Managing haematology and oncology patients during the COVID-19 pandemic: Interim consensus guidance

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Acknowledgments: The authors have no conflicts of interest to declare. The authors wish to acknowledge the endorsing organisations, and the following for review of the manuscript: Leanne Berkahn, Theresa Cole, Megan Crane, Nada Hamad, Eliza Hawkes, Mark Herzberg, Marie Malica, Nick Pavlakis, David Ross, Rachel Wiseman, Leeroy Williams and David Yeung. The authors also thank the Australasian Leukaemia and Lymphoma Group Consumer representative group for review and input to the manuscript.

Word, table and reference counts: Abstract 198 words; main text 4,657 words; 1 table and 1 box; 54 references

Abstract

A pandemic coronavirus, termed SARS-CoV-2, causes a respiratory illness called COVID-19 disease, which is often severe or life-threatening. Patients with cancer may have compromised immunity due to their disease or its treatment, and early reports suggest cancer is a risk factor for severe COVID-19 disease. Community transmission of SARS-CoV-2 has the potential to overwhelm healthcare services, compromising the delivery of cancer investigations and care. Pending further evidence, this interim consensus guidance summarises the clinical presentation and diagnosis of COVID-19 disease, provides factors to consider when managing patients with cancer, and discusses risk factors for severe COVID-19 disease. Possible actions for clinicians managing patients with cancer are suggested, and are phased according to the presence or absence of community transmission and disruption to normal healthcare provision. Clinicians may need to reassess the risks and benefits of cancer therapies, balancing the risks of tumour progression against those of infections or other treatment complications on a case-by-case basis, while ensuring measures are proportionate, equitable and transparent. Key communication points for patients are proposed, and the potential impacts of COVID-19 disease on transfusion practice, stem cell transplantation and cellular therapies, radiation oncology, clinical trial participation and provision of palliative care are discussed.

Key words

COVID-19, coronavirus, SARS-CoV-19, neoplasms, hematologic diseases, immunocompromised host, palliative care

Introduction

Following a cluster of viral pneumonia cases in late 2019, a novel coronavirus was isolated and reported in Wuhan, China in January 2020(1). This virus, now termed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causes a respiratory disease called COVID-19 in infected individuals. COVID-19 disease spread rapidly worldwide, meeting conventional definitions of a pandemic. Although 81% of patients with COVID-19 have a mild illness, 14% have severe illness requiring hospitalisation and supplemental oxygen, and the remaining 5% become critically ill with respiratory failure, septic shock and/or multi-organ dysfunction(1). Recent estimates of COVID-19 case fatality rates are around 2%, rising to 15% in patients aged 80 years or over(1).

By early March 2020, the first instances of community spread of COVID-19 were documented in Australia, and the first COVID-19 cases were diagnosed in New Zealand. Given the spread of COVID-19 disease in other countries, including the dramatic rise in case numbers in Europe and the United States in March 2020, a further rise in cases across Australasia over the following months appears likely. At present, no vaccine or specific antiviral therapy is available. The only measures available to prevent or delay community spread of COVID-19 are containment and rigorous case finding. Once COVID-19 becomes widespread within a community, quarantine and social distancing measures may slow its further spread, and have been adopted in many jurisdictions.

Patients with cancers are frequently immunosuppressed by their disease and/or treatment, and are at increased risk of severe complications of respiratory viruses(2).

Moreover, many haematology and oncology patients will have additional risk factors for severe COVID-19 disease, such as advanced age and comorbidities(3).

Early review of a Chinese national data repository suggested a disproportionately higher prevalence of cancer (mainly lung cancer) in patients with confirmed COVID-19, when compared to the general population(4); however no data are available on the incidence of COVID-19 in cancer patients compared to the general population(5). Early COVID-19 outcome data suggested a case fatality rate of 5.6% among patients with cancer(1), and one study suggested patients with cancer had a 3.5 times higher risk of severe COVID-19 disease(4). However, reported case numbers remain low, and the relative contribution of other risk factors, including age, to this risk is not clear(6). Haematopoietic stem cell transplant (HSCT) recipients could be at particularly high risk: prior to the emergence of SARS-CoV-2, progression of the less pathogenic seasonal coronavirus infections from the upper to lower respiratory tract occurred in up to 30% of HSCT recipients(7).

Patients with cancer could be at elevated risk of severe COVID-19 disease, while delivery of cancer therapies could be disrupted by quarantines, social distancing measures, and disruption to routine healthcare delivery by the pandemic. Pending more definitive evidence, this article presents interim guidance, based on expert opinion, to aid decision-making for clinicians treating patients with cancers. The suggestions provided here may be relevant to both adult and paediatric patients. As recommendations may change in light of new evidence or experience, we encourage clinicians to refer to the official information sources regularly, and the website of the

National Centre Infections in Cancer (https://cancerandinfections.org/) for updates to this guidance.

1. Clinical presentation, diagnosis and treatment considerations

Clinically, COVID-19 disease is most frequently associated with fever (90 – 98%), cough (59 – 76%) and lethargy (38 – 70%)(3, 8-10). Abnormalities on CT chest have been reported in 80 – 100% of admitted patients, with bilateral ground glass opacities the most common finding(3, 8, 10-12). Median time to development of dyspnoea is 5 – 8 days(3, 9) with median hospital admission stay of 7 – 10 days(3). In adults, intensive care admission has been reported in 26% of admissions at a median time of 12 days after illness onset, coinciding with onset of acute respiratory distress syndrome (ARDS).(10) Atypical clinical presentations of other infections are common among cancer patients receiving highly immunosuppressive therapies,(13) although whether this applies to COVID-19 disease is not yet known.

The clinical impact of COVID-19 disease in children with cancer or haematological malignancy is currently unknown. Although the mechanism is not clear, children appear less frequently affected by SARS-CoV-2, representing only 2% of COVID-19 presentations in a large Wuhan series, with no deaths reported in those under 10 years(1, 14). When symptomatic illness occurs in children, it is usually mild, with fever and cough most frequently reported. Diffuse pulmonary infiltrates in an asymptomatic child were recently described(15). However, while asymptomatic or mild illness following SARS-CoV-2 infection is the norm in otherwise well children, the risk of severe illness may be higher in the immunocompromised. This is highlighted by a

report of severe COVID-19 disease in a child receiving chemotherapy for acute lymphoblastic leukaemia(16).

Diagnosis can be made by specific RT-PCR of nasopharyngeal or oropharyngeal swabs and lower respiratory tract samples(3) with median viral shedding of 20 days (interquartile range 17 – 24 days)(10). Following infection, SARS-CoV-2 viral shedding might be more prolonged in patients with cancer: viral shedding of seasonal coronaviruses lasts up to 4 weeks in patients with cancer,(7) and shedding of other respiratory viruses is prolonged in immunosuppressed patients.(17) The SARS-CoV-2 virus can also be detected in stool samples. Although the impact of this on virus transmission remains uncertain, this should be considered in patients with therapy-associated diarrhoea or with stomas(18). Clinicians must note that the coronavirus testing incorporated in routine respiratory virus PCR panels may not detect SARS-CoV-2, and should verify suitability of the assays in local use for COVID-19 disease testing.

Interim guidance for the treatment of COVID-19 disease is available elsewhere(19). Antiviral therapies such as lopinavir-ritonavir and remdesivir are undergoing evaluation, and the role of anti-cytokine therapies such as tocilizumab for severe infections is under exploration. Pending further information, we suggest that management of COVID-19 disease should be similar for patients with and without cancer. Immunocompromised patients with suspected or confirmed COVID-19 should be discussed with an infectious disease or clinical microbiology specialist. However, clinicians should be aware of the following considerations for patients with cancer who develop symptoms of COVID-19 disease:

i. Among immunocompromised patients, the differential diagnosis of fever and respiratory symptoms is broad, and clinicians should be alert to the possibility of alternative or secondary infections, including bacterial, fungal or other viral infections. Early recognition and treatment of bacterial sepsis remains vital, particularly in severely neutropenic patients;

ii. Pneumonitis can occur following certain cytotoxic chemotherapies, immune checkpoint blockade or radiotherapy, and shares clinical and radiological features with COVID-19 disease. Corticosteroids should be considered if therapy-related pneumonitis is suspected, acknowledging that a detrimental impact of corticosteroids on the risk of severe COVID-19 disease has not been excluded;

iii. Temporary discontinuation of cancer therapies will be warranted for some patients with cancer who develop symptoms of COVID-19 disease, to minimise treatment-related immunosuppression or to reduce the risk of drug interactions. This should be undertaken in discussion with an oncologist or haematologist familiar with management of the malignancy, who can advise on the benefits and risks of pausing therapy.

For each of the reasons above, community assessment and management procedures developed for healthy people with COVID-19 disease may be less well suited for some patients with cancer.

2. Possible risk factors for severe COVID-19 disease

Established risk factors for severe COVID-19 disease in adults include advanced age and medical comorbidities(3). In-hospital death has been independently associated with higher age, higher Sequential Organ Failure Assessment (SOFA) score and

elevated D-dimer(10). Importantly, some laboratory findings associated with adverse COVID-19 disease outcomes, such as lymphopenia, neutrophilia, elevated D-dimer and elevated lactate dehydrogenase, are frequent in patients with cancer – the applicability of these biomarkers of COVID-19 disease severity to patients with cancer has not been established, and they should be interpreted with caution.

In an early report of patients with COVID-19 disease in China, receipt of chemotherapy or cancer surgery was a risk factor for severe complications(20). Patients with cancer were also reported to be at higher risk of severe complications including intensive care unit (ICU) admission, invasive ventilation or death(20) and deteriorated more rapidly (median of 13 days vs. 43 days). Receipt of cancer therapy or surgery within the preceding month was associated with an increased risk of severe events after adjusting for other factors (odds ratio 5.34, $p<0.01$)(20). However, the number of COVID-19 cases with cancer in this series was small and the contribution of confounding factors, including smoking, is not clear(5).

Risk factors for severe COVID-19 disease in children are currently unknown, although a study of seasonal coronaviruses in children found that co-infection, younger age and immunocompromise were associated with an increased risk of severe lower respiratory tract infection(21).

Specific risk factors for severe respiratory viral infection in patients with solid tumours are poorly described in the literature. Although many treatments for solid tumours do not cause prolonged severe lymphopenia or neutropenia, severe infection risk may be elevated due to disruption of mucosal barriers by chemotherapy-induced mucositis, or

due to altered anatomy and reduced physiological reserve due to the malignancy itself or as a consequence of surgery or radiotherapy(22). This may be of particular relevance to patients with lung cancer, who made up the majority of cancer patients affected by COVID-19 disease in an early report(20).

Among adult haematology and HSCT patients with seasonal coronavirus (not SARS-CoV-2) infections, the following risk factors for lower respiratory tract disease were identified (2, 7, 23): Age 50 years and above; receipt of corticosteroids; graft versus host disease (GvHD); lymphopenia; neutropenia; hypogammaglobulinaemia < 4 g/L.

Until specific risk factors for severe COVID-19 disease among patients with cancer have been identified, we suggest clinicians use their clinical judgement, referencing established risk factors for severe manifestations of other respiratory viruses, to evaluate an individual patient's risk of severe COVID-19 disease.

3. **Actions for consideration by haematologists and oncologists**

Healthcare system and policy responses to COVID-19 are evolving rapidly. Haematologists and oncologists should regularly review and follow institutional, specialist college, state-level and federal government recommendations. We encourage haematology and oncology representatives to engage with, and participate in, pandemic planning within their health organisations.

As many patients with cancer may be at increased risk of severe COVID-19 disease, we suggest clinicians take a proactive approach. In Table 1, we propose actions to consider, phased according to the presence or absence of community spread of

COVID-19 disease locally, and the capacity of healthcare services to deliver routine care. The actions suggested in Table 1 will not be appropriate for all settings, and are not exhaustive, but are intended to prompt discussion among clinicians planning their own service's COVID-19 response. At each phase, clinicians should review actions they could take to prepare for the subsequent phase; some units may elect to initiate later-phase actions at an earlier phase. The actions are cumulative – the measures in phases B and C are suggested in addition to the earlier phases. Measures should be reviewed regularly, and reversed once the situation allows. Institutional, local, state-wide or federal/national policies/recommendations (including for social distancing, isolation, quarantine or personal protective equipment use) are likely to cover some or all of these actions, and should take priority.

Social distancing measures, quarantine and visitor limitations will limit opportunities for family support and advocacy, impacting an important sense of connection and source of strength and wellbeing, particularly for Indigenous peoples. We recommend services recognise these impacts, and seek to counterbalance them with measures to ensure safe non-physical contact and support, such as facilitation of video and telephone contact. Refer to guidance for the delivery of culturally safe care.(24, 25)

The spread of COVID-19 disease can be rapid, and may overwhelm primary and acute care facilities(1, 26). This may be compounded by COVID-19 infection of medical personnel, quarantine requirements and school closures, all of which may impact staffing levels(3), and by disruption to supply chains, affecting medical supplies. If acute care facilities are overwhelmed, institutions might make alternative provisions for the care of patients with cancers. Adaptive measures could include increased use

of community care (including 'hospital in the home' services) or of private facilities. Clinicians may need to work flexibly to facilitate safe service provision in alternative settings.

Resource constraints may mandate prioritisation or modification of patients' cancer therapies. While it is anticipated that institutions will develop their own plans, which will take priority, we suggest individual patient decisions should be the responsibility of clinicians who are familiar with the malignancy, its treatment, and with other therapeutic options. Clinicians will have to balance the relative risks of developing COVID-19 disease while severely immunosuppressed, or of developing a severe treatment complication, against the risks of tumour progression, while taking into account the prevailing state of the healthcare service, and current or incipient medicine supply constraints.

We suggest discussing risks and benefits of any treatment modifications among clinical peers. Take particular account of the need to protect vulnerable populations, including indigenous peoples, who experience a higher burden of both cancer and infectious disease(27-31). We suggest any treatment modifications, and the reasons for them, are clearly documented in each patient's medical record, and are communicated to the patient and their primary care physician. Consider making arrangements to review treatment modifications once resource availability allows – in some circumstances it may be appropriate to resume a postponed treatment, or to complete an abbreviated treatment course.

The ethical principles of equity, proportionality and transparency apply to resource allocation decisions. Refer to relevant regulatory guidance, such as that provided in the Medical Council of New Zealand document, “Safe practice in an environment of resource limitation”(27), and to ethical frameworks, such as that outlined in the 2020 “Australian Health Sector Emergency Response Plan for Novel Coronavirus (COVID-19)”.(28) If crisis standards of care replace normal standards, conflicts with and between other ethical principles including justice, non-maleficence, beneficence and autonomy may become acute, and need to be openly acknowledged and addressed. Where available, objective national guidelines should be followed, and a fair decision-making process adopted, shared between appropriate senior medical staff. Staff involved with such decisions should be supported during and after the crisis has resolved.

4. Information for patients

Many patients with cancer, and their families, will be concerned or distressed about the impacts of COVID-19 disease. A list of suggested messages for clinicians to communicate to their patients with cancer is outlined in Box 1.

As COVID-19 disease recommendations are likely to change frequently, clinicians should direct patients towards the most up to date resources, from the Department of Health in Australia (https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert), and from the Ministry of Health in New Zealand (https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus).

Patients with family members or other close contacts who have suspected or confirmed COVID-19 disease, should aim to remain isolated from these contacts, and should inform their cancer centre of any quarantine requirements. The recommendations of the relevant health department regarding quarantine and isolation should be followed.

Steps should be taken to reduce the risk of patients with symptoms of COVID-19 disease, or with a known SARS-CoV-2 contact, presenting unannounced to cancer centers or clinics. We suggest cancer centers inform patients of the symptoms of COVID-19 disease, indicate criteria for seeking medical advice, and stating the appropriate mode of presentation. This may include use of a triage line, assessment in an acute care setting with isolation and testing facilities, or use of a dedicated community assessment facility. This advice should be consistent with institutional, state or federal guidance, and should be disseminated to receptionists, nursing and clinical staff, as well as to patients themselves. The advice should take account of the possibility that cancer patients presenting with fever may be at elevated risk of bacterial or fungal infection requiring prompt antimicrobial therapy, and that the differential diagnosis of fever should not be limited to COVID-19 disease (see Section 1).

Measures that might be widely implemented in a pandemic setting, and which may warrant modification for immunocompromised patients, include: community-based assessment; home treatment of COVID-19 disease; cohorting with other infected patients in a non-specialist ward; symptomatic COVID-19 treatment without confirmatory investigations or without empiric antibiotics. During the pandemic,

patients may be assessed and managed by clinicians unfamiliar with their medical history; we suggest patients are aware of and inform clinicians of their malignancy and its treatment.

We recommend patients with cancer review governmental advice and restrictions before undertaking domestic and overseas travel. Patients should ensure they travel with a sufficient supply of their medicines, taking into account the potential risk of being quarantined during or after their journey. Patients must be aware that in addition to a higher risk of infection with SARS-CoV-2, access to medical services may be difficult or impossible in regions or countries where COVID-19 disease has exceeded healthcare capacity.

5. Transfusion considerations

Transfusion support for patients with cancer and blood disorders accounts for the majority of outpatient red cell and platelet utilisation, and for a large fraction of inpatient transfusions(32).

Transfusion requires close patient monitoring, placing demands upon in- and outpatient cancer services, which could fall under strain during the COVID-19 pandemic. Visits to acute care facilities for transfusions exposes immunocompromised patients to patients or staff, some of whom might be shedding SARS-CoV-2. Community spread of COVID-19 may reduce the blood donor pool, and threaten blood supplies, due to deferral of donors, blood service staff shortages, or shortages of consumables and reagents. Finally, there have been no cases of transfusion-transmitted infections (TTI) documented and there is no precedent for transfusion

transmission of respiratory viruses, however SARS-CoV-2 viral RNA can be detected in the plasma of people with COVID-19 disease, and donor deferral is the only current mechanism in place to prevent transmission via blood components(33). Although pathogen reduction technologies (PRT) for platelets and plasma are effective for other coronaviruses, these are not in routine use in Australia or New Zealand, and no licensed PRT is available for whole blood or red cells(33). Updated information on risk of transfusion-transmission and donor deferrals in place to prevent TTI can be found from the Australian Red Cross Lifeblood website (https://www.transfusion.com.au) and AABB(34). Information about the National Blood Authority's response to COVID-19 and the National Blood Supply Contingency Plan is available from the National Blood Authority,(35) and the World Health Organization provides guidance for national blood services on managing blood supplies(36).

Community spread of COVID-19 disease, therefore, has the potential to diminish the donor pool, to threaten the capacity of cancer services to provide routine transfusion support, and to increase the risks that transfusion-dependent patients come into contact with other individuals with SARS-CoV-2. This may favour the adoption of more restrictive transfusion practices during community spread of COVID-19 disease, and especially if healthcare services experience capacity constraints.

Restrictive red cell transfusion strategies have been assessed in a variety of settings. Although optimal thresholds for outpatient transfusion of patients with haematological malignancies have not been established(37), and practice varies widely(38), preliminary data suggests more restrictive transfusion thresholds require fewer red cells(39). Red cell transfusion thresholds have been reviewed elsewhere(40), and the

most highly restrictive thresholds may be inappropriate in patients with cardiovascular disease(41). For some patients, iron, folic acid, vitamin B12 or erythropoietin may present alternatives to red cell transfusion, and should be considered, to limit transfusion requirement.

Due to their short shelf-life, platelets are likely to be impacted by blood supply shortages early. While prophylactic platelet transfusion reduces risk of bleeding following intensive chemotherapy for haematological cancers, an impact on survival has not been demonstrated(42). International guidelines recommend a 'no prophylactic platelet transfusion' strategy for asymptomatic patients with chronic bone marrow failure (including during low dose oral chemotherapy or azacitidine) and to consider no prophylactic platelet transfusions for well patients without bleeding after autologous stem cell transplantation(43). A trial to assess efficacy and safety of prophylactic tranexamic acid during severe thrombocytopenia after intensive chemotherapy is ongoing(44). In the event of healthcare capacity constraints or a threat to the supply of platelets for transfusion, clinicians should consider transfusing only those at highest risk of bleeding, and consider alternatives to platelet transfusion (such as tranexamic acid), restrictive platelet transfusion criteria and deferral of non-urgent therapies that may require platelet transfusion support.

6. Special situations

Bone marrow transplantation and cellular therapies

Both autologous and allogeneic haematopoietic stem cell transplantation (HSCT), and cellular cancer therapies, such as chimeric antigen receptor (CAR) T-cell therapies, present specific challenges, as they may place recipients at high risk of infection, often

for an extended period. Moreover, if healthcare services are overwhelmed by demand, there is a risk that transplant and cellular therapy recipients are unable to receive prompt intensive care therapy.

Regulatory and ethical considerations for modifying or deferring bone marrow transplants and/or cellular therapies mirror those for non-cellular therapies (see Section 3). Team-based discussion, application of the principles of equity, transparency and proportionality, and clear documentation of decisions and their reasons, with subsequent review once capacity allows, are recommended.

Recipients of autologous and allogeneic transplantation

Infection with respiratory viruses can present an increased mortality risk for HSCT recipients,(45) and transplantation of recipients with active respiratory infections is often delayed, where possible. Widespread community transmission of SARS-CoV-2 should be taken into account when considering the risks and benefits of proceeding to transplantation, which are likely to differ on a case-by-case basis. If community SARS-CoV-2 transmission is occurring, transplant recipients should be advised to self-isolate prior to the procedure. Inclusion of SARS-CoV-2 in pre-transplant infectious disease screening of symptomatic recipients should be considered if community transmission is present, a positive result prompting consideration of delay or deferment.

Post-transplant care should be guided by the principles outlined in previous sections, with particular attention to the period of greatest risk prior to immune recovery. Among adult HSCT recipients, the immunodeficiency scoring index (ISI), initially developed for respiratory syncytial virus, might assist with evaluation of the risk of progression to

lower respiratory tract disease and of mortality(46). The ISI has been applied to HSCT recipients with influenza virus infection(47), but it has not yet been validated for SARS-CoV-2 infection. Consideration should be given to early vaccination for respiratory pathogens (seasonal influenza and *S. pneumoniae*).

Allogeneic donor considerations

Most unrelated donor stem cell products in Australasia come from international donors(48). The complex logistics of cross-national allogeneic stem cell donation are vulnerable to disruption by the COVID-19 pandemic, and may be impacted by donor availability, donor site staffing, border restrictions, international flight changes, courier availability, and specialist laboratory staffing. Donor cancellation may occur at short notice between donor assessment and stem cell harvest, presenting the risk that recipients lack a stem cell product after myelosuppressive conditioning. Contingency planning could include securing back-up donors if possible, or collection, transportation, cryopreservation, and storage of the stem cell products at the transplant unit before commencing recipient conditioning.

It is unclear whether SARS-CoV-2 is transmissible by cellular therapy products. Viral RNA can be detected in plasma of COVID-19 patients, but the presence or absence of infectious virus has not been reported.(34) At the current time no recommendation can be made for testing of donors due to variable availability of PCR testing at donor collection centres and the lack of a serologic assay, but SARS-CoV-2 testing of donors may be adopted in future. Donors in all regions should be assessed for risk based on current knowledge of local COVID-19 prevalence, travel history, exposures and symptoms. Position statements have been provided by a number of transplant

organisations including the World Marrow Donor Association.(49) Donor registries and bone marrow transplant and cellular therapy societies have produced guidelines and position statements(49-52), which are frequently updated.

The impact of COVID-19 on international transport may also affect the supply chain for autologous chimeric antigen receptor T-cells. As for stem cell recipients, patients awaiting CAR T-cell therapies should consider self-isolation to minimise the risk of SARS-CoV-2 exposure during the period of greatest vulnerability.

Radiation oncology

Provision of radiation therapy should be guided by the principles outlined in Section 3. The lead time between radiotherapy planning and treatment may be days to weeks, while cessation of radiation therapy part-way through a treatment course may compromise outcomes. Radiation oncology services should attempt to anticipate staffing and other capacity constraints, which will be difficult in a rapidly-changing situation. Consider use of shorter fractionation schedules where this is an option(53), deferral of therapy, or omission of radiotherapy if the clinical benefit is low and the risk high. Radiation oncology services should screen patients for symptoms suggestive of COVID-19 disease, and adopt infection control measures. For some centres, this may include consideration of dedicating a linear accelerator for those with suspected or confirmed COVID-19 disease(53, 54).

Clinical trial participants

In accordance with principles of ICH GCP (paragraph 2.3), the “rights, safety, and well-being of the trial subjects are the most important considerations and should prevail

over interests of science and society."(55) At phases B and C (see Section 3), it may be necessary to reduce routine follow-up appointments, institute remote or telehealth reviews or modify treatment plans and strategies for treatment delivery in the interest of the study participant. If this will lead to protocol deviations or violations, clinicians should contact the medical monitor or sponsor of their study, and contact the relevant human ethics committee. International travel restrictions could affect trial monitoring, start-up and investigator meetings, and distribution of investigational products and laboratory samples. When enrolling new participants, Principal Investigators should take reasonable steps to ensure a trial is proceeding as usual, and consider the potential impact of COVID-19 disease on the capacity of their own centre to conduct study procedures according to the trial protocol. Consideration should be given to suspending accrual of new patients to ongoing trials and delaying opening of new trials based on availability of local resources.

Palliative Care

Palliative care will play a critical role during the COVID-19 pandemic, and will be a responsibility for all health care professionals(56). Cancer services should collaborate with specialist palliative care services when developing COVID-19 contingency plans.

Palliative care will involve managing symptoms of both cancers and of COVID-19 disease at all stages, including at the end of life. Other roles include rapid reassessment of an individual patient's goals if treatment plans are changed, helping patients and families navigate end-of-life care decisions during a period of societal and economic disruption, supporting care in the community to avoid unnecessary

hospitalisations, and delivering care in a culturally safe and responsive manner.(24, 25)

At the same time as raising demand, COVID-19 disease presents a threat to specialist palliative care service staffing and capacity. The delivery of palliative care will frequently need to be undertaken by primary treating teams, under the guidance of specialist palliative care services. Throughout the pandemic, clinicians should proactively discuss the goals of care with all patients with advanced cancers, and clearly document enduring powers of attorney or advance care plans.

Visitor restrictions on wards, quarantine or isolation requirements, and any imposition of travel restrictions or social distancing measures, are likely to complicate the planning and delivery of palliative care, and compete with cultural rituals and norms for end-of-life care and death. Increased use of telephone or video consultation will become necessary. Issues of trust, isolation, disconnectedness, and worries about abandonment should be proactively addressed(57). In particular, the impact of restriction or banning of hospital visitors on the presence of family and friends at life's end needs to be addressed with compassion and humanity. At all stages of the COVID-19 pandemic, for all patients, the principle of non-abandonment should be paramount.

Summary

The COVID-19 pandemic presents a challenge of global reach and significance, which is unprecedented in the era of modern haematology and oncology. We present interim COVID-19 guidance for clinicians caring for patients with cancer, who may be

particularly vulnerable both to severe COVID-19 disease, and to the potential impact of the pandemic on the provision of cancer investigations and treatment.

This is a rapidly-evolving situation, and we emphasise again that clinicians must regularly review and implement institutional, local, state-wide and federal/national policies, modifying or adapting the suggestions provided here as needed. Finally, given the potential severe impact of COVID-19 disease on people with cancer, we propose that oncologists and haematologists advocate for the timely application of public health measures or treatments that might contain, delay or mitigate the spread of COVID-19 disease.

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Table 1: Actions to consider, according to community-level COVID-19 transmission and healthcare capacity

Phase	Aims	Issue	Actions to consider
A: No apparent community-level COVID-19 transmission*	Reduce risk of nosocomial acquisition of respiratory viruses Inform & educate patients and staff	Staff education	Education or re-education, including of receptionists/administrators, ward/day unit staff, clinicians, allied health teams, radiation therapists & staff at patient hostels: • Hand hygiene practices • Use of PPE • Institutional policies for respiratory virus isolation • Policies to limit unwell ward visitors Importance of staying away from work if unwell with fever or respiratory symptoms Re-education around communication skills required for effective goals of care conversations
		Early identification of potential cases	Discuss patients hospitalised with febrile respiratory illnesses & no identified cause with infectious diseases or microbiology team regarding role of investigation for COVID-19
		Vaccination	Encourage staff & patient uptake of seasonal influenza vaccination
		Advice to patients	Advice for concerned patients (see Section 4) Instruction on how to present if febrile with respiratory symptoms Smoking cessation advice Pro-active engagement regarding goals of care and advance care planning for all patients to assist future decision making
B: Community-level COVID-19	Reduce risk of nosocomial SARS-CoV-2 acquisition	Clinics	Screen for COVID-19 disease symptoms before clinic or radiation treatment (e.g. via written information, telephone contact, or direct symptom enquiry) Conduct outpatient clinics away from acute care facilities Conduct selected consultations remotely (via telephone, video, written advice)

transmission; healthcare service provision as normal	Reduce risk of staff acquisition of SARS-CoV-2 Support any recommended social distancing measures		Defer some non-urgent new & follow-up appointments Limit visitors attending with patients
		Routine investigations	Review frequency & location of routine tests (e.g. blood tests, scans), which may bring patients with cancer into contact with those with respiratory symptoms
		In-department isolation/assessment facility (e.g. fever clinic)	Establish COVID-19 isolation/assessment process for haematology/oncology patients, aiming to avoid exposure to SARS-CoV-2 and to separate from other haematology/oncology waiting and treatment areas Stagger treatment times or locations
		Cancer therapy and supportive care	Optimise prophylactic measures (e.g. G-CSF, antimicrobial prophylaxis, immunoglobulin replacement) to reduce risk of infections requiring inpatient therapy Employ alternatives to transfusion (see Section 5) Reduce unnecessary immunosuppression if safe to do so Defer or delay selected non-time critical cancer therapies, including radiation treatment, if it will not compromise outcome Use shortened radiation protocols where safe to do so and compensate for breaks in treatment using appropriate fractionation schedules Ensure adequate supplies of all medicines & equipment required, including for symptom management and end of life care – e.g. opioids, syringe drivers
		Community or hospital-in-the-home services	Enhance capacity for community care as alternative to cancer centre or inpatient care
		Wards/inpatient care	Limit ward visitors Minimise non-essential hospital admissions Consider early discharge from hospital if safe to do so

			Reduce non-essential staff & student contact with inpatients
		Clinical meetings	Limiting meeting attendance to key attendees Use teleconferencing facilities when possible
		Education	Postpone non-essential face-to-face educational meetings Provide education via teleconferencing or other electronic formats Provide education into the management of COVID-19 disease, including symptoms
		Staff working arrangements and leave	Ask staff to work from home when not required in person Review upcoming annual and study leave to provide contingency for sickness/absence Define minimum staffing for provision of skeleton service Establish clear collaboration with specialist palliative care services across all settings with clear lines of responsibility for treatment decisions
C: Community-level COVID-19 transmission; healthcare service capacity exceeded	Reduce demand on acute services Prioritise and deliver urgent and essential cancer therapies Reduce risk of treatment complications that cannot be	Alternative treatment delivery settings	Implement any plans to deliver cancer investigation & treatment in alternate settings (e.g. in community or private healthcare facilities) Maximise use of remote consultations (via telephone, video, written advice) Implement plans to deliver end of life care in designated settings
		Treatment prioritisation and demand limitation meetings	Prioritise urgent and potentially-curative treatments Ensure equity, proportionality and transparency at all stages of illness and regarding all treatments; refer to ethical & regulatory guidance. Consider pre-identification of patients whose disease status would limit escalation of hospital based treatment and allow primary care decision makers the ability to minimise hospital in-patient overload Document decisions and review regularly
		Treatment modifications	If necessary, clinician-led modification of cancer treatments on case-by-case basis. Risk/benefit will vary. Seek peer review & support. Examples could include:

	adequately managed Ensure adequate staffing for essential services		• Oral alternatives to parental therapy • Selection of less myelosuppressive regimens • Abbreviated or shorter-course treatments • Schedules requiring less frequent cancer centre attendance • Deferral of treatment where appropriate Document & communicate decisions clearly, including to patients Arrange review of decisions at appropriate interval Utilisation telephone consultation/support between primary oncology care – specialist palliative care, with likely decrease in face to face patient assessments
		Transfusion support	Adopt restrictive transfusion thresholds (see Section 5)
		Staff leave	Cancel annual and study leave Implement plans for skeleton service provision

The lists of actions to consider are cumulative; actions suggested during phase B are in addition to those during phase A, and actions from all phases should be considered during phase C. PPE, personal protective equipment

*At the time of writing, some jurisdictions had already progressed past this phase

Box 1: Communication points regarding COVID-19 disease for patients with cancer

- Severe COVID-19 disease is possible in any individual, but patients with cancer may be at higher risk due to their disease and/or its treatment
- Preventing transmission of infection should be a high priority for patients and carers. Review, monitor, and closely adhere to recommendations from the Department of Health (Australia) or Ministry of Health (New Zealand) regarding hand hygiene, social distancing and other measures to avoid COVID-19 disease
- Reiterate smoking cessation advice
- No vaccine for COVID-19 is available, but vaccination against influenza (and against other infections if appropriate), and adherence to other recommended measures to reduce infection risk (e.g. prophylactic antimicrobials, limiting dusts & soil exposure if prolonged severe neutropenia) may reduce risk of other infections
- Provide advice on when, how and where to present for assessment if patients have symptoms suggesting COVID-19 disease, or have had recent contact with a person with COVID-19; not to present unannounced to the cancer center or clinic
- COVID-19 disease is not the only potential cause of fevers or respiratory symptoms; patients must still follow febrile neutropenia recommendations if applicable, and be alert to other side effects of treatment (including pneumonitis, if applicable)
- Patients should communicate their cancer diagnosis and any current treatments to clinicians, or to telemedicine advice providers, if under assessment for possible or proven COVID-19 disease or exposure. Consider proving patients with a copy of a recent clinic letter to carry.
- Provide advice on how to contact cancer center in case of difficulty obtaining medications due to increased demand or supply constraints
- If considering domestic or overseas travel, patients should follow governmental advice, advise their clinician and ensure they have sufficient medication for their journey, taking the risk of quarantine into account
- Direct towards patient information resources regarding COVID-19 specifically for cancer patients if available