Guidelines for the Management of Prostate Cancer

Quick Reference Version
**Diagnosis and Referral of Prostate Cancer - Overview**

**Suspicion of Prostate Cancer:**
- Elevated PSA and/or abnormal DRE (See Page 10 for Position Statement on Early Detection of Prostate Cancer)
- Symptoms which led to PSA/DRE
- Identified by Primary Care Physician

**Referral to Urologist**

**Prostate biopsy**
- Biopsy sample to Pathology Lab

**Staging Investigations**
- Serum PSA levels
- Consider bone scan (if PSA > 10 ng/mL or if Gleason Grade > 7, if disease is locally advanced, or if there are symptoms suggestive of metastases)
- CT or MRI pelvic scans, if PSA > 20 ng/mL
- Pelvic lymph node dissection, if PSA > 20 ng/mL, or if PSA > 10mg/L and Gleason Grade > 7

**Management by Risk Category**

- No Invasive Cancer Present
  - Continue to follow PSA levels (by Urologist or Family Physician) +/- biopsies

- Invasive Cancer Present

**Referral to Cancer Centre if Radiotherapy and/or Chemotherapy under consideration**
- See Page 2 for details

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1 - Quick Reference Version Guidelines for the Management of Prostate Cancer
Staging Prostate Cancer

TNM- T (Tumour) N (Node) M (Metastasis) Criteria

 Clinical Tumour Size (T):
 T0 No evidence of a primary tumour
 T1 Clinically inapparent tumour, neither palpable nor visible by imaging
 T2 Tumour confined within prostate
 T3 Tumour extends through prostate capsule
 T4 Tumour is fixed or invades adjacent structures

 Pathologic Tumour Size (pT):
 pT1 There is no pathologic T1 classification
 pT2 Organ confined
 pT3 Extraprostatic extension
 pT4 Invasion of bladder, rectum

 Clinical Node Involvement (N):
 N0 No metastasis to regional lymph nodes
 N1 Metastasis in regional lymph node(s)

 Pathologic Node Involvement (pN):
 pN0 No positive regional lymph nodes
 pN1 Metastasis in regional lymph node(s)

 Presence of Metastasis (M):
 M0 No distant metastasis
 M1 Distant metastasis present

Grading Criteria
Prostate adenocarcinomas are graded by the Gleason score: scores in the range 2-10.
• Well differentiated tumours (Gleason 2-6)
• Moderately differentiated tumours (Gleason 7)
• Poorly differentiated tumours (Gleason 8-10)
Grading not generally used for staging at Capital Health

Stage I
T1a N0 M0 Low Grade

Stage II
T1 N0 M0 Any Grade
T2 N0 M0 Any Grade

Stage III
T3 N0 M0 Any Grade
Any T N1 M0 Any Grade
Any T Any N M1 Any Grade

Stage IV
Any T Any N M0 Any Grade
Any T Any N M1 Any Grade

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Referral Criteria for Prostate Cancer

Referral Information:
• Letter of Referral*
• Laboratory Results*- CBC, PSA (including old results)
• Biopsy Pathology Reports
• Operative Reports (prostatectomy, orchietomy, other)
• Diagnostic Imaging Reports (TURP, bone scans, chest X-ray, CT scans, other)

* Specific information which is necessary for proper triage of referrals

Referral to Cancer Centre if Radiotherapy and/or Chemotherapy under consideration

Local Urologist
• Refer as per usual practice within local community or health care district

QEII Health Sciences Centre:
• Faxed referrals to the QEII Cancer Care Program (CCP) Referrals Office at 902-473-6079 (tel. 902-473-5140 or 902-473-6098).

Cape Breton Cancer Centre:
• Direct referrals to the Referrals/Booking office at 902-567-7774 (fax. 902-567-7911).

Urgent Referrals:
• For urgent or emergent referrals, in Halifax-page the appropriate specialist on call through the Locating service (902-473-2220); in Cape Breton-page the appropriate specialist on call through the Locating service (902-567-8000)
Initial Treatment Options for Prostate Cancer

**Low Risk:**
- T1-T2a
- Low PSA (<10 ng/mL)
- Low Gleason Grade (<6)

  - Prostatectomy
  - External beam radiotherapy alone
  - Brachytherapy (seed implant-not available in NS)
  - Expectant Management
  - Observation

**Intermediate Risk:**
- T2b-T2c
- PSA = 10-20 ng/mL
- Gleason Grade = 7

  - Neoadjuvant Androgen Deprivation Therapy (ADT) and radical external beam radiotherapy (RT) (ADT for 2-8 months prior to RT or concurrent with RT)
  - Dose-escalated conformal external beam (3D) radiotherapy
  - Prostatectomy
  - ADT as primary treatment if contraindication to radiotherapy and prostatectomy
  - Expectant Management
  - Observation (for patients with significant morbidity or poor life expectancy)

**High Risk:**
- T3-T4
- Gleason Grade ≥8
- PSA >20 ng/mL

  - Neoadjuvant ADT and external beam radiotherapy (including elective treatment of pelvic lymph nodes) PLUS 2 years adjuvant hormone treatment
  - Prostatectomy (for highly selected patients with low volume disease; NOT RECOMMENDED for T3b-T4 patients)
  - Post operative radiotherapy and/or ADT may be required
  - ADT as primary treatment in very high risk patients with low chance of cure
  - Observation (for patients with significant morbidity or poor life expectancy)
Observation

- Observation consists of medical follow up where it is unlikely that the patient will be treated with radiation therapy or surgery for cure due to a limited life expectancy or severe medical co-morbidities. Treatment at symptomatic progression will likely consist of ADT with additional interventions given with the intent of improving impairments in prostate cancer-specific health-related quality of life.

Expectant Management

- Expectant management involves actively monitoring the course of disease with the expectation to intervene if the cancer progresses or if symptoms become imminent.
- Patients with clinically localized cancers that are candidates for definitive treatment and choose expectant management should have regular follow up.
  - DRE and PSA every 6 months
  - Needle biopsy of the prostate may be repeated within 6 months of diagnosis if initial biopsy was < 10 cores or assessment discordant (e.g., palpable tumour contralateral to side of positive biopsy).
  - Needle biopsy should be performed within 18 months if > 10 cores obtained initially, then periodically
  - A repeat biopsy may be indicated for any sign of disease progression by exam or markers.

Follow-Up After Curative Therapy

- The goal of follow up is to detect recurrence and to monitor for side effects from the treatment.
- Followup visits should include reassessment and management of supportive care issues, including psychosocial, sexual and/or incontinence problems.
- Follow up schedule will depend on a number of factors:
  - the initial clinical or pathological stage of the disease
  - acute or chronic toxicities
  - post therapy PSA levels, or rising PSA levels

### After Curative Radiotherapy

<table>
<thead>
<tr>
<th>Year</th>
<th>Frequency</th>
<th>Provider</th>
<th>Tests</th>
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<tbody>
<tr>
<td>1-5</td>
<td>every 6-24 months</td>
<td>RO</td>
<td>Clinical assessment, DRE</td>
</tr>
<tr>
<td>1-5</td>
<td>every 3-4 months</td>
<td>RO</td>
<td>PSA *</td>
</tr>
<tr>
<td>&gt;5</td>
<td>every 1-3 years</td>
<td>RO</td>
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</tr>
<tr>
<td>&gt;5</td>
<td>every 3-6 months</td>
<td>RO</td>
<td>PSA</td>
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</tbody>
</table>

* Serum testosterone may be monitored in patients receiving ADT

### After Curative Radical Prostatectomy

<table>
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<tr>
<th>Year</th>
<th>Frequency</th>
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<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>every 3-12 months</td>
<td>U</td>
<td>PSA, Clinical assessment</td>
</tr>
<tr>
<td>3- Ongoing</td>
<td>every 6-12 months</td>
<td>U</td>
<td>PSA, Clinical assessment</td>
</tr>
</tbody>
</table>

RO: radiation oncologist  U: urologist  DRE: digital rectal examination  PSA: prostate specific antigen
ADT (Androgen Deprivation Therapy - Hormonal Regimens)

The choice of initial orchiectomy or androgen deprivation (hormonal) agent(s) for any individual patient will depend on many factors.

- Combined Androgen Blockade (CAB- LHRH agonist plus non-steroidal antiandrogen agent) is not routinely indicated.
- Monotherapy with nonsteroidal antiandrogens is not routinely indicated.
- After initial failure of ADT, secondary hormonal manipulation should be tried (e.g. addition of a non-steroidal antiandrogen or discontinuation of non-steroidal antiandrogen if already on).
- Other hormonal manipulations, such as ketoconazole or estrogens may be tried. Some phase II trials show a decline in PSA. There are no randomized data to support any survival advantage.

OPTIONS:

1. **Orchiectomy**
   The testicles are surgically removed. The procedure is done as an outpatient, usually done under local anesthetic. Surgical castration (orchiectomy) is permanent.

2. **LHRH Agonists**
   - Goserilin (Zoladex®) 3.6 mg SC Depot q28d OR 10.8 mg SC Depot q84d
   - Leuprolide (Lupron®-IM, Eligard®-SC) 7.5 mg IM/SC Depot q28d
     OR 22.5 mg IM/SC Depot q84d (3mo) OR 30 mg SC Depot q112d (4 mo)
     OR 45 mg SC Depot q168d (6mo)
   - Buserilin (Suprefact®) 6.3 mg SC Depot q56d OR 9.45 mg IM Depot q120d
   Note: Due to an initial rise in testosterone levels, patients should be given a non-steroidal antiandrogen (see below) for 2-4 weeks at the same time as their first LHRH agonist dose.

3. **Non-steroidal Antiandrogen Agents**
   - Flutamide (Euflex®) 250 mg PO TID
   - Bicalutamide (Casodex®) 50 mg PO daily, up to 150 mg PO daily to TID
   - Nilutamide (Anandron®) 50 mg PO BID or TID

4. **Other Hormonal Treatments**
   - Cyproterone (Androcur®) 50-100 mg PO BID or TID
   - Megestrol (Megace®) 80-160 mg PO daily
   - Ketoconazole (Nizoral®) 400 mg PO TID (+/- Hydrocortisone 20 mg qAM & 10 mg qPM)
   - Estrogens- e.g. Diethylstilbestrol 1 mg PO Daily
Post-Prostatectomy Management

Post-operative PSA Undetectable or PSA < 0.2 ng/mL

- **pT2, pT0 NX,N0 M0** (negative margin)
  - No therapeutic interventions, standard follow-up management

- **pT2 (positive margin), pT3a NX,N0 M0**
  - No therapeutic interventions, standard follow-up management
  - Radiation Therapy (+/- ADT)

- **pT3b NX,N0 M0**
  - Radiation Therapy (+/- ADT)
  - No therapeutic interventions, standard follow-up management
  - Radiation Therapy (+/- ADT)
  - ADT alone
  - No therapeutic interventions, standard follow-up management

Post-operative PSA Detectable PSA ≥ 0.2 ng/mL

- **pT4 NX,N0 M0**
  - Radiation Therapy (+/- ADT)
  - ADT alone
  - No therapeutic interventions

- **pTX N+ M0**
  - ADT alone
  - No therapeutic interventions, standard follow-up management

Salvage Therapy

- **Post-Prostatectomy**
  - Rising PSA or first post-operative PSA > 0.2 ng/mL
    - Radiotherapy
    - No therapeutic intervention

- **Post-Radiotherapy**
  - Selected subset of patients (e.g., low risk disease at diagnosis and long PSA doubling time and long disease-free interval) with three consecutive rises in PSA 3-4 months apart and PSA > 1.5 ng/mL
    - Prostatectomy
    - Brachytherapy (seed implant - not available in NS)
    - Cryotherapy (not available in NS)
    - No therapeutic intervention

Assess effect of treatment(s) on patient function (especially incontinence & sexual dysfunction) and psychosocial distress. Manage symptom(s) and distress as appropriate.
Metastatic and Incurable Prostate Cancer

Metastatic cancer or clinically detectable lymph node disease
- Immediate ADT
- Delayed ADT

High-risk disease (without proven metastases)
- Unlikely to be cured and/or
- Significant co-morbid disease
- Immediate or delayed ADT

Consider referral to Palliative Care service (see page 9) and/or provincial home care service

Hormone Refractory Prostate Cancer

Prostate cancer managed with ADT
• Rising PSA and/or
• Worsening radiographic disease and/or
• Worsening symptoms

Castrate Testosterone Level
- Yes
  - Castrate Testosterone Level
  - Secondary Hormonal Treatment
- No
  - Implement effective ADT

Persistent pain or other symptoms

Addition of anti-androgen agent to LHRH agonist or orchiectomy

Discontinuation of anti-androgen (if already on one)

Other Hormonal Treatment:
• Cyproterone
• Megestrol
• Ketoconazole
• Estrogen

Optimize analgesic therapy for pain management (see CCNS Guidelines for Management of Cancer-Related Pain)

Urological intervention (e.g. TURP)

Radiotherapy (localized or hemi-body)

Low dose steroids
(e.g. prednisone 5-10 mg/day or dexamethasone 1-2 mg/day)

Bisphosphonate therapy
(e.g. zoledronic acid 4 mg IV)
Management of Sexual Dysfunction

Pre-treatment assessment for normal sexual function

Initiate post-operative/post-treatment discussions (6-12 weeks after treatment):
• Consider institution of oral agents (sildenafil (Viagra®), tadalafil (Cialis®), vardenafil (Levitra®)) to conserve penile health
• Urologist/radiation oncologist

At 3-12 months post-treatment:
• Assess efficacy of oral agents and need for sexual function
• If ineffective, consider penile injection therapy
• Erectile Dysfunction clinic or urologist/radiation oncologist
• Consider couple counselling as appropriate

Reassess at 12 months:
• Sexual function, distress issues

Management of Incontinence

Pre-treatment visit:
• Assessment of bladder function
• Instruction on Kegel exercises
• Training on incontinence products
• Discussion with patient about incontinence

2-3 weeks post-operation (at time of catheter removal):
• Discussion with patient about incontinence
• Patient demonstration of Kegel exercises

Three months post-treatment:
• Discussion with patient about any incontinence
• Referral for Urodynamic studies, if necessary

One year post-treatment:
• Reassess level of continence, consider incontinence device if necessary

See Management of Psychosocial Issues (Full Version Part 8.12)
Management of Psychosocial Issues

Screening for Psychosocial Distress at diagnosis, and other significant transition points

Risk factors for psychosocial distress (e.g. depression, anxiety, adjustment disorders) in prostate cancer

Risk factors for distress:
- age < 60
- mental health history
- social isolation
- receiving ADT
- high burden of illness
- advanced stage of cancer
- unresolved urinary incontinence
- high sexual dissatisfaction
- multiple life stressors

Screening and intervention should include both the patient and his partner

Low Risk
- Periodic screening at diagnosis, six months after treatment completion, disease recurrence, progression to advanced disease

High Risk
- Routine screening at each visit through disease continuum

Referral as appropriate for identified psychosocial distress problem(s)

Management of Pain and Other Symptoms

Referral of a cancer patient who needs help with pain or symptom management, or for palliative care

To The Attending Oncology Team:
- See Full Version Page 23

To The Cancer Patient Navigator:
- 1-866-524-1234 from anywhere in Nova Scotia

To The District Palliative Care/Supportive Care Service:

South Shore Health:
- 902-634-7369 or 902-354-3436
South West Health:
- 902-742-3542 Ext. 414.
Annapolis Valley Health:
- 902-678-7381 Ext. 2270
Colchester East Hants Health Authority:
- 902-893-5554 Ext. 2306
Cumberland Health Authority:
- 902-667-5400 Ext. 6373
Pictou County Health:
- 902-752-7600 Ext. 4190
Guysborough Antigonish Strait Health Authority:
- 902-867-4296 or 902-867-4436
Cape Breton District Health Authority:
- 902-567-7846
Capital Health Cancer Care Program:
- 902-473-3119
Position Statement on Early Detection of Prostate Cancer

Background
Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer deaths in Canadian men. Nova Scotia has the third highest rate of deaths from prostate cancer in Canada.

CCNS Position on Early Identification of Prostate Cancer
Cancer Care Nova Scotia does not at this time support the implementation of a comprehensive population-based prostate cancer screening program for Nova Scotia. While we know that the PSA test may be used to detect early stage prostate cancer, there is insufficient evidence to suggest at this time that a decline in mortality rates from prostate cancer can be directly attributed to screening. As new evidence emerges, this statement will be re-evaluated.

Cancer Care Nova Scotia believes that early identification of prostate cancer requires a partnership between Nova Scotian men and their physicians.

• Men need to be aware of prostate cancer, and what it may mean for them.
• Men who have concerns about prostate cancer should discuss them with their physician.
• Physicians should discuss the potential benefits of early detection of prostate cancer with men over 50 who do not exhibit urological symptoms and those who are considered to be at greater risk for prostate cancer.

The risk of prostate cancer increases with age, especially after the age of 50. Men who have a family history of prostate cancer are more likely to develop prostate cancer. American evidence suggests that men of African heritage are at higher risk of prostate cancer. Physicians are encouraged to discuss the risks and benefits of prostate screening with men in a higher risk category beginning at the age of 40.

Early detection of prostate cancer involves the use of both the Digital Rectal Exam (DRE) and serum PSA determination. The PSA blood test may be used to detect prostate cancers at an early stage. This test is available to Nova Scotian men through their family physicians and following a discussion of the risks and benefits of prostate cancer screening. Men who have difficulty accessing this test through their physician should request a referral to another physician. It is important to recognize that PSA is accepted to be useful in the evaluation of symptomatic prostate disorders.

Guidelines for Health Professionals
The Genito-Urinary (GU) Cancer Site Team recommends that:

• Health professionals be aware of prostate cancer as the most common cancer in men.
• Health professionals recognize the increasing incidence of clinically significant prostate cancer reflecting the increased life expectancy of the current male population.
• Health professionals be aware of the natural history of prostate cancer. It is not advised to screen patients with significant co-morbidities or a limited life expectancy.
• Early detection of prostate cancer involves both the DRE and serum PSA determination.
• Age adjusted PSA reference values be the standard when PSAs are ordered.
• Appropriate counselling (including the risks and benefits of prostate cancer screening) be provided to men prior to initiating screening and that informed consent should be documented.
• Men who choose to be screened should be screened on an annual basis. The need for screening be re-evaluated as necessary based on the man’s health status.
• Student physicians continue to be trained in the technique of proper male genitourinary examination including DRE, and learning opportunities for practicing physicians be provided.
• Men who present with urological symptoms or have suspicious findings on physical examination require appropriate diagnostic investigations, including age-adjusted PSA and DRE regardless of age.

This statement was developed by the Genito-Urinary Cancer Site Team of Cancer Care Nova Scotia, with input from provincial stakeholders including health professionals and prostate cancer consumers. Release date: January, 2002.