Cancer in the context of COVID-19: Summary of emerging evidence (10)

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The CRI presents a selection of emerging research articles and clinical practice guidelines related to cancer and COVID-19, with a summary of their key findings/recommendations (links to the articles are embedded as hyperlinks in the titles). This is the tenth of our weekly compilation, which we plan to update and disseminate as the pandemic evolves globally and nationally.

This week, we highlight the latest research related to oncology services in COVID-19 outbreak contexts, including in resource-constrained settings. We hope that insights from these pieces of evidence will help guide how we rethink cancer prevention, treatment and care in the context of the ongoing pandemic, in view of its unprecedented implications for patients, healthcare providers and the community in general. We are keen to include research and guidelines from African and other low- and middle-income settings and will profile these as they become available. Previous weeks' editions can be found on the **CRI website,** as well as on **our Twitter page (@UctCri)**.

Caj et al. Which Cancer Type Has the Highest Risk of COVID-19 Infection? Journal of Infection. DOI: 10.1016/j.jinf.2020.05.028

Country context: Global

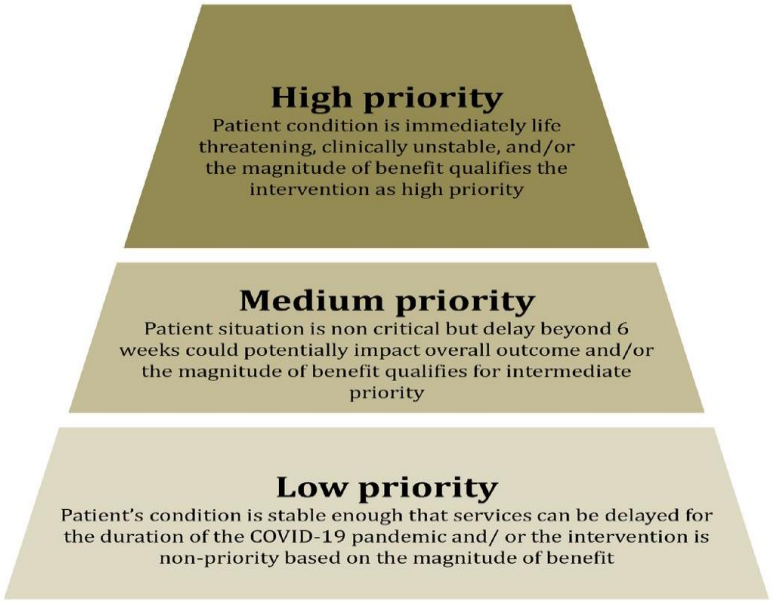
In this editorial correspondence, the authors share findings from their pan-cancer analysis using Tumour Immune Estimation Resource (TIMER) - a web server for comprehensive analysis of tumour-infiltrating immune cells. They found that the expression levels of Angiotensin-Converting Enzyme 2 (ACE2) in Esophageal carcinoma (ESCA), Kidney renal papillary cell carcinoma (KIRP), Lung adenocarcinoma (LUAD), Uterine Corpus Endometrial Carcinoma (UCEC) are high. Similarly, Transmembrane Protease Serine 2 (TMPRSS2) levels in Kidney Chromophobe (KICH), Prostate Adenocarcinoma (PRAD), Uterine Corpus Endometrial Carcinoma (UCEC) are also increased. Given the substantial evidence that ACE2 and TMPRSS2 are the receptors for SARS-CoV-2 to invade the human respiratory tract, the risk of COVID-19 infection in patients with these tumors is higher. They also found that only UCEC is co-expressing ACE2 and TMPRSS2 receptors; therefore, patients with UCEC carry the highest risk of COVID-19 infection.

Azambuja et al. ESMO Management and Treatment Adapted Recommendations in the COVID-19 Era: Breast Cancer. Oral Oncology. DOI: 10.1136/esmoopen-2020-000793

Country context: UK

This report, developed by an international panel of expert breast cancer health providers, aims to organise health interventions for breast cancer management and research in a tiered framework (high, medium, low value), formulating a scheme of prioritisation informed by clinical cogency and intrinsic value or magnitude of benefit. The public health tools and schemes for priority setting in oncology have been used as models, aspiring to capture clinical urgency, value in healthcare, community goals and fairness, while respecting the principles of benevolence, non-maleficence, autonomy and justice.

The figure below illustrates the proposed breast cancer patients' prioritisation framework:



The tables below detail the recommended prioritisation framework for specific breast cancer services:

Priorities for the management of breast cancer: Outpatient visit priorities for the management of breast cancer

Table 1 Outpatient visit priorities for the management of breast cancer

High priority	Medium priority	Low priority
Postoperative unstable clinical scenario (eg, haematoma, infection)	New diagnosis of non-invasive cancer. *Convert as many visits as possible to telemedicine visits.*	Established patients with no new issues: *refer to telemedicine*
New diagnosis of invasive breast cancer (for multidisciplinary tumour board discussion: biology and stage will drive priority)		Survivorship follow-up: *refer to telemedicine*
Breast cancer diagnosis during pregnancy	Postoperative visits in patients with no complications	Follow-up for patients at high risk of breast cancer (BRCA carriers, etc) or patients at high risk of relapse
On-treatment patients with new symptoms or side effects (depending on severity of symptoms/side effects, burden of progression, etc). *Convert as many visits as possible to telemedicine visits. Intensify safety monitoring for those patients on oral chemotherapy or endocrine therapy plus biological agents*		Psychological support visits (*convert to telemedicine*)

Priorities for the management of breast cancer: diagnostics and imaging

Table 2 Priorities for breast diseases: diagnostics and imaging

High priority	Medium priority	Low priority
Self-diagnosis of breast lump or other symptoms suggestive of malignancy	Further diagnostic imaging for BIRADS 4 screening mammogram in asymptomatic subjects.	Mammography-based population screening and risk-adapted breast screening programmes for asymptomatic subjects (eg, MRI or ultrasound).
Clinical evidence of locoregional relapse with surgical radical approach feasible (according to stage, histology and biological features of the disease)	Image-guided or clinically guided biopsy to ascertain a suspect of metastatic relapse.	Patients with abnormal findings at screening mammograms who can go to 6-month interval imaging (BIRADS 3).
Pathology assessment (histopathology or cytopathology) for abnormal mammograms or breast symptoms or a symptomatic metastatic relapse	Initial metastatic workup (according to stage and biological features) in patients with early stage invasive breast cancer.	In patients with early stage breast cancer, follow-up imaging, restaging studies, echocardiograms, ECGs and bone density scans can be delayed if clinically asymptomatic. In patients with metastatic breast cancer, we recommend symptoms-oriented follow-up. Imaging, restaging studies, echocardiograms and ECGs can be delayed or done at lengthened intervals. *Implement telemedicine follow-up*.
Further diagnostic imaging for BIRADS 5 screening mammogram in asymptomatic subjects	Echocardiograms in patients with early stage invasive breast cancer requiring with indication to anthracycline-based or anti-HER2 treatment.	

BIRADS, Breast Imaging-Reporting and Data System.

Priorities for the management of breast cancer: surgical oncology

Table 3 Priorities for breast disease: surgical oncology

High priority	Medium priority	Low priority
Breast cancer surgery complication with bleeding or indication to incision and drainage of a breast abscess and/or haematoma	Clinically low-risk primary breast cancer (eg, stage I/II ER-positive/PR-positive/HER2-negative, low-grade/low proliferative index tumours). *After multidisciplinary tumour board discussion consider starting neoadjuvant/preoperative endocrine therapy according to menopausal status and delay surgery*.	Excision of benign lesions and duct excision (fibroadenomas, atypia, papillomas).
Complications of reconstructing surgery (eg, ischaemia)	Discordant biopsies likely to be malignant.	Surgery of non-invasive breast cancer (in situ) except for extended high-grade DCIS.
Surgery in patients who have completed neoadjuvant chemotherapy-based treatment (or, in exceptional cases, with progression of disease during neoadjuvant treatment)	-	Discordant biopsies likely to be benign.
-	-	Immediate or delayed breast reconstruction with autologous tissue and/or implants.
Surgery in patients with invasive cancer for whom multidisciplinary tumour board may decide, case-by-case, to proceed with upfront surgery	-	Prophylactic surgery for asymptomatic high-risk patients.
Excision of malignant recurrence (depending on phenotype and extent)		
Breast cancer surgery during pregnancy (multidisciplinary treatment should be individualised according to stage and biology)	-	-

DCIS, ductal carcinoma in situ.

Priorities for the management of breast cancer: radiation oncology

Table 4 Priorities for breast cancer: radiation oncology

High priority	Medium priority	Low priority
Palliative treatment of acute spinal cord compression, symptomatic brain metastases, bleeding/painful inoperable breast masses or any urgent palliative radiation therapy, when control of symptoms cannot be achieved pharmacologically	Adjuvant postoperative radiation therapy for low-risk/intermediate-risk patients with breast cancer (aged <65 years and stage I/II luminal cancer, ER positive regardless of nodal status or positive margins). *Use of hypofractionated regimens should be considered to reduce hospital visits. Endocrine therapy can be started during the waiting interval.*	Elderly patients with low-risk breast cancer (aged >70 years, with low-risk stage I ER-positive/HER2-negative breast cancer): *starting adjuvant endocrine therapy is recommended while postponing radiation therapy.* Carcinoma in situ.
Patients already on radiation treatment	-	-
Adjuvant postoperative radiation therapy for high-risk patients with breast cancer (inflammatory disease at diagnosis, node-positive disease, triple-negative or HER2-positive breast cancer, residual disease at surgery postneoadjuvant therapy, young age (<40 years)	-	-

Priorities for the management of breast cancer: medical oncology—early breast cancer

Table 5 Priorities for breast cancer: medical oncology—early breast cancer

High priority	Medium priority	Low priority
Neoadjuvant and adjuvant chemotherapy for patients with triple-negative breast cancer Neoadjuvant and adjuvant chemotherapy in combination with targeted therapy for HER2-positive patients with breast cancer Neoadjuvant and adjuvant endocrine therapy±chemotherapy for high-risk ER-positive/HER2-negative breast cancer as defined by current guidelines	For postmenopausal women with stage I cancers, with low-intermediate grade tumours, lobular breast cancers endocrine therapy may be started first while surgery can be delayed.	Follow-up imaging, restaging studies, echocardiograms, ECGs and bone density scans can be delayed if patients clinically asymptomatic or clinical signs of response in the neoadjuvant setting.
Completion of neoadjuvant chemotherapy (with or without anti-HER2 therapy) that has already been initiated	For patients with low-risk genomic signatures/score prefer endocrine therapy alone.	-
Continuation of adjuvant capecitabine treatment in patients with high-risk triple-negative breast cancer, and T-DM1 in HER2-positive patients with high-risk breast cancer	Ongoing adjuvant trastuzumab alone may be postponed by 6–8 weeks in patients at high risk of complicated COVID-19 infection.	-
Continuation of standard adjuvant endocrine therapy in premenopausal and postmenopausal setting. *Use telemedicine to manage potential toxicity reported by patients*		
Continuation of treatment in the context of a clinical trial, provided patient benefits overweight risks, with possible adaptation of procedures without affecting patient safety and study conduct. *Regulatory agencies and sponsors may provide guidance on rules on study conduct during the pandemics*	-	-

Priorities for the management of breast cancer: medical oncology-metastatic breast cancer

Table 6 Priorities for breast cancer: medical oncology—metastatic breast cancer

High priority	Medium priority	Low priority
Early line chemotherapy, endocrine therapy, targeted agents or immune-checkpoint inhibitors likely to improve outcomes in metastatic disease (high priority to pertuzumab/ trastuzumab plus chemotherapy in HER2-positive breast cancer). Consider also, discussing case-by-case in multidisciplinary tumour board, endocrine therapy with CDK 4–6 inhibitors in ER-positive/ HER2-negative breast cancer, chemotherapy plus atezolizumab in PD-L1-positive TNBC	Second, third, beyond third-line treatment when therapy may provide clinical benefit and impact on outcome.	Bone agents therapy (zoledronic acid, denosumab) that are not needed urgently for hypercalcaemia, or not needed for pain control and in patients who are otherwise not in need for coming to the hospital (ie, receiving oral chemotherapy or endocrine therapy). Bone agents can be administered every 3 months.
Visceral crisis	Consider avoiding or delaying the addition of mTOR inhibitors or PIK3CA inhibitors (still not approved in European Union) to endocrine therapy, particularly in elderly patients with comorbidities.	If clinically asymptomatic follow-up imaging, restaging studies, echocardiograms and ECGs can be delayed or done at lengthened intervals.
Continuation of treatment in the context of a clinical trial, provided patient benefits overweight risks, with possible adaptation of procedures without affecting patient safety and study conduct. *Regulatory agencies and sponsors may provide guidance on rules on study conduct during the pandemics.*	Consider, discussing case-by-case, inclusion in a clinical trial, provided patient benefits overweight risks, with possible adaptation of procedures without affecting patient safety and study conduct.	-

mTOR, mammalian target of rapamycin; PD-L1, programmed death-ligand 1; PIK3CA, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; TNBC, triple-negative breast cancer.

Kapetanakis et al. Management of surgical lung cancer patients during the COVID-19 pandemic in the financially and resource strained Greek health care system. Journal of Surgical Oncology. DOI: https://doi.org/10.1002/jso.25988

Country context: Greece

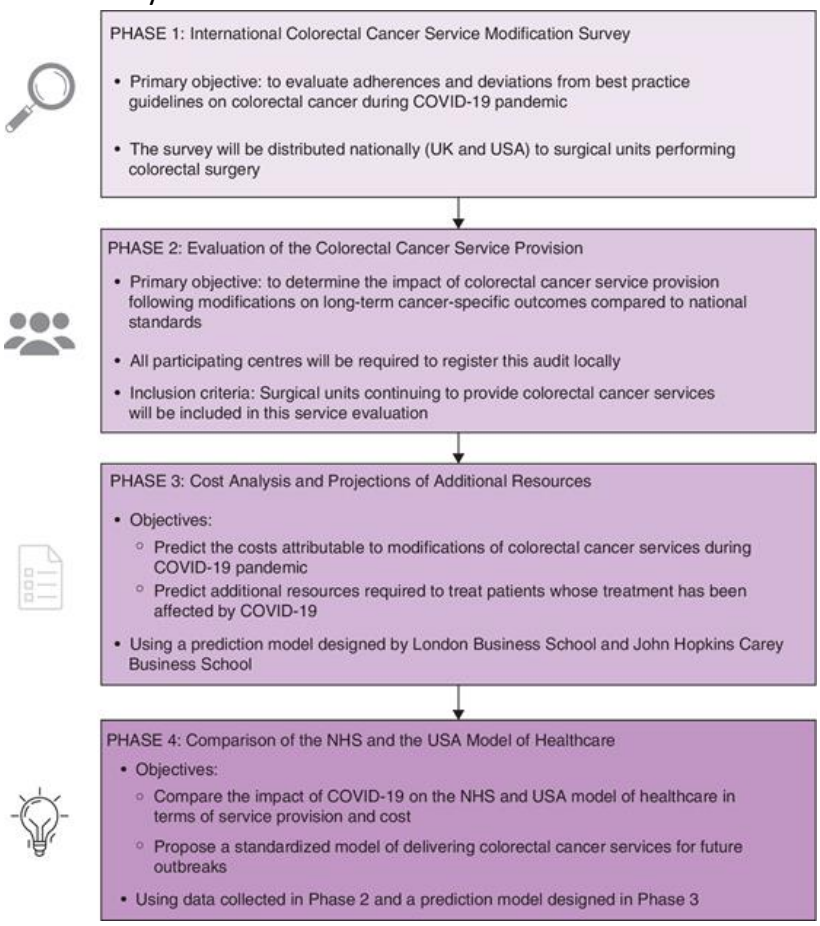
In this letter to the editor, the authors discuss the ethical dilemmas and worries that they as lung cancer specialists are facing during the COVID-19 outbreak. They present the necessary management adjustments they have to undertake for patients with operable lung cancer so as to continue providing them with quality medical care in a chronically resource-starved health system during this pandemic. They propose the following management recommendations for surgical lung cancer patients:

Lung cancer stage		
Ia-IIa	IIb-IIIa	IIIb
Postpone surgery for 8 wk following multidisciplinary team review	Induction chemotherapy for 2 cycles	Chemotherapy for downstaging according to established strategies
Surgery performed in certain low-risk patients with high potential for curative resection		Chemotherapy continued for 1 additional cycle or surgery performed in low-risk patients
6-wk follow-up with new imaging		Follow-up as per protocol

CRC COVID-19 Research Collaborative. Colorectal Cancer Services During the COVID-19 Pandemic. British Jorunal or Surgery. Doi: https://doi.org/10.1002/bjs.11706

Country context: UK

This article presents the protocol of a Colorectal Cancer (CRC) Collaborative study aiming to describe changes in colorectal cancer services in response to the COVID-19 pandemic, the impact that ensues, and sensible ways to navigate the ethical challenges of rationing services and sustaining care during the pandemic. The flow-chart below illustrates the planned phases of the study:



Adhikari et al. Caring of cancer patients during COVID-19: A real-life challenge. Indian Journal of Cancer.

Country Context: India

This article recommends approaches to making difficult decisions about how and when to provide cancer treatment in low-resource settings where the health systems have been overburdened by the COVID-19 pandemic:

1. Screening for patients: Separate entry points for cancer staff and patients; all patients to be asked a set of screening questions to identify COVID-19 patients; idenitify patients at "high-risk" (Patients on active chemotherapy/radical radiotherapy/immunotherapy, patients with hematological malignancies, hematopoietic stem cell transplant recipients (in last 6 months).

2. Medical management: Patients requiring chemotherapy can be stratified according to the risk and benefit. Those with the lowest risk and highest benefit should get the priority. Outpatient consultations for patients who do not need active management should be avoided to reduce hospital contact. All screening, surveillance and protocol-based diagnostic procedures can be rescheduled for later dates. Telemedicine, with the help of telephone or digital messaging/conferencing services, would be beneficial.
3. Surgical management: Elective surgical cases with a high likelihood of postoperative intensive care unit (ICU) or ventilator utilisation should be delayed considering the risk of infection and need of these resources for patients with COVID-19. All aerosol-generating procedures (e.g., endoscopy and intubation) should ideally be done in negative pressure rooms. A dedicated operating theatre should be kept to take care of suspected or confirmed COVID-19 patients with cancer, in case of emergency..
4. Radical radiotherapy or chemoradiotherapy with curative intent can be initiated in patients with rapidly proliferating tumors, especially when treatment has already been started. In aggressive tumours, where the residual disease is left after surgery, postoperative radiotherapy can be given. For less aggressive tumours, radical radiotherapy can be initiated if it is the first-line treatment done with curative intent. Palliative radiotherapy can be done if it reduces the usage of other treatment modalities.
5. Palliative care: Palliation is an ethical obligation, and we should strive for reasonable symptom control and comfort care for cancer patients in a pandemic. Ensure adequate medications are available to patients as repeated trips to hospital pharmacy is not desired. Medications such as opioids can be prescribed for longer than usual and telemedicine can be used to monitor patients' compliance with dosage.
6. Hospital infection control (HIC): This is the cornerstone in preventing nosocomial outbreaks of COVID-19 in cancer patients. Arrangements for the adequate supply of PPE along with earmarked donning and doffing area should be made with proper disinfection and biomedical waste management. This should be coupled with regular training for healthcare workers on the proper use of PPE. Whenever patients are suspected with COVID-19, use of PPE is advised, especially if aerosol-generating procedure done. Surgical masks and handwashing with alcohol-based hand rub should be provided to all cancer patients at the entrance and wards.

Parashar et al. Disease Site-Specific Guidelines for Curative Radiation Treatment During 'Limited Surgery' and 'Hospital Avoidance': A Radiation Oncology Perspective From the Epicenter of COVID-19 Pandemic. Cureus. Doi: 10.7759/cureus.8190

Country Context: USA

This article reviews evidence-based radiation therapy approaches for curable cancer patients during the COVID-19 pandemic. It focuses on three scenarios of cancer care: 1) radiation therapy as an alternative to surgery when immediate surgery is not possible, 2) radiation therapy as a 'bridge' to surgery, and 3) radiation options definitively or postoperatively, given the risk of hospitalisation with high-dose chemotherapy. In addition to site-specific recommendations on head anc neck, breast, bladder and colorectal cancers etc, they recommend the following general considerations:

1. When available, test cancer patients and staff for coronavirus infection and exposure
2. Follow or create safety protocols to prevent infections for patients and staff

3. Multidisciplinary discussion for each patient case (virtual or in-person with social distancing)
4. Short-course hypofractionated RT is preferred when feasible
5. Conservative (smaller) RT fields are preferred, if possible, to minimise RT-induced lymphopenia and reduce mucosal toxicity
6. Consider enrollment into clinical trials to collect data and information on this cohort of patients. Consider enrollment onto clinical trials if infected with the coronavirus.

They also recommend the following general considerations when treating cancer patients with radiation during COVID-19:

1. Aggressive and preemptive management of side effects
1. Includes early interventions, such as skin creams, anti-diarrheal, cough suppressant, anti-inflammatory, and nutritional supplements
2. Low threshold for hydration, pain management
3. Enhanced communication (consider virtual) with multidisciplinary teams (medical oncology, surgery, nutrition, occupational and physical therapy [OT/PT], social work, and wound care)

Buckstein et al. Experiencing the Surge: Report From a Large New York Radiation Oncology Department During the COVID-19 Pandemic. DOI: 10.1016/j.adro.2020.04.014

Country context: USA

This study reviews the impact of COVID-19 on a hospital system in New York on aspects of medicine, nursing, radiation therapy, and administration. It found that COVID-19 surge had a tremendous impact on the health system including cessation of all of surgeries, including oncologic surgery, as well as transfer of all inpatient oncology services to makeshift outpatient facilities. Radiation Oncology centres made aggressive efforts to reduce patients on treatment to protect patients and staff as well reallocate staff and space for more acute clinical needs. Patients on-beam were reduced by 27% from 172 to 125 by 4/1/20. Almost all visits were changed to telemedicine within 2 weeks. Infection rates and quarantine were quite low amongst staff and patients. The majority of residents were deployed into COVID-19 clinical settings.

Taub et al. COVID-19 and childhood acute lymphoblastic leukemia. Pediatric Blood & Cancer. DOI: https://doi.org/10.1002/pbc.28400

Country context: USA

In this letter to the editor, the authors draw the attention of paediatric oncologists to two critical questions: Can the isolation of children at home lead to an avoidance of exposure to viruses and the leukemia-inducing “second-hit?” and will this result in a decreased number of childhood Acute lymphoblastic leukemia (ALL) cases in the near future? Conversely, can the infection of predisposed children by COVID-19 (even those who may be clinically asymptomatic) act as a “second-hit,” leading to an increased number of ALL cases following this pandemic? They note that answers to these two potential scenarios may become evident in the near future with ongoing epidemiologic surveillance.

Sites:

International Society of Paediatric Oncology. COVID-19 Resources and Guidance

Country context: Global

This resource page provides current resources, tools and the latest information on COVID-19 as it relates to childhood cancer. It also provides a platform for paediatric oncologists and care providers to connect and collaborate, as well as access to a real-time pediatric cancer registry.

The UK Paediatric Oncology Coronavirus Cancer Monitoring Project. Infographic on COVID-19 in children with cancer. May 2020.

Country context: UK

Paediatric oncology centres in the UK have joined the the UK Paediatric Oncology Coronavirus Cancer Monitoring Project, registering cases of COVID-19 in children with cancer since the outbreak of the pandemic. Below is a summary of the data as of 18 May 2020.