Adapting care for older cancer patients during the COVID-19 pandemic: Recommendations from the International Society of Geriatric Oncology (SIOG) COVID-19 Working Group

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PII: S1879-4068(20)30366-0

DOI: https://doi.org/10.1016/j.jgo.2020.07.008

Reference: JGO 996

To appear in: *Journal of Geriatric Oncology*

Received date: 29 June 2020

Accepted date: 10 July 2020

Please cite this article as: N.M.L. Battisti, A.R. Mislang, L. Cooper, et al., Adapting care for older cancer patients during the COVID-19 pandemic: Recommendations from the International Society of Geriatric Oncology (SIOG) COVID-19 Working Group, *Journal of Geriatric Oncology* (2019), https://doi.org/10.1016/j.jgo.2020.07.008

Title

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Abstract

The COVID-19 pandemic poses a barrier to equal and evidence-based management of cancer in older adults. The International Society of Geriatric Oncology (SIOG) formed a panel of experts to develop consensus recommendations on the implications of the pandemic on several aspects of cancer care in this age group including geriatric assessment (GA), surgery, radiotherapy, systemic treatment, palliative care and research.

Age and cancer diagnosis are significant predictors of adverse outcomes of the COVID-19 infection. In this setting, GA is particularly valuable to drive decision-making. GA may aid estimating physiologic reserve and adaptive capability, assessing risk-benefits of either providing or temporarily withholding treatments, and determining patient preferences to help inform treatment decisions. In a resource-constrained setting, geriatric screening tools may be administered remotely to identify patients requiring comprehensive GA. Tele-health is also crucial to ensure adequate continuity of care and minimize the risk of infection exposure.

In general, therapeutic decisions should favor the most effective and least invasive approach with the lowest risk of adverse outcomes. In selected cases, this might require deferring or omitting surgery, radiotherapy or systemic treatments especially where benefits are marginal and alternative safe therapeutic options are available.

Ongoing research is necessary to expand knowledge of the management of cancer in older adults. However, the pandemic presents a significant barrier and efforts should be made to ensure equitable access to clinical trials and prospective data collection to elucidate the outcomes of COVID-19 in this population.

Keywords: geriatric oncology; older patients; COVID-19; SARS-CoV-2; competing risks; recommendations

Introduction

The COVID-19 pandemic requires the implementation of individualized approaches for the management of cancer in older adults. As of June 2020, there were more than 10 million cases and over 500,000 deaths worldwide.[1, 2] The actual cumulative death toll from COVID-19 is expected to be higher as reporting varies within each country. While the virus affects people of all ages, data have consistently shown that mortality is higher with increasing age and comorbidities.[3-6] The case fatality rates (CFR) in patients aged less than 70 years were reported as 0.3-3.5%.[7, 8] This is in contrast to the CFR of 8% in patients aged 70-79 years and around 15% in those aged over 80 years in China.[7] In Italy, epidemiological data shows that the mean age of patients dying from COVID-19 was 80 years,[9] with CFR rising with increasing age beyond 70 years: 12.5% (70-79), 19.7% (80-89) and 22.7% (over 90).[8] In the United States, the death rate in New York City among patients aged 75 years or older was more than 1,511 per 100,000 population[10].

COVID-19 represents an additional competing risk factor to consider when undertaking therapeutic decisions for older adults with cancer (Figure 1). The International Society for Geriatric Oncology (SIOG) advocates for intergrating geriatric assessment (GA) to drive decision-making in the management of older adults with cancer, especially during the COVID-19 pandemic. .

Older age and comorbidities such as cardiovascular disease, diabetes, chronic respiratory disease, chronic renal impairment, and cancer have been shown to increase risk for worse outcomes from COVID-19. [11, 12] In many older patients with cancer where management could be challenging, the risks of morbidity and mortality from acquiring COVID-19 must be considered when assessing risks and benefits of the decision to treat. Currently, personalized care should be the norm in treating older patients with cancer; with COVID-19, it becomes even more imperative that such an approach is followed to avoid the risk of over- or under-treatment [13] and minimize the risk of adopting an ageist approach.

In order to mitigate the negative impact of COVID-19 on the management of cancer in older adults. SIOG has brought together a COVID-19 Working Group including

members from different continents and with different specialties (surgery, radiation oncology, medical/geriatric oncology, geriatrics, hematology, nursing, pharmacy) to develop recommendations and an action plan based on expert opinion and evidence related to geriatric oncology and applied to these circumstances.

Impact of the COVID-19 pandemic on older adults with cancer

Cancer is a disease of older adults. On the other hand, baseline information from epidemiological data on specific cancer types, stage, and treatment at the time of COVID-19 infection are lacking. In the recently published COVID-19 and Cancer Consortium (CCC19) cohort, the median age of patients with cancer and COVID-19 was 66 years, and 56% were aged 65 years and older.[14] Mortality was found to be closely associated with age, with patients aged 65-74 and over 75 years having a relative risk of death of 11% and 25% respectively, compared to 6% for patients below the age of 65 years. In the TERAVOLT cohort of patients with thoracic malignancies and COVID-19, age was also closely associated with increased risk of death, with patients aged 65 years and older (OR 1.88, 95% CI 1.0-3.6).[15]

In general, COVID-19 is acquired by transmission of a respiratory virus via close contact, droplet spray or aerosol, with the duration of viral stability and viability maintained depending on various objects or surfaces.[16] Most local and national health organizations worldwide have implemented various means to mitigate viral transmission and allocate resources appropriately. Primary and secondary prevention measures have included home confinement and social distancing of patients with cancer, limiting their hospital visits where the risk of acquiring COVID-19 is high, and reducing iatrogenic immunosuppression and treatment-related toxicities, which often leads to inpatient admissions that could put pressure on already stretched resources.[17] Goals of care should be established early and documented clearly. These should be revisited periodically and must also include individualised discussions on advance care planning that should be based on the individual circumstances, particularly in the context of a pandemic.

Several geriatric-focused issues have been identified as a result of imposed quarantine and social distancing, including: 1) feelings of estrangement and neglect due to limited access to news or information, friends and family, particularly when access to digital technology is lacking; 2) decline in communication and comprehension not only due to isolation but also from wearing masks and face shields, more particularly so for hard-of-hearing patients who rely on lip reading and non-verbal cues; 3) loss of autonomy and ensuing dependency on others to provide basic needs such as medicines, food and other home supplies due to travel restrictions or lack of access to transportation; 4) disruption of established community support for seniors such as cleaning, shopping, and home maintenance to aid them to cope with daily life; 5) increased risk of deconditioning in the outpatient setting and following acute medical admissions. In addition, social restrictions and shielding can lead to significant decrease in physical activity which, in turn, can contribute to or accelerate loss of muscle mass and bone density, as well as mobility and functional impairment in older adults; [18, 19] and 6) institutionalized patients, such as those in a nursing care facility are at higher risk of acquiring COVID-19 infection, increased feelings of abandonment, as well as mental health problems.[20, 21]

The risk of delirium is especially important and underestimated, called by some experts the “silent epidemic within the pandemic.”[22, 23] Leading authorities on delirium have found that altered mental status may be one of the first signs of COVID-19 infection among vulnerable older adults, and that the current state of hospitals and other healthcare settings is becoming more “deliriogenic” as they restrict visitors, require all staff members to wear personal protective equipment (PPE), and minimize patient interaction to avoid exposure.[24] In these times, it is paramount to evaluate in the out-patient setting and stratify the risk of delirium in patients prior to administering any anticancer therapy. Hence, the impact of social isolation as a result of recommendations on physical distancing, risk of delirium, and decisions regarding anticancer treatment are important issues to assess and pro-actively address.[25]

Geriatric assessment

Older patients with underlying comorbidities have increased disease severity and mortality from COVID-19.[26] Chronological age alone should not drive decisions on whether or not to provide life-saving treatments during the pandemic,[27] and yet, older patients with cancer are likely to be doubly disadvantaged as health systems are overwhelmed.

Prior to this pandemic, frailty had been increasingly adopted as a superior predictor of adverse outcomes over chronologic age for older adults in multiple clinical settings. In the oncology setting, frailty has been proven to predict toxicity from treatment and mortality, and leading cancer societies have recommended GA to gauge frailty prior to treatment in older adults to assess such risks.[28-30] The decision to treat older patients with cancer is best guided with GA and discussed in a multidisciplinary setting to help care providers determine the best treatment options, predict treatment-related toxicities, and establish ongoing management for cancer and other competing risks.[31] GA is particularly valuable in a context where competing risks are more prevalent. GA may estimate physiologic reserve and adaptive capability, assess risk-benefits of either providing or temporarily withholding treatments, and determine patient preference to help inform treatment decisions.

Different tools, such as the Clinical Frailty Scale and the Frailty Index have been proposed to screen and stratify frailty in the setting of COVID-19.[32, 33] However, others have highlighted that their use has not been validated in these circumstances, and advocate for cautious implementation in the context of the pandemic as clear evidence is limited.[34, 35] Additional concerns about the widespread use of these tools include the need for standardized training to ensure accuracy in the assessment as well as a clear understanding of limitations and appropriateness of using these tools to inform, and not replace personalized discussions and care recommendations for older adults. In the majority of cases, in the interest of time to limit visits and infection exposure for professionals and patients, geriatric screening may be sufficient to identify the risk of frailty in some way. The selection of patients most likely to benefit from a multi-domain GA is a major challenge.

We recommend using screening tools that can be self-administered by patients, such as the G8 screening tool or Vulnerable Elders-13 Survey (VES13).[36] Once patients are identified as high-risk for frailty, we recommend further assessment by clinicians with geriatric expertise via telemedicine for assessment of function, cognitive reserve, mood and delirium, nutritional status, and social support using validated tools.

Telehealth has been implemented widely across settings in the midst of the current pandemic, and has been shown to be an effective modality [37] even for vulnerable populations.[38] Oncology-specific GA can also be conducted via telemedicine. One example was outlined by the University of Rochester Specialized Oncology Care and Research in the Elderly (SOCARE) and the Ohio State University group. They presented a framework for multi-domain GA that can be conducted mostly by telephone. This telemedicine version of the GA includes a pre-visit phone screen to identify areas of vulnerability and help guide decision-making for older adults with cancer (Table 1.[39]

More research on conducting GA in a time-efficient manner is needed and decision-making should incorporate patients' preferences and goals, especially in these times of heightened risk and uncertainty. Paired with the information derived from a GA, goal-concordant care is paramount in partnership with patients and caregivers in weighing the risks of COVID-19 exposure and anticancer treatments against the risks of delaying such treatment.

Surgery

Decision-making should be individualized and take into account the potential risk of pursuing, delaying or omitting surgery or choosing different surgical approaches. (Table 2). For example, open and endoscopic techniques have different intensive care requirements, whereas some operations may avoid or delay the need of alternative treatments (e.g., neoadjuvant chemotherapy) which may be less safe in the context of the pandemic. Along with patients' fitness and comorbidities that may influence postoperative outcomes, clinicians should consider factors related to the

tumor, such as its morbidity and mortality and the presence or absence of ongoing cancer-related symptoms, and those associated with the planned surgical procedure being considered, in order to ensure the most secure and safest approach to achieve local disease control.

Elective surgical procedures scheduled at inpatient facilities may be delayed.[40, 41] Nonetheless, the definition of “elective” is sometimes debatable. Apart from emergency operations, any essential procedures may include those where a delay by two or three months can significantly impact on outcomes and/or those where surgery is a crucial component of cancer management, such as for breast, colon, gastric, pancreatic, liver, bladder, renal, lung and brain tumors.[42, 43] Selected procedures aiming for rapid symptomatic relief and minimizing neurological complications should also be prioritized. Surgical management of non-invasive tumors, such as breast ductal in-situ carcinoma, can also be delayed since they are unlikely to impact on survival outcomes in this age group.

The risk of tumor progression with delayed radical surgery should also be balanced with the availability of resources. These include the availability of operating theatres that may been converted to intensive care units (ICUs), the local ICU and anesthetist capacity, the risk of surgical complications, and the expected recovery time.[44] The presence of pre-existing lung conditions that can increase the risk of complications should also be considered, along with the need to perform aerosol-generating procedures. For patients who require surgery, measures should be put in place to mitigate risks, such as preoperative testing and isolation, use of PPE and cohorting operations in COVID-19-free areas.

An observational study of 1,128 patients undergoing surgery and who had a confirmed COVID-19 infection within 7 days before or 30 days after the procedure reported more than 2-fold increase in 30-day mortality for those aged 70 and older (OR 2.30).[45] Consequently, the most effective surgical procedures with minimal invasiveness, least post-operative morbidity, and fastest recovery time should be prioritized in this age group.

Delaying surgery may be appropriate for selected older patients while monitoring the cancer behaviour until the outbreak is under control. For example, a 60-day delay to surgery for stage I-II breast cancer patients had no detrimental impact on outcomes in a retrospective analysis from a single academic hospital.[46] Less toxic systemic treatment such as endocrine therapy or radiotherapy may be considered means to delay surgery in selected cases, as discussed below. Nonetheless, predicting when the outbreak will end, even at a local level remains a significant challenge.

As surgery gets delayed, prehabilitation may be adopted during pandemic to ensure that fitness to treatment is achieved or maintained while waiting, to minimize post-op morbidity and mortality, which may include physical exercise, nutritional support, as well as management of comorbidities, health risks and psychosocial factors.[47] However, such intervention should be implemented in the context of the recommended strategies to minimize the risk of COVID-19 transmission.

In certain circumstances, omitting surgery may be appropriate when the impact on symptoms and survival is minimal or if a safe and effective alternative systemic treatment is available. For example, the use of primary endocrine therapy for older patients with early-stage ER-positive, HER2-negative breast cancer is supported by evidence demonstrating no positive impact of surgery on overall survival (OS).[48-50]

Radiotherapy

Similarly, the use of radiation therapy (RT) in older patients should be prioritized based on its intent, expected benefits, and tumor characteristics in the context of patients' fitness and preference (Table 2). In the older age group, social issues, traveling constraints, daily hospital visits, and patients' concerns regarding exposure may represent significant challenges requiring careful consideration.

Furthermore, radiation dose, fractionation and techniques should be optimized and adapted to the emergency context. In the curative setting, hypofractionated regimens and shorter schedules might be preferable.[51] For example, a short course of

neoadjuvant RT should be favored over a more prolonged course of chemoradiotherapy for older patients with locally advanced rectal cancer, with the aim of minimizing the need for hospital attendance and the chances of myelosuppression.[52] For early breast cancer, 15% of patients enrolled in the FAST-Forward study experimental arm were aged 70 years and older and this trial confirmed non-inferiority of a shorter course of adjuvant RT (26 Gy in 5 fractions) compared with a standard regimen of 40 Gy in 15 fractions.[53] Modest hypofractionation can also be considered for patients with early prostate cancer.[54] Such regimens are appropriate alternatives to minimize the risk of infection exposure in older patients. Despite its role still being debated, intraoperative RT may be considered to spare older adults undergoing surgery from having subsequent outpatient appointments.[55, 56] Specific guidance is available on RT regimens for patients with hematological malignancies. [57]

In the palliative setting, patients should be offered the smallest number of fractions to minimize the need to attend the hospital and potential exposure to infection. For bony pain relief, a single 8 Gy fraction should be favored as equally effective as multiple fractions.[58] A single fraction also can be offered in case of metastatic cord compression.[59] The role of whole brain RT for the management of brain metastases remains controversial as medical treatments might already be beneficial with regard to symptom control.[60] In contrast, stereotactic body RT (SBRT) might still be appropriate in the context of its better safety profile, which is particularly relevant in frail and older individuals.[61]

RT should be delayed in the absence of any significant impact on cancer management outcomes. On the other hand, in cases of curative intent or rapidly progressive disease, the risks of delaying RT might outweigh the risks of COVID-19 exposure and infection.[62] Patients already undergoing RT should be offered a discussion about the risks and benefits of continuing it based on individual goals of care.[51, 63]

For patients with early-stage breast cancer, RT can be safely delayed for up to five months for those receiving chemotherapy followed by endocrine therapy.[64] RT can be delayed by 3-6 months for patients with early prostate cancer in case of low-risk

disease while aiming for either active surveillance or upfront androgen deprivation therapy (ADT);[65, 66] in cases of high-risk disease, RT can be delayed for up to 2-3 months while starting patients on ADT.[67]

In the curative setting, survival gains may be modest in older patients in the context of competing risks of mortality including COVID-19 and careful consideration should be given to balancing risks and benefits. Treatments reducing the risk of locoregional recurrence in the absence of any survival improvement may be appropriately omitted.[68] For older patients with low-risk disease, breast radiotherapy can be safely omitted.[69, 70] Also, adding a RT boost for patients with early-stage breast cancer does not improve survival outcomes and might cause additional toxicities in older patients. In the palliative setting, RT should be pursued when any other options, including medical treatment (such as analgesia and bisphosphonates for bone pain), have been exhausted.

Finally, in the context of the pandemic, RT in the form of either SBRT or conventional fractionation may represent a reasonable alternative to surgery in selected cases, such as older patients with stage I-II non-small cell lung cancer.[71] SBRT may be valuable in this setting in view of the limited number of fractions required (usually 1-5) to spare patients potentially prolonged admission and postoperative complications. Combined data from two trials comparing SBRT with surgery showed better 3-year overall survival for SBRT and no differences in locoregional and distant recurrence, although this analysis should be interpreted with caution in view of the small number of patients enrolled.[72] The practicalities of reducing infection risk within the radiotherapy department and educating patients on appropriate safety measures is discussed in detail elsewhere.[73, 74]

Systemic treatment

The potential benefits of systemic treatments (including chemotherapy, targeted therapy, endocrine therapy and immunotherapy) in terms of tumor control are unchanged during a pandemic. However, risks may be higher especially for treatments causing myelosuppression or requiring frequent hospital visits and

increased infection exposure. Nonetheless, the balance of risks and benefits remains uncertain as there is no evidence suggesting that changing or withholding systemic treatment is beneficial during a pandemic (Table 2).[75] Therefore, decision-making should again be individualized based on consideration of tumor biology, type of systemic therapy, patients' general health status and preferences in the context of the presence of cancer-related symptoms (in cases of active disease), local prevalence of COVID-19, the availability of healthcare system resources, and the risk of infection exposure. Guidelines focusing on delivering specific systemic treatments during the pandemic are also available.[63]

Models based on GA have been developed to predict chemotherapy toxicity and may aid therapeutic decisions in older patients. Therefore, their implementation is particularly appropriate in the context of the ongoing COVID-19 pandemic. The Cancer and Aging Research Group (CARG) model takes into account age, type of cancer, proposed chemotherapy regimen, renal and hematologic function, hearing, along with GA domains such as ability to take medications, physical activity and social activity.[76, 77] The Chemotherapy Risk Assessment Scale for High age (CRASH) is based on the specific chemotherapy regimen being considered as well as laboratory values (creatinine, albumin, hemoglobin, lactate dehydrogenase, liver function tests) and assessments of functional, mental, and nutritional status.[78]

In the curative setting, chemotherapy should be considered if indicated and in the presence of clear survival benefits, which may be less established in the older age group.[79] If possible, a shorter treatment duration should also be considered. In the palliative setting, shared decision-making should also take into account the hazards of worsening symptoms and functional status, which may lead to losing the opportunity to treat.[80] Discontinuing chemotherapy may be an option for some patients with low volume disease or after attaining ongoing disease, especially if alternative non-myelosuppressive agents are available, such as endocrine therapy for hormone receptor-positive breast cancer patients.

In general, evidence-based chemotherapy regimens that require less frequent dosing should be favored in order to minimize the need for hospital attendance, especially in cases of high local prevalence of COVID-19. If available and

appropriate, oral agents should be considered in place of intravenous treatments, as long as there is evidence to support this change. For example, capecitabine can substitute for fluorouracil in managing colorectal malignancies without compromising outcomes.[81] Whenever possible, physicians should attempt to utilize existing evidence to choose strategies shown to be of similar efficacy (in both the younger and older population) over more intensive and/or toxic regimens. Relevant examples include offering three instead of six months of adjuvant chemotherapy for patients with stage III colon cancer,[82] utilizing a 40% dose reduction of combined oxaliplatin and capecitabine chemotherapy for frail or older patients with metastatic gastric cancer [83], or opting for best supportive care alone over chemotherapy for vulnerable/frail patients with advanced lung cancer.[84]

Primary prophylaxis with granulocyte colony-stimulating factors is advisable for patients receiving chemotherapy in view of the higher risk of myelosuppression in older individuals.[85-87] Home-drawn blood service can also be considered, along with setting up courier drug delivery and home treatment administration systems to minimize the need to travel to the hospital. The National Comprehensive Cancer Network (NCCN) has issued a toolkit to facilitate the shifting of systemic anticancer treatments for hematologic malignancies from inpatient to outpatient setting.[88]

In older patients with hematological malignancies, the risk of disease and treatment-related lymphopenia and neutropenia should also be considered and integrated in decision-making.[89] Likewise, the need for anti-CD20 monoclonal antibodies should be critically evaluated in view of the adverse impact of lymphopenia on COVID-19 outcomes.[90] Data are limited on the impact of immunotherapy on COVID-19 and potential risks and benefits should be balanced and personalized in older patients. Nonetheless, the less frequent dosing of some immunotherapy agents is particularly attractive in this context to minimize the need for hospital visits.[91]

Systemic treatment given in the adjuvant setting can be delayed within the accepted timing for each tumor type. For example, for patients with colorectal or lung cancer, it can be safely postponed for up to 8 weeks,[92, 93] and for those with breast cancer for up to 12 weeks after surgery.[94] Older patients should not be denied systemic treatments on the basis of chronological age alone. Instead, the decision to treat

should consider individual circumstances that are likely to influence a significant impact on survival or symptom control, including life expectancy, comorbidities and tumor biology, in the context of patients' preferences.

Systemic therapies may also be considered as effective means to delay surgery in selected cases. A neoadjuvant endocrine approach is particularly valuable for older patients with estrogen receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer, as aromatase inhibitors are associated with low toxicity and reasonable response rates at 3-4 months.[95] ADT may also be considered preoperatively for selected older adults with prostate cancer, although evidence on its impact on radical resection rates is still scarce.[96, 97] Despite the benefits, the use of upfront chemotherapy, e.g. taxanes, in the pandemic setting is more questionable in view of the higher risk of myelosuppression and infections in the older age group, the need for more hospital visits and clinician-patient contact, not unless the risks are outweighed by the benefits of rapid disease control to allow a curative resection,[85, 86, 98] although patients' preferences remain crucial.[99]

Palliative care

Despite the scarcity of health resources brought on by the pandemic, attention needs to be paid for the provision and maintenance of palliative care services. COVID-19 restrictions and physical distancing guidelines have resulted in reduced access to available information, care and supports from families and friends, as well as social and personal care services that allow older persons, including those living with disabilities, to cope at home. Older persons with cancer may present with symptoms associated with their malignancy or treatment toxicity, exacerbation of comorbidities or COVID-19 that may require hospital admission for critical care and/or referral to palliative care.

Early discussion of advance care plans should be implemented to determine patients' preferences and treatment goals. Telemedicine can also facilitate communication with older adults in home settings and institutions as appropriate. Clinicians should also ensure prompt and adequate communication with families and

support older patients during end of life care in critical and palliative care setting, including psycho-social and spiritual support. Infection control procedures should apply also to palliative care settings. The demand for palliative care services (at home or residential care facilities, in hospitals or hospices) may increase and this should be adapted to respond rapidly and flexibly during the pandemic,[100] within the scope of availability of staff and other health-care resources.

Survivorship

Cancer survivors include people who have completed initial treatment with no evidence of active disease or those living with progressive disease who may be receiving cancer treatment but are not in the terminal phase of illness [101]. Older people account for more than two-thirds of cancer survivors [102]. However, COVID-19 may disproportionately impact older cancer survivors' physical health and psychosocial wellbeing, which may lead to unintended consequences in the long-term [103]. Despite social and outdoor activities being on hold due to COVID-19 restrictions, it is recommended to avoid sedentary lifestyle by maintaining physical activity by integrating exercise into the daily routine [104].

Delivery of high-quality, tailored, person-centred survivorship care to address the unique needs of older cancer survivors during the pandemic is challenging. Nonetheless, as evidence here is still lacking, the recommendations valid for the general population should apply also to older cancer survivors.

Research

The COVID-19 pandemic presents a further major barrier to participation in clinical trials for older adults with cancer, who are already under-represented in oncology studies.[105] Screening and/or enrolment for certain clinical trials have been either halted or prioritized in several research programs worldwide.[106] Nonetheless, where feasible, it is imperative to continue facilitating the access of older patients to clinical trials to minimize the impact of the pandemic on the expansion of knowledge

relevant for this age group while complying with current regulations and limiting the consequences on study integrity.[107, 108] The US Food and Drug Administration and the European Medicines Agency have issued specific recommendations on this topic.[109, 110]

In addition, more evidence on the impact of the COVID-19 pandemic in older adults with cancer is warranted. With many preventive (i.e. COVID-19 vaccine) trials underway, inclusion of eligible older patients with cancer should be considered. As recently outlined by the CARG investigators,[25] multicenter and international collaborations and novel methods of rapid dissemination will be crucial to elucidate the interaction between global health measures (rather than age alone) and oncological outcomes, along with endpoints particularly meaningful for older adults, such as function and quality of life.

Recommendations and action plans

COVID-19 is an emerging and rapidly evolving condition that warrants tailored care and assessment depending on the disease prevalence. As society grapples with the pandemic and how best to deliver cancer care in older patients, there is an urgent need to act now to protect the vulnerable and mitigate the projected negative outcomes in this age group. As this is unlikely to be the last pandemic that we will encounter, it is imperative to take this unique opportunity to learn and devise management plans for both present and future use. It should also be acknowledged that the previously mentioned recommendations may lead to different implementation depending on the stage of the pandemic. Whilst data are still emerging and median follow-up from published trials is short to make robust conclusions, the SIOG Working Group has developed a number of recommendations on the management of older adults with cancer and future directions, which are outlined in Table 2.

Acknowledgments

Dr Battisti would like to acknowledge the support of the Cridlan Ross Smith Charitable Trust and the NIHR Biomedical Research Centre at The Royal Marsden NHS Foundation Trust and the Institute of Cancer Research, London, UK. Dr Lichtman is supported by the NCI Cancer Center Support Grant (P30CA008748).

Figure 1 – Factors to consider in treatment decision-making for older patients with cancer during the COVID-19 pandemic.

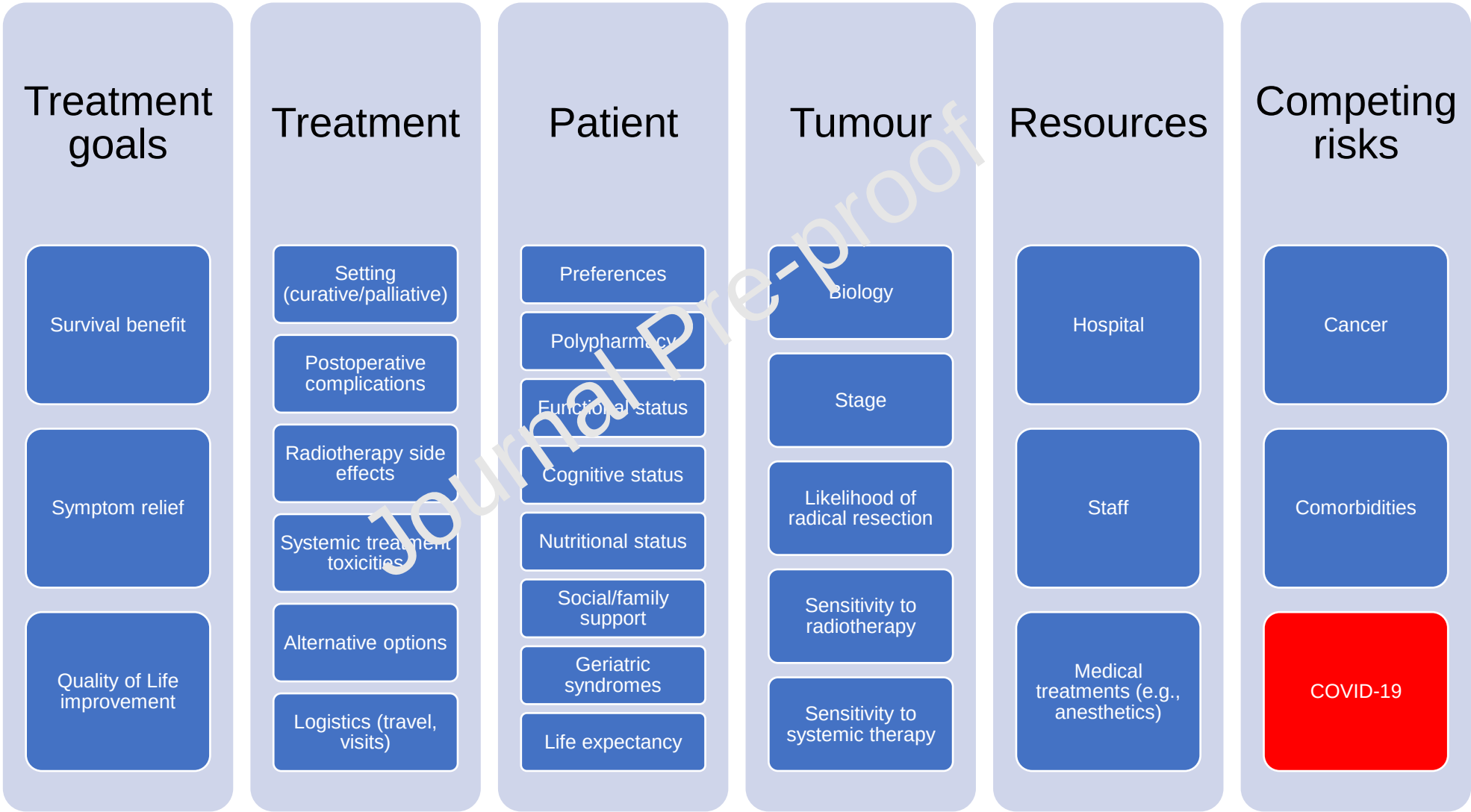

Table 1 – The modified telehealth University of Rochester Specialized Oncology Care and Research in the Elderly (SOCARE) geriatric assessment *[adapted from: DiGiovanni G et al, J Geriatr Oncol, 2020]*

GA domain	Modified tele-health SOCARE GA
Functional status	**OARS: Instrumental Activities of Daily Living** 1) Can you use the telephone? 2) Can you get to places out of walking distance? 3) Can you go shopping for groceries or clothes (assuming you have transportation)? 4) Can you prepare your own meals? 5) Can you do your housework? 6) Can you take your own medicines? 7) Can you handle your own money? 8) Can you walk about one block? **Fall history** 1) In the past year, have you fallen down? 2) About how long ago was your most recent fall? **Fatigue rating** 1) Do you experience fatigue and weakness? 2) If yes, rate your fatigue on a scale of 1-10 (10 = severe, 0 = absence).
Hearing	1) How is your hearing (with a hearing aide, if needed)? 2) If hearing is fair to totally deaf, how much does it interfere with activities?
Comorbidities	**Comorbidity review**

	Completed by geriatric oncologist during visit
Polypharmacy	**Medication review** Nurse Navigator confirmed current medications and provided list to SOCARE pharmacist for review and potential recommendations
Nutrition	**Weight loss** 1) Have you lost weight in the past 6 months (involuntarily)? 2) What is your weight now? 3) What was your weight 6 months ago?
Cognition	**Blessed Orientation Memory Concentration** Conducted in person by occupational therapist during visit
Social support	1) Who do you live with? 2) Who is your main social support?
Psychological status	**PHQ-2** 1) In the last two weeks, how often have you been bothered by(0 =Not at all, 1=Several days, 2 = More than half the days, 3 = Nearly every day) a) Limited interest/pleasure in doing things? b) Feeling down, depressed, or hopeless?

Abbreviations: GA: geriatric assessment; OARS: Older Americans Resources and Services; MOS: Medical Outcomes Survey; PHQ-2: Patient Health Questionnaire 2.

Table 2 – Summary of the International Society of Geriatric Oncology (SIOG) COVID-19 Working Group recommendations on various domains of cancer care.

Care domains	Recommendations	
General interventions	• Maintain physical distancing to reduce risk of exposure and viral transmission • Implement strict infection control policies in residential care facilities and hospitals, and minimize or discourage all non-essential visits • Deploy telehealth care via telephone or video link to protect both the patient and the clinician and provide continuity of care despite social containment • Encourage digital literacy and provide access to online technologies to maintain social network with family, friends, support workers and care providers • Implement a coordinated and pragmatic treatment journey to rationalize and/or minimize hospital appointments • Identify early, periodically re-evaluate and clearly document the goals of care • Consider advance care planning discussions where appropriate	
Care domains	**Recommendations**	**Practical examples**
Geriatric assessment	• Implement remote geriatric screening as a more time- and resource-efficient strategy to select older patients requiring a more comprehensive assessment • Conduct geriatric assessments by implementing telehealth via platforms in compliance with local	• Self-administered screening tools: G8, VES-13 • SOCARE team telehealth-geriatric assessment

	electronic health care regulations • Adopt a "virtual" geriatric-focused multidisciplinary team approach through the use of videoconferencing platforms to enable tumor board meetings in compliant with local regulations	
Surgery	• Prioritize surgical management based on patients' global health status and wishes, setting (curative versus palliative), type of surgery and risk of complications, need for general or local anesthetics, expected recovery time, availability of hospital resources, presence of cancer-related symptoms • Defer noncritical surgery especially if neoadjuvant non-myelosuppressive systemic treatment options are available and while ensuring adequate disease behavior monitoring • Consider omitting surgery in selected cases if no clear survival or symptom control benefit especially if safe systemic or radiotherapy options are available	• Use local anesthetics if appropriate • Consider neoadjuvant endocrine therapy to defer breast cancer surgery for HR-positive, HER2-negative breast cancer • Consider primary endocrine therapy instead of surgery for HR-positive, HER2-negative breast cancer
Radiotherapy	• Prioritize radiation therapy approaches based on patients' global health status and wishes, setting (curative versus palliative), fractionation and dosing,	• Hypofractionation for breast cancer • Short- course neoadjuvant radiotherapy for rectal cancer

	risk of side effects, availability of hospital resources, presence of cancer-related symptoms • Delay noncritical radiotherapy within disease-specific safe time intervals in the adjuvant setting especially if systemic treatment options are available • Omit radiotherapy if no clear survival or symptom control benefit	• Single-fraction radiotherapy for palliative purposes • Intraoperative radiotherapy for breast cancer • Stereotactic radiotherapy for early non-small cell lung cancer or central nervous system metastases • Consider ADT to delay radiotherapy for early prostate cancer • Avoid radiotherapy boost for early breast cancer
Systemic therapy	• Prioritize systemic treatments based on patients' global health status and wishes, setting (curative versus palliative), class of agents, expected toxicities, availability of hospital resources, presence of cancer-related symptoms • Implement the use of chemotherapy toxicity prediction tools • Implement home delivery services for oral agents, home blood service and home treatment administration if available	• CARG or CRASH chemotherapy toxicity prediction tools • Neoadjuvant endocrine therapy for HR-positive, HER2-negative early breast cancer, particularly for those with lobular histology or Luminal-A like subtype • Primary endocrine therapy for HR-positive, HER2-negative early breast cancer

	• Prescribe primary G-CSF prophylaxis to limit risk of myelosuppression • Delay noncritical systemic treatments within disease-specific safe time intervals in the adjuvant setting • Omit systemic therapy if no clear survival or symptom control benefit	• Substitute oral for intravenous preparation, i.e. oral vinorelbine for day 8 treatment; capecitabine for fluorouracil for the treatment of GI malignancies • Consider omitting adjuvant chemotherapy for patients with low-risk HR-positive, HER2-negative breast cancer and in low-risk Stage II colorectal cancer • Consider 3 over 6 months adjuvant treatment for Stage 3 colorectal cancer • Omit oxaliplatin in Stage 3 colorectal cancer where the benefit in older patients is lacking • Consider ADT to delay surgery and/or radiotherapy for early prostate cancer • Preference for a less frequent treatment dosing schedule, i.e. CAPOX vs. FOLFOX; 6-weekly vs. 3-weekly pembrolizumab

Palliative Care	• Discuss advance care plans to determine care preferences and goals, such as do not attempt cardiopulmonary resuscitation orders, endotracheal intubation, or dialysis • Use telemedicine and videoconferencing to facilitate communications with older persons in home settings and institutions as appropriate and evaluate their efficacy • Use palliative care techniques to communicate with families and support older patients dying in critical and palliative care settings • Provide WHO recommended infection control procedures and other guidance on PPE, as well as psycho-social and spiritual support to staff in hospitals, nursing homes, hospices and community settings to ensure well-being and resilience
Survivorship	• Avoid sedentary lifestyle by integrating home based physical exercises into daily routine • Either or a combination of 150 minutes of moderate intensity or 75 minutes of vigorous intensity of physical activity per week, depending on the pre-existing level of function • Schedule short active breaks during the day, which may include standing every hour, walk around the block or walk several times inside the house, or follow regimen from online exercise class • Practice meditation, mindfulness and deep breathing exercise • Integrate cognitively stimulating activities, i.e. puzzles, reading, or board games • Monitor nutrition, avoid substance abuse, and control comorbidities by coordinating with the primary care provider

Abbreviations: VES-13: Vulnerable Elders Survey-13; HR: hormone receptor; HER2: human epidermal growth factor receptor 2; CARG: Cancer and Aging Research Group; CRASH: Chemotherapy Risk Assessment Scale for High age; G-CSF: granulocyte

colony-stimulating factor; ADT: androgen deprivation therapy; SOCARE: University of Rochester Specialized Oncology Care and Research in the Elderly; WHO: World Health Organization.

References

1. ; Available from: https://www.worldometers.info/coronavirus/.
2. Organization, W.H. *Novel Coronavirus (COVID-19) Situation*. 2020; Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019
3. Kuderer, N.M., et al., *Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study.* The Lancet.
4. Lee, L.Y.W., et al., *COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study.* Lancet, 2020.
5. Liang, W., et al., *Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China.* Lancet Oncol, 2020. **21**(3): p. 335-337.
6. Zhou, F., et al., *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.* Lancet, 2020. **395**(10229): p. 1054-1062.
7. *[The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China].* Zhonghua Liu Xing Bing Xue Za Zhi, 2020. **41**(2): p. 145-151.
8. Livingston, E. and K. Bucher, *Coronavirus Disease 2019 (COVID-19) in Italy.* JAMA, 2020. **323**(14): p. 1335-1335.
9. Sanità, I.S.d., *Characteristics of SARS-CoV-2 patients dying in Italy. Report based on available data on May 28th, 2020*. 2020.
10. *Death rates for COVID-19 in New York City as of June 8, 2020, by age group (per 100,000 people)*. 2020 [cited 2020 11/06/2020]; Available from: https://www.statista.com/statistics/1103867/coronavirus-death-rates-by-age-new-york-city/.
11. Richardson, S., et al., *Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area.* Jama, 2020.
12. Wang, B., et al., *Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis.* Aging (Albany NY), 2020. **12**(7): p. 6049-6057.
13. DuMontier, C., et al., *Defining Undertreatment and Overtreatment in Older Adults With Cancer: A Scoping Literature Review.* J Clin Oncol, 2020: p. Jco1902809.
14. Kuderer, N.M., et al., *Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study.* Lancet, 2020. **395**(10241): p. 1907-1918.
15. Garassino, M.C., et al., *COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study.* The Lancet Oncology.
16. van Doremalen, N., et al., *Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1.* New England Journal of Medicine, 2020. **382**(16): p. 1564-1567.
17. Fratino, L., et al., *Coronavirus: Older Persons With Cancer in Italy in the COVID-19 Pandemic.* Front Oncol, 2020. **10**: p. 648.
18. Grimmer, M., et al., *Mobility related physical and functional losses due to aging and disease - a motivation for lower limb exoskeletons.* J Neuroeng Rehabil, 2019. **16**(1): p. 2.
19. Paterson, D.H. and D.E. Warburton, *Physical activity and functional limitations in older adults: a systematic review related to Canada's Physical Activity Guidelines.* Int J Behav Nutr Phys Act, 2010. **7**: p. 38.
20. Armitage, R. and L.B. Nellums, *COVID-19 and the consequences of isolating the elderly.* Lancet Public Health, 2020. **5**(5): p. e256.

21. Petretto, D.R. and R. Pili, *Ageing and COVID-19: What is the Role for Elderly People?* Geriatrics (Basel), 2020. **5**(2).
22. Helms, J., et al., *Neurologic Features in Severe SARS-CoV-2 Infection.* New England Journal of Medicine, 2020. **382**(23): p. 2268-2270.
23. Mao, L., et al., *Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China.* JAMA Neurol, 2020.
24. O'Hanlon, S. and S.K. Inouye, *Delirium: a missing piece in the COVID-19 pandemic puzzle.* Age Ageing, 2020.
25. Mohile, S., et al., *Perspectives from the Cancer and Aging Research Group: Caring for the vulnerable older patient with cancer and their caregivers during the COVID-19 crisis in the United States.* J Geriatr Oncol, 2020. **11**(5): p. 753-760.
26. Onder, G., G. Rezza, and S. Brusaferro, *Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy.* Jama, 2020.
27. Balducci, L. and G. Colloca, *Natural disaster and rationing of care.* J Geriatr Oncol, 2020. **11**(5): p. 750-752.
28. Mohile, S.G., et al., *Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology.* Journal of Clinical Oncology, 2018. **36**(22): p. 2326-2347
29. Cohen, H.J., et al., *Frailty as determined by a comprehensive geriatric assessment-derived deficit-accumulation index in older patients with cancer who receive chemotherapy.* Cancer, 2016. **122**(24): p. 3865-3872.
30. Guerard, E.J., et al., *Frailty Index Developed From a Cancer-Specific Geriatric Assessment and the Association With Mortality Among Older Adults With Cancer.* J Natl Compr Canc Netw, 2017. **15**(7): p. 894-902.
31. Goede, V. and R. Stauder, *Multidisciplinary care in the hematology clinic: Implementation of geriatric oncology.* J Geriatr Oncol, 2019. **10**(3): p. 497-503.
32. *COVID-19 rapid guideline: critical care in adults* 2020, National Institute for Health and Care Excellence.
33. Bellelli, G., et al., *Frailty index predicts poor outcome in COVID-19 patients.* Intensive care medicine, 2020: p. 1-3.
34. Chong, E., et al., *COVID-19: Use of the Clinical Frailty Scale for Critical Care Decisions.* J Am Geriatr Soc, 2020.
35. Moug, S., et al., *Decision-Making in COVID-19 and Frailty.* Geriatrics (Basel), 2020. **5**(2).
36. Decoster, L., et al., *Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations†.* Ann Oncol, 2015. **26**(2): p. 288-300.
37. Hollander, J.E. and B.G. Carr, *Virtually Perfect? Telemedicine for Covid-19.* N Engl J Med, 2020. **382**(18): p. 1679-1681.
38. Calton, B., N. Abedini, and M. Fratkin, *Telemedicine in the Time of Coronavirus.* J Pain Symptom Manage, 2020.
39. DiGiovanni, G., et al., *Development of a telehealth geriatric assessment model in response to the COVID-19 pandemic.* J Geriatr Oncol, 2020. **11**(5): p. 761-763.
40. *CDC guidance for health care facilities* 2020 [cited 2020 12/06/2020]; Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-hcf.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fhealthcare-facilities%2Fguidance-hcf.html.

41. *Maintaining essential health services: operational guidance for the COVID-19 context*. 2020 [cited 2020 12/06/2020]; Available from: https://www.who.int/publications/i/item/covid-19-operational-guidance-for-maintaining-essential-health-services-during-an-outbreak.
42. *Cancer Surgery and COVID19.* Ann Surg Oncol, 2020. **27**(6): p. 1713-1716.
43. *COVID-19 and Surgery*. 2020 [cited 2020 12/06/2020]; Available from: https://www.facs.org/covid-19.
44. Sud, A., et al., *Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic.* Ann Oncol, 2020.
45. *Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study.* Lancet, 2020.
46. Mansfield, S.A., et al., *Timing of Breast Cancer Surgery-How Much Does It Matter?* Breast J, 2017. **23**(4): p. 444-451.
47. Silver, J.K., *Prehabilitation May Help Mitigate an Increase in COVID-19 Peripandemic Surgical Morbidity and Mortality.* Am J Phys Med Rehabil, 2020. **99**(6): p. 459-463.
48. Hind, D., et al., *Surgery versus primary endocrine therapy for operable primary breast cancer in elderly women (70 years plus).* Cochrane Database Syst Rev, 2006(1): p. Cd004272.
49. Chakrabarti, J., et al., *A randomised trial of mastectomy only versus tamoxifen for treating elderly patients with operable primary breast cancer-final results at 20-year follow-up.* Crit Rev Oncol Hematol, 2011. **78**(3): p. 260-4.
50. Johnston, S.J., et al., *A randomised trial of primary tamoxifen versus mastectomy plus adjuvant tamoxifen in fit elderly women with invasive breast carcinoma of high oestrogen receptor content: long-term results at 20 years of follow-up.* Ann Oncol, 2012. **23**(9): p. 2296-300.
51. *COVID-19 FAQs*. 2020 [cited 2020 12/06/2020]; Available from: https://www.astro.org/Daily-Practice/COVID-19-Recommendations-and-Information/COVID-19-FAQs.
52. Marijnen, C.A.M., et al., *International expert consensus statement regarding radiotherapy treatment options for rectal cancer during the COVID 19 pandemic.* Radiother Oncol, 2020. **148**: p. 213-215.
53. Murray Brunt, A., et al., *Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial.* The Lancet, 2020. **395**(10237): p. 1613-1626.
54. Dearnaley, D., et al., *Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial.* The Lancet Oncology, 2016. **17**(8): p. 1047-1060.
55. Vaidya, J.S., et al., *Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial.* The Lancet, 2010. **376**(9735): p. 91-102.
56. Esposito, E. and M. Douek, *Update on intraoperative radiotherapy: new challenges and issues.* Ecancermedicalscience, 2018. **12**: p. 793-793.
57. Yahalom, J., et al., *ILROG emergency guidelines for radiation therapy of hematological malignancies during the COVID-19 pandemic.* Blood, 2020. **135**(21): p. 1829-1832.

58. Chow, R., et al., *Single vs multiple fraction palliative radiation therapy for bone metastases: Cumulative meta-analysis.* Radiotherapy and Oncology, 2019. **141**: p. 56-61.
59. Hoskin, P.J., et al., *Effect of Single-Fraction vs Multifraction Radiotherapy on Ambulatory Status Among Patients With Spinal Canal Compression From Metastatic Cancer: The SCORAD Randomized Clinical Trial.* JAMA, 2019. **322**(21): p. 2084-2094.
60. Mulvenna, P., et al., *Dexamethasone and supportive care with or without whole brain radiotherapy in treating patients with non-small cell lung cancer with brain metastases unsuitable for resection or stereotactic radiotherapy (QUARTZ): results from a phase 3, non-inferiority, randomised trial.* The Lancet, 2016. **388**(10055): p. 2004-2014.
61. Davis, J.N., et al., *Stereotactic body radiotherapy for centrally located early-stage non-small cell lung cancer or lung metastases from the RSSearch(®) patient registry.* Radiat Oncol, 2015. **10**: p. 113.
62. Nagar, H. and S.C. Formenti, *Cancer and COVID-19 - potentially deleterious effects of delaying radiotherapy.* Nat Rev Clin Oncol, 2020. **17**(6): p. 332-334.
63. *COVID-19 rapid guideline: delivery of radiotherapy. NICE guideline [NG162]*. 2020, National Institute for Health and Care Excellence (NICE).
64. Olivotto, I.A., et al., *Intervals longer than 20 weeks from breast-conserving surgery to radiation therapy are associated with inferior outcome for women with early-stage breast cancer who are not receiving chemotherapy.* J Clin Oncol, 2009. **27**(1): p. 16-23.
65. Crook, J., et al., *Final Report of Multicenter Canadian Phase III Randomized Trial of 3 Versus 8 Months of Neoadjuvant Androgen Deprivation Therapy Before Conventional-Dose Radiotherapy for Clinically Localized Prostate Cancer.* International Journal of Radiation Oncology*Biology*Physics, 2009. **73**(2): p. 327-333.
66. Neal, D.E., et al., *Ten-year Mortality, Disease Progression, and Treatment-related Side Effects in Men with Localised Prostate Cancer from the ProtecT Randomised Controlled Trial According to Treatment Received.* European Urology, 2020. **77**(3): p. 320-330.
67. Ghadjar, P., et al., *Use of androgen deprivation and salvage radiation therapy for patients with prostate cancer and biochemical recurrence after prostatectomy.* Strahlentherapie und Onkologie, 2018. **194**(7): p. 619-626.
68. Simcock, R., et al., *COVID-19: Global radiation oncology's targeted response for pandemic preparedness.* Clin Transl Radiat Oncol, 2020. **22**: p. 55-68.
69. Hughes, K.S., et al., *Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343.* J Clin Oncol, 2013. **31**(19): p. 2382-7.
70. Matuschek, C., et al., *The benefit of adjuvant radiotherapy after breast conserving surgery in older patients with low risk breast cancer- a meta-analysis of randomized trials.* Radiat Oncol, 2017. **12**(1): p. 60.
71. Schneider, B.J., et al., *Stereotactic Body Radiotherapy for Early-Stage Non-Small-Cell Lung Cancer: American Society of Clinical Oncology Endorsement of the American Society for Radiation Oncology Evidence-Based Guideline.* J Clin Oncol, 2018. **36**(7): p. 710-719.

72. Chang, J.Y., et al., *Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials.* Lancet Oncol, 2015. **16**(6): p. 630-7.
73. Simcock, R., et al., *COVID-19: Global radiation oncology's targeted response for pandemic preparedness.* Clinical and Translational Radiation Oncology, 2020. **22**: p. 55-68.
74. Tsang, Y., et al., *Meeting the challenges imposed by COVID-19: Guidance document by the ESTRO Radiation TherapisT Committee (RTTC).* Technical Innovations & Patient Support in Radiation Oncology, 2020. **15**: p. 6-10.
75. Russell, B., et al., *Associations between immune-suppressive and stimulating drugs and novel COVID-19-a systematic review of current evidence.* Ecancermedicalscience, 2020. **14**: p. 1022.
76. Hurria, A., et al., *Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study.* J Clin Oncol, 2011. **29**(25): p. 3457-65.
77. Hurria, A., et al., *Validation of a Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer.* J Clin Oncol, 2016. **34**(20): p. 2366-71.
78. Extermann, M., et al., *Predicting the risk of chemotherapy toxicity in older patients: the Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score.* Cancer, 2012. **118**(13): p. 3377-86.
79. Giordano, S.H., et al., *Use and outcomes of adjuvant chemotherapy in older women with breast cancer.* J Clin Oncol, 2006. **24**(18): p. 2750-6.
80. Ueda, M., et al., *Managing Cancer Care During the COVID-19 Pandemic: Agility and Collaboration Toward a Common Goal.* J Natl Compr Canc Netw, 2020: p. 1-4.
81. Hofheinz, R.D., et al., *Chemoradiotherapy with capecitabine versus fluorouracil for locally advanced rectal cancer: a randomised, multicentre, non-inferiority, phase 3 trial.* Lancet Oncol, 2012. **13**(6): p. 579-88.
82. Grothey, A., et al., *Duration of Adjuvant Chemotherapy for Stage III Colon Cancer.* New England Journal of Medicine, 2018. **378**(13): p. 1177-1188.
83. Hall, P.S., et al., *Optimising chemotherapy for frail and elderly patients (pts) with advanced gastroesophageal cancer (aGOAC): The GO2 phase III trial.* Journal of Clinical Oncology, 2019. **37**(15_suppl): p. 4006-4006.
84. Corre, R., et al., *Use of a Comprehensive Geriatric Assessment for the Management of Elderly Patients With Advanced Non–Small-Cell Lung Cancer: The Phase III Randomized ESOGIA-GFPC-GECP 08-02 Study.* Journal of Clinical Oncology, 2016. **34**(13): p. 1476-1483.
85. Dees, E.C., et al., *A prospective pharmacologic evaluation of age-related toxicity of adjuvant chemotherapy in women with breast cancer.* Cancer Invest, 2000. **18**(6): p. 521-9.
86. Schild, S.E., et al., *The outcome of combined-modality therapy for stage III non-small-cell lung cancer in the elderly.* J Clin Oncol, 2003. **21**(17): p. 3201-6.
87. Gómez, H., et al., *Elderly patients with aggressive non-Hodgkin's lymphoma treated with CHOP chemotherapy plus granulocyte-macrophage colony-stimulating factor: identification of two age subgroups with differing hematologic toxicity.* J Clin Oncol, 1998. **16**(7): p. 2352-8.
88. *Toolkit: Providing Oncology Treatments in the Outpatient Setting*. 2020.

89. von Lilienfeld-Toal, M., et al., *Frequently asked questions regarding SARS-CoV-2 in cancer patients—recommendations for clinicians caring for patients with malignant diseases.* Leukemia, 2020. **34**(6): p. 1487-1494.
90. von Lilienfeld-Toal, M., et al., *Frequently asked questions regarding SARS-CoV-2 in cancer patients-recommendations for clinicians caring for patients with malignant diseases.* Leukemia, 2020. **34**(6): p. 1487-1494.
91. Lala, M., et al., *A six-weekly dosing schedule for pembrolizumab in patients with cancer based on evaluation using modelling and simulation.* Eur J Cancer, 2020. **131**: p. 68-75.
92. Bos, A.C., et al., *Timing of adjuvant chemotherapy and its relation to survival among patients with stage III colon cancer.* Eur J Cancer, 2015. **51**(17): p. 2553-61.
93. Burdett, S., et al., *Adjuvant chemotherapy for resected early-stage non-small cell lung cancer.* Cochrane Database Syst Rev, 2015(3): p. Cd011430.
94. Kupstas, A.R., et al., *Effect of Surgery Type on Time to Adjuvant Chemotherapy and Impact of Delay on Breast Cancer Survival: A National Cancer Database Analysis.* Ann Surg Oncol, 2019. **26**(10): p. 3240-3249.
95. Spring, L.M., et al., *Neoadjuvant Endocrine Therapy for Estrogen Receptor-Positive Breast Cancer: A Systematic Review and Meta-analysis.* JAMA Oncol, 2016. **2**(11): p. 1477-1486.
96. Powell, I.J., et al., *Neoadjuvant therapy before radical prostatectomy for clinical T3/T4 carcinoma of the prostate: 5-year followup, Phase II Southwest Oncology Group Study 9109.* J Urol, 2002. **168**(5): p. 2016-9.
97. Scolieri, M.J., A. Altman, and M.I. Resnick, *Neoadjuvant hormonal ablative therapy before radical prostatectomy: a review. Is it indicated?* J Urol, 2000. **164**(5): p. 1465-72.
98. Crivellari, D., et al., *Burdens and benefits of adjuvant cyclophosphamide, methotrexate, and fluorouracil and tamoxifen for elderly patients with breast cancer: the International Breast Cancer Study Group Trial VII.* J Clin Oncol, 2000. **18**(7): p. 1412-22.
99. Williams, C.P., et al., *Importance of quality-of-life priorities and preferences surrounding treatment decision making in patients with cancer and oncology clinicians.* Cancer, 2020.
100. *Policy Brief: The Impact of COVID-19 on older persons*. 2020.
101. *Two million reasons - the Cancer Survivorship Agenda: Why we need to support people with or beyond cancer*. 2008: London.
102. Bluethmann, S.M., A.B. Mariotto, and J.H. Rowland, *Anticipating the "Silver Tsunami": Prevalence Trajectories and Comorbidity Burden among Older Cancer Survivors in the United States.* Cancer Epidemiol Biomarkers Prev, 2016. **25**(7): p. 1029-36.
103. Nekhlyudov, L., et al., *Addressing the needs of cancer survivors during the COVID-19 pandemic.* J Cancer Surviv, 2020: p. 1-6.
104. *Stay physically active during self-quarantine*. 2020 27/06/2020]; Available from: https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/technical-guidance/stay-physically-active-during-self-quarantine.
105. Scher, K.S. and A. Hurria, *Under-representation of older adults in cancer registration trials: known problem, little progress.* J Clin Oncol, 2012. **30**(17): p. 2036-8.

106. Waterhouse, D.M., et al., *Early Impact of COVID-19 on the Conduct of Oncology Clinical Trials and Long-Term Opportunities for Transformation: Findings From an American Society of Clinical Oncology Survey.* JCO Oncology Practice. **0**(0): p. OP.20.00275.
107. de Paula, B.H.R., et al., *Recommendations from national regulatory agencies for ongoing cancer trials during the COVID-19 pandemic.* Lancet Oncol, 2020. **21**(5): p. 624-627.
108. Fleming, T.R., D. Labriola, and J. Wittes, *Conducting Clinical Research During the COVID-19 Pandemic: Protecting Scientific Integrity.* Jama, 2020.
109. *FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency: Guidance for Industry, Investigators, and Institutional Review Boards*. 2020, Food and Drug Administration.
110. *Guidance on the management of clinical trials during the COVID-19 (coronavirus) pandemic*. 2020, European Medicines Agency.