Prostate Cancer Foundation

Prof Mohamed Haffejee
Head Academic Committee of the Prostate Cancer Foundation of South Africa

Urologist and Robotic Surgeon
University of the Witwatersrand
The Prostate Cancer Foundation of South Africa

VISION: Empowering South Africans through information and education, to act appropriately and minimise the impact of prostate cancer.

MISSION: To engage all South Africans through education, awareness, advocacy and research in addressing the prevention, treatment and ultimately cure of prostate cancer.
Patron of the Prostate Cancer Foundation of South Africa: ARCHBISHOP EMERITUS DESMOND TUTU

“If prostate cancer is detected at an early stage, the chance of survival and even cure is greatly increased.”

These are wise words from a wise man who is also the patron of the Prostate Cancer Foundation of South Africa: Archbishop Emeritus Desmond Tutu.

He knows what he is talking about because he was diagnosed and successfully treated for Prostate Cancer in 1997.
The Prostate Cancer Foundation of South Africa - Empowering South Africans through information and education, to act appropriately and minimise the impact of prostate cancer

“Every man is at risk for Prostate Cancer!”

Despite the massive impact that prostate cancer has on the health of men (it is estimated that 1 in 6 men will be affected), we are still not sure what causes it and why it affects some men and not others.

Fortunately, screening for prostate cancer is relatively simple and inexpensive and if detected early treatment results are highly successful. Of course, that doesn’t mean that we should stop researching the causes.

Unfortunately many men are still unaware of which screening tests are necessary, and at what age the tests need to be done. That’s why we are here, and if you’re reading this pamphlet then you can probably help too.
Visit the website at http://www.prostatecancerfoundation.co.za/ for more information on prostate cancer.
Revised Prostate Cancer Diagnostic and Treatment Guidelines 2013
The Prostate Cancer Foundation of South Africa
Publication Date: August 2013

ORIGINAL AUTHORS before 2012:
Prof. M. Haffejee, Prof. S. Wentzel, Prof. C.F. Heyns, Prof S.B.A. Mutambirwa, Dr. L. Coetzee, Dr C Steinmann, Dr P Porteus, Dr M Mackenzie, Dr M Bongers, Dr M. Bolus, Dr R. Rencken, Dr S. Kamba, Dr T. Naidoo, Dr B. Rapoport

These guidelines have subsequently been reviewed, adapted and updated by The Prostate Cancer Foundation of South Africa and in their current format represent only the views and opinions of the Prostate Cancer Foundation of South Africa.

AUTHORS AND REVIEWERS OF 2013 VERSION:
Dr. L. J. E. Coetzee MBChB(Pret.), MMed(Urol.)SA, F.C.S(Urol.)SA, Fellow in Uro-Oncology (Duke Univ. USA); Prof. S. B. A. Mutambirwa MBChB(Zim.), F.C.S(Urol.)SA, MMed(Urol.)SA; Dr. G.F.G.O. De Muelenare MBChB, MMed(RadT), MD; Prof. M. Haffejee MBCh(Wits), FC(Urol)SA; Dr. M. Mackenzie MBCh(Wits), FRCS Ed., F.C.S(Urol)SA, FHKCS.; Dr. P. T. Paradza MBChB(UZ), FC Rad(SA)Onc.

These guidelines were reviewed and are endorsed by The South Africa Urological Association (SAUA) in 2013:

SAUA REVIEWERS:
Prof. S. B. A. Mutambirwa, Prof. R. Barnes, Dr. M. Bigalke, Dr. M. Bongers, Dr. P. Chetty, Dr. L. Coetzee, Prof. M. L. S. de Kock, Prof. M. Haffejee, Prof. C. F. Heyns, Dr. M. Mackenzie, Dr. E. M. Moshokoa, Dr. A. Naudé, Dr P. Porteus, Prof. A M. Segone, Prof. S. Wentzel.

These guidelines are in the process of being reviewed by:
The South African Society of Medical Oncology (SASMO)
The South African Society of Clinical and Radiation Oncologists (SASCRO)
Revised guidelines will be published after obtaining the input of these societies
IMPORTANT:

Diagnostic and treatment guidelines are intended only as a guide for clinicians and patients.

The obligation to be fully informed of the latest available information pertaining to the diagnosis and treatment of prostate cancer lies with the clinician.

Diagnostic and treatment guidelines cannot factor in the individual characteristics of each patient, and it is therefore the clinician’s responsibility to determine whether the guidelines are relevant for each individual patient that they diagnose and treat.
Prevention of PCA

The use of 5-alpha-reductase inhibitors (5ARIs – finasteride & dutasteride) has been shown to reduce prostate cancer risk in placebo-controlled clinical trials.

Two large randomised studies showed that PCa diagnosed in men on 5ARI treatment was of higher grade than in the placebo group. These drugs are effective in the treatment of lower urinary tract symptoms in men with benign prostatic hyperplasia (BPH) but can currently not be recommended for prevention of PCa.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

- Digital rectal examination (DRE) and serum prostate specific antigen (PSA) screening of asymptomatic men reduces PCa mortality but increases overdiagnosis and overtreatment and is unavailable under the current state health system in RSA.
Give Prostate Cancer the finger!

Do your part to help "BEAT PROSTATE CANCER"

1. Get tested - have your DRE
   Have a Digital Rectal Examination (DRE) annually from the age of 40. A DRE is done for men to check for growths in or enlargement of the prostate gland. A tumour in the prostate can often be felt as a hard lump.

2. Sponsor an event or make a donation
   The more awareness that we can create about prostate cancer, the more enabled we will be to motivate men to undergo annual screening. We also need funding to be able to conduct research so that we can better understand all aspects of the disease. If you have the resources to assist us we’d love to meet with you to explore how we can work together to:

3. Visit our website
   Go to www.prostate-ca.co.za for more information about prostate cancer and how to beat it.

Beat Prostate Cancer

Head Office: 011-7911791
E-mail: info@prostate-ca.co.za
Website: www.prostate-ca.co.za
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

- PSA testing is recommended in males with a life expectancy of more than 10 years in the following situations:
  
  From the age of 40:
  - in black African patients
  - in those with a positive family history of prostate and/or breast cancer in a first degree relative

  From the age of 45 years in all other males.
  - in addition patients with a history of lower urinary tract symptoms (LUTS) and/or clinical suspicion of prostate cancer regardless of age group

Periodic reassessment will be determined by the initial PSA and DRE result.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

Diagnostic approach to prostate assessment

- A focused urological history
- Clinical examination form the basis of all assessments.

- DRE is recommended in all patients.
  - An abnormal DRE is suggested by the presence of nodules, asymmetry, irregularity, and tethering of the overlying mucosa.
  - A normal DRE does not exclude prostate cancer.
- DRE should include palpation of the rectum and inspection of the faeces.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

Prostate specific antigen (PSA)

PSA related to cancer screening:
- is not reliable in the presence of active urinary tract infection (UTI), recent urinary tract instrumentation and/or urinary retention.

Treat the UTI and repeat the PSA after 6 weeks.

Routine DRE does not elevate PSA significantly.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

PCA3

Is a urine test having the advantage over PSA that it is specific to prostate cancer and not other conditions such as BPH and prostatitis.

May be of value:
- in stratifying risk categories in patients in whom prostate cancer is suspected.
- in patients who have had one or more negative prostate biopsies and who demonstrate a rising PSA,
- patients with atypical acinar proliferation (ASAP) lesions
- even patients on active surveillance, who may be spared an unnecessary biopsy.

This test is done on the first (10ml) post prostate massage urine. PCA3 is not currently recommended to be used in place of PSA testing.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

Indications for prostate biopsy

The indications for prostate biopsy include an abnormal DRE and/or a total PSA above the age related norm.
At first presentation if DRE is normal and PSA is below 10 a repeat PSA in 6 weeks is advised.

Normal age related total PSA reference range:
- 40 – 50 years: 0 - 2.5 ng/ml
- 50 – 60 years: 0 - 3.5 ng/ml
- >60 years: 0 - 4.0 ng/ml
Indications for prostate biopsy

Free to total PSA ratio (FT) and complex PSA should be performed at the clinician’s request in men with a total PSA above the age related reference range but less than 10ng/ml with a negative first prostate biopsy in order to improve decision making in addition to the DRE. If FT is > 20% follow up as opposed to re biopsy is the preferred option.

An increased PSA velocity, (defined as an increase of greater than 0.75ng/ml or 25% per year) is also an indication for a prostate biopsy.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

Biopsy technique

Antibiotic prophylaxis is essential and oral quinolones are recommended as the first choice.

Written informed consent is required even if biopsy is done without local anaesthesia as an outpatient procedure.

Diagnosis can be made without biopsy in elderly patients with a clinically malignant prostate on DRE, markedly raised PSA and/or other clinical evidence of advanced PCa.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

Biopsy technique

Trans-rectal ultrasound (TRUS) images are of limited value in diagnosing prostate cancer. Its most important use is to place needle biopsies accurately. TRUS guided biopsies are optimal, but digital guidance is acceptable if TRUS is not available. Digitally guided biopsies can be used to target palpable nodules. It is recommended that between six and twelve biopsy cores be taken depending on the size of the prostate and localization of the lesion. Biopsy cores should include lateral, para-sagittal and suspicious areas. More biopsies can be taken at the discretion of the urologist but runs the risk of altering the dynamics of active surveillance (AS) and resulting in overtreatment.
B. DETECTION, DIAGNOSIS AND SCREENING OF PROSTATE CANCER

Indications for repeat biopsy

The indications for repeat biopsy are complex and this decision should be based on extensive discussion between the patient and his urologist including the histological finding of high grade prostatic intraepithelial neoplasia [PIN III] and atypical small acinar proliferation (ASAP), rising PSA, DRE changes and possibly use of PCA3.
C. CLINICALLY LOCALIZED PROSTATE CANCER

Various staging investigations including bone scan, CT scanning, TRUS, lymph node dissection (LND) and MRI may be utilized. Since the incidence of skeletal metastases is negligible when PSA is below 10, bone scans are only advised when PSA is > 10 and/or Gleason score is 8 – 10 and/or T Stage is > T2.

- Radical prostatectomy – (RP)
  - Retropubic
  - Perineal
  - Laparoscopic
  - Robotic assisted laparoscopic

- Radiotherapy (RT)
  - External beam (3-dimensional conformal or intensity modulated)
  - Interstitial brachytherapy

- Cryotherapy

- High intensity focused ultrasound (HIFU)

- Androgen deprivation therapy (ADT)

- Deferred treatment
  - Active surveillance
  - Watchful waiting

Are still experimental outside clinical trials
C. CLINICALLY LOCALIZED PROSTATE CANCER

Active surveillance (AS)

Active surveillance is an increasingly recognized management option for men with low-risk prostate cancer. Despite encouraging evidence for oncologic efficacy and reduction in morbidity, several barriers contribute to the underuse of this management strategy. Consistent selection criteria as well as identification and validation of triggers for subsequent intervention are essential.

Active surveillance consists of regular monitoring of patients with the intent of curative treatment if disease progression occurs. Patients should commit to a regular follow-up with DRE and PSA. A repeat biopsy is indicated after 12 – 24 months or if there is any sign of disease progression by examination or markers.
C. CLINICALLY LOCALIZED PROSTATE CANCER

Active surveillance (AS)

Active surveillance is an option in men with a tumor matching or approaching the definition of "indolent" or insignificant which would include:

- PSA < 10ng/ml
- Gleason score ≤ 6
- Stage T1-2a
- PSA density < 0.15-0.2
- ≤ 50% of PCa in any biopsy core
Watchful waiting (WW)

Watchful waiting consists of regular monitoring of patients with intent of palliative treatment with disease progression. Patients should commit to a regular follow-up with DRE and PSA.

These are usually patients with low risk disease and/or with life expectancy below 10 years and/or an existing co-morbidity profile which places them at risk of death from other causes in less than ten years.
D. RISK STRATIFICATION

Risk stratification is an important part in planning the most appropriate treatment option for the patient and assessing potential outcomes.

**Low risk disease**

- T1 to T2a clinical stage
- Gleason score of 2 to 6
- PSA less than 10ng/ml

If life expectancy is less than ten years then treatment options include watchful waiting. If the life expectancy exceeds ten years then treatment options include active surveillance, external beam radiotherapy (ERBT), interstitial brachytherapy (IB) and radical prostatectomy (RP).
D. RISK STRATIFICATION

Intermediate risk disease

T2b – T2c clinical stage and/or
Gleason 7 (3+4) and/or
PSA 10 – 20ng/ml

If the expected survival is less than ten years then treatment options include watchful waiting. If the life expectancy exceeds ten years then treatment options include active surveillance, external beam radiotherapy, interstitial brachytherapy and radical prostatectomy with a lymph node dissection or combinations of the above.
D. RISK STRATIFICATION

High risk disease

Clinical stage T3a or T3b and/or
Gleason 7 (4+3) to 10 and/or
PSA>= 20

This group represents locally advanced but potentially curable
disease. Initial therapeutic options include radiotherapy with ADT,
radical prostatectomy with pelvic lymph node dissection, ADT
alone or trimodal therapy (brachytherapy plus EBRT plus ADT).
E. FAILED LOCAL THERAPY

Post radical prostatectomy
In the presence of positive margins options include, ADT, radiation therapy and WW. Where the histology reveals positive lymph nodes or seminal vesicle involvement then ADT and/or ERBT are the preferred options.

Rising PSA post definitive management
Options include WW, ADT and targeted radiotherapy to pelvis/prostate bed or metastatic lesions.

Post radiation therapy
Management options for recurrences following radiotherapy or brachytherapy include ADT, watchful waiting and possibly salvage radical prostatectomy in highly selected cases.
F. LOCALLY ADVANCED OR METASTATIC PROSTATE CANCER

The standard treatment for locally advanced PCa is ADT which delays clinical progression and improves quality of life (QOL). At this stage, chemotherapy should be considered only in castrate resistant PCa (CRPC). RP and RT can be considered in selected cases in combination with ADT.

The goals of treatment are delayed disease progression, improved quality of life and possibly increased survival. The choice of treatment is dependent on an informed patient decision and also on the availability of treatment, costs and complications.

The other standard indication for ADT is metastatic PCa. Symptomatic patients with localised prostate cancer unsuitable for curative treatment represent a further indication.
F.  LOCALLY ADVANCED OR METASTATIC PROSTATE CANCER

Types of ADT

First line

**Medical**
- Parenteral oestrogens
- Luteinizing hormone releasing hormone (LHRH) antagonists
- Luteinizing hormone releasing hormone (LHRH) agonists
- Antiandrogens
- Combinations of above

**Surgical**
- Bilateral orchidectomy or
- Seminectomy
- Combination of above with antiandrogens

Second line

Ketoconazole
Withdrawal of antiandrogens
Corticosteroids
F. LOCALLY ADVANCED OR METASTATIC PROSTATE CANCER

Chemotherapy

First line = Docetaxel / Carbazitaxel

Second line = Abiraterone

In CRPC the use of chemotherapy may be indicated. Neuro-endocrine differentiation represents a small subset in which platinum based chemotherapy is indicated.
F. **LOCALLY ADVANCED OR METASTATIC PROSTATE CANCER**

**Treatment options (androgen sensitive disease unless otherwise stated)**

<table>
<thead>
<tr>
<th>TNM</th>
<th>Primary recommended</th>
<th>Optional</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1, T2, N0, M0</td>
<td>See above</td>
<td>Neo-adjuvant LHRH agonist prior to radiotherapy</td>
</tr>
<tr>
<td>T3, T4, N0, M0</td>
<td>ADT plus RT or RP</td>
<td>Bicalutamide monotherapy</td>
</tr>
<tr>
<td>N+</td>
<td>Continuous ADT</td>
<td>Intermittent / sequential ADT</td>
</tr>
<tr>
<td>M+</td>
<td>Continuous ADT</td>
<td>Anti-androgen therapy 14 days prior to LHRH agonists to prevent flare/spinal compression Intermittent / sequential ADT</td>
</tr>
<tr>
<td>M+ CRPC</td>
<td>ADT must continue plus chemotherapy (taxanes +/- corticosteroids)</td>
<td>ADT in addition to: Mitoxantrone, Corticosteroid Estramustine and vinblastine Platinum based chemotherapy Strontium, samarium Bisphosphonate Denosumab, PCa vaccines, MDV3100, Carbazitaxel, Abiraterone acetate</td>
</tr>
</tbody>
</table>
1. Although surgical and medical castration have been shown to have equivalent efficacy, surgical castration is unacceptable to some men. On the other hand long term LHRH therapy usually is more expensive and requires patient compliance.

2. Early ADT has been shown to delay time to progression and may have a survival benefit over delayed ADT in locally advanced PCa.

3. Intermittent therapy could be used as there may be a reduction in side effects as well as cost. Efficacy of intermittent therapy as opposed to continuous ADT remains to be proven, but has shown some QOL benefits.

4. Timing of chemotherapy is important as chemotherapeutic agents are more effective in patients with good performance status. Chemotherapy should be considered after failure of 2 lines of ADT. After 3 cycles of chemotherapy re-evaluate for response. If there is a significant reduction of PSA and/or improvement in symptom score, response is implied. There is currently no clear indication for second line chemotherapy. Carbazitaxel is registered for use after failure of docetaxel.

5. Patient monitoring on ADT includes regular history, examination and appropriate laboratory and radiological investigations. Patients on chemotherapy may require more frequent evaluation.
G. PREVENTION AND TREATMENT OF COMPLICATIONS RELATED TO PROSTATE CANCER THERAPY

These complications are possibilities for each mode of therapy and will differ depending on patient factors, facilities and the intrinsic nature of the procedure performed.

1. Erectile dysfunction
2. Stricture/Bladder neck stenosis
3. Incontinence
4. Radiation proctitis
5. Radiation cystitis
6. Urinary retention
7. Gynecomastia
8. Hot flushes
9. Osteoporosis associated with ADT
10. Depression
1. **Erectile dysfunction**

**Epidemiology**
- Frequently coexists in patients with PCa
- Immediate after surgery, tendency to improve
- Develops later after radiation therapy - tendency to worsen with time
- Incidence comparable at 2 years after both surgery and radiation

**Prevention**
- Nerve sparing surgery
- Early phosphodiesterase-5 (PDE$_5$) inhibitor therapy, vacuum device or intra-cavernosal prostaglandin after radical prostatectomy
- Bicalutamide as monotherapy or intermittent ADT
- Active surveillance

**Treatment of erectile dysfunction**
- Phospho-diesterase 5 (PDE$_5$) inhibitors
- Intracavernosal therapy
- Vacuum device
- Penile prosthesis
G. PREVENTION AND TREATMENT OF COMPLICATIONS RELATED TO PROSTATE CANCER THERAPY

2. Stricture/Bladder neck stenosis
   Prevention
   - Optimal surgical and radiation technique
   - Active surveillance
   Treatment
   - Dilatation
   - Optical urethrotomy
3. **Incontinence**

**Epidemiology**
- Can occur after both surgery and radiation therapy or be independent of PCa treatment. Incidence, pathogenesis and treatment are different
- Always exclude local or systemic cause of incontinence (including medication)

**Prevention**
- Active surveillance
- Nerve sparing surgery
- Controlled exposure to radiation
- Pelvic floor exercise peri-operatively
### 3. Incontinence

<table>
<thead>
<tr>
<th>Mild (1-2 pads per day)</th>
<th>Moderate (2-5 pads per day)</th>
<th>Severe (&gt;5 pads per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic floor exercise</td>
<td>Pelvic floor exercise</td>
<td>Artificial sphincter</td>
</tr>
<tr>
<td>Bulking agents</td>
<td>Bulking agents</td>
<td>Penile clamp</td>
</tr>
<tr>
<td>Biofeedback</td>
<td>Slings</td>
<td>Urethral occlusion devices</td>
</tr>
<tr>
<td>Pharmacological:</td>
<td>Penile clamp</td>
<td></td>
</tr>
<tr>
<td>$\alpha$-stimulants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticholinergics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta_3$ Agonists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urethral occlusion devices</td>
<td>Urethral occlusion devices</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Artificial sphincter</td>
<td></td>
</tr>
</tbody>
</table>

**NOTES** for invasive management of incontinence:
- Wait at least two years, if patient continues to improve
- If no improvement, wait one year
G. PREVENTION AND TREATMENT OF COMPlications RELATED TO PROSTATE CANCER THERAPY

4. **Radiation proctitis**
   (and other bowel complications after radiation therapy)

   - CO₂ laser therapy
   - Formalin instillation
   - Prednisone enema
   - Hyperbaric oxygen
   - Colostomy/Laparotomy
   - Generally avoid biopsy of rectal lesion
G. PREVENTION AND TREATMENT OF COMPLICATIONS RELATED TO PROSTATE CANCER THERAPY

5. **Radiation cystitis**

- Clorpactin, silver nitrate, formalin instillation
- Prednisone instillation
- Hyperbaric oxygen
- Urinary diversion
G. PREVENTION AND TREATMENT OF COMPLICATIONS RELATED TO PROSTATE CANCER THERAPY

6. **Urinary retention**

- Alpha blockers
- Catheterization
- TUR prostate (recommended to wait at least 6-10 months after real time brachytherapy)
- Urethral stricture management
7. **Gynecomastia**

**Epidemiology**
Can be primary or secondary to any hormonal manipulation, but is of special importance when bicalutamide 150 mg monotherapy (B-150) is used.

**Notes on B-150 therapy:**

**Prevention**
Prophylactic mastectomy or single dose (10Gy) radiotherapy or 3 consecutive doses of 250 cGy; prophylactic EBRT significantly reduces incidence if employed prior to initiation of therapy.

**Treatment**
Subareolar mastectomy
G. PREVENTION AND TREATMENT OF COMPLICATIONS RELATED TO PROSTATE CANCER THERAPY

8. Hot flushes

Prevention and treatment
- Lifestyle, Diet
- Cyproterone acetate
- Bicalutamide monotherapy
- Intermittent ADT
- Clonidine
- Low dose oestrogen and or progesterone
G. PREVENTION AND TREATMENT OF COMPLICATIONS RELATED TO PROSTATE CANCER THERAPY

9. **Osteoporosis associated with ADT**

- Prevention and treatment
- Lifestyle/Exercise/Diet
- Bicalutamide monotherapy
- Intermittent ADT
- Calcium supplementation
- Vitamin D
- Bisphosphonates
- Denosumab
G. PREVENTION AND TREATMENT OF COMPLICATIONS RELATED TO PROSTATE CANCER THERAPY

10 Depression

Prevention and treatment
Lifestyle/Exercise/Diet
Evaluate patients regularly/referral to psychiatrist/psychologist
Anti-depressants
H. TREATMENT OF COMPLICATIONS OF ADVANCED PROSTATE CANCER AND CRPC

I. Local complications

A. Infiltration

<table>
<thead>
<tr>
<th>Peri-prostatic LUTS + retention</th>
<th>ADT naive</th>
<th>CRPC</th>
<th>Palliation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ADT</td>
<td>TUR prostate</td>
<td>Suprapubic catheter</td>
</tr>
<tr>
<td></td>
<td>± Transurethral resection prostate (TURP)</td>
<td>± EBRT</td>
<td>Urinary diversion</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prostate stents</td>
</tr>
<tr>
<td>Ureter</td>
<td>ADT</td>
<td>Assess general condition and decide on palliation</td>
<td>Only if good performance status</td>
</tr>
<tr>
<td></td>
<td>Bypass - J-stents</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nephrostomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>EBRT and/or</td>
<td>EBRT and/or Colostomy</td>
<td>Colostomy for obstruction</td>
</tr>
<tr>
<td></td>
<td>ADT and/or Colostomy</td>
<td></td>
<td>Pain relief</td>
</tr>
<tr>
<td></td>
<td>Colostomy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
H. TREATMENT OF COMPLICATIONS OF ADVANCED PROSTATE CANCER AND CRPC

I. Local complications

B. Urethral / Bleeding

Cystoscopy + transurethral resection and fulguration in combination with ADT

- Stop
  - Follow-up
    - Mild
      - Medical
        - Oestrogens
        - Tranexamic acid
      - Radiotherapy
    - Severe
      - Radiotherapy ± Embolization (Internal iliac artery)
      - Urinary diversion
- Recurrence
II. Systemic Complications

<table>
<thead>
<tr>
<th></th>
<th>ADT Naïve</th>
<th>CRPC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lymphatic obstruction</strong></td>
<td>ADT</td>
<td>Supportive therapy</td>
</tr>
<tr>
<td><em>(Lymphoedema)</em></td>
<td>Supportive therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Hematogenous metastases</strong></td>
<td>ADT</td>
<td>1st line Bisphosphonates + chemotherapy</td>
</tr>
<tr>
<td>1. Skeletal</td>
<td>Bisphosphonates</td>
<td>2nd line Symptomatic Asymptomatic</td>
</tr>
<tr>
<td></td>
<td>EBRT</td>
<td>Symptomatic</td>
</tr>
<tr>
<td></td>
<td>Analgesics</td>
<td>Asymptomatic Follow-up</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EBRT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Isotopes (Strontium, Samarium)</td>
<td></td>
</tr>
<tr>
<td><strong>2. Soft tissue</strong></td>
<td>ADT</td>
<td>Palliation</td>
</tr>
<tr>
<td></td>
<td>EBRT</td>
<td>+ Chemotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+ Radiotherapy</td>
</tr>
<tr>
<td><strong>3. Bone marrow metastases</strong></td>
<td>ADT</td>
<td>Treat medical condition on merit (e.g. blood</td>
</tr>
<tr>
<td></td>
<td>Treat medical condition on merit (e.g. blood transfusion)</td>
<td>transfusion)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anaemia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disseminated Intravascular</strong></td>
<td>Coagulation (DIC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>4. Spinal cord compression</strong></td>
<td>Emergency orchidectomy</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
<td>Supportive measures</td>
</tr>
<tr>
<td></td>
<td>EBRT</td>
<td>EBRT</td>
</tr>
<tr>
<td></td>
<td>Spinal decompression</td>
<td>Spinal decompression</td>
</tr>
</tbody>
</table>
"There is life after Prostate Cancer"

Patron of the Prostate Cancer Foundation: Archbishop Emeritus Desmond Tutu

BEAT Prostate Cancer Foundation of South Africa
Who is the Prostate Cancer Foundation of SA?

The Prostate Cancer Foundation is an organisation led by a group of people who have a direct interest in prostate cancer. It includes some of South Africa’s top medical specialists who diagnose, treat and research prostate cancer on a daily basis. It also includes members from pharmaceutical and medical companies who provide the treatments for prostate cancer and who help fund the foundation’s costs and projects and volunteer their time to help us to implement our programmes.

The foundation also provides a forum for men and their families whose lives have been directly affected by prostate cancer. Some are involved in assisting others who have recently been diagnosed, some have been willing to share their story on our website and some have provided donations.

It is this involvement of the medical specialists who research and treat prostate cancer, the companies that develop the treatments, and the patients and their families affected by the disease that make our organisation unique and enables us to fight the disease from all angles. We hope you’ll join us in the fight so that together we can:

“BEAT PROSTATE CANCER”

How can you help beat Prostate Cancer?

If you are a man over the age of 40 and have never been screened for Prostate Cancer this is the single most important thing that you can do!

Screening for Prostate Cancer

Two tests are used to check for Prostate Cancer:

1. The Prostate Specific Antigen test (PSA)

For a PSA test blood is drawn and sent to the lab. This test gives an indication of whether something is wrong with your prostate. It could be cancer or it could just be an infection so don’t panic if it comes back high, your doctor will do further tests to determine exactly what’s wrong. It’s not just the score that’s important, but also how much it has changed year-on-year. As the PSA test is not completely fool proof, you will also need to go for a DRE.

2. The Digital Rectal Examination (DRE) also known as “The Finger”

A DRE involves your doctor inserting a gloved and lubricated finger into the rectum so that they can feel the prostate for any abnormal lumps. Some men are afraid that this test is going to be painful but that’s just not true. It’s a minute of minor discomfort

A simple DRE could save your life!
If you organise wellness days or wellness programmes

You are in the unique position to be able to arrange for education and awareness about prostate cancer which can help save lives. You may even be able to organise PSA tests for the men over 45 in your organisation. Call us, we have education and promotional materials and can arrange for on-site PSA testing.

If you have lost a loved one to Prostate Cancer

The most devastating result of prostate cancer is when it leads to the death of a loved one. Nothing can bring that person back, but we would like to afford you the opportunity to pay tribute to the person whom you lost to prostate cancer through our memorial wall on our website. This will also enable friends and family members to make donations in memory of the person that you lost to prostate cancer. All donations will help us in the on-going fight to:

“BEAT PROSTATE CANCER”

“Go for an annual check-up!”
Understanding Cancer

- **Cancer** begins in **cells**, the building blocks that make up **tissues**.
- Tissues make up the **organs** of the body.
- Normally, cells grow and divide to form new cells as the body needs them. When cells grow old, they die, and new cells take their place.
- Sometimes, this orderly process goes wrong. New cells form when the body does not need them, and old cells do not die when they should. These extra cells can form a mass of tissue called a growth or **tumor**.
- Tumors can be **benign** or **malignant**.
• **Benign tumors** are not cancer:
  – Benign tumors are rarely life-threatening.
  – Generally, benign tumors can be removed. They usually do not grow back.
  – Cells from benign tumors do not invade the tissues around them.
  – Cells from benign tumors do not spread to other parts of the body

• **Malignant tumors** are cancer:
  – Malignant tumors are generally more serious than benign tumors. They may be life-threatening.
  – Malignant tumors often can be removed. But sometimes they grow back.
  – Cells from malignant tumors can invade and damage nearby tissues and organs.
  – Cells from malignant tumors can spread (metastasize) to other parts of the body.
  – Cancer cells spread by breaking away from the original (primary) tumor and entering the bloodstream or lymphatic system.
  – The cells invade other organs and form new tumors that damage these organs. The spread of cancer is called metastasis.
The Prostate

- The prostate is part of a man's reproductive system.
- It is located in front of the rectum and under the bladder.
- It surrounds the urethra, the tube through which urine flows.
- A healthy prostate is about the size of a walnut.
- The prostate makes part of seminal fluid.
- During ejaculation, seminal fluid helps carry sperm out of the man's body as part of semen.
- Male hormones (androgens) make the prostate grow.
- The testicles are the main source of male hormones, including testosterone.
- The adrenal gland also makes testosterone, but in small amounts.
- If the prostate grows too large, it squeezes the urethra. This may slow or stop the flow of urine from the bladder to the penis.
Epidemiology

- Third most common cause of death from cancer in men in the Western world\(^1\)
- First and second most commonly diagnosed cancer in men in the US and EU, respectively\(^2\)-\(^3\)
- 237,800 men were newly diagnosed in the EU in 2004 accounting for 15.5% of all male cancers\(^2\)

\(^3\)Greenlee RT et al. *CA Cancer J Clin*. 2000, 50, 7-33
Age-specific incidence rates of prostate cancer in UK (1975-2001)

http://info.cancerresearchuk.org/cancerstats/prostate/incidence/
A man with prostate cancer may not have any symptoms. For men who have symptoms of prostate cancer, common symptoms include:

- **Urinary problems**
  - Not being able to urinate
  - Having a hard time starting or stopping the urine flow
  - Needing to urinate often, especially at night
  - Weak flow of urine
  - Urine flow that starts and stops
  - Pain or burning during urination

- Difficulty having an *erection*

- Blood in the urine or semen

- Frequent pain in the lower back, hips, or upper thighs

- Often, these symptoms are not due to cancer. BPH, an infection, or another health problem may cause them.

- Any man with these symptoms should tell his doctor so that problems can be diagnosed and treated as early as possible. He may see his regular doctor or a *urologist*.

- A urologist is a doctor whose specialty is diseases of the urinary system
Risk Factors

• No one knows the exact causes of prostate cancer.
• Doctors often cannot explain why one man develops prostate cancer and another does not.
• However, we do know that prostate cancer is not contagious.
• You cannot "catch" it from another person.
• Research has shown that men with certain risk factors are more likely than others to develop prostate cancer. A risk factor is something that may increase the chance of developing a disease.
• Studies have found the following risk factors for prostate cancer:

• **Age:** Age is the main risk factor for prostate cancer.
  – This disease is rare in men younger than 45.
  – The chance of getting it goes up sharply as a man gets older.

• **Family history:** A man's risk is higher if his father or brother had prostate cancer.

• **Race:** Prostate cancer is more common in African American men than in white men, including Hispanic white men. It is less common in Asian and American Indian men.

• **Certain prostate changes:**
  – Men with cells called high-grade *prostatic intraepithelial neoplasia* (PIN) may be at increased risk for prostate cancer.
  – These prostate cells look abnormal under a microscope.

• **Diet:**
  – Some studies suggest that men who eat a diet high in animal fat or meat may be at increased risk for prostate cancer.
  – Men who eat a diet rich in fruits and vegetables may have a lower risk.
Screening

• Your doctor can check you for prostate cancer before you have any symptoms.

• Screening can help doctors find and treat cancer early.

• **Digital rectal exam**: The doctor inserts a lubricated, gloved finger into the rectum and feels the prostate through the rectal wall. The prostate is checked for hard or lumpy areas.

• **Blood test for prostate-specific antigen (PSA)**: A lab checks the level of PSA in a man's blood sample. A high PSA level is can be caused by BPH or prostatitis (inflammation of the prostate). Prostate cancer may also cause a high PSA level.

• The digital rectal exam and PSA test can detect a problem in the prostate. They cannot show whether the problem is cancer or a less serious condition. Your doctor will use the results of these tests to help decide whether to check further for signs of cancer.
Prostate-specific antigen (PSA)

• Serin protease produced almost exclusively by the epithelial cells of the prostate
• Contributes to increase sperm motility
• Normally found in low concentration in serum (<4 ng/ml)
• Not specific of prostate cancer. Can be raised in benign prostatic hyperplasia, prostatitis, urological manipulations
• Continuum prostate cancer risk at all PSA values. No cut-off with simultaneous high sensitivity and specificity to detect cancer.

Thompson *JAMA* 2005, 294, 66-70
TNM system
- Tumor, node, metastasis
  - T stage: T1 (incidental tumor) through T4 (locally advanced disease)
  - N stage: NO (no spread to lymph nodes) through N1 (spread to lymph nodes)
  - M stage: M0 (no spread to distant organs) through M1 (spread to bones or distant organs)

Figure 2: Tumor stages
More precise methods lead to earlier treatment

Grading and staging prostate cancer

- Gleason system
  - Grades degree of irregularity of biopsied cancer cells
  - Predicts aggressiveness of disease
    - Grade 1 (relatively little change) to grade 5 (significant change)
    - Sum of the 2 most prevalent grades found in biopsy samples represents total Gleason score (2–10)
    - Gleason score > 7 indicates more aggressive cancer

Figure 1: Gleason grades
Metastasis

- Lung
- Liver
- Bone
- Epidural space
Bone scan
Men with prostate cancer have many treatment options. The treatment that is best for one man may not be best for another.

Treatment may involve
- surgery,
- radiation therapy,
- hormone therapy.
- watchful waiting,
Treatment Methods

• Cancer treatment is either *local therapy* or *systemic therapy*:

• **Local therapy**: Surgery and radiation therapy are local treatments. They remove or destroy cancer in the prostate. When prostate cancer has spread to other parts of the body, local therapy may be used to control the disease in those specific areas.

• **Systemic therapy**: Hormone therapy is systemic therapy. Hormones are given to control cancer that has spread.

• The treatment that is right for you depends on the stage of the cancer, the grade of the tumor, your symptoms, and your general health. Your doctor will describe your treatment choices and the expected results.
Prognosis at initial diagnosis

— 95% of patients are initially diagnosed with localized or regional disease
  • 5-year survival: 100%

— 5% of patients are initially diagnosed with metastatic disease
  • 5-year survival: 34%
Radical prostatectomy

Figure 1: Structures removed during radical prostatectomy
Radiotherapy and cryotheraphy

- External Beam Radiation
- Brachytherapy
- Cryotherapy

Figure 1: Brachytherapy/seed implantation
## Hormone/androgen-deprivation therapy

<table>
<thead>
<tr>
<th>General benefits</th>
<th>General risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Clinical improvement in up to 80% of recipients</td>
<td>- Fatigue</td>
</tr>
<tr>
<td></td>
<td>- Tumor flare = bone pain, bladder dysfunction</td>
</tr>
<tr>
<td></td>
<td>- Sexual dysfunction</td>
</tr>
<tr>
<td></td>
<td>- Loss of libido</td>
</tr>
<tr>
<td></td>
<td>- Hot flashes</td>
</tr>
<tr>
<td></td>
<td>- Spinal metastases → spinal cord compression = lower back pain, weakness in lower extremities, difficulty excreting</td>
</tr>
</tbody>
</table>
Orchiectomy (surgical castration)
— Complete removal of testes
— Currently not commonly done

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cost</td>
<td>• Psychological effect</td>
</tr>
<tr>
<td>• Compliance</td>
<td>• Erectile dysfunction</td>
</tr>
<tr>
<td>• Low mortality rates</td>
<td>• Hot flashes</td>
</tr>
<tr>
<td></td>
<td>• Rapid clinical response (24–48 hours postsurgery)</td>
</tr>
<tr>
<td></td>
<td>• Loss of libido</td>
</tr>
<tr>
<td></td>
<td>• Infection at wound site</td>
</tr>
</tbody>
</table>