frontline-of-SARS-CoV-2-outbreak
US Oncology Nursing Society	Information for nurses regarding COVID-19 including interim guidelines for PPE use during pandemic – updated daily	https://www.ons.org/coronavirus?utm_source=hl&utm_medium=email&utm_campaign=weeklyupdate_member_corona
US Centers for Disease Control	Managing anxiety and stress related to COVID-19 (in English and Spanish)	https://www.cdc.gov/coronavirus/2019-ncov/prepare/managing-stress-anxiety.html
US American Psychological Association	Guidance for psychologists, practitioners and health professionals and links to resources including resources for parents and caregivers	https://www.apa.org/practice/programs/dmhi/research-information/pandemics
Italy - University of Verona HEMOT Helmet for EMOTions	“Coronavirus: Psychological tips for children and adolescents’ emotions” (PDF) in 17 languages	https://www.hemot.eu/2020/02/28/public-health-emergency/#English
COVID-19 Chinese Consultation Center	Resource sharing, online handbook of COVID-19 prevention and treatment, and medical expert communication center	https://covid-19.alibabacloud.com/
Union for International Cancer Control	Information for adult cancer patients and survivors with links to online resources in English, French and Spanish.	https://www.uicc.org/news/cancer-and-coronavirus-coping-double-challenge?