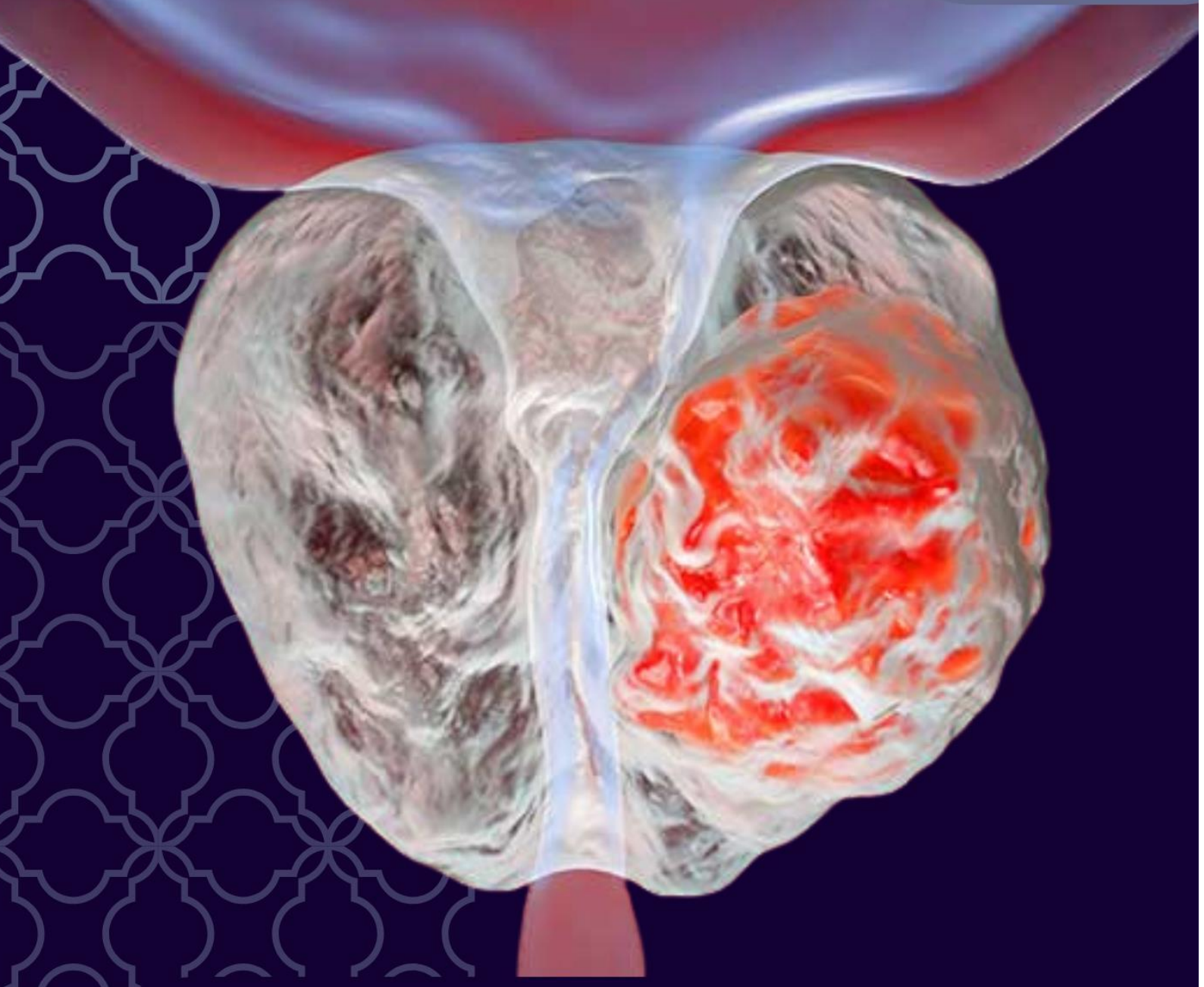
National Guideline for the diagnosis and treatment of

Prostate Cancer

2025



World Health Organization
Maldives

Ministry of Health
Republic of Maldives

Version Number	Version Date	Description of change
1	08/12/2025	Initial release

DOCUMENT NUMBER: MOH-QA/G/25/214-0

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Published by:	Ministry of Health, Maldives

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1. INTRODUCTION

Prostate cancer is a growing public health concern in the Maldives, reflecting a global trend of increasing incidence with aging populations[1]. While comprehensive national cancer registry data remain limited, hospital-based reports from Indira Gandhi Memorial Hospital (IGMH) and Tree Top Hospital indicate that prostate cancer is among the top ten malignancies affecting Maldivian men, accounting for approximately 7–8% of all male cancers[2]. Most cases present at advanced or metastatic stages due to the lack of organized screening programs, limited awareness, and delays in referral and diagnosis.

In the Maldives, diagnostic capacity for prostate cancer is primarily concentrated in Malé, with histopathological confirmation and PSA testing available at tertiary centers. Advanced imaging modalities such as MRI pelvis, bone scans, and PSMA PET-CT are often performed overseas under Aasandha coverage[2]. As life expectancy increases and the burden of non-communicable diseases rises, establishing a national framework for early detection, risk-based management, and follow-up of prostate cancer has become essential.

This document adapts key international standards, including those from the **European Society for Medical Oncology (ESMO)** and the **National Comprehensive Cancer Network (NCCN)**, to the Maldivian healthcare context.

2. LITERATURE REVIEW

Globally, prostate cancer is the **second most common cancer in men** and the **fifth leading cause of cancer-related deaths**[1]. The incidence varies widely, with the highest rates observed in high-income regions such as North America, Northern Europe, and Oceania, largely due to widespread PSA screening[5]. In contrast, South Asian nations, including the Maldives, Sri Lanka, and India, report lower incidence rates but higher proportions of advanced disease at diagnosis[6].

The **introduction of PSA testing** in the 1990s significantly altered prostate cancer epidemiology, leading to earlier detection but also raising concerns regarding overdiagnosis and overtreatment[7]. The **European Randomized Study of Screening for Prostate Cancer (ERSPC)** demonstrated that PSA-based screening reduced prostate cancer mortality by 20% over 13 years[8], while the **Prostate,**

Lung, Colorectal, and Ovarian (PLCO) trial found no significant difference in overall mortality[9]. These contrasting results have shaped the nuanced approach to PSA-based screening worldwide.

Recent advances include **risk stratification**, **active surveillance** for low-risk disease, and **multimodal therapy** for high-risk or metastatic cases. Novel androgen receptor inhibitors such as abiraterone, enzalutamide, and apalutamide have significantly improved survival in metastatic settings[10]. Genomic profiling and PSMA PET-CT imaging now guide more precise treatment decisions.

3. SIGNS AND SYMPTOMS

Prostate cancer often develops insidiously, with many men remaining asymptomatic in early stages. When symptomatic, presentations may include:

- **Lower urinary tract symptoms (LUTS):** Frequency, urgency, nocturia, hesitancy, weak stream.
- **Hematuria or hematospermia.**
- **Pelvic or perineal discomfort.**
- **Bone pain or pathological fractures** (indicative of metastases).
- **Unintentional weight loss or fatigue.**

Differentiation between benign prostatic hyperplasia (BPH) and malignancy requires appropriate clinical and biochemical evaluation[6].

4. SCREENING AND EARLY DETECTION

4.1 Target Population

- **Average risk:** Men aged **55 to 70 years and above.**
- **High risk:** Men aged **45 years and above** with family history (first-degree relative with prostate cancer).

4.2 Screening Protocol

- **Prostate-Specific Antigen (PSA):** Annual or biennial testing based on baseline results.
- **Digital Rectal Examination (DRE):** Annually for men >50 years or >45 with risk factors.

Interpretation of PSA Levels:

PSA Level (ng/mL)	Recommended Action
<2.5	Routine repeat every 2 years
2.5–4.0	Repeat PSA and DRE in 6–12 months
>4.0	Refer for urologist evaluation and possible biopsy

4.3 Diagnostic Workup:

- Transrectal ultrasound (TRUS) or MRI-guided biopsy.
- Serum PSA and free/total PSA ratio.
- MRI pelvis and bone scan for staging when indicated[3].
- BRCA testing cases with family history of pancreatic/ colorectal cancer.

5. REFERRAL PATHWAYS IN THE MALDIVES

Primary Care / Regional Hospitals:

- Men with elevated PSA (>4 ng/mL), abnormal DRE, or clinical suspicion should be referred to IGMH or Tree Top Hospital for evaluation.

Tertiary Centers (IGMH, Tree Top Hospital, ADK Hospital):

- Diagnostic confirmation via biopsy and staging imaging.
- Multidisciplinary team (MDT) review involving urology, oncology, radiology, and pathology.
- Treatment based on NCCN/ESMO-aligned risk categories[3].

Overseas Referral (Aasandha Mechanism):

- For PET-CT, brachytherapy, or advanced radiotherapy not available locally.
- For patients requiring novel systemic agents.

Follow-up Coordination:

- Shared-care model between tertiary and regional hospitals.
- Electronic registry tracking for long-term outcomes[2].

6. STAGING AND RISK STRATIFICATION

Risk stratification follows the NCCN framework[3]:

Risk Group	Clinical / Pathologic Features
Very Low	cT1c, Grade Group 1, PSA <10 ng/mL, <3 positive cores, PSA density <0.15
Low	cT1–cT2a, Grade Group 1, PSA <10 ng/mL
Intermediate	cT2b–cT2c, Grade Group 2–3, PSA 10–20 ng/mL
High	cT3a or Grade Group 4–5 or PSA >20 ng/mL
Very High	cT3b–cT4 or primary Gleason 5 or multiple high-risk features

Staging imaging includes MRI pelvis and bone scan for intermediate/high risk, and CT chest/abdomen/pelvis for advanced disease.

7. TREAMENT

7.1 LOCAL and LOCALLY ADVANCED PROSTATE CANCER (NCCN)

Clinically localized, very low-risk prostate cancer: Active surveillance is the preferred approach for most men with very low-risk prostate cancer. However, definitive local therapy, including radiation therapy (RT) or radical prostatectomy, may be offered to select patients who have a higher likelihood of disease progression under active surveillance or who prefer a more immediate, definitive treatment despite the low-risk status.

Clinically localized, low-risk prostate cancer: For men with low-risk prostate cancer and a life expectancy greater than 10 years, both definitive therapy (such as radical prostatectomy, brachytherapy, or external beam radiation therapy) and active surveillance are viable options.

Clinically localized, intermediate-risk prostate cancer: For men with intermediate-risk prostate cancer, both radiation therapy (RT) and radical prostatectomy are appropriate treatment options. Men receiving radical RT should have neoadjuvant and concurrent ADT for 4-6 months (ESMO). Active surveillance can be considered for those with favorable intermediate-risk disease,

Clinically localized, high-risk prostate cancer: combination of external beam radiation therapy (RT), brachytherapy, and androgen deprivation therapy (ADT), or radical prostatectomy ± lymphadenectomy. Men receiving radical RT for high-risk disease should have long-course ADT (18-36 months). (ESMO)

Locally advanced and very high-risk prostate cancer: Treatment options typically include external beam radiation therapy (RT), with or without brachytherapy, and long-term androgen deprivation therapy (ADT), or radical prostatectomy. In cases where patients have biopsy grade group 5 disease, our preference leans toward external beam RT combined with brachytherapy and ADT over radical prostatectomy. Neoadjuvant docetaxel Chemotherapy may be offered before radiotherapy for young, fit men with very high-risk localised prostate cancer

Postoperative Radiotherapy (ESMO)

Following RP, patients should have their serum PSA level monitored, with salvage RT recommended in the event of PSA failure. Adjuvant postoperative RT after RP is not routinely recommended.

Treatment of relapse after local treatment (ESMO)

Salvage RT should start early (e.g. PSA <0.5 ng/ml) [III, B]. Concomitant ADT for 6 months or bicalutamide 150 mg daily for 2 years may be offered to men having salvage RT. Men having SRT to the prostate bed may be offered pelvic nodal RT.

Men with biochemical relapse after radical RT who may be candidates for local salvage or metastasis-directed treatment should undergo imaging with PET-CT. Early ADT alone is not recommended for men with biochemical relapse unless they have a rapid PSA doubling time, symptomatic local disease or proven metastases

Men starting ADT for biochemical relapse, in the absence of metastatic disease, should be offered intermittent rather than continuous treatment

7.2 NON-METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Apalutamide, darolutamide or enzalutamide should be considered as options for men with M0 (on bone scan and CT) CRPC and a high risk of disease progression

7.3 METASTATIC HORMONE-NAÏVE PROSTATE CANCER

ADT is recommended as first-line treatment of mHNPC in combination with abiraterone/ prednisone or or apalutamide or or enzalutamide

RT to the primary tumour combined with the systemic treatment is recommended for patients with low volume mHNPC

ADT alone is recommended as first-line systemic treatment of mHNPC in men who are unfit for abiraterone, apalutamide, enzalutamide and docetaxel

For men starting on ADT, management to prevent CTIBL is recommended

7.4 METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Abiraterone or enzalutamide is recommended for asymptomatic/mildly symptomatic men with ChT-naive mCRPC. Docetaxel is recommended for men with mCRPC. In patients with mCRPC in the post-docetaxel setting, abiraterone, enzalutamide and cabazitaxel are recommended options.

In patients with bone metastases from CRPC at risk for clinically significant skeletal-related events (SREs), a bisphosphonate or denosumab is recommended. 223Ra is recommended for men with bone-predominant, symptomatic mCRPC without visceral metastases. 223Ra is not recommended in combination with abiraterone and prednisolone. The use of a second AR inhibitor (abiraterone after enzalutamide or vice versa) is not recommended.

7.5 PALLIATIVE CARE

A single fraction of external beam RT is recommended for palliation of painful, uncomplicated bone metastasis

In patients with bone metastases from CRPC at risk for clinically significant SREs, a bisphosphonate or denosumab is recommended

MRI of the spine to detect subclinical cord compression is recommended in men with CRPC with vertebral metastases

Urgent MRI of the spine to detect cord compression is very strongly recommended in men with CRPC with vertebral metastases and neurological symptoms.

8. FOLLOW-UP AND MONITORING

Clinical Situation	Follow-up Schedule	Key Investigations
Active Surveillance	PSA every 6 months, DRE annually	Repeat biopsy/MRI every 2–3 years
Post-Radical Prostatectomy	PSA at 3, 6, 12 months, then annually	Imaging if PSA >0.2 ng/mL
Post-Radiotherapy	PSA every 6 months for 5 years	MRI/bone scan if PSA rise confirmed
On ADT	Every 3–6 months	PSA, testosterone, metabolic profile, DEXA annually
mCRPC	Every 3 months	PSA, ALP, LFTs, imaging every 6–9 months

Lifestyle measures include exercise, adequate calcium/vitamin D, smoking cessation, and limiting alcohol. DEXA monitoring is advised for men on long-term ADT[4].

9. ANNEX I: RADIOTHERAPY PROTOCOLS AND FRACTIONATION SCHEDULES

1. Radical (Definitive) External Beam Radiotherapy (EBRT)

Conventional Fractionation

- **Total Dose:** 74–80 Gy
- **Fraction Size:** 1.8–2.0 Gy
- **Schedule:** 37–40 fractions over ~8 weeks
- **Indication:** Localized disease when hypofractionation not feasible.
- **ADT:** 4–6 months (intermediate risk), 18–36 months (high/very high risk).

Moderate Hypofractionation (Preferred)

- **Total Dose:** 60 Gy in 20 fractions (3 Gy/fx) or 70 Gy in 28 fractions (2.5 Gy/fx).
- **Schedule:** 4–6 weeks.
- **Evidence:** CHHiP, PROFIT trials confirm non-inferiority to conventional RT.

Ultra-Hypofractionation (SBRT)

- **Total Dose:** 36.25–40 Gy in 5 fractions (7.25–8 Gy/fx).
- **Schedule:** 1–2 weeks.
- **Indication:** Low to favorable intermediate-risk disease.

Brachytherapy

- **LDR Monotherapy:** I-125: 145 Gy, Pd-103: 108 Gy.
- **HDR Boost:** 15 Gy × 1 (with EBRT 46 Gy/23 fx) or 10.5 Gy × 2 (with EBRT 45 Gy/25 fx).

2. Post-Operative (Adjuvant and Salvage) RT

Adjuvant RT

- **Dose:** 64–66 Gy in 32–36 fractions (1.8–2 Gy/fx).
- **Timing:** 4–6 months post-surgery, PSA <0.1 ng/mL.
- **Field:** Prostate bed ± pelvic nodes.

Early Salvage RT

- **Indication:** PSA ≥0.2 ng/mL (rising).
- **Dose:** 66–70 Gy (2 Gy/fx).
- **ADT:** 6 months may improve control (RTOG 9601).

Pelvic Nodal RT

- **Pelvic Field:** 45–50.4 Gy/25–28 fx.
- **Boost:** To 66–70 Gy to prostate bed.

3. Technique and Planning Notes

- IMRT/IGRT recommended. MRI-fusion for contouring.
- Dose Constraints: Rectum V70 <15%, Bladder V65 <25%, Femoral heads Dmax <50 Gy.
- Daily image guidance preferred.
- Hydrogel spacers reduce rectal dose where available.

4. Summary Table

Setting	Total Dose	Fraction Size	Duration	ADT Duration	Notes
Conventional EBRT	74–80 Gy	1.8–2.0 Gy	7–8 weeks	4–36 mo	Standard baseline
Hypofractionated EBRT	60 Gy	3 Gy	4 weeks	4–36 mo	Preferred approach
SBRT	36.25–40 Gy	7.25–8 Gy	1–2 weeks	Optional	Low/intermediate risk
Adjuvant RT	64–66 Gy	2 Gy	6–7 weeks	None–6 mo	For adverse pathology
Salvage RT	66–70 Gy	2 Gy	6–7 weeks	6 mo	Start PSA <0.5 ng/mL

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