A Canadian framework for managing prostate cancer during the COVID-19 pandemic: Recommendations from the Canadian Urologic Oncology Group and the Canadian Urological Association

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Introduction

The COVID-19 pandemic has had an unprecedented impact on all aspects of healthcare. One widespread strategy to mitigate the burden of disease is to limit nonessential exposure to healthcare settings by canceling office visits and non-emergent surgeries. The underlying concern is that there is an unknown proportion of patients and staff who are asymptomatic carriers and testing capacity is insufficient to test everyone¹. The COVID-19 pandemic presents a unique challenge for oncology for several reasons. Patients with cancer might be more likely to get COVID-19 and have serious adverse outcomes, including intensive care admissions, ventilator requirements and death^{2,3}. Furthermore, patients undergoing surgery, including select oncologic cases, may be at high risk for postoperative mortality⁴. In addition, intubation is a procedure that carries high risk of spreading the virus to members of the healthcare team present in the operating room. These complexities in cancer care have resulted in the release of several guidelines regarding management of oncology patients during the COVID-19 era⁵⁻⁹. Two recent Canadian Urological Association (CUA) publications outline recommendations on surgical

triaging and the use of systemic therapies in genitourinary malignancies^{7,9}. The purpose of this publication is to provide a multidisciplinary framework focused on prostate cancer management in the setting of the COVID-19 global pandemic within the Canadian context.

General principles

- 1. This consensus statement is a guide to help physicians manage prostate cancer during the acute phase of a pandemic. Treatment prioritization must take into account regional differences in infection rates, resource capacity and mitigation efforts. The current pandemic has had a widespread reach across all Canadian communities, but we recognize that the degree of impact varies, and that provincial and institutional policies are not uniform. Physicians must continue to monitor a continuously evolving situation and make adjustments to clinical decisions as deemed appropriate.
- 2. The risk of serious morbidity resulting from SARS-CoV-2 infection may outweigh the competing risk of prostate cancer in many men. Observation of prostate cancer in carefully selected patients does not increase long-term mortality^{10,11}, and therefore short-term treatment delays are unlikely to lead to disease progression and worse outcomes. All management decisions should be based on this core principle.
- 3. Appropriate patient counseling and shared decision making is strongly encouraged. Men diagnosed with prostate cancer have increased anxiety and psychological distress^{12,13}. This will undeniably become amplified in the setting of a global health crisis. Despite resource restrictions and changes in treatment recommendations, physicians must continue to address the needs of patients and involve them in the decision-making process. This approach may decrease patient anxiety levels and improve outcomes once regular practice resumes.
- 4. Prioritization must be given to limiting exposures of patients and healthcare workers to SARS-CoV-2. Implementation of telehealth visits significantly reduces the risk of infection among frontline personnel and patients, but also preserves critically needed hospital resources. For these reasons, telehealth visits are strongly encouraged. In-person consultations should be limited to men with new symptoms, those requiring a physical examination and for the evaluation and management of treatment-related serious adverse events. In men who require an in-person assessment, consideration should be given to not repeating visits when two specialists are consulted, nor when pre-operative assessment is needed. The healthcare provider should coordinate their needs to minimize patient's visits.

Screening and detection

- 1. The CUA endorses prostate cancer screening and detection in appropriately selected men¹⁴. However, the public health benefit from these recommendations is derived from long-term implementation and has no role in an acute setting. Therefore, we recommend cessation of routine prostate-specific antigen (PSA) screening in asymptomatic men until resolution of this pandemic.
- 2. In men with a suspicion of asymptomatic localized prostate cancer (based on PSA testing or clinical exam) we recommend delay of further investigations. This includes digital rectal examination (DRE), cross sectional or prostate imaging and transrectal ultrasound (TRUS) guided or perineal biopsies. These procedures increase patient and occupational exposure to SARS-CoV-2, utilize healthcare resources and are unlikely to improve patient outcomes in the short term. MRI has become a preferred imaging modality for diagnosis and staging of prostate cancer, however access is currently restricted and therefore its use should be limited for staging of high-risk cases when clinically indicated (see below). The risk of TRUS biopsy related sepsis is of particular concern given the potential severity of this complication, which can lead to hospitalization and further risk of exposure to the virus. A secondary concern is that of possible fecal SARS-CoV-2 transmission arising from the gastrointestinal tract¹⁵. In rare cases where a diagnosis of prostate cancer may change immediate management, we recommend that TRUS biopsies are performed using adequate PPE¹⁶ and strict adherence to appropriate antimicrobial prophylaxis. The risk of fecal transmission during a DRE is unknown and, to our knowledge, international societies have not addressed use of PPE during the examination. We recommend adherence to institutional Infection Prevention and Control (IPAC) guidelines. If unavailable, we recommend at minimum use of droplet precautions with mask, eye protection, gown and gloves.

Treatment prioritization strategies

Treatment recommendations depend on the predicted severity of disease, which we have defined below using National Comprehensive Cancer Network (NCCN) guidelines¹⁷.

- 1. Localized low risk prostate cancer (very low, low and favourable intermediate risk (FIR) groups).
 - General principle: In men with asymptomatic low risk prostate cancer, deferral of further investigations and treatments is recommended until return to routine clinical activities.
 - I. In patients currently on or choosing **active surveillance** short-term suspension of active surveillance protocols is recommended where appropriate, including in person clinic visits, DRE, PSA testing, imaging (including MRI) and repeat biopsy.

- II. In men choosing **surgical treatment** for low or FIR disease, delays of up to several months to one year from diagnosis to radical prostatectomy (RP) do not appear to worsen biochemical recurrence rates¹⁸⁻²⁰. The length of delay until adverse outcomes occur is unknown, however 6-12 months is likely appropriate based on these retrospective series. Therefore, in men with newly diagnosed low risk prostate cancer (including FIR) consider delay of RP until return to routine elective procedures. Neoadjuvant androgen deprivation therapy (ADT) to bridge the COVID-19 related delay to RP should not be used in this patient population.
- III. In men electing to proceed with **radiation therapy** (RT), a delay in treatment is also recommended. There is no role for neoadjuvant ADT in men with low risk prostate cancer, and it is not routinely used for FIR disease. Consultation with and referral to radiation oncology is advised where appropriate.
- IV. In patients on **ongoing surveillance following definitive therapy** for low- and FIR disease consider decreasing frequency of PSA testing and deferring in-office clinic appointments, particularly for patients greater than 1 year since surgery or RT.
- 2. Localized high risk prostate cancer (unfavorable intermediate risk (UIR), high risk (HR) and very high risk (VHR) groups)
 - I. For **new consults**, we recommend proceeding with diagnostic interventions and staging investigations in these patients pending resource availability, since a finding of metastatic disease would significantly alter management.
 - II. Patients with UIR, HR and VHR prostate cancer who choose **radiation treatment** should begin neoadjuvant ADT (NADT), as per current best practice recommendations. Four to 6 months of NADT is appropriate for patients with UIR note that RTOG 9910 showed that 9 months of ADT did not improve local control, biochemical disease-free survival, cancer-specific mortality, metastasis-free survival, or overall survival²¹. Hypofractionated RT protocols should be considered to minimize patient visits.
 - III. UIR, HR and VHR patients electing to proceed with **radical prostatectomy** require special consideration. Within the current COVID-19 climate many centers are deferring non-emergent surgical cases, therefore a delay in time to RP from diagnosis may be expected. In a retrospective analysis of UIR, HR and VHR patients, a treatment delay for up to 6 months did not affect BCR or recurrence free survival²², whereas a study of HR and VHR cases only suggested no adverse oncologic outcomes from a 3-month delay²³. Hence, a delay of 3 months may be considered in places where surgical resource capacity is limited.
 - IV. **Neoadjuvant ADT prior to RP** for localized prostate cancer is not recommended outside of a clinical trial because current best available evidence suggests no overall survival benefit²⁴. However, there is a significant improvement in multiple

pathological variables, including nodal metastases and positive margins with an acceptable safety profile²⁴. In a randomized study comparing 3- and 8-month durations of NADT prior to RP, patients in the 8-month group had ongoing pathological and biochemical regression of localized prostate cancer, suggesting safety of this approach²⁵. Therefore, this option may be considered in patients with UIR, HR and VHR disease during the COVID-19 crisis if prolonged surgical delays are expected. Patients should be aware that this is not standard practice, and the risk-benefit discussion should be documented. Use of androgen receptor axis targeted therapies (ARAT) in this context remains experimental and is not recommended.

- V. For patients on **surveillance following definitive therapy for high risk prostate cancer** we recommend ongoing PSA testing and imaging, if needed, to assess for recurrent disease. Consideration may be given to decreased frequency of testing in men who have been disease free for 2 years or greater, and to transition them to telehealth visits.
- 3. Advanced prostate cancer (clinical nodal involvement, biochemical recurrence post primary treatment (BCR), metastatic disease)
 - I. Patients with newly diagnosed advanced prostate cancer are complex and require comprehensive and preferably multi-disciplinary assessment. We recommend considering in-person clinic consultations for these men depending on clinical scenario. Full staging evaluation, including laboratory testing, and imaging is also recommended.
 - II. In men with high risk features post RP, early salvage RT is recommended over up front adjuvant RT^{26,27}. Men with BCR and no evidence of metastases should have ongoing PSA and imaging assessments as indicated, and the frequency should be dictated by disease risk and PSA doubling time. Hypofractionated RT protocols should be considered to minimize patient visits.
 - III. Men with newly diagnosed **node positive prostate cancer** without evidence of further metastases should receive ADT and consideration for external beam RT as per current best practice. Hypofractionated RT protocols should be considered. Abiraterone has also shown benefit in these patients²⁸, however this must be balanced with requirement for laboratory monitoring and physical examination. Therefore, we would recommend a delay of abiraterone therapy for of up to 6 months from time of diagnosis.
 - IV. In men with **newly diagnosed metastatic hormone sensitive prostate cancer** (HSPC), we recommend treatment with an ARAT over docetaxel chemotherapy in addition to ADT. While outcomes of prostate cancer patients infected with SARS-CoV-2 are unknown, cancer patients with a history of receiving

- chemotherapy within 1 month are at higher risk for severe illness². Chemotherapy administration is also associated with more intense resource utilization and risk exposure.
- V. Men with **oligometastatic HSPC** may benefit from ADT (with or without an ARAT) with external beam RT to the prostate^{29,30}. We recommend withholding or delaying RT in this setting during the pandemic. If RT is administered, a hypofractionated course should be considered.
- VI. In men with a **new diagnosis of high risk (PSADT < 10 months) non-metastatic castrate resistant prostate cancer** (nmCRPC) we recommend consideration of apalutamide, enzalutamide or darolutamide per current standard of care³¹⁻³³. In nmCRPC patients with a prolonged PSADT we recommend considering a decrease in the frequency of imaging.
- VII. In men with a **new diagnosis of metastatic castrate resistant prostate cancer** (mCRPC) who have not previously been treated with an ARAT, we recommend this therapy over chemotherapy for the reasons discussed above. Another option may be Radium-223 in men with bony metastases, however the benefit must be weiged against the risk of pancytopenia. Men should be referred to medical oncology for discussion of risks and benefits of systemic therapy within the COVID-19 setting.
- VIII. In men with painful **bone metastases** or bone metastases at high risk of fracture (weight bearing bone such as vertebra/pelvis/femur) we recommend referral to radiation oncology for a short course of palliative radiotherapy.

Special considerations

- 1. The **treatment of localized or locally advanced prostate cancer** within the COVID-19 context requires complex decision making, not only with respect to timing but also choice of treatment modality. Surgery and brachytherapy carry the risk of serious complications, require utilization of hospital resources and have increased risk of SARS-CoV-2 exposure to patients and healthcare personnel. External beam RT mitigates some of these risks, however patients are subject to multiple, repeated outpatient hospital visits. Many RT groups have instituted short course interim policies leaning heavily on stereotactic body RT techniques³⁴. The optimal choice and timing of treatment ultimately requires shared decision making and multidisciplinary collaboration.
- 2. For **robotic-assisted laparoscopic prostatectomy or laparoscopic RP** there may be an increased risk for aerosolization of the virus³⁵. Although this has not yet been directly linked to SARS-CoV-2, urologists performing minimally invasive surgery should take necessary precautions to mitigate this possibility, including use of filter devices^{16,35}.

There are several filter devices available on the market, and they have been summarized elsewhere 16.

- 3. **For patients on ADT**, strong consideration should be given to using longer acting depots and implementing home injection programs where available in order to decrease patient and healthcare practitioner exposures.
- 4. Special consideration should be given to patients on **bone targeted therapies**, specifically denosumab. For men with mCRPC receiving monthly dosing, self-injections should be encouraged when possible to limit exposure to healthcare personnel. The frequency of laboratory monitoring (calcium specifically) and associated exposure risk present an added challenge during the COVID-19 crisis. This must be balanced with the net benefit of therapy. In patients who are unable to or refusing laboratory testing during the pandemic, we recommend temporary discontinuation of denosumab, or consideration of longer treatment intervals (eg. 3 instead of 1 month).
- 5. For **patients receiving abiraterone**, the home monitoring program should be instituted to avoid unnecessary hospital and clinic visits.
- 6. For **patients receiving and progressing on abiraterone**, the switch from prednisone to dexamethasone is commonly practiced and may delay the time to initiation of chemotherapy³⁶. This may be advantageous in the setting of COVID-19. However, practitioners must be aware that there is currently a global shortage in access to dexamethasone.
- 7. Many institutions have **restricted visitor access**. This challenge may be of particular concern to patients with advanced prostate cancer, cognitive challenges or language barriers, whose caregivers are highly involved in treatment decisions and information synthesis. Patients should be encouraged to use technology (video, telephone) to enhance discussion and comprehension during the clinic visit.
- 8. Men with advanced prostate cancer are generally older, frail, and have multiple comorbidities in addition to an advanced malignancy. This makes them a vulnerable population during the COVID-19 pandemic. Patients and their families should be encouraged to discuss **substitute decision making and advanced directives**. A useful framework on this subject is discussed elsewhere³⁷.

9. One of the major repercussions of COVID-19 is the potential for **economic instability and occupational insecurity**. Many younger patients may not have continuing access to drug coverage benefits as a result. Use of **compassionate drug access programs**, if available, is strongly encouraged for these cases.

Conclusions

The COVID-19 pandemic has resulted in extraordinary challenges to healthcare systems, which raises several concerns for the treatment of prostate cancer patients. Herein we provide a framework for Canadian physicians managing this complex malignancy during a global health crisis, as summarized in Table 1. The proposed recommendations act as a guide and must be considered in the context of a fluctuating and evolving environment. They do not address the impact of potentially delayed care on the healthcare system once operations return to pre-COVID-19 levels. We recognize that this is a complex issue and that delayed care may result in challenging triaging decisions in the future, however these recommendations are meant to guide physicians during the acute crisis phase. We note that population-wide changes to prostate cancer care are not unprecedented, with one population-based study showing a decrease in PSA detectable prostate cancer diagnoses and increased use of conservative management during the Great Recession³⁸. We believe that the principles in this statement may remain applicable under future resource constraints.

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Figures and Tables

Table 1. Summary of treatment recommendations for prostate cancer during COVID-19 pandemic				
	In-person consult	Diagnostic investigations (imaging, biopsy)	Treatment	Post-treatment monitoring
Very low-risk Low-risk Favourable intermediate-risk	Not recommended	Not recommended	Recommend delaying until pandemic resolution	Recommend delaying active surveillance protocols
Unfavourable intermediate-risk High-risk Very high-risk	May be considered, depending on clinical scenario	Recommended	Neoadjuvant ADT for patients choosing RT Consider neoadjuvant ADT prior to RP if extended delay to surgery Consider delaying definitive therapy (up to 3 months from diagnosis)	Recommend ongoing surveillance Consider decreasing frequency of PSA and imaging if >2 years since definitive therapy and stable
Locally advanced or metastatic	May be considered, depending on clinical scenario	Recommended	Recommended (see text for details)	Close surveillance of patients on treatment is recommended to monitor for disease progression and AEs

ADT: androgen deprivation therapy; AE: adverse events; PSA: prostate-specific antigen; RP: radical prostatectomy; RT: radiotherapy.