MINISTRY OF HEALTH AND SOCIAL WELFARE

GUIDELINES FOR NATIONAL PROSTATE CANCER SCREENING AND TREATMENT

TECHNICAL COMMITTEE

JANUARY 2015

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ABBREVIATIONS

ORCI	Ocean Road Cancer Institute
MNH	Muhimbili National Hospital
KCMC	Kilimanjaro Christian Medical Centre
Pca	Prostate Cancer
PSA	Prostatic Specific Antigen
DRE	Digital rectal Examination
MOHSW	Ministry of Health and Social Welfare
QOL	Quality of life
APHFTA	Association of Private Health Facilities in Tanzania
TRUS	Trans-rectal Ultrasound

SUMMARY

Carcinoma of the prostate also known as Prostate cancer (Pca), is the development of cancer in the prostate, a gland in the male reproductive system. Most prostate cancers are slow growing; however, some grow relatively fast. About 99% of Pca occur in those over the age of 50. Having a first degree relative with the disease increases the risk 2 to 3 fold; and it is more common among Africans than among Caucasians. Worldwide, prostate cancer is the second most frequently diagnosed cancer (at 15% of all male cancers) and the sixth leading cause of cancer death in males worldwide. In Tanzania, it is estimated that each year there are 3434 new patients diagnosed with prostate cancer and 2752 dying from the disease per annum. Combined data from ORCI, MNH and KCMC shows that each year there are approximate 404 new prostate cancer cases recorded; however this data might not reflect the true picture of the disease due to lack of population-based cancer registry.

Provision of prostate cancer prevention services in Tanzania has been done by different stakeholders particularly by ORCI and 50Plus campaign; although specialists from MNH, zonal hospitals and private hospitals have also played a great role. However, in the absence of national guidelines, this has created difficulties in the implementation of a national Pca prevention service due to uncoordinated efforts. Thus, these guidelines will provide a platform for coordination of the Pca prevention and control services in the country.

The primary endpoint of screening has two main aspects, reduction in mortality from PCa; and a maintained QoL as expressed by quality-of-life-adjusted gain in life years (QUALYs). Prostate cancer screening is one of the most controversial topics in urological literature. Thus, an individualized risk-adapted strategy for screening might be offered to a well-informed man with at least 10-15 years of individual life expectancy. However, this approach may still be associated with a substantial risk of overdiagnosis. It is therefore important to identify carefully those patient cohorts likely to benefit most from individual early diagnosis, taking into account the potential balances and harms involved.

In Tanzania it is recommended that men have a chance to make an informed decision with their health care provider about whether to be screened for prostate cancer. The recommendation for screening is; should take place at age 50 for men who are at average risk of prostate cancer and are expected to live at least 10 more years; should take place starting at age 45 for men at high risk of developing prostate cancer (men who have a first-degree relative (father, brother) diagnosed with prostate cancer at an early age); and for those with negative results, screening should be done biennial (every two years) until age 65. After age 65, screening should be done annually until age 70. After age 70, Pca screening is individualized through discussion between the doctor and the client.

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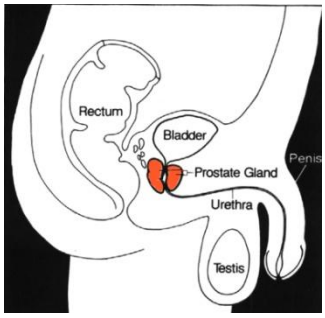
INTRODUCTION

Carcinoma of the prostate also known as Prostate cancer (Pca), is the development of cancer in the prostate, a gland in the male reproductive system (1). Most prostate cancers are slow growing; however, some grow relatively fast (2,3). The cancer cells may spread from the prostate to other parts of the body, particularly the bones and lymph nodes (4).



Factors that increase the risk of prostate cancer include: older age, a family history of the disease, and being African (2,3,4). About 99% of cases occur in those over the age of 50. Having a first degree relative with the disease increases the risk 2 to 3 fold. It is more common among Africans than among Caucasians. Other factors that may be involved include a diet high in processed, red meat, or milk products or low in certain vegetables (4).

BURDEN OF PROSTATE CANCER

Worldwide, as of 2012, prostate cancer is the second most frequently diagnosed cancer (at 15% of all male cancers) and the sixth leading cause of cancer death in males worldwide (5,6). Rates of prostate cancer vary widely across the world. Prostate cancer is least common among Asian men and most common among black men, with figures for white men in between (7). The table below shows the burden of prostate cancer worldwide and in selected regions (8).

Table: Estimated Incidence, Mortality and Prevalence of prostate cancer worldwide in 2012

Estimated numbers (thousands)	Cases	Deaths	5-year prevalence.
World	1112	307	3924
More developed regions	759	142	2937
Less developed regions	353	165	987
WHO Africa region (AFRO)	52	37	135
WHO Americas region (PAHO)	413	85	1539
WHO East Mediterranean region (EMRO)	19	12	47
WHO Europe region (EURO)	437	101	1579
WHO South-East Asia region (SEARO)	39	25	123
WHO Western Pacific region (WPRO)	153	46	499
IARC membership (24 countries)	808	157	3064
United States of America	233	30	980
China	47	23	104
India	19	12	64
European Union (EU-28)	362	72	1343

In Tanzania, based on data from Globocan 2012 (9), it is estimated that each year there are 3434 new patients diagnosed with prostate cancer. These comprise 10.1% of the total number of cancer patients estimated to occur nationwide in Tanzania. Similarly, it is estimated that there are

about 2752 deaths due to prostate cancer per annum in Tanzania. It should be noted there is no population-based cancer registry in Tanzania thus the data from Globocan is used to estimate the national data, and it may overestimate or underestimate actual data. The table below shows some selected cancer types occurring in Tanzania based on Globocan data (9).

Table: Incidence, Mortality and Prevalence of selected cancer types for Tanzania, both sexes

Cancer	Incidence			Mortality			5-year prevalence		
	Number	(%)	ASR (W)	Number	(%)	ASR (W)	Number	(%)	Prop.
Kaposi sarcoma	5266	15.5	14.5	3570	15.1	12.3	8397	11.9	32.0
Breast	2732	8.1	19.4	1355	5.7	9.7	8570	12.1	64.8
Cervix uteri	7304	21.6	54.0	4216	17.8	32.4	18489	26.1	139.8
Prostate	3434	10.1	34.6	2752	11.6	27.9	8926	12.6	68.4

Data from Ocean Road Cancer Institute (ORCI) shows that prostate cancer incidence has been increasing steadily over the years. In year 2006, there were 51 new prostate cancer patients who attended ORCI while in 2013 there were 116 new prostate cancer patients (10). The mean age of the patients was 59.6 years and majority of the patients were from Dar es Salaam. It should be noted that the number of prostate cancer patients who attend at ORCI is grossly underestimated because majority of the patients with prostate cancer are treated by urologist in major hospitals of Tanzania and do not come to ORCI. Those who attend ORCI mostly are those with advanced stage disease requiring radiotherapy, chemotherapy and hormonotherapy.

The above information is in agreement with data from the Unit of Urology of Muhimbili National Hospital which shows that each month there are about 20 new cases of prostate cancer attended; this translates into about 240 new prostate cancer patients per year at MNH in 2014 (11). Furthermore, data from Kilimanjaro Christian Medical Centre shows that each month there are about 4 new prostate cancer patients attended; and this translates into 48 new prostate cancer patients per year in 2014 (personal communication).

SYMPTOMS OF PROSTATE CANCER

Early prostate cancer usually causes no symptoms. Sometimes, however, prostate cancer does cause symptoms, often similar to those of diseases such as benign prostatic hyperplasia (12).
The most common presentation of prostate cancer are;

- Age – usually present at age 60 years and above; but it occur even at younger age
- Most patients are asymptomatic diagnosed during examination either by postate-specific antigen or digital rectal examination
- With advanced cancer, symptoms may include urinary obstruction, hematuria and bone pains from bone metastasis
- Prostate cancer that has metastasize to the spine can also compress the spinal cord, causing leg weakness and urinary and fecal incontinence

INITIATIVES FOR PROSTATE CANCER PREVENTION

In Tanzania, the initiatives for prostate cancer prevention and control have been running for decades but not at the national level, mostly it has been done at institutional level. Public education on prostate cancer awareness through the media, have been conducted through interviews by doctors from ORCI, MNH, 50Plus campaign and others. Furthermore, ORCI has been in the forefront of advocating for prostate cancer prevention through distribution of awareness posters and brochures to the public during the Sabasaba and Nanenane trade fairs in Dar es Salaam and Dodoma, respectively as well as in its cancer screening clinic. 50plus campaign has also been advocating for prostate cancer prevention in public rallies through distribution of brochures and posters.

Screening and early detection of prostate cancer has been done in an opportunistic fashion in some hospitals and clinics such as ORCI, MNH, and other urological clinics whereby individuals who need prostate cancer testing undergo risk assessment as well as screening and early detection for prostate cancer using PSA and/or DRE, respectively.

Mass screening for prostate cancer using PSA and DRE has been done at a limited capacity in the country, mainly by 50plus campaign using PSA test among rural communities and by ORCI using PSA testing among Members of Parliament in Dodoma; and on 4th February of each year while marking World Cancer Day.

RATIONALE FOR GUIDELINES ON NATIONAL PROSTATE CANCER SCREENING AND TREATMENT

The burden of prostate cancer in the country is increasing partly due to aging population as well as probably an increase in the exposure to risk factors among the population. In addition, an increase in awareness among the population might also have led to the increase in the number of prostate cancer patients attending hospitals in the country. Majority of the patients are diagnosed at advanced stage of the disease in which case curative treatment is not an option.

Prostate cancer prevention initiatives in the country has been done at institutional level mostly by ORCI and 50Plus campaign; and not in most cases not coordinated. This has resulted in different strategies for the prostate cancer prevention programs in the different institutions and communities, hence difficult in assessment of its outcome. Furthermore, the services are not available throughout the country which has resulted in inequitable access to the service.

Knowing the fact that considerable amount of national health care burden is taken by the private health care facilities, and majority of Pca patient are early detected and managed in the private facilities; it is found to be appropriate to identify and include private health facilities in the national campaigns for Pca screening and treatment.

Therefore Tanzania needs a national guideline for prostate cancer screening and treatment in order to address the above shortcomings in the prevention of prostate cancer in the country. Furthermore, there is a need to have national guidelines which will help to inform the general

public as well as the implementers on clear and balanced information about screening and treatment for prostate cancer.

PROSTATE CANCER SCREENING AND EARLY DETECTION - CURRENT EVIDENCE

Population or mass screening is defined as the systematic examination of asymptomatic men (at risk) and is usually initiated by health authorities. In contrast, early detection or opportunistic screening consists of individual case findings, which are initiated by the person being screened (patient) and/or his physician. The primary endpoint of both types of screening has two main aspects (13):

- Reduction in mortality from PCa;
- At least, a maintained QoL as expressed by quality-of-life-adjusted gain in life years (QUALYs).

Prostate cancer mortality trends range widely from country to country in the industrialized world. Decreased mortality rates due to PCa have occurred in most Western countries but the magnitude of the reduction varies between countries. The reduced mortality seen recently in the USA is considered to be partly due to a widely adopted aggressive PCa screening policy. However, there is still no evidence that prostate-specific antigen (PSA) screening reduces mortality due to PCa.

Prostate cancer screening is one of the most controversial topics in urological literature. A huge number of passionate papers, discussions and debates have been produced, as well as at least three large prospective RCTs initially published in 2009 (14,15,16). The great importance of this subject requires the highest-quality evidence, which can only be obtained by a systematic literature search of published trials or cohorts summarized in a structured meta-analysis. The subgroup analysis of cohorts that are part of a large trial, or mathematical projections, can never provide evidence and are only useful for generating hypotheses.

The main summary of findings from literature published on PCa screening is the Cochrane review published in 2013 (17). This review was based on an up-to-date systematic literature search during November 2012 and is an update of a 2010 paper with the same methodology. Its findings are as follows (17):

- Screening was associated with an increased diagnosis of PCa (RR: 1.3; 95% CI: 1.02-1.65).
- Screening was associated with more localized disease (RR: 1.79; 95% CI: 1.19-2.70) and less advanced PCa (T3-4, N1, M1) (RR: 0.80; 95% CI: 0.73-0.87).
- From the results of five RCTs, representing more than 341,000 randomized men, no PCa-specific survival benefit was observed (RR: 1.00; 95% CI: 0.86-1.17). This was the main objective of all the large trials.
- From the results of four available RCTs, no overall survival benefit was observed (RR: 1.00; 95% CI: 0.96-1.03).

Moreover, screening was associated with minor and major harms such as over diagnosis and overtreatment. Surprisingly, the diagnostic tool (i.e. the biopsy) was not associated with any mortality in the selected papers, which is in contrast with some other known data (18,19). The

impact on the patient's overall QoL is still unclear. It appears to be minimal in some subgroup analysis, but significant in others. This has led to strong advice against population-based systematic screening in all countries, including Europe (13). Nevertheless, at 11 years of median follow-up, the ERSPC has shown a 21% reduction in PCa-specific mortality and a 29% reduction after adjustment for non-compliance. However, there is still no overall survival benefit (20).

Thus, an individualized risk-adapted strategy for early detection might be offered to a well-informed man with at least 10-15 years of individual life expectancy. However, this approach may still be associated with a substantial risk of overdiagnosis (13). It is therefore important to identify carefully those patient cohorts likely to benefit most from individual early diagnosis, taking into account the potential balances and harms involved. Men at elevated risk of having PCa are those aged above 50 years, or with a family history of PCa and aged more than 45 years, or African-Americans. In addition, men with PSA > 1 ng/ML at 40 years and > 2 ng/mL at 60 years are also at increased risk of PCa-related mortality or a diagnosis of advanced or metastatic disease.

Early PSA testing could be used to detect these cohorts of men at risk and in need of further follow-up. However, the long-term benefit for survival and QoL of such an approach remains to be proven at a population level. Informed men requesting an early diagnosis should be given a PSA test and undergo a DRE. The optimal intervals for PSA testing and DRE follow up are unknown, and it has varied between several prospective trials. A risk-adapted strategy might be considered based on the initial PSA level. This could be every 2 years for those initially at risk, or postponed up to 8 years in those not at risk. The age at which attempts to make an early diagnosis of PCa should be stopped remains controversial but is influenced by an individual's life expectancy. Men who have less than a 15-year life expectancy are unlikely to benefit. Furthermore, although there is not a simple tool to evaluate individual life expectancy, co-morbidity is at least as important as age. Based on the tools currently available, an individualized strategy will diagnose many insignificant lesions (above 50% in some trials), most of which will not require any form of active treatment. It is important to realise that breaking the link between diagnosis and active treatment is the only way to decrease overtreatment, while still maintaining the potential benefit of individual early diagnosis for men requesting it.

Table: Pros and cons to the PSA test.

Pros of PSA screening	**Cons of PSA screening**
PSA screening may help you detect prostate cancer early.	Some prostate cancers are slow growing and never spread beyond the prostate gland.
Cancer is easier to treat and is more likely to be cured if it's diagnosed in the early stages of the disease.	Not all prostate cancers need treatment. Treatment for prostate cancer may have risks and side effects, including urinary incontinence, erectile dysfunction or bowel dysfunction.
PSA testing can be done with a simple, widely available blood test.	PSA tests aren't fullproof. It's possible for your PSA levels to be elevated when cancer isn't present, and to not be elevated when

	cancer is present.
For some men, knowing is better than not knowing. Having the test can provide you with a certain amount of reassurance — either that you probably don't have prostate cancer or that you do have it and can now have it treated.	A diagnosis of prostate cancer can provoke anxiety and confusion. Concern that the cancer may not be life-threatening can make decision making complicated.
The number of deaths from prostate cancer has gone down since PSA testing became available.	It's not yet clear whether the decrease in deaths from prostate cancer is due to early detection and treatment based on PSA testing or due to other factors.

The United States Preventive Services Task Force has analyzed the data from the PLCO, ERSPC, and other trials and estimated that, for every 1,000 men ages 55 to 69 years who are screened every 1 to 4 years for 10 years (21):

- 0 to 1 death from prostate cancer would be avoided.
- 100 to 120 men would have a false-positive test result that leads to a biopsy, and about one-third of the men who get a biopsy would experience at least moderately bothersome symptoms from the biopsy.
- 110 men would be diagnosed with prostate cancer. About 50 of these men would have a complication from treatment, including erectile dysfunction in 29 men, urinary incontinence in 18 men, serious cardiovascular events in 2 men, deep vein thrombosis or pulmonary embolism in 1 man, and death due to the treatment in less than 1 man.

PROSTATE CANCER SCREENING PROCEDURES

There are in principle two tests that may be used in mass screening, PSA (prostate specific antigen) and DRE (digital rectal examination) which are usually followed by prostatic biopsy for those with suspicious findings. The PSA test is simple, cheap, safe and acceptable. However the prostatic biopsy, required to investigate positive results, is less acceptable and carries significant risks. The accuracy (sensitivity and specificity) of the PSA test is difficult to determine. There is no good standard against which to test it, since prostatic biopsy may itself miss 10% to 30% of cases. Also, biopsies are not normally done on men with a negative PSA, so it is difficult to assess the number of false negative tests and measure sensitivity of the PSA test. Testing does not differentiate between the relatively harmless tumours and those that are likely to be fatal; therefore it is not specific for clinically important disease. Digital examination is less acceptable and less accurate than PSA testing

Digital Rectal Examination

Most prostate cancers are located in the peripheral zone of the prostate and may be detected by DRE. In about 18% of all patients, PCa is detected by a suspect DRE alone, irrespective of the PSA level. A suspect DRE in patients with a PSA level up to 2 ng/mL has a positive predictive value of 5-30%. An abnormal DRE is associated with an increased risk of a higher Gleason score and should therefore be considered an indication for prostate biopsy.

Prostate-Specific Antigen

Prostate specific antigen (PSA) is a protein made by the prostate. Most PSA is released into semen. Some of it is released into the blood. If there is a problem with the prostate, the PSA level in the blood can become elevated. The use of PSA as a serum marker has revolutionized the diagnosis of PCa. PSA is a kallikrein-like serine protease produced almost exclusively by the epithelial cells of the prostate, which is organ- but not cancer specific. Thus, serum levels may be elevated in the presence of benign prostatic hypertrophy (BPH), prostatitis and other non-malignant conditions such as after DRE, urinary tract infections, and sexual intercourse. The level of PSA as an independent variable is a better predictor of cancer than suspicious findings on DRE or transrectal ultrasound (TRUS). There are many different commercial test kits for measuring PSA, but no commonly agreed international standard exists. PSA may be measured quantitatively by immunoassay in a laboratory or by qualitatively using rapid test kits. The normal total PSA concentration in human serum on whole blood is 0.1 –2.6 ng/ml. The level of PSA is a continuous parameter: the higher the value, the more likely the existence of PCa.

Table: PSA level by age

Age (years)	Normal total PSA range (µg/L)
younger than 50	0.0–2.5
50–59	0.0–3.5
60–69	0.0–4.5
70 and older	0.0–6.5

Prostate Biopsy

The need for a prostate biopsy should be determined on the basis of the PSA level and/or a suspicious DRE. The patient's age, potential co-morbidities, and the therapeutic consequences should all also be considered. Risk stratification is becoming an important tool for reducing unnecessary prostate biopsies. The first elevated PSA level should not prompt an immediate biopsy. The PSA level should be verified after a few weeks by the same assay under standardized conditions (i.e. no ejaculation, no manipulations such as catheterisation, cystoscopy or transurethral resection, and no urinary tract infections) in the same diagnostic laboratory, using the same methods. It is now considered the standard of care to perform prostate biopsies guided by ultrasound. Although a transrectal approach is used for most prostate biopsies, some urologists prefer to use a perineal approach. The cancer detection rates from perineal prostate biopsies are comparable to those obtained from transrectal biopsies. The ultrasound-guided perineal approach is a useful alternative in special situations. Some of the complications of prostate biopsy are shown in the table below.

Table: Percentage of complications per biopsy session, irrespective of the number of cores

Complications	**Percentage of biopsies affected**
Haematospermia	37.4
Haematuria> 1 day	14.5
Rectal bleeding < 2 days	2.2

Prostatitis	1.0
Fever > 38.5°C (101.3°F)	0.8
Epididymitis	0.7
Rectal bleeding > 2 days ± requiring surgical intervention	0.7
Urinary retention	0.2
Other complications requiring hospitalization	0.3

Pathology of Prostate Needle Biopsies

Prostate core biopsies taken from different sites are usually sent to the pathology laboratory in separate vials and should be processed in separate cassettes. Diagnosis of PCa is based on histological examination.

RECOMMENDATIONS FOR PROSTATE CANCER SCREENING/EARLY DETECTION

The Tanzania technical committee on prostate cancer screening/early detection concurs with American Cancer Society (ACS) recommendations that men have a chance to make an informed decision with their health care provider about whether to be screened for prostate cancer. The decision should be made after getting information about the uncertainties, risks, and potential benefits of prostate cancer screening. Men should not be screened unless they have received this information.

- The discussion about screening should take place at age 50 for men who are at average risk of prostate cancer and are expected to live at least 10 more years. Thus, prostate cancer screening for low risk men should start at age 50.
- The discussion should take place starting at age 45 for men at high risk of developing prostate cancer. This includes men who have a first-degree relative (father, brother) diagnosed with prostate cancer at an early age (younger than age 65). Thus, prostate cancer screening for high risk men should start at age 45.
- For those with negative results, screening should be done biennial (every two years) until age 65. After age 65, screening should be done annually until age 70. After age 70, Pca screening is individualized through discussion between the doctor and the client.

Because prostate cancer often grows slowly, men without symptoms of prostate cancer who do not have a 10-year life expectancy should not be offered testing since they are not likely to benefit. Overall health status, and not age alone, is important when making decisions about screening. Even after a decision about testing has been made, the discussion about the pros and cons of testing should be repeated as new information about the benefits and risks of testing becomes available. Further discussions are also needed to take into account changes in the patient's health, values, and preferences.

The patient flow chart in a prostate cancer screening program is attached as appendix 1

The estimates for a prostate cancer screening program; an example for Dar es Salaam is attached as appendix 2

PROSTATE CANCER STAGING

Clinical Staging

The assessment of prostate cancer (PCa) extent is usually made by DRE and PSA measurement, and supplemented with bone scan and computed tomography (CT) or MRI in specific situations. Staging is usually done based on TNM classification.

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor not palpable or visible by imaging
T1a	Tumor incidental histologic finding in ≤5% of tissue resected
T1b	Tumor incidental histologic finding in >5% of tissue resected
T1c	Tumor identified by needle biopsy (because of elevated prostate specific antigen [PSA] level)
T2	Tumor confined within prostate; tumors found in 1 or both lobes by needle biopsy but not palpable or reliably visible by imaging
T2a	Tumor involves one-half of 1 lobe or less
T2b	Tumor involves more than one-half of 1 lobe but not both lobes
T2c	Tumor involves both lobes
T3	Tumor extends through the prostatic capsule; invasion into the prostatic apex, or the prostatic capsule is classified not as T3 but as T2
T3a	Extracapsular extension (unilateral or bilateral)
T3b	Tumor invading seminal vesicle(s)
T4	Tumor fixed or invades adjacent structures other than seminal vesicles (eg, bladder, levator muscles, and/or pelvic wall)
Regional lymph nodes (N)	
NX	Regional lymph nodes were not assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)
Distant metastasis (M)*	
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph nodes(s)
M1b	Bone(s)

M1c	Other site(s) with or without bone disease
*If more than 1 site of metastasis is present, use the most advanced category (pM1c).	

Pathology staging

Prostate cancer is also given a grade called a Gleason score, which is based on how much the cancer looks like healthy tissue when viewed under a microscope.

Histopathologic grade (G)	
GX	Gleason score cannot be assessed
Gleason ≤6	Well differentiated (slight anaplasia)
Gleason 7	Moderately differentiated (moderate anaplasia)
Gleason 8-10	Poorly differentiated or undifferentiated

Group staging

Prostate cancer group staging is categorized into four main stages; these are important for planning treatment options and prognosis

Stage	T	N	M	PSA*	Gleason
I	T1a-c	N0	M0	PSA < 10	Gleason ≤6
	T2a	N0	M0	PSA < 10	Gleason ≤6
	T1-T2a	N0	M0	PSA X	Gleason X
IIA	T1a-c	N0	M0	PSA < 20	Gleason 7
	T1a-c	N0	M0	PSA ≥10 but < 20	Gleason ≤6
	T2a	N0	M0	PSA < 20	Gleason ≤7
	T2b	N0	M0	PSA < 20	Gleason ≤7
	T2b	N0	M0	PSA X	Gleason X
IIB	T2c	N0	M0	Any PSA	Any Gleason
	T1-2	N0	M0	PSA ≥20	Any Gleason
	T1-2	N0	M0	Any PSA	Gleason ≥8
III	T3a-b	N0	M0	Any PSA	Any Gleason
IV	T4	N0	M0	Any PSA	Any Gleason
	Any T	N1	M0	Any PSA	Any Gleason
	Any T	Any N	M1	Any PSA	Any Gleason
*If PSA or Gleason is not available, grouping should be determined by T stage and/or either PSA or Gleason, as available.					

PROSTATE CANCER TREATMENT

The treatments available for localized prostate cancer such as that found at screening are: radical prostatectomy (surgery), radiotherapy and "watchful waiting." In this third case (also known as "active monitoring") men are followed up and only treated if there is evidence of disease progression.

The outlook for men with localized prostate cancer can be excellent, and watchful waiting can produce survival rates similar to those of more aggressive treatment. Screen-detected cancers are mostly of this type. Treatment, however, can cause harm as well as benefit. The principal adverse events of surgery are sexual dysfunction (approx 79.6%) and urinary incontinence (approx 9.6%). Surgery can be fatal in 0.1% to 0.3% of cases. Radiotherapy can cause sexual dysfunction (approx 6.5%), as well as urinary symptoms and diarrhea or rectal bleeding.

Depending on the situation, the treatment options for men with prostate cancer may include:

- Expectant management (watchful waiting) or active surveillance
- Surgery
- Radiation therapy
- Cryosurgery (cryotherapy)
- Hormone therapy
- Chemotherapy
- Bone directed treatment

These treatments are generally used one at a time, although in some cases they may be combined. The treatment choosen take into account:

- Age and expected life span
- Any other serious health conditions
- The stage and grade of the cancer
- Patient feelings (and your doctor's opinion) about the need to treat the cancer
- The likelihood that each type of treatment will cure your cancer (or provide some other measure of benefit)
- Patient feelings about the possible side effects from each treatment

Stage I

These prostate cancers are small (T1 or T2a) and have not grown out of the prostate. They have low Gleason scores (6 or less) and low PSA levels (less than 10).

- They usually grow very slowly and may never cause any symptoms or other health problems.
- For men without any prostate cancer symptoms who are elderly and/or have other serious health problems that may limit their lifespan, active surveillance is often recommended.
- For men who wish to start treatment, radiation therapy (external beam or brachytherapy) or radical prostatectomy may be options.

- Men who are younger and healthy may consider active surveillance (knowing that they may later need to be treated), radical prostatectomy, or radiation therapy (external beam or brachytherapy).

Stage II

Stage II cancers have not yet grown outside of the prostate gland, but are larger, have higher Gleason scores, and/or have higher PSA levels than stage I tumors. Compared with stage I prostate cancers, stage II cancers that are not treated with surgery or radiation are more likely to eventually spread beyond the prostate and cause symptoms.

- As with stage I cancers, active surveillance by following PSA levels is often a good option for men whose cancer is not causing any symptoms and who are elderly and/or have other serious health problems.
- Radical prostatectomy and radiation therapy (external beam or brachytherapy) may also be appropriate options.

Treatment options for men who are younger and otherwise healthy may include:

- Radical prostatectomy (often with removal of the pelvic lymph nodes). This may be followed by external beam radiation if your cancer is found to have spread beyond the prostate at the time of surgery, or if the PSA level is still detectable a few months after surgery.
- External beam radiation only*
- Brachytherapy only*
- Brachytherapy and external beam radiation combined*

*All of the radiation options may be combined with several months of hormone therapy if there is a greater chance of recurrence based on PSA level and/or Gleason score.

Stage III

Stage III cancers have grown outside of the prostate capsule but have not reached the bladder or rectum (T3). They have not spread to lymph nodes (N0) or distant organs (M0). These cancers are more likely to come back (recur) after treatment than earlier stage tumors.

Treatment options at this stage may include:

- External beam radiation plus hormone therapy
- External beam radiation plus brachytherapy, possibly with a short course of hormone therapy
- Radical prostatectomy in selected cases (often with removal of the pelvic lymph nodes). This may be followed by radiation therapy.

Men who have other medical problems may be given less aggressive treatment such as hormone therapy (by itself) or even active surveillance.

Stage IV

Stage IV cancers have already spread to nearby areas such as the bladder or rectum (T4), to nearby lymph nodes (N1), or to distant organs such as the bones (M1). A few T4 cancers may be curable using some of the same treatments for stage III cancers above. But most stage IV cancers cannot be cured with standard treatment.

Treatment options may include:

- Hormone therapy
- External beam radiation plus hormone therapy (in selected cases)
- Surgery (TURP) to relieve symptoms such as bleeding or urinary obstruction
- Treatments aimed at bone metastases, such as denosumab (Xgeva), a bisphosphomate like zoledronic acid (Zometa), or a radiopharmaceutical such as strontium-89, samarium-153 or radium-223.
- Chemotherapy
- Active surveillance (for those who have another serious illness)

Treatment of stage IV prostate cancer may also include treatments to help prevent or relieve symptoms such as bone pain.

EQUIPMENT AND SUPPLIES FOR PROSTATE CANCER SCREENING AND TREATMENT

Level 1: Provide prostate cancer education, risk assessment and screening using rapid PSA test kits and DRE

- Questionnaires and attendance cards
- Health education materials- brochures, banners
- PSA rapid test kits
- Examination beds
- Examination gloves
- Lubricants (K-Y jelly etc)
- Examination beds screens

Level 2 (Referral hosp): Provide advanced prostate cancer assessment and investigations including quantitative PSA testing, transrectal ultrasound and biopsy as well as pathology services

- PSA immunoassay machine – for quantitative PSA measurement
- Examination gloves
- Trucut needles
- Syringes
- Vacutainers
- Transrectal ultrasound machine and biopsy probes/needles
- Biopsy specimen vials/cassettes
- Slides
- Pathology reagents for staining
- Xylocaine
- Microscopes

Level 3 (National hospitals/Specialized hospital): Provide treatment to prostate cancer patients

- Operating theatre (with all supplies needed for surgical management
- Radiotherapy machines
- Chemotherapy
- Hormonotherapy

REFERENCES

1. National Cancer Institute. Prostate Cancer. Accessed at www.cancer.gov/cancertopics/types/prostate. Retrieved 5 January 2015.
2. World Health Organization. *World Cancer Report 2014*. 2014. pp. Chapter 5.11. ISBN 9283204298.
3. National Cancer Institute Prostate Cancer Treatment. Accessed at www.cancer.gov/cancertopics/treatment/prostate. Retrieved 5 January 2015.
4. Ruddon H, Raymond W. (2007). *Cancer biology* (4th ed. ed.). Oxford: Oxford University Press. p.223. ISBN 9780195175431.
5. International Agency for Research on Cancer (IARC). *World Cancer Report 2014*, World Health Organization. 2014. ISBN 978-92-832-0432-9.
6. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D (2011). "Global cancer statistics". *A Cancer Journal for Clinicians* **61** (2): 69–90.
7. American Cancer Society. Overview: Prostate Cancer—What Causes Prostate Cancer? American Cancer Society (2 May 2006). Retrieved on 5 January 2015
8. IARC. Cancer fact sheet. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Accessed on 5 January 2015
9. IARC. Population cancer fact sheet – Tanzania. Accessed on 5th January 2015 at http://globocan.iarc.fr/Pages/fact_sheets_population.aspx
10. Ocean Road Cancer Institute. Facts about Ocean Road Cancer Institute: Building capacity for cancer services in Tanzania. January 2014
11. Muhimbili National Hospital. Urology unit mortality meeting. December 2014
12. Miller DC, Hafez KS, Stewart A, Montie JE, Wei JT (September 2003). "Prostate carcinoma presentation, diagnosis, and staging: an update form the National Cancer Data Base". *Cancer* **98** (6): 1169–78.
13. European Urological Association. Prostate cancer guidelines. Prostate cancer update 2014.
14. Andriole GL, Crawford ED, Grubb RL 3rd, et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med 2009 Mar;360 (13):1310-9.
15. Schröder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized. European study. N Engl J Med 2009 Mar;360(13):1320-8.
16. Hugosson J, Carlsson S, Aus G, et al. Mortality results from the Göteborg randomised population based prostate-cancer screening trial. Lancet Oncol 2010 Aug;11(8):725-32.
17. Ilic D, Neuberger MM, Djulbegovic M, et al. Screening for prostate cancer Cochrane Database Syst Rev 2013 Jan. http://www.ncbi.nlm.nih.gov/pubmed/23440794
18. Andriole GL, Crawford ED, Grubb RL 3rd, et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med 2009 Mar;360(13):1310-9.
19. Schröder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. N Engl J Med 2009 Mar;360(13):1320-8.
20. Schröder FH, Hugosson J, Roobol MJ, et al. ERSPC Investigators. Prostate-cancer mortality at 11 years of follow-up. N Engl J Med 2012 Mar;366(11):981-90.
21. US Preventive Service Task Force. Recommendation for prostate cancer screening. http://www.uspreventiveservicestaskforce.org. Accessed on 5th January 2015