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INTRODUCTION

Coronaviruses are important human and animal pathogens. At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world. In February 2020, the World Health Organization designated the disease COVID-19, which stands for coronavirus disease 2019 [1]. The virus that causes COVID-19 is designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); previously, it was referred to as 2019-nCoV.

On January 30, 2020, the WHO declared the COVID-19 outbreak a public health emergency of international concern and, in March 2020, began to characterize it as a pandemic, in order to emphasize the gravity of the situation and urge all countries to take action in detecting infection and preventing spread.

The WHO has indicated three priorities for countries [2]:

- Protecting health workers
- Engaging communities to protect those at highest risk of severe disease (eg, older adults and those with medical comorbidities)
- Supporting vulnerable countries in containing infection

The rapidly expanding COVID-19 acute respiratory pandemic has impacted all areas of daily life, including medical care. The primary intervention to slow disease spread has been physical distancing, hand and respiratory hygiene, and staying home as much as possible. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Personal preventive measures'.)

Delivering care for patients with cancer during this crisis is challenging given the competing risks of death from cancer versus death or serious complications from SARS-CoV-2, and the likely higher lethality of COVID-19 in immunocompromised hosts [3,4]. Many patients with cancer are struggling to receive treatment for their cancers due to hospitals canceling or delaying surgeries and other procedures, including chemotherapy and radiation therapy. There is also concern that patients who are otherwise healthy and have curable cancers that require timely implementation of surgery, chemotherapy, or radiation have unfortunately concluded that the risk of contracting COVID-19 may outweigh the benefits of cancer treatment [5]. Inadequate supplies of personal protective equipment (PPE) for health care providers, limited hospital capacity, including intensive care units (ICUs), and lack of point-of-care testing and seroprevalence data further complicate the difficulty.

This topic will discuss issues related to balancing the risk from treatment delay versus harm from COVID-19, ways to minimize the compromise of physical distancing during care delivery, how limited healthcare resources can be appropriately and fairly allocated, and reviews the recommendations for cancer care during the COVID-19 epidemic from expert groups [6-12].

Issues pertaining to the coronavirus in the general population are discussed elsewhere, as are issues related to particular patient populations.

- (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention".)
- (See "Coronavirus disease 2019 (COVID-19): Critical care and airway management issues".)
- (See "Coronavirus disease 2019 (COVID-19): Myocardial infarction and other coronary artery disease issues".)
- (See "Coronavirus disease 2019 (COVID-19): Considerations in children".)
- (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Pregnant and breastfeeding women'.)
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INCIDENCE AND PREVALENCE IN CANCER PATIENTS

The prevalence of cancer in those with COVID-19 has varied across reports.

Although limited, the best information on incidence of COVID-19 among patients with cancer comes from Wuhan, China [3]. Of the 1524 patients with cancer admitted to an oncology department over a six-week period from December 2019 to February 2020, 0.79 percent (12 patients) had infection with SARS-CoV-2. Although this infection rate was higher than the cumulative incidence in the community served by the hospital (0.37 percent), these patients were all sick enough to be admitted, and this report does not address the incidence of COVID-19 among community-dwelling outpatients with cancer.

Other studies, also from Wuhan, China, suggest that among those with COVID-19, approximately 1 to 2 percent have cancer [13-16]. On the other hand, a higher prevalence of cancer in those with COVID-19 have been reported from the New York City area (in one report of 5700 hospitalized patients with COVID-19, 6 percent had cancer [17]), and in Lombardy, Italy (8 percent of the patients admitted to the intensive care unit [ICU] for COVID-19 had either active or prior history of malignancy [18]). In another report, 20 percent of the deaths from COVID-19 in all of Italy were in patients with active cancer [19]. As the infection becomes more widespread, the population concurrently challenged by cancer and COVID-19 will undoubtedly expand asymmetrically across different geographies and risk cohorts. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Spectrum of illness severity and case fatality rates' and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Impact of age'.)

CLINICAL PRESENTATION AND OUTCOMES

As in non-cancer populations, the clinical characteristics of COVID-19 in patients with cancer usually include fever, dry cough, dyspnea, chills, muscle pain, headache, sore throat, rigors, and a loss of taste or smell (table 1). Reddish-purple nodules on the distal digits similar in appearance to pernio (chilblains) have also been described, mainly in children and young adults with documented or suspected COVID-19 ("COVID-toes"). (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Clinical manifestations'.)

Although COVID-19 is typically more severe and lethal among older people [20], people of any age with underlying medical conditions are at increased risk if they contract the virus [21]. These conditions include active or past history of cancer, particularly if they recently received or are continuing to receive treatment. However, data are extremely limited and more studies are needed.

Data on the clinical characteristics of SARS-CoV-2 infected cancer patients are limited by small sample sizes. One is a report of 28 patients with COVID-19 from three hospitals in Wuhan, China

[22]:

- Regarding demographics, 67 percent were male, the median age was 65 years, and the most frequent cancer type (7 of 28, 25 percent) was lung cancer. Eight were suspected to be from hospital-associated transmission.
- Clinical characteristics included fever in 82 percent, dry cough in 81 percent, and dyspnea in 50 percent. Lymphopenia was present in 82 percent and 75 percent were anemic.
- In terms of clinical course, more than one-half of the patients had severe disease (15 of 28, 54 percent), and six required admission to the ICU (21 percent). There were more severe events among the seven patients who had received chemotherapy, radiotherapy, targeted therapy, or immunotherapy within the last 14 days, relative to those who had not received treatment with the last 14 days (hazard ratio [HR] 4.079, 95% CI 1.086-15.322). The finding of patchy consolidation on admission computed tomography (CT) was also associated with a greater risk of severe disease (HR 5.438, 95% CI 1.498-19.748).
- At the time of analysis, the outcome was fatal in 8 patients (29 percent); 10 had been discharged, and 10 remained in hospital.

Is illness more severe in patients with malignancy? — Accumulating data suggest that the likelihood of a severe illness from COVID-19 is higher among patients with cancer, particularly those with hematologic malignancies and lung cancer.

- Much of the early data were derived from patients treated in Wuhan, China:
  - A meta-analysis of four retrospective studies totaling 1356 COVID-infected patients, all treated in China, addressed the severity of complications from the disease in patients with malignancy [23-27]. Although patients with cancer accounted for a higher proportion of individuals with severe disease (3.9 versus 1.4 percent of those with non-severe disease, odds ratio 2.29, 95% CI 1.00-5.23), there were only 33 cancer patients in all four studies, and the number of events overall was very low.
  - Additional information comes from an analysis of 105 patients with cancer hospitalized for COVID-19 in 14 hospitals in Wuhan, China, over a seven-week period, whose outcomes were compared with a control group of 536 patients without cancer, and matched for age, hospital, and hospitalization time [28]. Lung cancer was the most frequent malignancy (n = 22), followed by gastrointestinal (n = 13), breast (n = 11), or thyroid cancer (n = 11), and hematological malignancy (n = 9). Compared with the matched controls without cancer, patients with cancer had higher observed death rates (odds ratio [OR] 2.34, 95% CI 1.15-4.77), higher rates of ICU admission (OR 2.84, 95% CI 1.59-5.08), a greater likelihood of

severe symptoms (OR 2.79, 95% CI 1.74-4.41), and a two-fold higher likelihood of requiring invasive mechanical ventilation. Notably, cancer patients also experienced more in-hospital infections (19 versus 1.5 percent) and were more likely to be smokers (34 versus 9 percent), which could have accounted for some of these differences. Patients with hematologic malignancies, lung cancer, and metastatic cancer had the highest frequency of severe events, but the number of patients in each category was small.

- Data are emerging in other populations:

  - An analysis of 5688 patients diagnosed with laboratory-confirmed COVID-19 over a five-week period in a single New York City health system included 334 patients with cancer (6 percent); most had breast (n = 57) or prostate cancer (n = 56), followed by lung (n = 23), urothelial (n = 18) and colorectal cancer (n = 16) [29]. After adjusting for age, cancer patients aged 66 to 80 were intubated significantly more frequently than those without a diagnosis of cancer (relative risk [RR] 1.76, 95% CI 1.15-2.70); no significant difference was found in other age groups. Although cancer patients under age 50 had a fivefold higher mortality rate than those in this age group without cancer (RR 5.01, 95% CI 1.55-16.2), mortality rates from COVID-19 were not significantly higher in older patients with cancer compared with those without cancer.

  - A higher case-fatality ratio (CFR) for patients with COVID-19 and a cancer diagnosis relative to those without cancer was seen in a second report from a different New York City Hospital system [30]. Over a three-week period, 218 COVID-19-positive patients with a diagnosis of malignancy were identified, and 61 died, with a CFR of 37 percent for hematologic malignancies, and 25 percent for solid tumors, which included 6 deaths in 11 with lung cancer (CFR 55 percent). When compared with an age- and sex-matched cohort of 1090 patients with COVID-19 infection but without cancer from the same hospital system and same time period, the CFR for cancer patients was double that of noncancer patients (28 versus 14 percent). In multivariate analysis, the higher mortality rate in cancer patients was associated with older age, multiple comorbidities (heart and chronic lung disease, but not diabetes or chronic kidney disease), need for ICU support, and elevated levels of D-dimers, lactate dehydrogenase, and lactate. Few patients were on active oncologic therapy, and the impact of specific treatments, including immunotherapy, could not be assessed.

    The particularly high mortality rates among lung cancer patients is discussed in more detail below. (See 'Patients with lung cancer' below.)

- Similarly, in a small case series from Spain, among 34 patients being followed for a hematologic malignancy who were hospitalized with COVID-19, there was a high mortality rate [31]. Overall 11 died (CFR 32 percent). In multivariate analysis, hematologic status of relapsed/refractory, or stable without remission (as distinguished from remission without treatment or watch and wait), ECOG performance status ≥2 (table 2), and the presence of moderate to severe ARDS were all independently associated with poorer survival.

WHICH CANCER PATIENTS SHOULD GET SARS-COV-2 TESTING?

Patients with COVID-19 symptoms or a known COVID-19 exposure — Cancer can be an immunocompromised state, and many cancer treatments can further compromise the immune system. As such, cancer patients with fever or lower respiratory findings (eg, cough, dyspnea, hypoxia) are among the highest priority for COVID-19 testing. Subsequent approach, depending on the results of SARS-CoV2 testing, is discussed below. (See 'Approach to those who have had SARS-CoV-2 testing' below.)

These patients should also be evaluated for alternative causes of their symptoms other than COVID-19, such as influenza, bacterial pneumonia, pulmonary progression of their underlying cancer (eg, lymphangitic spread), or treatment-related side effects such as postsurgical or systemic therapy related pulmonary events (eg, atelectasis, pulmonary embolism, pneumonitis, pulmonary edema/fluid overload, immunotherapy-related pneumonitis, etc). Other symptoms (eg, chills, muscle pain, sore throat) also raise the suspicion for COVID-19 and may warrant testing. (See 'Differentiating lymphangitic spread, pneumonitis, and COVID-19' below and "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Clinical suspicion and criteria for testing' and "Toxicities associated with checkpoint inhibitor immunotherapy" and "Radiation-induced lung injury".)

We also recommend COVID-19 testing for cancer patients with an exposure to someone with confirmed COVID-19. Particular considerations for testing of lung cancer patients are discussed below. (See 'Patients with lung cancer' below.)

Patients admitted to the hospital — Some hospitals are testing all patients who are admitted to inpatient units, irrespective of whether they have a cancer diagnosis or symptoms of COVID-19. While such a strategy is reasonable, and is supported by the National Comprehensive Cancer Network (NCCN) [32], local testing availability will dictate whether it is feasible.

Elective surgeries, including many cancer surgeries, have not been performed during the COVID-19 pandemic, but as the pandemic wanes, some institutions are starting to perform elective procedures. (See 'Cancer surgery' below.)

Some institutions are routinely performing COVID-19 testing for all patients regardless of symptoms before scheduling elective surgery, and some states have specific mandates or advisories for testing. A joint statement from the American Society of Anesthesiologists (ASA) and the Anesthesia Patient Safety Foundation (APSF) recommends that in areas of high COVID-19 prevalence, testing for COVID-19 should be performed for all patients prior to non-emergency surgery, and that surgery should be delayed until the patient is no longer infectious and has recovered from COVID-19. (See "Coronavirus disease 2019 (COVID-19): Anesthetic concerns, including airway management and infection control", section on 'Preoperative COVID-19 testing for elective surgery'.)

Should asymptomatic patients receiving immunosuppressive therapy be tested? — For patients with cancer without symptoms of COVID-19, guidance regarding SARS-CoV-2 testing is evolving, and the approach among UpToDate experts is variable. Some institutions are routinely testing all cancer patients 48 to 72 hours prior to immunosuppressive therapies and prior to medical procedures. This policy is supported by updated guidelines from the Infectious Disease Society of America, which now recommends SARS-CoV-2 RNA testing in asymptomatic individuals before immunosuppressive procedures, regardless of a known exposure to COVID-19 [33]**.** According to these guidelines, immunosuppressive procedures are defined as cytotoxic chemotherapy, solid organ or stem cell transplantation, long acting biologic therapy, cellular immunotherapy, or high-dose corticosteroids.

Other institutions follow a selective approach to testing, based upon the individual clinician's judgment as to the immunosuppressive potential of the specific regimen (eg, testing would be preferred prior to highly immunosuppressive treatments such as methotrexate, vinblastine, doxorubicin plus cisplatin [MVAC], or cisplatin/etoposide; but not for less myelosuppressive regimens such as gemcitabine or docetaxel monotherapy, or single agent immunotherapy). Specific considerations for patients with lung cancer are discussed below. (See 'Patients with lung cancer' below.)

However, test availability is still limited in many jurisdictions. ASCO guidelines on this subject recommend following state public health directives and guidance on who should be tested and how the tests should be conducted. As testing becomes more widely available, it may be reasonable to test asymptomatic patients who will be receiving immunosuppressive anticancer therapy or who are believed to otherwise be at risk for serious complications from COVID-19. Results of such testing can inform decisions about delaying cancer therapy and increase the protection of health care providers and other patients.

The approach depending on SARS-CoV-2 test results is discussed below. (See 'Approach to those who have had SARS-CoV-2 testing' below.)

APPROACH TO THOSE WHO HAVE HAD SARS-COV-2 TESTING

Positive test for SARS-CoV-2 infection

Holding immunosuppressives and COVID-19 management considerations

- In general, immunosuppressive cancer therapy should be withheld in patients who test **positive for SARS-CoV-2 infection**.
    - However, although data are very limited, a case report has suggested that the Bruton's tyrosine kinase inhibitor ibrutinib for patients with a chronic hematologic malignancy may be a possible exception [34], and continuation of this class of drugs should be considered on a case-by-case basis [35].
    - For patients receiving glucocorticoids for management of their cancer or toxicities of treatment, our approach depends on the indication, but data are absent in this area. For example, if patients are on high-dose steroids and tapering is acceptable, we would do so. However, we recognize that for certain indications, for example steroids for severe immune-related adverse events or edema from central nervous systems, discontinuation of glucocorticoids is not possible.

      For patients who are receiving glucocorticoids, the decision as to whether to continue or discontinue in a patient diagnosed with COVID-19 must be individualized, and depends in part on the dose and indication for the glucocorticoid. As an example, decision-making for high-dose glucocorticoids in a patient with brain metastases or epidural spinal cord compression, or a serious immunotherapy-related adverse event is more difficult, and must be addressed on a case-by-case basis.
- Additionally, some oral non-immunosuppressive therapies such as hormonal therapies or drugs targeting activating mutations (eg, epidermal growth factor receptor [EGFR] inhibitors or BRAF/MEK inhibitors) may be continued on a case-by-case basis.

Regarding management of COVID-19, many mild cases (eg, fever, cough, and/or myalgias without dyspnea or hypoxia) and asymptomatic infections can be managed conservatively at home, if individuals can be adequately isolated. However, patients with more severe disease may warrant a higher level of care.

Importantly, if a cancer patient with late-stage disease or with significant comorbid health conditions affecting the heart or lungs acquires severe COVID-19 and requires mechanical ventilation, the prognosis is likely to be dismal [36]. It is therefore imperative for clinicians to have proactive

discussions with patients about goals of care and advance care planning, especially for those with advanced cancer [37]. Depending on state regulations, patients should be offered the option of completing a Physician Order for Life-Sustaining Treatment (POLST) form and/or other type of out-of-hospital do not resuscitate (DNR) order, especially if they would not want to receive cardiopulmonary resuscitation (CPR) or mechanical ventilation. In the absence of an advance directive, a patient with underlying severe chronic illness and acute respiratory failure from COVID-19 who is getting worse despite maximal therapy may be appropriate for a unilateral DNR order to reduce the risk of medically futile CPR to patients, families, and health care workers. This may occur through informed consent with the patient or his/her surrogate, or occasionally, informed assent [37].

Consultation with a palliative care specialist may be beneficial, although access to essential palliative care services may be limited in the face of high demand in all countries during the pandemic [38,39]. Helpful communications guides for clinicians on a wide range of pertinent topics related to COVID-19 are available from VitalTalk.

Management of COVID-19 is discussed in further detail elsewhere. (See "Coronavirus disease 2019 (COVID-19): Management in hospitalized adults" and "Coronavirus disease 2019 (COVID-19): Outpatient management in adults".)

When can cancer treatment be safely restarted? — While there are no universally accepted guidelines as to when cancer therapies can be safely restarted after COVID-19 diagnosis, given that reinfection rates and their consequences are unknown, the effects of further suppressing or augmenting a patient's immune system quickly after COVID-19 must be weighed heavily against the risks of their unique tumor's biology.

- Our approach for most patients, which draws upon available guidelines and individual centers' "best practices," is to hold immunosuppressives until symptoms from COVID-19 have resolved. Once symptoms have resolved, we retest for SARS-CoV-2 and proceed with planned cancer therapies only if a negative result is obtained. However, given a significant false negative rate in first-generation test kits, two consecutive negative tests ≥24 hours apart can be considered.

  However, clinical judgment and individualized decision-making is needed, particularly in settings in which curative therapies are being withheld. As an example, in advanced testicular cancer, delaying chemotherapy for any extended period of time is usually not appropriate, and the risk/benefit ratio would favor continuing treatment even if the patients had persistent viral shedding but felt clinically well. Serological assays to identify SARS-CoV-2 antibodies are being developed and are discussed below. Once validated and widely available, such assays can be used to identify patients with previous exposure and possible immunity.

Examples of approaches taken by expert groups and at other institutions are as follows:

- For cancer patients diagnosed with COVID-19, ASCO recommends that immunosuppressive cancer treatments be held until symptoms are resolved (including resolution of fever without the use of antipyretics) and there is some certainty that the virus is no longer present (eg, a negative SARS-CoV-2 test), a position that is generally concordant with United States Centers for Disease Control and Prevention (CDC) test-based strategies for discontinuing home isolation, as well as guidelines for returning to work for health care workers who have recovered from a SARS-CoV-2 infection or have had an exposure. These are discussed elsewhere.

- However, the CDC guidelines are more stringent than ASCO in one respect, calling for negative results of a US Food and Drug Administration (FDA) emergency use authorized molecular assay for COVID-19 from at least **two** consecutive negative nasopharyngeal swab specimens collected ≥24 hours apart. An exception to this general recommendation would be if the cancer is rapidly progressing and the risk/benefit assessment favors proceeding with cancer treatment.

  Similarly, the World Health Organization (WHO) recommends that to be released from home isolation, the patient must test negative using two samples collected at least 24 hours apart; where testing is not possible, confirmed patients should remain isolated for an additional two weeks after symptoms resolve.

- However, the United Kingdom National Institute for Health and Care Excellence (NICE) has published rapid guidance on the delivery of anticancer therapy that suggests treatment may be initiated or resumed after only **one** negative SARS-CoV-2 test. Similar guidelines are followed at some institutions in the United States. However, given a significant false negative rate in first-generation test kits, two consecutive negative tests may be considered.

- At some institutions, sending patients who have been cleared to resume treatment to an isolated infusion center, away from the main infusion center, may be recommended. This position stems from concerns as to the limitations of test strategies, and that some proportion of recovered patients who initially test negative might in fact be persistent virus shedders [40].

Regardless of the timing of reinitiation of treatment, physical distancing rules and contact limitation remain essential components of cancer treatments amid the pandemic to protect the patient, the health care workers, and other non-COVID-19 patients being treated in the same center.

Management of persistent virus shedding — In general, patients with persistent viral shedding despite symptom resolution should stay on precautions/isolation until they convert to a

negative test. However, decisions must be individualized, carefully weighing the risks and benefits of withholding versus restarting treatment.

There appears to be a wide range in the duration of viral shedding, which may depend on severity of illness. However, an important point is that detecting viral RNA via a polymerase chain reaction (PCR)-based test does not necessarily mean that infectious virus is present. There may be a threshold of viral RNA level below which infectivity is unlikely. For example, according to CDC, among those who continue to have detectable RNA, concentrations of detectable RNA three days following recovery are generally in the range at which replication-competent virus cannot be reliably isolated; additionally, isolation of infectious virus from upper respiratory specimens more than nine days after illness onset has not yet been documented [41]. This subject is discussed in detail elsewhere. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Viral shedding and period of infectivity'.)

Nevertheless, there is no way to distinguish patients who remain infectious from those who do not, and therefore decisions regarding reinitiation of cancer treatments must be individualized, particularly if the withheld treatments are potentially curative, and the period of persistent viral shedding is prolonged.

Negative test for SARS-CoV-2 infection — In such patients, the approach depends on whether the patient is symptomatic, and if so, the cause for the respiratory symptoms and the cancer in question. For those in whom respiratory symptoms are mild, following an approach that is similar to those without respiratory symptoms may be appropriate. (See 'General considerations regarding cancer management' below and 'Cancer type-specific guidance' below.)

However, travel history, recent contacts, and prevailing local public health conditions should be considered given the imperfect negative predictive value of current COVID-19 testing, which is discussed in detail elsewhere. Retesting may be needed if the index of suspicion is high.

For those with more severe symptoms, management will depend on the underlying etiology and goals of care. Careful consideration for non-COVID-19 and potentially cancer and/or treatment-related etiologies causing similar constellations of symptoms must always be considered.

Role of serologic testing — Serologic tests detect antibodies to SARS-CoV-2 in the blood. Those that have been adequately validated may help identify patients who have had COVID-19 or exposure to SARS-CoV-2. However, there are many unknown factors, including sensitivity, specificity, and positive and negative predictive value [42,43]; how much immunity is conferred by a prior infection, and for how long; and the level and types of antibodies that indicate immunity.

Additionally, while serologic tests may be able to identify some patients with current infection (particularly those who present late in the course of illness), it is less likely that antibodies will be reactive in the first several days to weeks of infection, and therefore serologic tests offer little utility for diagnosis in the acute setting. This subject is discussed elsewhere. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Serology to identify prior infection'.)

GENERAL CONSIDERATIONS REGARDING CANCER MANAGEMENT

Delivering cancer care during the COVID-19 crisis is challenging given the competing risks of death from cancer versus death or serious complications from infection, and the likely higher lethality of COVID-19 in immunocompromised hosts, including those with cancer. Other challenges include cancellations of in-office visits; delays in routine cancer screening [44]; surgery postponements or cancellations; physical distancing in the office, clinic, and infusion rooms; and the transition to telemedicine for many visits. (See 'Minimizing the compromise of physical distancing during cancer care delivery' below.)

There is no "one size fits all" approach to delivering cancer care during the COVID-19 pandemic, and no international guidelines. Treatment decisions must be made on a case-by-case basis. Relevant issues are expanded upon in the following sections. Conceptual frameworks for balancing cancer risk versus infection risk, and practical approaches for managing cancer patients during the pandemic are presented below. (See 'Conceptual framework for balancing competing risks' below.)

General care — The American Society of Clinical Oncology (ASCO) suggests the following guidance for general care from the United States Centers for Disease Control and Prevention (CDC), as described in the links below:

- General Health Care Facility and Health Care Professional guidance
- Clinical care guidance
- Home care guidance
- High-risk subpopulation guidance

In addition to general guidance provided by the CDC, the following points have been emphasized in the ASCO recommendations:

- Patients should be informed regarding the symptoms of COVID-19, and trained in proper handwashing, hygiene, and minimizing exposure to sick contacts and large crowds.

- At this time, no specific evidence or guidance on mask use for patients with cancer has been published. Patients and clinicians are urged to follow the CDC's general recommendations on mask wear, which now recommends that everyone should wear a cloth face cover when they go out in public, as well as guidance from local health authorities.

  There is no guidance or evidence to suggest that N95 masks are required for cancer patients. However, most institutions and clinical practices are requiring health care workers, patients, and visitors to wear a surgical face mask within the facility. (See 'Allocation of limited health care resources' below.)

- In general, as recommended by the CDC, any clinic visits that can be postponed without risk to the patient should be postponed. This includes routine surveillance visits to detect cancer recurrence. In many cases, the recommended frequency of these visits is already considered a range (eg, three to six months), so extending the time between evaluations may still be within the recommendations. (See 'Minimizing the compromise of physical distancing during cancer care delivery' below.)

- For cancer patients with fever or other symptoms of infection, a comprehensive evaluation should be performed, as per usual medical practice. (See 'Patients with COVID-19 symptoms or a known COVID-19 exposure' above.)

- Prescreening via telephone calls or digital platforms for COVID-19 symptoms and exposure history prior to planned in-person clinic visits is recommended, if possible [45]. Screening clinics should be developed to allow for patients with symptoms to be evaluated and tested in a dedicated unit with dedicated staff.

Further information is available within UpToDate on the evaluation, diagnosis, and screening for COVID-19 that are not specific to cancer patients. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Diagnosis' and "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings", section on 'Measures for all patients, visitors, and personnel'.)

Cancer diagnosis and staging — In general, as recommended by the CDC, any clinic visits that can be postponed without risk to the patient should be postponed. As an example, this might include a patient who is clinically suspected of disease with a low risk of rapid progression (eg, minor suspicious findings on mammography).

ASCO guidelines state that there is no evidence that COVID-19 infection interferes with or has an effect on the diagnosis and staging of cancer. In a patient newly diagnosed with cancer, it is

reasonable to limit staging procedures and pretreatment evaluation only to those that are most necessary to inform development of the initial care plan.

Cancer surgery

- **Delaying elective surgeries** – The CDC's guidance for health care facilities and guidance from the World Health Organization (WHO) suggests that "elective surgeries" at inpatient facilities should be rescheduled, if possible. However, clinicians and patients need to make individual determinations, based on the potential harms of delaying needed cancer-related surgery; in many cases these surgeries cannot be considered "elective." Some have distinguished a subset of nonemergent cancer surgeries as being "essential cancer surgery," including surgical management of brain tumors, as well as breast, colon, stomach, pancreas, liver, bladder, kidney, and lung resections [46]. These are generally cancers that cannot wait two to three months and have a significant chance of benefiting from the surgery.

  The American College of Surgeons has validated this approach, noting that cases that involve cancers that may progress without treatment should be performed as resources permit, to minimize the need for emergency procedures, which are often more complicated and more likely to consume limited resources. In addition, another category of essential surgeries are selective palliative procedures being performed for acute relief of pain and suffering or acute neurologic deficits that are not manageable by other means [46]. However, if a surgery will likely require postoperative intensive care, the capacity of available intensive care units (ICUs) should be considered as part of decision-making.

  In some cases, neoadjuvant therapy may be used as a means of delaying surgery. As an example, patients with rectal cancer may undergo chemoradiotherapy plus upfront chemotherapy (total neoadjuvant therapy) rather than chemoradiotherapy alone as a means of delaying surgery. (See "Neoadjuvant chemoradiotherapy, radiotherapy, and chemotherapy for rectal adenocarcinoma", section on 'Total neoadjuvant therapy for locally advanced tumors'.)

  In other situations where neoadjuvant hormonal therapy is not routinely considered (eg, early stage breast cancer, high-risk prostate cancer), it may be reasonable to offer neoadjuvant therapy or to simply delay surgery rather than proceeding to upfront surgery. The risks of tumor progression with delay in definitive surgery should be weighed against the potential added burden on hospital resources, case complexity, and the risk of exposure to COVID-19. However, neoadjuvant therapy that requires clinic visits, clinician-patient contact, or that is immunosuppressive must also be viewed with the potential incremental risks to the patient.

  Specific guidance for decision-making for cancer surgery on a disease-by-disease basis is available from the American College of Surgeons, from the Society for Surgical Oncology, from

an international Urologic Oncology Group, and from the European Society of Surgical Oncology.

- **When should elective surgeries be resumed?** – As health care facilities consider resuming elective surgical cases, the American College of Surgeons and other groups have issued the following recommendations [47,48]:

  - SARS-CoV-2 infection rates should be on a downward trend for at least two weeks at the facility's geographic location
  - Resource utilization, including ICU bed and personal protective equipment (PPE), must be carefully calibrated
  - Testing of patients and employees must be strongly considered
  - Prioritization and scheduling of cases must be managed carefully by all key stakeholders.

  Other resources for resuming cases are available [49,50].

Radiation therapy — Some patients receiving radiation therapy (RT) with curative intent or for rapidly progressive tumors may reasonably proceed with therapy, as the risks of delaying treatment may outweigh the risks of COVID-19 exposure and infection. Where available, alternative regimens should be offered. As an example, an international expert consensus statement has recommended that neoadjuvant short course RT be preferred over long-course chemoradiotherapy for patients with locally advanced rectal cancer during the pandemic [51]. (See "Neoadjuvant chemoradiotherapy, radiotherapy, and chemotherapy for rectal adenocarcinoma", section on 'Short-course radiotherapy'.)

For those receiving RT for symptom control, or for whom an alteration of schedule is unlikely to significantly impact outcome, treatment should be delayed or adjusted. According to the American Society for Radiation Oncology (ASTRO), if hypofractionated schedules are considered reasonable, they should be considered. Similarly, the International Lymphoma Radiation Oncology Group has issued guidance on alternative radiation treatment schemes in blood cancer during the COVID-19 pandemic [52].

For patients who are actively undergoing RT with established treatment plans, the decision to continue requires careful consideration of indications, dose already delivered, and risks and benefits. ASTRO suggests that cancellation or delay in cancer treatment may be an appropriate option for patients with COVID-19, after a reassessment of the patient's goals of care. Recommendations are also available from an international Radiation Oncology Group called the Global Radiation Oncology Targeted Response. NICE has published a rapid guideline on the delivery of radiation in cancer patients.

Systemic anticancer treatments — There is no direct evidence to support changing or withholding chemotherapy or immunotherapy in patients with cancer [53], and routinely withholding critical anticancer or potentially immunosuppressive therapy is not recommended for those who do not have COVID-19. The approach to patients who have a positive test for SARS-CoV-2 is discussed above. (See 'Positive test for SARS-CoV-2 infection' above.)

The balance of potential harms that may result from delaying or interrupting treatment versus the potential benefits of possibly preventing or delaying COVID-19 infection is very uncertain. ASCO recommends that clinical decisions be individualized, and consider factors such as the curability of the cancer, the risk of cancer recurrence with treatment delay, modification or interruption; the number of cycles of therapy already completed; and the patient's tolerance of treatment. NICE has published a rapid guideline on delivery of systemic anticancer treatments.

- **Chemotherapy** – Administration of chemotherapy is determined on a case-by-case basis. The decision is influenced by the likelihood of cure or extension of life from the cancer treatments, the potential risks of delaying treatment, the patient's tolerance of treatment, where they are in the planned treatment course, the local incidence of coronavirus and availability of necessary resources, and whether testing for SARS-CoV-2 has been performed. (See 'Should asymptomatic patients receiving immunosuppressive therapy be tested?' above.)

  In general, adjuvant therapy with curative intent should likely proceed, despite the threat of SARS CoV-2 infection during therapy. Shorter treatment duration should be considered, where feasible. (See "Adjuvant therapy for resected stage III (node-positive) colon cancer", section on 'Duration of therapy'.)

  For patients receiving palliative therapy for metastatic disease, the decision to continue requires careful consideration of indications, response to treatment already delivered, and risks and benefits of continued treatment. In some cases, treatment delays may lead to worsening symptoms and performance status and the loss of the opportunity to treat [36]. Considerations should include how such delays require hospital admission for palliation of symptoms, which would further stress available resources. Shared decision-making is paramount.

  Considerations for chemotherapy treatment during the COVID-19 pandemic set forth by ASCO include the following:

  - For patients in deep remission who are receiving maintenance therapy, stopping chemotherapy may be an option. Similarly, for those in whom the benefit of adjuvant chemotherapy is expected to be small and where non-immunosuppressive therapies are available (eg, hormone therapy for hormone receptor-positive early breast cancer or

prostate cancer), it may be reasonable to omit chemotherapy in consideration of the risks of COVID-19.

- Oral chemotherapy and home infusion of chemotherapy drugs (if logistically feasible) may be options for some, but require coordination with the oncology team to ensure that patients are taking their treatments correctly.

  A toolkit is available from the National Comprehensive Cancer Network (NCCN) to assist in shifting traditionally inpatient chemotherapy regimens into the outpatient setting, primarily for patients with hematologic malignancies [54].

- If a particular cancer center is heavily affected by coronavirus infections, it may be reasonable to alter the chemotherapy schedule so that fewer visits are needed or to arrange infusion at a less affected cancer center.

- Lymphopenia seems to be a specific risk factor for adverse outcomes from COVID-19 and other coronaviruses [55,56]. This has led some expert groups to recommend critical reevaluation of the need for drugs that inhibit B cells, such as anti-CD20 monoclonal antibodies, during the pandemic [57]. Specific guidance for treatment of hematologic malignancies on a disease-by-disease basis is available from the American Society of Hematology.

The use of prophylactic growth factors is discussed below. (See 'Supportive care' below.)

- **Immunotherapy** – At this time, there are no data regarding whether checkpoint inhibitor therapy increases, decreases, or has no effect on the severity of coronavirus infection and the immune response to it. Of particular concern is treatment-related pneumonitis, which may increase the risk of serious complications if the patient develops COVID-19. For those with a known coronavirus exposure, it is recommended to hold treatment until it is clear that the patient will not develop COVID-19. (See 'Patients with COVID-19 symptoms or a known COVID-19 exposure' above.)

  Updated guidelines from ASCO suggest that the potential harms and benefit of therapy with these agents should be carefully considered for each patient. The role of SARS-CoV-2 testing for patients initiating immunotherapy is discussed above. (See 'Should asymptomatic patients receiving immunosuppressive therapy be tested?' above.)

  Less frequent drug administration is an option for patients who are already receiving the drug. One modeling study suggested that pembrolizumab 400 mg every six weeks leads to similar exposures as every three week administration of a single dose of either 200 mg or 2 mg/kg [58]. The safety and efficacy of this extended dosing option has been shown in patients with

advanced melanoma [59], and this is an appropriate option for some patients receiving pembrolizumab monotherapy, particularly in areas where the prevalence of SARS-CoV-2 is high. Both the US Food and Drug Administration and the European Medicines Agency have approved a new dosing regimen of 400 mg every six weeks for pembrolizumab across all currently approved adult indications, in addition to the current 200 mg every three week dosing regimen [60,61]. (See "Immunotherapy of advanced melanoma with immune checkpoint inhibition", section on 'Dosing considerations'.)

Decisions regarding whether it is appropriate to use combination versus single agent immunotherapy will need to be individualized. The risks of immune-related adverse effects (irAEs) associated with ipilimumab-containing combination regimens (or other immunotherapy combinations), including the risks of hospitalization and associated COVID-19 exposure, should be weighed against the diminished efficacy of single agent therapy, in each particular setting. Other considerations are similar as to those receiving chemotherapy. (See "Toxicities associated with checkpoint inhibitor immunotherapy".)

- **Allogeneic hematopoietic cell transplantation** – Although there are limited data regarding the impact of COVID-19 in transplant candidates and donors and cellular therapy recipients, there is sufficient concern that COVID-19 could have a significant impact on posttransplant or post-therapy outcomes. Decisions on whether hematopoietic cell transplantation should be delayed must be individualized.

  The American Society of Hematology has published a list of frequently asked questions (FAQs) that pertain to treating hematologic malignancies during the COVID-19 pandemic, many of which address the role of induction and consolidation therapies, including hematopoietic cell transplantation in many malignancies. In addition, the Fred Hutchinson Cancer Research Center and the Seattle Cancer Care Alliance have provided guidance on stem cell transplantation and COVID-19 that may be of value.

  Considerations from ASCO include the following:

  - It may be prudent to test potential donors for COVID-19 even in an absence of evidence of transmission by blood transfusion.
  - As a general precaution, visitation post-transplant may need to be limited and visitors may need to be screened for symptoms and potential exposure.

Supportive care — ASCO has set forth the following recommendations for supportive care during cancer therapy:

- There is no known role for prophylactic antiviral therapy for COVID-19 in any patient, including immune suppressed patients.

- Flushing of ports can occur at intervals as long as every 12 weeks, and patients who are capable of flushing their own devices should be encouraged to do so. However, the process of training may itself be a source of exposure and access to sterile supplies at home may be limited. (See 'Managing subcutaneous ports' below.)

- Transfusions should be given according to usual practice guidelines, if possible, with consideration of erythropoietin-stimulating agents if severe or life-threatening anemia is anticipated or if blood products become scarce due to lack of donations. If anemia is due to bleeding, tumor embolization, volume expanders, and antifibrinolytic agents (eg, epsilon aminocaproic acid or tranexamic acid, where available) can be offered as a temporizing measure; iron infusions are another option for those in less immediate need. In the operating room, the use of cell saver may also be appropriate.

  For patients in need of other blood products such as fresh frozen plasma (FFP) or platelets, care should be individualized based on the indications, severity, and alternatives. Donor-directed transfusions should be encouraged from patient family members in order to help sustain blood product supply during the pandemic.

- For patients who are febrile and likely to be neutropenic based on the timing of their cancer treatments, it may be reasonable to prescribe empiric antibiotics if the patient seems stable by clinical assessment (in person or via telemedicine evaluation). It is preferable that further evaluation be pursued, if necessary, outside of the emergency department.

- Although myeloid growth factor support is typically administered for those at high risk for febrile neutropenia (>20 percent), it may be reasonable for patients with a lower level of expected risk for febrile neutropenia with treatment (eg, >10 percent) to be prescribed prophylaxis with growth factor support.

NCCN guidelines for cancer care during the pandemic have also lowered the threshold for the use of myeloid growth factors to include those regimens with a febrile neutropenia risk of 10 to 20 percent [62].

Glucocorticoids — Glucocorticoids are widely used in cancer patients, for example, for chemotherapy- or radiation-induced nausea and vomiting; infusion-related reactions; management of edema in patients with brain metastases or epidural spinal cord compression; and in conjunction with hormone therapies such as abiraterone, to reduce the likelihood of treatment-related mineralocorticoid deficiency. Although data are limited regarding the impact of glucocorticoids on

host immunity to COVID-19 in patients with cancer [53], we typically continue glucocorticoids, if they are indicated, in cancer patients who **do not** have suspected or documented COVID-19. Discussion on the approach to cancer patients with COVID-19 is found above. (See 'Holding immunosuppressives and COVID-19 management considerations' above.)

Select indications for glucocorticoids in cancer are discussed elsewhere. (See "Prevention and treatment of chemotherapy-induced nausea and vomiting in adults" and "Infusion-related reactions to therapeutic monoclonal antibodies used for cancer therapy" and "Management of vasogenic edema in patients with primary and metastatic brain tumors" and "Treatment and prognosis of neoplastic epidural spinal cord compression", section on 'Symptomatic and preventive care'.)

Advance care planning — Proactive advance care planning is important for all cancer patients, but is particularly critical given the additional risk of COVID-19. Aligning the care that is delivered with the patient's values and goals of care in the setting of an acute life-threatening illness is important, especially for patients with chronic, life-limiting disease. Individuals who are most likely to develop severe illness will be older and have a greater burden of chronic illness; these are the very populations who may wish to forego prolonged life support, should the need arise. If an oncology patient with late-stage disease or with significant comorbid health conditions affecting the heart or lungs develops COVID-19 and requires mechanical ventilation, the prognosis is likely to be dismal [36]. (See 'Patients with COVID-19 symptoms or a known COVID-19 exposure' above.)

Because of these issues, it is imperative for clinicians to have proactive discussions with patients about advance care planning, especially for those with advanced cancer [37]. This should include the use of advance directives or other expressions of end-of-life preferences, and clear documentation of these conversations, especially if they take place during a telehealth visit.

Helpful communications guides for clinicians on a wide range of pertinent topics related to COVID-19, including preferencing and proactive planning, are available from VitalTalk.

The following resources are available from the Center to Advance Palliative Care (CAPC) and Respecting Choices:

- CAPC COVID-19 Response Resources
- Respecting Choices COVID-19 Tools and Resources

For cancer patients with COVID-19, who are at increased risk of needing mechanical ventilation or ICU care, a conversation about Physician Orders for Life Sustaining Treatment (POLST) is appropriate. Additional information is available at National POLST.

Post-treatment surveillance — ASCO suggests that any clinic visits that can be postponed without risk to the patient should be postponed. This includes routine surveillance in patients who have

completed treatment or those on active surveillance considered to be at relatively low risk of recurrence or disease progression, and those who are asymptomatic during the follow-up period. In situations where existing recommendations provide frequency ranges for interventions (eg, every three to six months), it is reasonable to delay scheduled interventions to the longest recommended frequency duration. Remote monitoring of such patients using telehealth may be adopted.

Mental health issues — Globally, the COVID-19 pandemic is leading to mental health problems such as stress, anxiety, depressive symptoms, insomnia, denial, anger, and fear [63]. Cancer patients on and off treatment may have additional feelings of anxiety, fear, and vulnerability for disease recurrence or progression. As resources become constrained, cancer patients may feel loneliness and isolation as they watch their system swamped with cases that literally freeze them out. (See 'Allocation of limited health care resources' below.)

Specific resources are available for patients. (See "Society guideline links: Coronavirus disease 2019 (COVID-19) – Resources for patients".)

Clinicians are also at risk for increased anxiety and stress because of [64,65]:

- Physical isolation from friends and family
- Worry about their own health and health of family, peers, and colleagues
- Competing demands of typical daily workload and COVID-19 response especially coupled with changes in family care responsibilities
- Difficult choices and challenges in patient care, worry about patients, and the need to support patients and families during reduced visitation

ASCO has recommended mental health resources with tips on enhancing coping. The suggestions include avoiding information overload, and taking a break from news and social media regarding COVID-19. There is also a set of tips for enhancing mental and physical health during the pandemic.

Resources are also available from the National Alliance on Mental Illness and a wide variety of other groups. (See 'Society guideline links' below and "Coronavirus disease 2019 (COVID-19): Psychiatric symptoms and disorders".)

In addition, helpful communications guides for clinicians on a range of potentially stressful topics specific to COVID-19, including counseling when coping needs a boost or emotions are running high, and for notifying a family member of a loved one's death by telephone, are available from VitalTalk.

CANCER TYPE-SPECIFIC GUIDANCE

Conceptual framework for balancing competing risks — There are no international guidelines to address the management of cancer patients in any infectious pandemic. An algorithmic approach to solid tumors diagnosed during the pandemic has been proposed by an international group [66], but decision-making about whether specific treatments can be safely postponed or not requires a conceptual framework for balancing competing risks of the cancer and infection.

A conceptual approach to decision-making regarding immediate cancer treatment during the COVID-19 pandemic has been described, which attempts to balance the risk of progression with delay of cancer care versus the risk for significant morbidity from COVID-19 (figure 1) [67]. The list below presents examples that are meant to provide general guidance. Specific patient comorbidities as well as values and preferences must also be considered in each case. Specific considerations for lung cancer patients are discussed below. (See 'Patients with lung cancer' below.)

- Based on **low risk** of progression in certain cancers, it may be safe to **delay for more than three months** certain treatments, regardless of age.
    - Examples include surgery and radiation (where indicated) for the following:
        - Nonmelanoma skin cancer.
        - Hormone receptor positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer in postmenopausal women. In such women, neoadjuvant endocrine therapy can be administered.
    - Similarly, medical oncology treatments may be delayed for chronic hematologic cancers such as chronic lymphocytic leukemia (CLL). Specific guidance is available from the American Society of Hematology.
- Based on **intermediate risk** of progression in other cancers, **a delay of approximately three months** may be acceptable in the some settings, particularly for individuals 50 and older. Examples are outlined below.
    - Surgery for the following:
        - Intermediate or high-risk prostate cancer (androgen deprivation may be started in the interim); the oncologic safety of delaying radical prostatectomy in this setting is supported by an analysis of data from the National Cancer Database [68].
        - Colon cancer with low risk for imminent obstruction.
        - Low-risk melanoma.
    - Radiation for post-resection endometrial cancer and high-risk resected prostate cancer.

- In selected cases, chemotherapy for advanced metastatic breast, colorectal, lung, and other solid tumors. However, these are difficult decisions, and must be individualized. For some patients with rapidly progressive metastatic disease or a high tumor burden, a delay of three months could be catastrophic. In such cases, shared decision-making is critically important. In contrast, active surveillance may be an appropriate option for some patients with slow-growing advanced disease, such as some patients with indolent or low tumor burden metastatic clear cell renal cancer [69]. (See "Systemic therapy of advanced clear cell renal carcinoma", section on 'Active surveillance'.)

- By contrast, given a **high risk** of progression in certain cancers, ideally there would be **no delay** in treatments for the following individuals under age 70, although for older individuals, benefits of immediate treatment must be balanced against the risks. Examples are as follows:

  - Surgery for the following:

    - ≥2 cm lung mass
    - Colon cancer with imminent obstruction
    - Type 2 endometrial cancer
    - Pancreatic, ovarian, or liver mass(es) suspicious for malignancy
    - High-risk non-muscle invasive or muscle invasive urothelial cancer

  - Radiation for the following:

    - Lung cancer
    - Locally advanced rectal cancer
    - Head and neck cancer

  - Chemotherapy for the following:

    - Acute leukemia, large cell lymphoma, Hodgkin lymphoma, symptomatic myeloma, and all other non-low-grade hematologic cancers
    - Metastatic testicular cancer
    - Small cell lung cancer
    - Most head and neck cancers, except thyroid

Other conceptual frameworks for prioritizing radiation and systemic treatment for cancer during the pandemic are available [70].

In addition to potentially altering therapeutic protocols, other actions that have been suggested to increase the safety of managing oncologic care during the COVID-19 pandemic include screening all patients, caregivers, staff, and providers for COVID-19 symptoms; limiting exposure to sick contacts while on anticancer therapy; minimizing nonessential follow-up visits; restricting visitors to both outpatient and inpatient facilities; increasing engagement in telehealth and phone visits rather than in-person clinic visits; and prescribing oral drugs that can be taken at home, rather than injectable agents requiring administration in an infusion center, whenever possible.

Guidance from expert groups — Guidance is available from several expert groups on how care for certain cancer types should be affected by COVID-19.

The following is not an exhaustive list, and additional society guideline links are provided elsewhere. (See 'Society guideline links' below.).

- **Breast cancer** – In addition to guidance on breast cancer surgery from the American College of Surgeons, the Society of Surgical Oncology, the American Society of Breast Surgeons and European Society of Medical Oncology (ESMO) have published brief, high-level guidance on prioritization for multidisciplinary care in breast cancer, and guidelines for radiation therapy for early breast cancer are available from an international group [71]. Guidelines for triage, prioritization, and treatment of breast cancer during the pandemic are also available from at least two international consortiums of breast cancer experts [72,73].

- **Gastrointestinal cancers** – In addition to guidance on colorectal surgery from the American College of Surgeons, and on gastrointestinal tract cancer surgery from the Society of Surgical Oncology and ESMO, an American group of oncologists has developed recommendations for minimizing risks to patients with gastrointestinal malignancies [74], and recommendations are also available from the US Colorectal Cancer Alliance. Recommendations for management of colorectal cancer are available from the National Comprehensive Cancer Network (NCCN) [75].

- **Genitourinary cancers** – In addition to guidance from ESMO, Canadian guidelines on prioritizing systemic therapy for patients with genitourinary malignancies are available, and there are also recommendations for triage of urologic surgeries during the COVID-19 pandemic from a multidisciplinary group [76]. Recommendations for appropriate triage of outpatient procedures have also been proposed [77], and NCCN has recommendations for management of prostate cancer during the pandemic [75].

- **Gynecologic cancers** – In addition to guidance form ESMO, and the American College of Surgeons, guidance for management of these cancers is available from the Society of Gynecologic Oncology, the National College of French Gynecologists and obstetricians [78], from the editors of the International Journal of Gynecologic Cancer [79], and from the International Gynecologic Cancer Society.

- **Head and neck cancer** – Specific triage recommendations for head and neck cancer surgery are available from The University of Texas MD Anderson Cancer Center [80], and from a joint consensus group of the French Society of Otolaryngology, Head and Neck Surgery and the French Society of Head and Neck Carcinology [81]. A group from the United Kingdom has developed an evidence-based triage system for assessment of patients with diagnosed or suspected head and neck cancer using outpatient telemedicine consultations [82].

- **Hematologic malignancy** – In addition to guidelines from the American Society of Hematology, the American Society of Transplantation and Cellular Therapy (ASTCT), the European Society for Blood and Marrow Transplantation (EBMT), and ESMO, the Seattle Cancer Care Alliance has published guidance on managing patients with hematologic malignancies [83], and there are also recommendations from a Brazilian task force [84]. The International Lymphoma Radiation Oncology Group has issued guidance on alternative radiation treatment schemes in blood cancer during the COVID-19 pandemic [52]. Additionally, an international group has published recommendations on the care of older patients with multiple myeloma [85]. United States Cutaneous Lymphoma consortium has published recommendations on treatment of cutaneous lymphoma [86], and the NCCN also has short-term recommendations for the management of T-cell and primary cutaneous lymphomas during the pandemic [75].

- **Hepatocellular carcinoma** – In addition to ESMO, the International Liver Cancer Association has issued guidance on management of HCC during the COVID-19 pandemic, as has the American Association for the Study of Liver Diseases (AASLD) [87] and the French Association for the Study of the Liver [88]. Additional information on issues relevant to solid organ transplantation is available elsewhere. (See "Coronavirus disease 2019 (COVID-19): Issues related to solid organ transplantation".)

- **Lung cancer** – In addition to the American College of Surgeons, the Thoracic Surgery Outcomes Research Network has published guidance on triage for thoracic surgery in patients with thoracic malignancy [89]. Additionally, ESMO has laid out specific guidelines for the types of lung cancer care that should be considered high priority (should not be delayed), medium priority (should not be delayed more than six weeks), and low priority (patient condition is stable enough that services can be delayed for the duration of the pandemic, or the intervention is

unlikely to have a significant magnitude of benefit). Guidance in the form of Frequently Asked Questions (FAQs) is provided by the International Association for the Study of Lung Cancer (IASLC), and short-term recommendations for non-small cell lung cancer management during the pandemic are available from the NCCN [75]. Guidelines for management of lung cancer during the pandemic are also forthcoming from an American group [90].

Additional considerations for care of lung cancer patients during the COVID-19 pandemic are provided below. (See 'Patients with lung cancer' below.)

- **Neurooncology** – Joint guidance on care of patients with brain tumors and brain metastases is available from the American Association of Neurological Surgeons/Congress of Neurological Surgeons Tumor Section/Society for Neuro-Oncology [91], and specific guidance for management of glioma patients is available from an international multidisciplinary group [92].

- **Neuroendocrine and endocrine tumors** – Guidance in managing neuroendocrine tumors during the COVID-19 pandemic are available from the North American Neuroendocrine Tumor Society (NANETS).

  Guidelines for surgical triage for neuroendocrine and endocrine tumors are available from the Society of Surgical Oncology.

- **Skin cancer** – Recommendations for prioritization of treatment for melanoma are available from ESMO and the Society of Surgical Oncology, and short-term recommendations for management of melanoma, as well as for non-melanoma skin cancers during the pandemic are available from NCCN [75]. In addition, an Italian group has provided recommendations for prioritization and management of skin cancers during the pandemic [93].

- **Sarcoma** – Recommendations for multidisciplinary management of sarcoma are available from the Society of Surgical Oncology and ESMO.

SPECIAL CONSIDERATIONS

Upper aerodigestive tract procedures — Because of the spread of SARS-CoV-2 through respiratory droplets, health care workers who come in contact with the upper aerodigestive tract during diagnostic or therapeutic procedures (eg, otolaryngologists-head and neck surgeons, upper gastrointestinal tract endoscopists) are particularly at risk. A set of safety recommendations has been developed to guide evaluation and surgery of the head and neck during the pandemic [94]. At many institutions, testing for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is mandatory before such procedures are undertaken in patients. Given the significant risks of treating upper aerodigestive tract diseases in patients with COVID-19 and the uncertain but

considerably lower specificity of current tests, two negative tests spaced ≥24 hours apart have been recommended for these patients. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Microbiologic diagnosis'.)

Other alternatives, such as computed tomography (CT)-guided biopsies, should be explored, if feasible.

Differentiating lymphangitic spread, pneumonitis, and COVID-19 — Some systemic cancer treatments are associated with a risk of pneumonitis (eg, immune checkpoint inhibitors, gemcitabine, mechanistic (previously referred to as mammalian) target of rapamycin (mTOR) inhibitors). (See "Toxicities associated with checkpoint inhibitor immunotherapy", section on 'Pneumonitis' and "Pulmonary toxicity associated with antineoplastic therapy: Molecularly targeted agents" and "Pulmonary toxicity associated with systemic antineoplastic therapy: Clinical presentation, diagnosis, and treatment" and "Pulmonary toxicity associated with antineoplastic therapy: Molecularly targeted agents", section on 'Rapamycin and analogs'.)

In other cases, new infiltrates on radiographic imaging may reflect disease progression (eg, lymphangitic spread). Besides the fact that treatment-related pneumonitis might increase the risk of serious complications if the patient develops COVID-19, it may be difficult to distinguish therapy effect versus disease progression versus viral infection. In this setting, treatment should be held until it is clear that the diagnosis is **not** COVID-19. Testing for COVID-19 is appropriate in such circumstances, similar to the approach taken for patients with new respiratory symptoms. (See 'Patients with COVID-19 symptoms or a known COVID-19 exposure' above.)

Managing subcutaneous ports — The typical frequency for maintenance flushing of subcutaneous ports is once every four to six weeks. However, at least some data suggest that extending the maintenance flushing interval of implanted ports in adult oncology patients to once every 12 weeks is safe and effective [95]. Patients who are capable of flushing their own devices may be encouraged to do so. However, the process of training may itself be a source of exposure and access to sterile supplies at home may be limited. (See 'Supportive care' above.)

Cancer survivors — It is unclear if cancer survivors who have completed treatment are at increased risk for COVID-19 and its complications; such risk may be influenced by the type of cancer, treatment received, and patient age and comorbid medical conditions. The duration of time off therapy may be important, although late and long-term effects of prior treatment (ie, pulmonary or cardiac toxicities, persistent immunosuppression) may pose risks.

Patients with long-term immune suppression may be at increased risk of infection. However, ASCO guidelines suggest that no recommendations can be made to alter care for these patients beyond the care they would normally receive. These high-risk patients should follow all of the general

measures (eg, social isolation) advised by the CDC to minimize their exposure to potential infection. Patients who receive intravenous immunoglobulin should continue to receive it at the prescribed dose and schedule.

Common questions about COVID-19 and answers for patients and cancer survivors are available from the American Society of Clinical Oncology (ASCO) and the National Coalition for Cancer Survivorship (NCCS) [96]. In addition, a compilation of selected COVID-19 resources for cancer survivors and health care providers in the United States is available [97].

Patients with lung cancer

- **SARS-CoV-2 testing** – Some have advocated for SARS-CoV-2 testing in all lung cancer patients, regardless of symptomatology, given that these patients often have baseline pulmonary deficits and other comorbidities [98,99]. Although this is not yet standard practice everywhere, it is a reasonable approach if adequate testing is available.

- **Risk** – There remains a lack of clarity regarding the effect of current versus previous cancer treatments and other comorbidities on the incidence and severity of COVID-19 [5]. However, patients with lung cancer may be at higher risk for acquiring COVID-19 than the general population; the disease may be more severe, and more often fatal, and COVID-19 may interfere with effective diagnostic and therapeutic lung cancer management [99]. It has also been postulated that smoking history and prior tobacco-related lung damage increase the incidence and severity of SARS-CoV-2 infection [98,100]. Given all of these issues, such patients should be particularly cautious about exposure to COVID-19, given that many have baseline respiratory comorbidity or impairment due to the cancer itself, and should immediately report any new or changing symptoms to their clinicians.

  Evolving data indicate a high rate of severe disease and mortality from COVID-19 in patents with lung cancer:

  - In preliminary results of a multi-institutional international registry study including 200 patients with thoracic cancer also diagnosed with COVID-19 infection through laboratory tests, or with suspected COVID-19 infection based on exposure and symptoms, the majority of patients were hospitalized (76 percent), and one third of these patients died [101]. Despite the high rate of hospitalization, only 9 percent were admitted to an ICU, and 2.5 percent were mechanically ventilated, which could have influenced the high mortality rate. It has been suggested that these low numbers were potentially the result of equipment shortages or institutional policy.

Regarding characteristics of included patients, approximately three-quarters of patients had metastatic disease. Approximately one third of all patients were receiving chemotherapy alone, one quarter were receiving immunotherapy alone, and 19 percent were receiving a tyrosine kinase inhibitor alone. However, in univariate analysis, there were no factors that were identified, including active cancer treatment, as being associated with mortality.

- In a report cited above from a hospital system in New York City, the case fatality rate for individuals with lung cancer diagnosed with COVID-19 was 55 percent (6 of 11) [30]. (See 'Is illness more severe in patients with malignancy?' above.)

- In a small series of seven patients from Wuhan, China, undergoing lung resection who contracted COVID-19 in the perioperative period, three died (mortality rate 42 percent) [102].

- **Impact on diagnosis and treatment**

  - Distinguishing lung cancer evolution from a potential COVID-19 superinfection on the basis of radiologic or clinical presentation can be difficult. The main CT findings of COVID-19 pneumonia can overlap with CT findings that are often found in patients with progressive lung cancer. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Imaging findings'.)

    In addition, the worsening pulmonary symptoms during lung cancer progression can be similar to that typical of COVID-19. (See "Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical features, diagnosis, and prevention", section on 'Clinical manifestations'.)

  - Adding further complexity, pneumonitis can also be induced by immune checkpoint inhibitor immunotherapy, an effective and widely used standard of care treatment for lung cancer in various treatment lines and settings [103]. Although the risk of pneumonitis is approximately 2 percent in patients treated with immune checkpoint inhibitors for a variety of cancers, it may be higher in patients with lung cancer [104]. The clinical symptoms and radiologic imaging findings associated with pneumonitis may overlap with those of COVID-19.

    Pneumonitis may also complicate molecularly-targeted therapies such as osimertinib and standard cytotoxic chemotherapy. Furthermore, cytotoxic chemotherapy can have immunosuppressive effects. (See "Pulmonary toxicity associated with antineoplastic

therapy: Molecularly targeted agents" and "Pulmonary toxicity associated with antineoplastic therapy: Cytotoxic agents".)

- The clinical and biologic aggressiveness of many lung cancers often does not allow for anticancer therapy to be withheld or postponed.

- **Treatment**

  - Specific guidance for lung cancer treatment during the COVID-19 pandemic is available from several expert groups. (See 'Cancer type-specific guidance' above.)

Clinical trials — Clinical research has transformed cancer management and is often seamlessly integrated into routine oncologic care, offering eligible patients additional treatment options. The COVID-19 pandemic presents a major barrier to enrollment and ongoing participation in clinical trials, and it is leading programs to halt or prioritize screening and/or enrollment for certain clinical trials, and cease research-only visits [105]. The US FDA, the European Medicines Agency, and other international bodies have released guidance for sponsors and study sites to ensure the safety of trial participation, while maintaining regulatory compliance and minimizing risks to study integrity [106].

MINIMIZING THE COMPROMISE OF PHYSICAL DISTANCING DURING CANCER CARE DELIVERY

Patients undergoing cancer care including diagnosis, counseling, active treatment, and surveillance are highly exposed to medical centers, providers, staff, and other patients. This results in a massive number of personal contact points and a large number of potential opportunities for viral transmission for both patients and caregivers. ASCO guidelines recommend adoption of telemedicine visits for patients not requiring a physical exam, treatment, or in-office diagnostics.

An important point is that while telemedicine is an important paradigm for patient provider communication, in an effort to maximize physical distancing, it has the potential to interrupt important aspects of the patient's relationships with the care team. This can lead to miscommunication and misunderstandings as well as avoidable delays and even adverse events related to improper care. As patients and providers utilize telephone and video platforms to communicate and deliver care, both must accept the benefits as well as the risks. Operationalizing televisit workflows to mimic those that providers and patients are accustomed to in person may be helpful to maintain familiarity and avoid missed opportunities to improve care and communication.

At the same time, personal contact often provides confidence, reassurance, and comfort that the patient is receiving optimal care. For patients who are already coming in to the cancer center for imaging, procedures, surgeries, radiation therapy, or infusions, a face-to-face visit remains an important option, with the usual precautions (masks, strict attention to hand hygiene). In general, minimizing time in waiting rooms, rearranging patient contact areas to maximize physical distancing, augmenting early discharge planning efforts, executing prompt and safe discharge events, minimizing visitors, instituting pharmacy deliveries, and anticipating/avoiding the possibility of urgent care/emergency department visits (eg, consider more delayed removal of drains/catheters based on risk benefit profile) are all necessary steps in creating a safe experience [107]. Both ASCO and the National Comprehensive Cancer Network have issued recommendations for oncology practices to keep patients with cancer, as well as their caregivers and health care staff, as safe as possible during the COVID-19 pandemic [45].

ALLOCATION OF LIMITED HEALTH CARE RESOURCES

The COVID-19 pandemic is challenging health care systems worldwide and raising important ethical issues, especially regarding the potential need for rationing health care in the context of scarce resources and crisis capacity.

Limited availability of personal protective equipment (PPE) has complicated medical care of patients with suspected or documented COVID-19 (and other transmissible conditions) worldwide. In general, physical distancing and barrier protective measures are the most potent forms of COVID-19 avoidance. We suggest following the CDC recommendations on face mask wearing. Further measures to prevent viral spread are discussed elsewhere. (See "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings", section on 'Infection control in the health care setting'.)

Local and regional considerations and policies should be informed on prevailing conditions. Special attention should be paid to augmenting PPE for care providers in close contact with known COVID-19-positive patients and those who manage the airway and respiratory tracts. Rapidly emerging data suggest that PPE such as N95 masks can safely be sterilized for reuse. In the United States, the CDC offers guidance on optimizing the supply of PPE when sudden increases in patient volume threaten a facility's PPE capacity. Strategies include canceling non-urgent procedures or visits that would warrant use of PPE, prioritizing the use of certain PPE for the highest risk situations, and cautious extended or limited reuse of PPE. This subject is discussed in detail elsewhere. (See "Coronavirus disease 2019 (COVID-19): Infection control in health care and home settings", section on 'When PPE is limited'.)

Beyond the care of individual patients, oncology clinicians may face the reality of rationing care due to limited resources, particularly hospital and intensive care unit (ICU) capacity. In the face of limited resources, clinicians must consider carefully what cancer treatments are most likely to be successful, symptom-relieving, or life-saving, and identify those patients who are likely to get the greatest benefit from treatment [36,108]. If treatments are withheld, from a medico-legal standpoint, national and local guideline standards should be followed [109,110]. ASCO has released guidance on allocation of limited resources during the COVID-19 pandemic [111]. They emphasize that decisions regarding allocation of scarce resources should be separated from bedside decision-making. In addition, interim guidelines for use during the COVID-19 pandemic are available from the Oncology Nursing Society (ONS) for use of PPE during clinical oncology care and for safe handling and administration of hazardous cancer drugs. (See "Coronavirus disease 2019 (COVID-19): Critical care and airway management issues", section on 'Surge capacity and scarce resource allocation'.)

While high quality of and accessibility to care remains the greatest concern of providers, as resources become constrained, cancer patients may feel that their disease progression may become collateral damage to healthcare shortages and deferrals. Neither patients nor clinicians have any significant experience with rationing of care. Addressing fears such as these is critical to an open dialogue and may lead to opportunities to improve communication and prioritize care goals and shared decision-making. (See 'Mental health issues' above.)

Helpful communications guides for clinicians on a range of topics specific to COVID-19, including limitations in resources, are available from VitalTalk.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored disease-specific guidelines (including those for hematology and oncology patients) from selected countries and regions around the world are provided separately. (See "Society guideline links: Coronavirus disease 2019 (COVID-19) – International and government guidelines for general care" and "Society guideline links: Coronavirus disease 2019 (COVID-19) – Guidelines for specialty care" and "Society guideline links: Coronavirus disease 2019 (COVID-19) – Resources for patients".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading

level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Coronavirus disease 2019 (COVID-19) overview (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Delivering cancer care during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is challenging given the competing risks of death from cancer versus death from infection, and the higher lethality of COVID-19 infection in immunocompromised hosts, among other reasons. Clinicians must balance the risks of delaying cancer treatments versus the risks for SARS CoV-2 exposure and the potential increased vulnerability to adverse outcomes from COVID-19, while navigating the disruption in care associated with physical distancing and limited health care resources. (See 'Introduction' above.)

- Data are limited but suggest that the likelihood of a severe illness from COVID-19 is higher among patients with cancer, particularly if they recently received or are continuing to receive treatment. It is unclear if cancer survivors who have completed treatment are at increased risk for COVID-19 and its complications; such risk may be influenced by the type of cancer, treatment received that could have resulted in long-term cardiopulmonary toxicity or immune system compromise, time since treatment, patient age and comorbid medical conditions. (See 'Is illness more severe in patients with malignancy?' above and 'Cancer survivors' above.)

- For cancer patients with lower respiratory symptoms and/or signs (eg, fever, cough, dyspnea, or hypoxia), or those with exposure to someone with confirmed COVID-19, we proceed with testing for SARS-CoV-2. These patients should also be evaluated for alternative causes of their symptoms. (See 'Patients with COVID-19 symptoms or a known COVID-19 exposure' above.)

    - For patients who test positive, immunosuppressive cancer treatments should be held at least until symptoms from COVID-19 have resolved. Some oral non-immunosuppressive therapies may be continued on a case-by-case basis.

- While there are no universally accepted guidelines as to when immunosuppressive cancer therapies can be safely restarted after COVID-19 diagnosis, the effects of further suppressing or augmenting a patient's immune system quickly after COVID-19 must be weighed heavily against the risks of their unique tumor's biology. Our approach for most patients, which draws upon available guidelines and individual centers' "best practices," is to hold immunosuppressives until symptoms from COVID-19 have resolved. Once symptoms have resolved, we retest for SARS-CoV-2 and proceed with planned cancer therapies only if a negative result is obtained. However, given a significant false negative rate in first-generation test kits, two consecutive negative tests ≥24 hours apart can be considered.

  However, there is no consensus on this issue, and at some institutions, more stringent guidelines are advocated, with delayed reinitiation of treatment until asymptomatic for at least 14 days and with two negative tests, at least 24 hours apart. Clinical judgment and individualized decision-making is needed, particularly in settings in which curative therapies are being withheld. (See 'When can cancer treatment be safely restarted?' above.)

  Patients with persistent viral shedding despite symptom resolution should stay on precautions/isolation until they convert to a negative test. Decision-making about reinitiation of chemotherapy is particularly difficult in these patients, particularly if the withheld treatments are potentially curative, and decisions must be individualized, carefully weighing the risks and benefits of withholding versus restarting treatment.

- For patients who test negative, the approach depends on the cause for the respiratory symptoms and the cancer in question.

- For patients without lower respiratory symptoms or signs or a known exposure, cancer patients are urged to follow the CDC's general recommendations in this regard, which are now that everyone should wear a cloth face cover when they go out in public. All patients should be informed regarding the symptoms of COVID-19, and trained in proper handwashing, hygiene, and minimizing exposure to sick contacts and large crowds. (See 'Should asymptomatic patients receiving immunosuppressive therapy be tested?' above.)

- Guidance regarding SARS-CoV-2 testing for asymptomatic cancer patients is evolving. Some institutions are routinely testing all cancer patients 48 to 72 hours prior to immunosuppressive therapies and prior to medical procedures. This policy is supported by updated guidelines from the Infectious Disease Society of America. However, test availability is still limited in many jurisdictions. Local and state public health directives and guidance on who should be tested,

and the logistics for carrying out testing should be followed. (See 'Should asymptomatic patients receiving immunosuppressive therapy be tested?' above.)

- A decision-making approach regarding immediate versus delayed cancer treatment during the COVID-19 pandemic is presented above, which balances the estimated risk of progression with delay of cancer care versus the risk for significant morbidity from COVID-19 (figure 1). Additionally, several groups have laid out cancer type-specific guidance during the COVID-19 pandemic. However, individual patient morbidities and values and preferences must also be weighed in these decisions. (See 'Cancer type-specific guidance' above.)
    - Clinicians should proactively discuss goals of care and advance care planning, including advance directives, especially for those with advanced cancer who are or may be infected with COVID-19. (See 'Advance care planning' above.)
- Given the number of opportunities for viral transmission for both patients and caregivers during cancer care, the use of video and/or telephone visits is encouraged, but both clinicians and patients must accept the benefits as well as the risks. When patients must receive in-person care, specific strategies can be used to accomplish physical distancing (eg, minimizing time in waiting rooms, minimizing/restricting visitors, instituting pharmacy deliveries, and avoiding emergency department visits, when possible). (See 'Minimizing the compromise of physical distancing during cancer care delivery' above.)
- Limited availability of personal protective equipment (PPE) has complicated medical care of patients with suspected or documented COVID-19 (and other transmissible conditions) worldwide. In general, physical distancing and barrier protective measures are the most potent forms of COVID-19 avoidance. We suggest following the CDC recommendations on facemask wearing and optimizing the supply of PPE when sudden increases in patient volume threaten a facility's PPE. (See 'Allocation of limited health care resources' above.)
- Clinicians are at high risk for stress during the COVID-19 pandemic for a number of reasons. ASCO guidelines contain mental health resources with tips on enhancing coping and enhancing mental and physical health during the pandemic. (See 'Mental health issues' above.)

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