WHITE PAPER ON PROSTATE CANCER

Recommendations for the EU Cancer Plan to tackle Prostate Cancer

European Association of Urology

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EXECUTIVE SUMMARY

Prostate Cancer is on the rise, and is the most frequent cancer in Europe with important consequences for healthcare systems. Every year, around 450,000 European men are diagnosed with Prostate Cancer. It has overtaken colorectal cancer, and is now the second commonest cause of male cancer death. Prostate Cancer killed 107,000 men in Europe in 2018 and thus, is not an indolent disease, killing more men than breast cancer kills women. It is a chronic disease that causes many emotional and social problems for patients and their families.

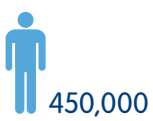
Efficient and effective action for Prostate Cancer patients depends on a coherent European strategy, and a common approach to mobilising and integrating resources. Saving lives and ensuring a high quality of life of Prostate Cancer patients during and after treatment requires immediate European action. **The EU Cancer Plan is a unique opportunity to facilitate a more coordinated and harmonised European approach to Prostate Cancer.**

In this update of the 2017 White Paper on Prostate Cancer, we provide the latest general information on prevention, early detection and awareness raising, treatment and care, survivorship and quality of life and research and innovation. It highlights the key challenges in tackling Prostate Cancer and improving patient outcomes, and presents recommendations on what can be done by the EU at European level in the fight against Prostate Cancer.

The EU Cancer Plan is a chance for wider recognition of Prostate Cancer as a European healthcare problem and to engage in closer collaboration between EU institutions and Member States, healthcare professionals, patient representatives and their families to agree an approach to tackling it.

As this white paper was being drafted, health systems and clinicians across the world are rising to the challenges of COVID-19 while citizens are being asked to socially distance themselves in order to stop further outbreaks. We do not yet know the full impact of COVID-19 but we know there will be a need for a review of how the current situation impacts upon treatment and care for Prostate Cancer patients. There will also need to be a review on the sustainability of Europe's healthcare systems, including its productive sector of scientific and healthcare professional education and patient associations.

PROSTATE CANCER



INCIDENCE
450,000 men in Europe are diagnosed with prostate cancer every year.

PREVALENCE
More than two million European men are living with prostate cancer.

AGE
1 in 7 men in Europe will develop prostate cancer before the age of 85.

MORTALITY
107,000 European men die of prostate cancer each year.

COSTS
€9 billion with healthcare accounting for €5.8 billion.

RECOMMENDATIONS FOR EU ACTION ON PROSTATE CANCER

The EU Cancer Plan is a chance for wider recognition of Prostate Cancer as a European healthcare problem and to engage in closer collaboration between EU institutions and Member States, healthcare professionals, patient representatives and their families to agree an approach to tackling it.

Our recommendations on Prostate Cancer to the European Commission in light of the EU Cancer Plan, are as follows:

PREVENTION, EARLY DETECTION AND AWARENESS RAISING

- The **EU Health Programme** in 2021-2027 should support **an EU wide awareness raising campaign on Prostate Cancer**.
- The EU Cancer Plan should mandate and endorse **clinical guidelines on early detection and diagnosis of Prostate Cancer** which can be taken up by EU Member States in their National Cancer Plans. The guidelines should use as a basis the most recently agreed clinical guidance, such as the EAU guidelines on Prostate Cancer.[1]

TREATMENT AND CARE

- The EU should promote **high quality, standardised and integrated care**, with a focus on patient-centred, multidisciplinary approach, either following the model of Prostate Cancer Centres of excellence[2] or in Prostate Cancer Units[3]
- **Health Technology Assessment (HTA)** legislation should support the prompt and consistent HTA for new screening, diagnostic, therapeutic and rehabilitation technologies in order to provide the basis for effective, efficient, targeted and optimised allocation of resources and specific Prostate Cancer services.
- Access to **innovative treatments and personalised medicines** should be made fast and equitable to all Prostate Cancer patients who can benefit from them at an **affordable price**. Effective implementation must be matched by demonstration of impact on outcomes (both clinical and economic).

SURVIVORSHIP AND QUALITY OF LIFE OF PATIENTS

- **Implementation of survivorship plans as part of the National Cancer Plans must be part of the EU cancer plan**, including specific plans for Prostate Cancer patients. Taking advantage of electronic patient-reported outcome measures (PROMs) for Quality of Life will get patients engaged in their own cancer journey.
- The EU should support an EU-wide **comparative study on the economic impact of cancer for patients** (including Prostate Cancer patients and their families) and society at large.

RESEARCH AND INNOVATION

The health cluster of **Horizon Europe** should:

- **Prioritise Prostate Cancer research** to allow better identification/discrimination between significant and insignificant cancers and in **areas of personalised cancer medicine** which should a) allow better identification of patients who will benefit from a particular treatment thus minimising costs for non-justified use of novel therapy agents and b) delay onset of tumour progression on the basis of appropriate knowledge on biomarkers and validated targets. In order to be able to achieve this goal, integrative projects with **novel models, bioinformatics analyses, and advanced technologies** should be supported.
- Dedicate funding to **research on comorbidities** to fill existing gaps in research and better understand disease interactions.
- **Continue and increase funding for big data projects in Prostate Cancer** which have been started during the 2014-2019 Commission. It is of utmost importance to support sustainability of the developed registries and databases.
- **Leverage and harness expertise and experience** of healthcare professionals, patient groups and healthy men as a soundboard for the **Cancer research mission** and potential actions on Prostate Cancer.
- Support **pragmatic solutions for facilitating General Data Protection Regulation (GDPR) compliant processing of personal data in health for secondary purposes including research**.
- Fund **digital skills training for healthcare professionals** to prepare them for the digital era, including on Artificial Intelligence (AI), robotic surgery and endoscopy.

1. PREVENTION

ESTABLISHED RISK FACTORS

The three well-established risk factors for Prostate Cancer are increasing age, ethnic origin and family history.

INCREASING AGE

The risk of developing Prostate Cancer increases with age. The average age at the time of diagnosis of Prostate Cancer is 69 years. By 2060, there will be an increase of around 32 million in the number of men aged over 65. [4]

ETHNIC ORIGIN

Prostate Cancer is most commonly diagnosed in men of African descent and least in Asian men. It is still unknown what causes these differences.

FAMILY HISTORY

Men with a family history of Prostate Cancer are at higher risk of developing the condition themselves. There is also a link between risk of Prostate Cancer and men with the BRCA2 gene (the same gene as breast cancer). Family history is an often lacking or insufficiently explored risk factor.

INCREASING AGE AFRICA FAMILY HISTORY

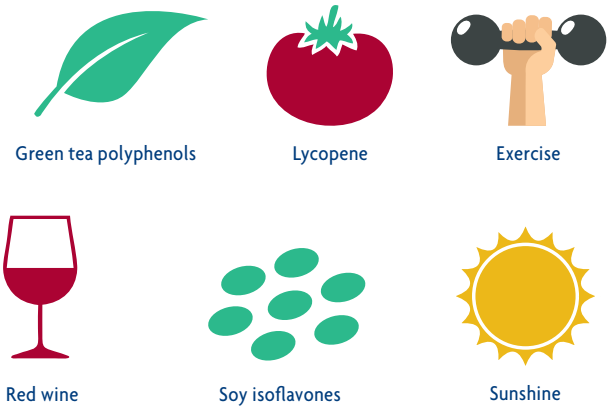
RISK FACTORS WITH CONFLICTING OR LIMITED EVIDENCE

A meta-analysis evaluated the association between metabolic syndrome, its components and the risk of Prostate Cancer. Among the individual components of the syndrome (body mass index, dysglycemia or dyslipidemia, high triglycerides, low HDL cholesterol) only hypertension and waist circumference (›102cm) are associated with a trend towards higher risk of Prostate Cancer , increasing it by 15% (p=0.035) and 56% (p=0.07) respectively. Although associations vary with geography, metabolic syndrome is weakly associated with Prostate Cancer risk.[5] A recent systematic review and meta-analysis demonstrated that hypertension may be associated with an increased risk of Prostate Cancer. Well-designed studies are needed to confirm these preliminary findings.[6] There is still conflicting evidence regarding the association of obesity (body mass index ≥ 30) and the risk of developing Prostate Cancer. However, obese men with Prostate Cancer are more likely to have aggressive disease.[7] Exogenous factors such as obesity may have an important impact on the progression of Prostate Cancer.

"OBESE MEN WITH PROSTATE CANCER ARE MORE LIKELY TO HAVE AGGRESSIVE DISEASE"

NO HIGH-LEVEL EVIDENCE –BASED PREVENTIVE MEASURES FOR PROSTATE CANCER

Beside the ways to reduce the cancer risk overall[8], there is currently no high-level evidence that more specific preventive measures may reduce the risk of Prostate Cancer , in particular. Given the epidemiological differences between Asia, North America, Northern and Southern Europe, it seems that dietary differences (a diet low in animal fat and rich in fruits, cereals and vegetables, specifically non-fermented soy containing isoflavones, a group of phenolic compounds that are considered to be bioactive), may contribute to a lower risk of Prostate Cancer. A balanced diet and regular exercise are recommended because they are beneficial for overall health. It is advisable for all Prostate Cancer patients to exercise and maintain a healthy weight.



Green tea polyphenols Lycopene Exercise

Red wine Soy isoflavones Sunshine

Currently, there are no data to suggest that pharmacological intervention would reduce the progression of Prostate Cancer. Although it seems that 5-alpha-reductase inhibitors (5-ARIs) have potential benefits in preventing or delaying the development of Prostate Cancer[9], it must be weighed against the harm of treatment as well as the potential for an increased risk of detecting high-grade Prostate Cancer[10]. None of these agents are EMA approved for Prostate Cancer prevention. There are conflicting data on the association between the use of aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) and Prostate Cancer risk.[11] A meta-analysis and the results of the REDUCE study did not confirm a preventive effect of statins on Prostate Cancer risk.[12] Results of a recent Danish study using nationwide high-quality registry data indicate that statins may lower the mortality rate of Prostate Cancer.[13] Further studies based on Big Data are required. Currently, there is no high-level evidence that preventive measures may reduce the risk of Prostate Cancer.[14]

However, it is suggested that green tea polyphenols, soy isoflavones, phytoestrogens, lycopene, red wine[15] and sunshine may have a favourable effect on Prostate Cancer prevention.

Based on the findings from a recent meta-analysis, red meat or processed meat intake do not appear to be associated with increased risk of Prostate Cancer.[16]

Researchers continue to look for foods and dietary supplements that can help lower Prostate Cancer risk. The options of Prostate Cancer chemoprevention should be further explored and future research should focus on determining the target population. The link between obesity and Prostate Cancer risk and whether weight loss might reduce the Prostate Cancer risk should also be investigated in well-designed studies on large cohorts.

2. EARLY DETECTION

DIAGNOSTIC TOOLS

PSA TESTING

PSA testing is a test that measures the amount of prostate specific antigen (PSA) in the blood. PSA values may be used to estimate the risk of Prostate Cancer in men. A raised PSA level may be an indication of Prostate Cancer but it is not specific to cancer. PSA levels may be raised by a benign enlargement of the prostate, a urinary infection or prostatitis (infection of the prostate) or following ejaculation. Conversely, men with Prostate Cancer may have low or normal levels of PSA. Clinicians do however have decades of experience on how to use PSA to diagnose Prostate Cancer as part of a tried and tested diagnostic strategy.

DIGITAL RECTAL EXAMINATION

Another diagnostic tool is digital rectal examination (DRE) in which the doctor puts a gloved, lubricated finger into the rectum to feel the prostate gland. DRE is less effective to detect tumours at an early stage, but will successfully diagnose late stage cancers.

IMAGING BEFORE PROSTATE BIOPSY

The availability of Multiparametric Magnetic Resonance Imaging (mpMRI) substantially changed the diagnostic paradigm of localised Prostate Cancer. MRI images are characterised by a high sensitivity and a high negative predictive value for aggressive disease.[17, 18] At the same time, it also has the ability to ignore small insignificant Prostate Cancer.[19, 20] Therefore, mpMRI has been proposed as a test to further optimize the identification of men at risk of having significant Prostate Cancer who should be considered for a prostate biopsy.[21]

The use of dedicated high quality mpMRI before prostate biopsy allows for the detection of a higher proportion of significant prostate cancers compared to random biopsies. **This leads to a reduction of more than 10% of diagnosing insignificant diseases and a 30% reduction in the number of unnecessary biopsies**.[22] The implementation of early detection strategies that include dedicated high quality mpMRI would avoid a substantial number of unnecessary prostate biopsies and other disease diagnoses.[23,24] Further optimization of MRI protocols will continue, such as comparing current MRI Protocol to a shorter one to evaluate the accuracy of bi (or tri) parametric MRI. It is important to high quality MRI available to more men using shorter protocols with preserved quality. Computerised image analysis by Artificial Intelligence (AI) will certainly play an important role in reducing the variability between less experienced readers and make the reading faster. Several algorithms are under development and need additional funding support.

CLINICAL TOOLS

Alongside the digital rectal examination (DRE), the clinician can take a number of risk factors into account that are helpful to identify those individuals that need closer follow-up or eventually further investigations like, for instance, MRI. Men at risk are those with a family history of Prostate Cancer, men of Afro-American origin, and those with a BRCA2 mutation(breast cancer gene). Also an elevated PSA Density (relates PSA to the volume of the prostate, and larger prostates may have an higher PSA level in the blood) indicates further investigation. Risk calculators using these different tools have been developed by the ERSPC (European Randomized Screening study for Prostate Cancer) and by PCPT (Prostate Cancer Prevention Trial) and are readily available on the internet.[25] They are able to percentwise report the likelihood that someone has Prostate Cancer.

NOVEL MOLECULAR TESTS

Different molecular biomarkers in blood and urine have been proposed to identify men with significant Prostate Cancer. These tools based on algorithms including PSA or other proteins and clinical information can identify clinically significant disease with better accuracy than PSA alone and further decrease the risk of overdiagnosis.[26,27,28,29] They provide complimentary information that enhance prediction of high-grade Prostate Cancer. Their integration with other tools such as mpMRI might ultimately reduce the number of unnecessary biopsies without increasing the risk of missing a significant disease.[30,31] More studies are needed to identify the best early detection algorithm by integrating risk calculators, mpMRI and molecular tests in a model with family history and other clinical information.

BIOPSY

A prostate biopsy is used if the PSA is too high, if there is a suspicious result of digital rectal examination, a rapid PSA increase or suspicion at mpMRI. Prostate biopsy is the only test that can confirm a Prostate Cancer diagnosis.

CONCERNS OVER EARLY DETECTION OF PROSTATE CANCER

Some clinicians and health systems have been reluctant to recommend PSA testing for two main reasons:

- **Overdiagnosis** is defined as the detection of a disease in men who don't experience any symptoms at the moment of detection and would not develop any symptoms during their lifetime if not identified by early detection activities.[32] The risk of overdiagnosis has been estimated to be as high as 40% in screening-detected Prostate Cancer[33] and is particularly important given the slow development of the disease itself.[34] This applies particularly to men with decreased life expectancy or those with lower PSA values, where the beneficial effect of treatment is limited.[35,36]

- Although PSA screening reduces the risk of mortality, its main drawback is a substantial number of unnecessary biopsies and detection of insignificant cancers, which in the past led to **overtreatment**.[37,38] The issues related to overdiagnosis and overtreatment are the main drivers for recommendations against PSA screening. **However, there are no large studies on the patient´s perspective of overdiagnosis and overtreatment.** The view of healthcare providers may not be identical to patient´s experience and this consideration must continue to be explored in the development and implementation of early detection programmes. In addition, as stated above, there are now diagnostic tools and enhanced knowledge that when effectively implemented will significantly reduce risk of overdiagnosis and overtreatment.

BENEFITS OF EARLY DETECTION OF PROSTATE CANCER

In a nutshell, early detection of Prostate Cancer saves lives, increases quality of life outcomes for Prostate Cancer patients, and decreases costs for public funded health systems.

Globally, men die an average six years younger than women, and for reasons that are largely preventable. One of the main reasons behind this is that many men remain ill-informed about their health. If performed correctly, early detection of Prostate Cancer can play an important part of enhancing men's understanding of their health as part of an informed decision making process with healthcare professionals.

DECREASING MORTALITY AND RAISING QUALITY OF LIFE

Making the decision to conduct a PSA test depends on many factors, including the policy of the doctor or hospital, or the national health policies of the country. Age and family history are always crucial. The main advantage of PSA testing is that men at higher risk for Prostate Cancer are more likely to get an early diagnosis and may need less aggressive treatment. Early stages of Prostate Cancer are mostly asymptomatic but can be easily cured with less severe consequences and at a lower price (80% cheaper than treating late advanced Prostate Cancer). Early detected tumours means there is less damage to the urethral sphincter (incontinence) and to the erectile nerves (impotence) in case of surgery and no need for androgen deprivation in case of radiotherapy. Advanced cancer is less amenable for cure, with more functional complications and can become metastatic and castrate resistant. The treatment of this disease stage is extremely expensive, only to prolong life by an average of two years with poor quality of life.

"IF PERFORMED CORRECTLY, EARLY DETECTION OF PROSTATE CANCER CAN PLAY AN IMPORTANT PART OF ENHANCING MEN'S UNDERSTANDING OF THEIR HEALTH AS PART OF AN INFORMED DECISION MAKING PROCESS WITH HEALTHCARE PROFESSIONALS. "

Before the PSA blood test became available, up to a half of Prostate Cancer patients died of the disease. Since PSA was introduced to detect Prostate Cancer at an early stage, the mortality from Prostate Cancer has decreased more dramatically than for any other cancer[39], at the cost however of so called over-diagnosis and overtreatment.

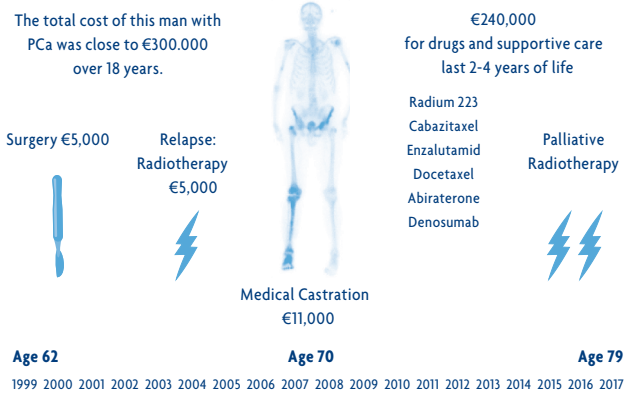
The European Randomised Study of Screening for Prostate Cancer(ERSPC) demonstrates that PSA screening reduces disease specific mortality by 21%, which is equivalent to one death prevented per 781 men invited for screening or one per 27 Prostate Cancer detected. The evidence shows that after 20 years of follow-up the number of patients needed to screen and diagnose Prostate Cancer decreased to 101 and 13, respectively, to prevent one Prostate Cancer death.[40,41] As such, PSA screening results in mortality reduction are obviously better than in breast or colon cancer screening.[42] This decrease in Prostate Cancer death becomes more and more significant with longer follow up (more than 50% after 19 years).[43]

Recent studies in the UK and the USA have also demonstrated that cutting back on PSA screening has a direct correlation with 'too late' detection of the diseases and a rise in mortality rates from Prostate Cancer.[44] Similarly, in Germany, 49 % of Prostate Cancers were diagnosed at a locally advanced level in 2017, whereas in 2008, only 29 % where diagnosed at this later stage.

DECREASING COSTS

An important benefit for European public funded health systems, is that early detection of Prostate Cancer creates costs savings compared with later stage Prostate Cancer. Even though they need to be repeated, PSA tests and a good quality mpMRI scans are cheaper[45] than the treatment of advanced and metastatic disease, which only marginally improves survival.[46] While the costs of robot-assisted radical prostatectomy, which is one of the most used treatments for early Prostate Cancer, does not exceed €15,000 per patient[47], the costs for the management of patients with castration- resistant, non-curable Prostate Cancer can be estimated in approximately €140,000 per patient per year up to €300,000 during a patient's lifetime in Western countries.[48]

COST OF PROSTATE CANCER CARE



CURRENT EVIDENCE BASED RECOMMENDATIONS ON EARLY DETECTION OF PROSTATE CANCER[49]

Current evidence shows that early detection of Prostate Cancer by PSA based risk-adapted early diagnosis in well informed men, will undoubtedly decrease Prostate Cancer mortality dramatically at a reasonable cost.[50]

Currently, only 48 % of all men in Europe are aware of Prostate Cancer risk and PSA testing. The first important step in early detection is awareness raising on Prostate Cancer to the healthy male population.

Awareness raising and building a culture of well-informed men is of utmost importance. Therefore, the EAU (and other international organisations) have designed patient information material to help men to become better informed on whether they should have a PSA test or not with all the pro and cons clearly explained. These information leaflets are not just to be distributed among the healthy population but there is a need to help GP's to guide their patients through the information and informed consent process. PSA based population screening in non-informed men may in fact lead to problems of overdiagnosis and treatment again and this must be avoided. The important first step is awareness raising and accurate information to healthy men. This is why we believe the EU Health Programme should fund a European awareness raising campaign which will include resources which can be used with the general public, healthcare practitioners and schools/higher education facilities. It will also be necessary to address the taboos connected to Prostate Cancer caused by its link to sexual life.

Compared to the classic (previous) diagnostic strategy (that is, PSA and direct biopsies), PSA can be used more cleverly, by applying MRI and further risk stratification tools in men at increased risk, that might need to undergo biopsy. This combined approach in well-informed men will allow a substantial reduction of the number of men that need to undergo biopsy (up to 70%) and reduce over-diagnosis by up to 20%. Risk calculators, biomarkers, and molecular tests can further improve the identification of men with significant Prostate Cancer and reduce the risk of overdiagnosis. Well established management strategies such as withholding active therapy (through active surveillance) for non-life-threatening Prostate Cancer can reduce overtreatment (by up to 25%). With the application of MRI guided active surveillance for all low and some intermediate risk Prostate Cancers, it is now possible to better and non-invasively guide these patients.

A strong understanding of active surveillance as a viable treatment option by both patients and clinicians is a critical element of any early detection programme. The EAU has clear clinical Prostate Cancer deferred treatment guidelines as well as patient information leaflets. In order to improve the uptake of guidelines, the EAU is conducting a large scale project throughout its network to understand the obstacles met across Europe in implementing clinical guidelines.

3. TREATMENT AND CARE

HOW IS PROSTATE CANCER TREATED ?

The most important factors for selecting treatment are the stage and the aggressiveness of the disease. Other factors are individual life expectancy, general state of health and the preference of the individual patient who may give more weight to aspects of quality of life. It should also be borne in mind that individual recommendations may depend on the country and health care system. Optimal management of all stages should ideally be discussed and decided in dedicated Prostate Cancer centres by a multi-disciplinary team (MDT)

LOCALISED AND LOCALLY ADVANCED PROSTATE CANCER

Localised Prostate Cancer is where the cancer is limited to the prostate gland and has not spread. Locally advanced Prostate Cancer is where the cancer has broken through the capsule surrounding the prostate gland.

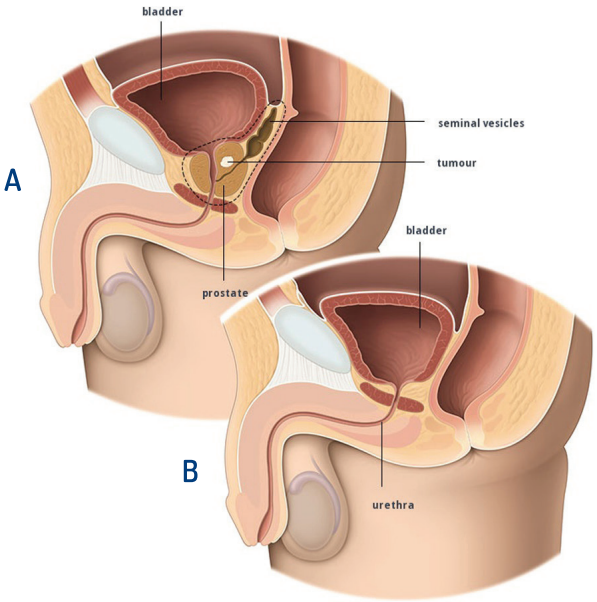
ACTIVE SURVEILLANCE

A way of not immediately treating a recently detected localised Prostate Cancer, but monitoring the disease using serum PSA levels and repeat biopsies to delay or avoid active treatment and possible side effects. Many active surveillance (AS) protocols nowadays include MRI which can be repeated to see if a tumour progresses but also to reduce the need for re-biopsies.

Active treatment options will be proposed when signs of progression occur. AS is an alternative to radical treatment for patients with the lowest risk for progression and with a life expectancy of at least 10 years. (Because of the connotations in the public mind concerning any form of cancer the option of postponing radical treatment by AS may be seen by some men as counter-intuitive). Where men with a low-risk diagnosis are being offered such treatment options they may need significant additional advice on the pros and cons and a clear understanding of the likely post treatment effects of radical treatments in terms of the patient's quality of life. In order to avoid reluctance of patients to accept AS as opposed to active treatment, patients should be informed of the possibility of this option at the time of initial PSA testing.

RADICAL PROSTATECTOMY

A surgical treatment in which the entire prostate and the seminal vesicles are removed. When there is an increased risk of regional metastases, pelvic lymph nodes are removed in the same procedure.



Situation before (A) and after (B) radical prostatectomy.

RADIATION THERAPY

To control and destroy cancer cells via external beam radiation therapy or internal radiation therapy (brachytherapy). Radio-therapy can be given either alone or combined with androgen deprivation therapy.

ANDROGEN DEPRIVATION THERAPY

Hormonal therapy to stop the production or block the action of male sex hormones (androgens) that promote tumour growth. In the past, men were sometimes offered orchiectomy (the surgical removal of the testicles) to stop the production of testosterone. Today, androgen deprivation therapy with drugs has replaced this approach as effective, less invasive and the effects are reversible to a certain extent. A wide variety of drugs are now available and treatment most often consists of:

- Continuous gonadotropin releasing hormone (GnRH) agonist or antagonist therapy (depot injections)
- Maximal androgen blockade (MAB): combination of GnRH with anti-androgens (oral)
- Intermittent androgen deprivation therapy

WATCHFUL WAITING

A way of monitoring as a less intensive type of follow-up, relying more on changes in a man's symptoms to decide if treatment is needed. Other treatment options will be selected only when symptoms appear. It is a palliative treatment modality for patients not eligible for local curative treatment and those with a shorter life expectancy.

EXPERIMENTAL LOCAL TREATMENTS

- Cryosurgical ablation: a minimally invasive surgical treatment in which controlled freezing kills the cancer cells.
- High-intensity focused ultrasound (HIFU): uses the energy of high-frequency sound waves to heat and destroy the cancer cells.
- Photodynamic therapy: a less invasive perineal approach with tissue ablation on the tumour bearing through the side the prostate through laser beams after injection of a photosensitising drug.

METASTATIC PROSTATE CANCER

Where cancer has spread to other parts of the body and can no longer be cured. The treatment will try to slow the growth of the tumour and the metastases.

For patients with newly diagnosed metastatic Prostate Cancer, a combination of hormonal therapy and either radiotherapy, chemotherapy, or new hormonal approaches has shown to improve survival dramatically. In patients with low volume metastasis, hormone therapy combined with palliative radio-therapy to the primary tumour also improves the outcome.

METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCR PC)

This stage of the disease develops in most men under treatment with hormone therapy for metastatic or non-metastatic disease. The tumour and metastases continue to grow because the Prostate Cancer cells no longer respond to hormonal castration treatment. This generally occurs 2-3 years after hormonal therapy starts. Research on mCRPC is ongoing and additional treatments can emerge quickly.

NEW HORMONAL AGENTS

Addition of abiraterone acetate, apalutamide or enzalutamide when ADT is no longer effective.

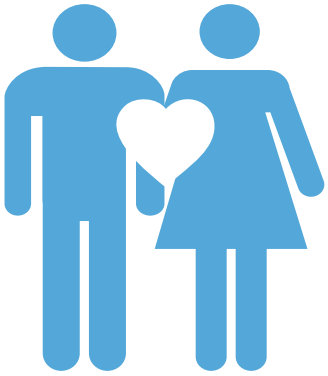
CHEMOTHERAPY

Uses chemicals to kill or stop the growth of metastatic cancer cells (e.g. docetaxel and cabazitaxel).

BONE-SEEKING AGENTS

Ra-223 is an intravenously administered bone seeking radionuclide that has been associated with improved survival in patients with bone only mCRPC. Prostate-specific membrane antigen (PSMA)-ligand labelled with Lutetium-177 is a new radioligand therapy in phase 3 clinical trials. Results are expected to be presented this year. Several studies on other forms of radioligand- and radioimmunotherapy (RLT and RIT) are ongoing. Zoledronic acid and denosumab are bone targeted agents that can be used to decrease the risk of skeletal-related complications, that result from metastases in the bones.

4. QUALITY OF LIFE AND SURVIVORSHIP



In 2019, Europa Uomo, the European Prostate Cancer Coalition, conducted a survey among Prostate Cancer patients, receiving nearly 3,000 contributions from 24 countries. The preliminary results reveal that the respondents quality of life is more impacted than previously imagined. Sexual dysfunction is the major negative consequence of Prostate Cancer treatments and fatigue, incontinence, insomnia and depression are other important factors. Patients who are on the second or later treatment due to cancer recurrence, have worse scores across all measurements.

As the number of Prostate Cancer survivors is increasing, patients, general practitioners and the broader public should be better informed about the needs of cancer survivors in order to improve their quality of life. Prostate Cancer and its treatment affects men physically and emotionally. It may have a significant impact on their everyday life, work, social life and sexuality. It can also have a significant impact on partners and family members.

Patients need to obtain balanced and fair information on the advantages as well as the adverse side-effects of their treatment plans. They need to be able to decide on their own choices and preferences (adapted to their level of acceptance, culture and societal expectations).

If the patients have no symptoms of Prostate Cancer they can usually continue with their daily activities. However, just as importantly, they may be anxious about their prognosis. This may make them feel nervous and depressed. If Prostate Cancer progresses, survivors may need help from family, friends, or professional home carers to do their daily activities. After surgery or other treatment, such as radiotherapy or chemotherapy, they will probably feel tired or sick and may have to stop working at least for a period of time.

Treatment of Prostate Cancer will have several side effects which may interfere with daily life. Common side effects of radiation therapy are a burning sensation when urinating, urinary frequency and anal irritation. Radical prostatectomy may cause stress urinary incontinence. Another common risk of radical prostatectomy is erectile dysfunction (impotence), which also exists with radiotherapy. Younger Prostate Cancer patients should be informed about existing fertility preservation techniques. Androgen deprivation therapy has serious side effects including osteoporosis, anaemia, hot flashes, erectile dysfunction and loss of libido, loss of muscle mass, breast tenderness and growth of breast tissue, decline in cognitive function, depression, weight gain, metabolic changes, and an increased risk of cardiovascular events. It would be beneficial for more research on co-morbidities associated with Prostate Cancer to be conducted. The side effects of treatment or the fact that patients feel too sick or tired can make it difficult for them to take part in social activities. This can make them feel lonely or isolated from others.

The role of patient organisations is pivotal to provide support and more detailed information about coping with Prostate Cancer in relation to the socio-economic difficulties and their cancer survivorship way of life. In particular, the EAU plays a role in providing more and better information to patient organisations for them to raise awareness on the specific needs of Prostate Cancer patients on:

- Physical, psychological, sexual, and nutritional rehabilitation
- Late effects related to the treatment, with particular regard to the metabolic syndrome
- The issue of returning to work after the acute treatment phase

Many middle-aged men in Europe and North America are notorious for not maintaining a healthy lifestyle. If they are obese on diagnosis, the importance of adopting lifestyle changes, during and after treatment, should be emphasised - including a healthy diet and regular physical activity. Evidence is building that exercise can help men with Prostate Cancer to reduce their symptoms and improve their quality of life. Therefore, it is likely that exercise and lifestyle adaptations may be important for men with Prostate Cancer as early as possible after diagnosis. Secondary and tertiary prevention are essential for all patients.

After treatment for Prostate Cancer, a PSA test and eventually a digital rectal examination, will be performed during regular follow-up visits. Follow-up is important to check general health, to manage any side effects from treatment, to watch for a return of the Prostate Cancer (known as recurrent Prostate Cancer), and to watch for other types of cancers.

All the steps of proper follow-up should be included into a personalised Prostate Cancer survivorship cancer plan, to empower individual patients and make sure that each patient would have all the information and would retain full control over his life after the acute treatment.

5. RESEARCH AND INNOVATION

PREVENTION OF LIFE-THREATENING CANCERS

Networks of researchers are working on exciting research into early detection programmes for prostate and other cancers. Latest technological advancements, particularly in whole-exome sequencing, proteomics and machine learning algorithms, now allow for application of 'omics' biomarkers, liquid biopsies and digitalised novel PSA early detection programmes as decision support tools. More research is needed to allow better identification/discrimination between significant and insignificant cancers. Big data initiatives are ongoing to support these research activities.

NEW THERAPIES AND TREATMENTS

European urological research networks present a number of strengths in terms of translational research. Several groups are internationally recognised in developing patient-derived xenografts from individuals with resistant cancers. They have also continuously contributed to high-level research on androgen receptors which allows development of alternative therapies and new anti-androgens. Europe has particular expertise in experimental and translational studies on therapy resistance and European collaborative researchers are recognised for research on cytokines in terms of biomarkers and therapy targets. EAU members also develop innovative viral- and immunotherapies.

Currently, use of most drugs is empiric and rarely guided by appropriate biomarkers/molecular classification, thereby resulting in unnecessary significantly higher costs of novel drugs due to poor selection of the right patients who are good candidates for them. These initiatives are of high importance as they are paving the way towards personalised medicine approaches.

QUALITY OF LIFE AND SURVIVORSHIP

Patients and their families need to be put at the centre of innovations, which need to be linked to clinical practice guidelines. This process allows us to obtain unique insights into what are the best outcomes for patients, and what are the most effective solutions, the best value for money, and importantly also, what solutions best maintain or improve quality of life. Such measures are possible because of the close connection to patients through large patient networks.

Male fertility is also an important strand which runs through this work and has a link to the 'health through the life course' and 'environmental and social health determinants' priorities of the Health cluster of Horizon Europe. Male fertility is a key section of the EAU Guidelines on Sexual and Reproductive Health; it is impacted not only by some urological cancers but can result from treatment of urological cancers.

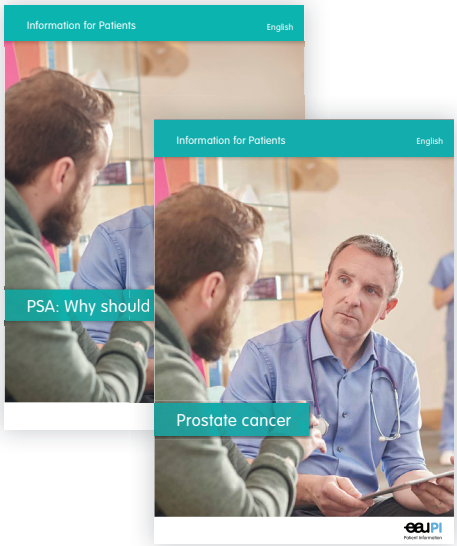
Big data and digitalisation

PIONEER (www.prostate-pioneer.eu), an Innovative Medicines Initiative (IMI) funded project as part of the Big Data for Better Outcomes Programme, has started to build a big data platform on Prostate Cancer drawing in data sets from the EAU network of clinical trials and registries. The next step for this will be to link with electronic health record (EHR) and genomics data. The aim of PIONEER is to use big data to address key knowledge gaps related to the screening, diagnosis and treatment of Prostate Cancer patients.

6. THE ROLE OF THE EUROPEAN ASSOCIATION OF UROLOGY

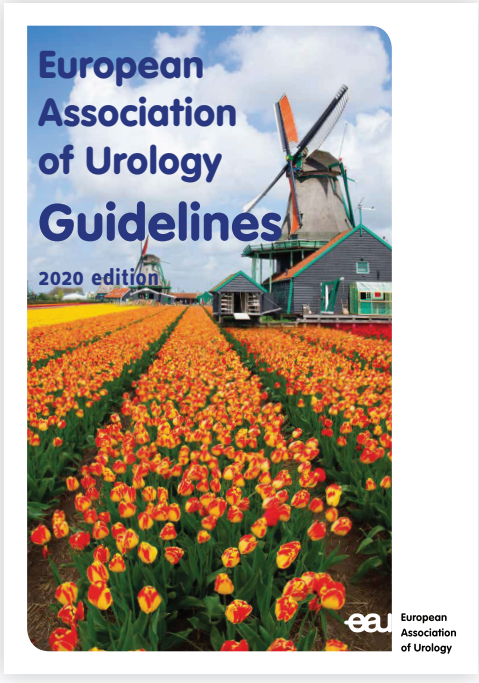
The EAU is the leading authority within Europe on urological practice, research and education. Over 18,000 medical professionals are members and contribute to our mission: to raise the level of urological care throughout Europe and beyond.

The EAU has carried out a range of activities specifically focused on Prostate Cancer which have contributed to improve medical practice and patient care in different ways.



EDUCATION

The EAU provides the latest scientific evidence, expert recommendations and high quality information on Prostate Cancer for medical professionals and patients (e.g. patient information leaflets) in 16 European languages. The European School of Urology (ESU) meets the educational needs of urologists on behalf of the EAU Education Office. Medical professionals benefit from online education, webinars, teaching courses and surgical training. The up-to-date information provided is in line with the EAU Prostate Cancer guidelines to guarantee consistency in content and quality.



EAU GUIDELINES

The Prostate Cancer panel EAU Guidelines Office has prepared guidelines (www.uroweb.org) to assist practicing clinicians in making evidence-based treatment decisions and improve patient care. They are implemented and updated annually based on a structured literature search and systematic reviews. The Prostate Cancer panel consists of an international multidisciplinary group of urologists, radiation oncologist (official representative of ESTRO), medical oncologists, two radiologists (official representatives of ESUR), a nuclear medicine specialist (official representative of EANM), an oncogetriatric specialist (official representative from SIOG) and a patient stakeholder organisation representative. The current corpus of 21 EAU Clinical Practice Guidelines covers the breadth of the urological field and are endorsed by over 70 national urological societies globally including all EU Member States.

The Prostate Cancer guidelines are officially endorsed by the European Society for Therapeutic Radiology and Oncology (ESTRO), the International Society of Geriatric Oncology (SIOG) as well as the European Society of Nuclear Medicine (EANM) and the European society of Urogenital Radiology (ESUR). They are critical for improving and harmonisation of cost-efficient care for all EU citizens.

PATIENT INFORMATION AND ADVOCACY

The EAU's Patient Information Initiative has produced patient information leaflets on Prostate Cancer with the help of medical experts, patient organistations, specialised nurses and Prostate Cancer patients. All participated in the writing and critical review of the information ensuring it is understandable for the general public. The medical facts in these patient information leaflets are consistent with EAU guidelines ensuring the information is unbiased and reliable.

EAU patient information offers detailed information on diagnosis and treatment of localised, advanced and metastatic Prostate Cancer as well as on palliative care and a frequently asked questions section for patients and their relatives. To better understand the treatment path, EAU patient information on Prostate Cancer is supported by educational images that illustrate diagnostic and surgical procedures.

The EAU patient information on Prostate Cancer is part of the *EAU Patient Information Project (patients.uroweb.org)*.

The EAU Patients Advocacy Group (EPAG) was started in 2019 with an objective to increase and improve patient involvement in EAU activities, patient empowerment and engagement in the development, dissemination and impact assessment of guidelines and patient information and to support educational events for patients and patient associations. This joint effort is to draw from each other's expertise in order to take on the challenges that come with expanding activities on a European level that have significant impact and force change in legislation, as well as the involvement of patients in clinical care, research and medical congresses in the field of oncology and non-oncology diseases.

RESEARCH

Patient platforms, professional networks and cutting-edge research supported by the EAU cover all phases of the research cycle from basic to clinical practice guidelines implementation research, and training to support the uptake of innovation, harmonize care and demonstrate impact.

Our clinical practice guidelines development based on evidence-based medicine is one of the core activities of the EAU to educate and train our current and future healthcare professionals, and to allow for successful deployment of innovative research outcomes and novel knowledge generated and validated within the scientific society through appropriate clinical trials.

Research is another core activity of the EAU. The EAU Section of Urological Research (ESUR), aiming to promote basic and clinical research in the field of urology and related areas, acts as a platform for researchers in different disciplines, in order to improve the coordination of research (from experimental to clinical trials and big data/real-world evidence). The EAU also has its own Research Foundation (RF), whereby our members can apply for funds to promote, facilitate and stimulate clinical and basic research in European urology. The RF acts as sponsor of multicentre studies and several registries (www.uroweb.org/research). We set out to achieve this mission by acting as a bridge between urological centres across the European Union, research organisations and the EAU membership.

7. WHAT HAS THE EU DONE SO FAR?

EU MILESTONES ON CANCER

Although significant advances are being made in the fight against the disease, cancer remains a key public health concern and a tremendous burden on European societies. It is for this reason that a range of activities on cancer have taken place at EU level to help Member States in the fight against cancer.

In 2003, the EU Health Ministers unanimously adopted a Council Recommendation on cancer screening, setting out principles of best practice in the early detection of cancer. The Recommendation invited all Member States to take common action to implement national population-based screening programmes for breast, cervical and colorectal cancer, with appropriate quality assurance at all levels.

The EU Joint Action on Cancer Control (CANCON) was launched to develop an EU Guide on Quality Improvement in Comprehensive Cancer Control. The successor of CANCON, the Innovation Partnership on Action Against Cancer (iPAAC) is continuing this valuable work among EU member states. The previous Health Commissioner Andriukaitis had indicated in response to a parliamentary question[51] that iPAAC would collect new evidence for the possible inclusion of Prostate Cancer screening programmes into National Cancer Plans, however very little progress has yet been made on this issue.

The EU's Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases also includes cancer as a priority.

The European Commission through the Joint Research Council has also initiated a ground-breaking project to develop a European quality assurance scheme for breast cancer services underpinned by accreditation and referring to high quality, evidence-based guidelines.[52]

Alongside this, the European Commission, through its consecutive Research Programmes such as Horizon 2020, has supported a number of EU collaborative research projects in cancer, including projects specifically focused on Prostate Cancer.

8. RECOMMENDATIONS FOR EU ACTION ON PROSTATE CANCER

The EU Cancer Plan is a chance for wider recognition of Prostate Cancer as a European healthcare problem and to engage in closer collaboration between EU institutions and Member States, healthcare professionals, patient representatives and their families to agree an approach to tackling it.

Our **recommendations** on Prostate Cancer to the European Commission in light of the EU Cancer Plan, are as follows:

PREVENTION, EARLY DETECTION AND AWARENESS RAISING

- The **EU Health Programme** in 2021-2027 should support an **EU wide awareness raising campaign on Prostate Cancer**. There are now multiple published research studies that provide robust evidence confirming that early detection of Prostate Cancer saves lives. Therefore, it is time for the EU Health Programme to promote awareness of the benefits of early detection of Prostate Cancer. In parallel, it is important that the EU health programme addresses the knowledge gap that exists on the benefits of an early detection programme by supporting educational resources that ensures that men at risk make an informed choice.

- The EU Cancer Plan should mandate and endorse **clinical guidelines on early detection and diagnosis of Prostate Cancer** which can be taken up by EU Member States in their National Cancer Plans. We believe this action will lead to much better harmonization of approach to early detection across the EU. This will dramatically reduce mortality rates from Prostate Cancer and will also help to increase the number of well-informed men and ensure better quality of life outcomes at a reasonable cost. The guidelines should use as a basis the most recently agreed clinical guidance, such as the EAU guidelines on Prostate Cancer.[53]

TREATMENT AND CARE

- The EU should promote **high quality, standardised and integrated care**, with a focus on patient-centred, multidisciplinary approach, either following the model of Prostate Cancer Centres of excellence[54] or in Prostate Cancer Units[55]
- **Health Technology Assessment** (HTA) legislation should support the prompt and consistent HTA for new screening, diagnostic, therapeutic and rehabilitation technologies in order to provide the basis for effective, efficient, targeted and optimised allocation of resources and specific Prostate Cancer services. Meaningful involvement of all stakeholders, including patients, healthcare professionals, consumer, public health organisations and academia in the process is necessary to get a clearer understanding on societal needs and preferences.
- Access to **innovative treatments and personalised medicines** should be made fast and equitable to all Prostate Cancer patients who can benefit from them at an **affordable price**. Effective implementation must be matched by demonstration of impact on outcomes (clinical and economic).

SURVIVORSHIP AND QUALITY OF LIFE OF PATIENTS

- **Implementation of survivorship plans as part of the National Cancer Plans must be part of the EU Cancer Plan**, including specific plans for Prostate Cancer patients. Taking advantage of electronic patient-reported outcome measures (PROMs) for Quality of Life will get patients engaged in their own cancer journey.
- The EU should support an **EU-wide comparative study on the economic impact of cancer for patients** (including Prostate Cancer patients and their families) and society at large.

RESEARCH AND INNOVATION

The health cluster of **Horizon Europe** should:

- **Prioritise Prostate Cancer research** to allow better identification/discrimination between significant and insignificant cancers and in **areas of personalised cancer medicine**

which should a) allow better identification of patients who will benefit from a particular treatment thus minimising costs for non-justified use of novel therapy agents and b) delay onset of tumour progression on the basis of appropriate knowledge on biomarkers and validated targets. In order to be able to achieve that goal, integrative projects with **novel models, bioinformatics analyses, and advanced technologies** should be supported.

- Dedicate funding to **research on comorbidities** to fill existing gaps in research and better understand disease interactions.
- **Continue and increase funding for big data projects in Prostate Cancer** which have been started during the 2014-2019 Commission, like the IMI funded PIONEER project (www.prostate-pioneer.eu) which is building a unique big data platform and state-of-the-art analytics to improve Prostate Cancer outcomes. With increased financial support for data linkage, data input, and connection of registries, clinical practice guidelines and clinical trial data with Electronic Health Records (EHR) in collaboration with the proposed European Cancer Knowledge Centre and the European health data space, it will be possible to make clear advances in transforming lives of Prostate Cancer patients through more effective research into their conditions, identification of new treatment strategies and in the digital transformation of healthcare. One concrete example of this is computerised image analysis by AI which could play an important role in increasing accuracy, reducing variability and speeding up the reading of suspected Prostate Cancer tumours. Several algorithms are under development and additional funding support is needed for careful evaluation of the new tools. It is of utmost importance to support sustainability of the developed registries and databases.
- **Leverage and harness expertise and experience** of healthcare professionals, patient groups and healthy men as a soundboard for the **Cancer research mission** and potential actions on Prostate Cancer.
- Support **pragmatic solutions for facilitating GDPR compliant processing of personal data in health for secondary purposes including research**, taking forward the gold-standard work of the ERNs, the European Commission and the European Data Protection Board on a consent model for ERNs (through the **EU Health Programme 2020 Joint Action** on GDPR and the health)
- Fund digital skills training for healthcare professionals to prepare them for the digital era, including on AI, robotic surgery and endoscopy.

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ACKNOWLEDGEMENTS

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REFERENCES

1 Mottet N., Cornford P., van den Bergh R.C.N., Briers E., De Santis M., Fanti S., Gillessen S., Grummet J., Henry A.M., Lam T.B., Mason M.D., van den Kwast T.H., van den Poel H.G., Rouvière O., Schoots I.G., Tilki D., Wiegel T.; members of the EAU–EANM-ESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Edn. presented at the EAU Annual Congress Amsterdam 2020. ISBN: 978-94-92671-07-3. Publisher: EAU Guidelines Office. Place published: Arnhem, The Netherlands. https://uroweb.org/guideline/prostate-cancer/

2 Wirth, et al. The European Prostate Cancer Centres of Excellence: A Novel Proposal from the European Association of Urology Prostate Cancer Centre Consensus Meeting, Eur Urology 76 (2 019) 179 – 18 6

3 Valdagni, Van Poppel et al, Prostate Cancer Unit Initiative in Europe: A position paper by the European School of Oncology, Critical Reviews in Oncology/Hematology, 2015

4 https://ec.europa.eu/eurostat/statistics-explained/index.php/People_in_the_EU_-_population_projections#An_ageing_society

5 Esposito K, et al. Effect of metabolic syndrome and its components on prostate cancer risk: meta-analysis. J Endocrinol Invest 36:132-9, 2013

6 Liang Z, et al. Hypertension and risk of prostate cancer: a systematic review and meta-analysis. Sci Rep 6:31358, 2016

7 Alshaker H, et al. Leptin signalling, obesity and prostate cancer: molecular and clinical perspective on the old dilemma. Oncotarget 6:35556-63, 2015

8 www.cancer-code-europe.iarc.fr

9 Epstein JI, et al. A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. Eur Urol 69:428-35, 2016

10 Mottet N., Cornford P., van den Bergh R.C.N., Briers E., De Santis M., Fanti S., Gillessen S., Grummet J., Henry A.M., Lam T.B., Mason M.D., van den Kwast T.H., van den Poel H.G., Rouvière O., Schoots I.G., Tilki D., Wiegel T.; members of the EAU–EANM-ESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Edn. presented at the EAU Annual Congress Amsterdam 2020. ISBN: 978-94-92671-07-3. Publisher: EAU Guidelines Office. Place published: Arnhem, The Netherlands. https://uroweb.org/guideline/prostate-cancer/

11 Huang TB, et al. Aspirin use and the risk of prostate cancer: a meta-analysis of 24 epidemiologic studies. Int Urol Nephrol 46:1715-28, 2014

12 Freedland SJ, et al. Statin use and risk of prostate cancer and high-grade prostate cancer: results from the REDUCE study. Prostate Cancer Prostatic Dis 16:254-9, 2013

13 Benzon Larsen S, et al. Statin use and prostate cancer mortality, 31th Annual EAU Congress, Munich, 11-15 March 2016. Available at: http://uroweb.org/wp-content/uploads/EAU16-Benzon-Larsen-press-release.pdf, 2016. Last accessed October 2016

14 Mottet N., Cornford P., van den Bergh R.C.N., Briers E., De Santis M., Fanti S., Gillessen S., Grummet J., Henry A.M., Lam T.B., Mason M.D., van den Kwast T.H., van den Poel H.G., Rouvière O., Schoots I.G., Tilki D., Wiegel T.; members of the EAU–EANM-ESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Edn. presented at the EAU Annual Congress Amsterdam 2020. ISBN: 978-94-92671-07-3. Publisher: EAU Guidelines Office. Place published: Arnhem, The Netherlands. https://uroweb.org/guideline/prostate-cancer/

15 Van Poppel H, Tombal B. Chemoprevention of prostate cancer with nutrients and supplements. Cancer Manag Res 3:91-100, 2011

16 Bylsma LC, Alexander DD. A review and meta-analysis of prospective studies of red and processed meat, meat cooking methods, heme iron, heterocyclic amines and prostate cancer. Nutr J 14:125, 2015

17 Gandaglia, G., et al., The Problem Is Not What to Do with Indolent and Harmless Prostate Cancer-The Problem Is How to Avoid Finding These Cancers. Eur Urol, 2016. 70(4): p. 547-548.

18 Futterer, J.J., et al., Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging? A Systematic Review of the Literature. Eur Urol,2015. 68(6): p. 1045-53.

19 Gandaglia, G., et al., The Problem Is Not What to Do with Indolent and Harmless Prostate Cancer-The Problem Is How to Avoid Finding These Cancers. Eur Urol, 2016. 70(4): p. 547-548.

20 Futterer, J.J., et al., Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging? A Systematic Review of the Literature. Eur Urol,2015. 68(6): p. 1045-53.

21 Ahmed, H.U., et al., Diagnostic accuracy of multi-parametric

MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet, 2017. 389(10071): 815-822.

[22] Kasivisvanathan, V., et al., MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med, 2018. 378(19): p.1767-1777

[23] Grenabo Bergdahl, A., et al., Role of Magnetic Resonance Imaging in Prostate Cancer screening: A Pilot Study Within the Goteborg Randomised Screening Trial. Eur Urol, 2016. 70(4): p. 566-573.

[24] Alberts, A.R., et al., Characteristics of Prostate Cancer Found at Fifth Screening in the European Randomized Study of Screening for Prostate Cancer Rotterdam: Can We Selectively Detect High-grade Prostate Cancer with Upfront Multivariable Risk Stratification and Magnetic Resonance Imaging? Eur Urol, 2017.

[25] http://www.prostatecancer-riskcalculator.com/

[26] Vickers, A.J., E.A. Vertosick, and D.D. Sjoberg, Value of a Statistical Model Based on Four Kallikrein Markers in Blood, Commercially Available as 4Kscore, in All Reasonable Prostate Biopsy Subgroups. Eur Urol, 2018. 74(4): p. 535-536.

[27] Zappala, S.M., et al., Clinical performance of the 4KscoreTest to predict high-grade Prostate cancer at biopsy: A meta-analysis of us and European clinical validation study results. Rev Urol, 2017. 19(3): p. 149-155.

[28] Loeb, S., et al., Prostate Health Index improves multivariable risk prediction of aggressive prostate cancer. BJU Int, 2017. 120(1): p. 61-68.

[29] Van Neste, L., et al., Detection of High-grade Prostate Cancer Using a Urinary Molecular Biomarker-Based Risk Score. Eur Urol, 2016. 70(5): p. 740-748.

[30] Fenstermaker, M., et al., Risk Stratification by Urinary Prostate Cancer Gene 3 Testing Before Magnetic Resonance Imaging-Ultrasound Fusion-targeted Prostate Biopsy Among Men With No History of Biopsy. Urology, 2017. 99: p. 174-179.

[31] Briganti, A., et al., Active Surveillance for Low-risk Prostate Cancer: The European Association of Urology Position in 2018. Eur Urol, 2018. 74(3): p. 357-368.

[32] Marcus, P.M., et al., Conceptualizing overdiagnosis in cancer screening. J Natl Cancer Inst, 2015. 107(4).

[33] Draisma, G., et al., Lead time and overdiagnosis in prostate specific antigen screening: importance of methods and context. J Natl Cancer Inst, 2009. 101(6): p. 374-83

[34] Abdollah, F., et al., Cancer-specific and other-cause mortality after radical prostatectomy versus observation in patients with prostate cancer: competing-risks analysis of a large North American population-based cohort. Eur Urol, 2011. 60(5): p. 920-30.

[35] Vickers, A.J., et al., Empirical estimates of prostate cancer overdiagnosis by age and prostate-specific antigen. BMC Med, 2014. 12: p. 26.

[36] Vickers, A., et al., Individualized estimation of the benefit of radical prostatectomy from the Scandinavian Prostate Cancer Group randomized trial. Eur Urol, 2012. 62(2): p. 204-9.

[37] Martin, R.M., et al., Effect of a Low-Intensity PSA-Based Screening Intervention on Prostate Cancer Mortality: The CAP Randomized Clinical Trial. JAMA, 2018. 319(9): p. 883-895.

[38] Loeb, S., et al., Overdiagnosis and overtreatment of prostate cancer. Eur Urol, 2014. 65(6): p. 1046-55.

[39] EAU Policy Paper on PSA Screening for PCa found at http://epad.uroweb.org/wp-content/uploads/EAU_policy-briefing_PSA.pdf p. 6

[40] Osses, D.F., et al., Results of Prostate Cancer Screening in a Unique Cohort at 19yr of Follow-up. Eur Urol, 2018.

[41] Minozzi S, et al. European Code against Cancer 4th Edition: Process of reviewing the scientific evidence and revising the recommendations. Cancer Epidemiol 39 Suppl 1:S11-9, 2015

[42] EAU Policy Paper on PSA Screening for PCa found at http://epad.uroweb.org/wp-content/uploads/EAU_policy-briefing_PSA.pdf p. 6

[43] Osses, D.F., et al., Results of Prostate Cancer Screening in a Unique Cohort at 19yr of Follow-up. Eur Urol, 2018

[44] EAU Policy Paper on PSA Screening for PCa found at http://epad.uroweb.org/wp-content/uploads/EAU_policy-briefing_PSA.pdf p. 7

[45] For example, PSA tests cost approximately Đ10 and a good quality mpMRI costs around Đ136 based on average cost in Belgium.

[46] Cornford, P., et al., EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part II: Treatment of Relapsing, Metastatic, and Castration-Resistant Prostate Cancer. Eur Urol, 2017. 71(4): p.630-642.

[47] Forsmark, A., et al., Health Economic Analysis of Open and Robot-assisted Laparoscopic Surgery for Prostate Cancer Within the Prospective Multicentre LAPPRO Trial. Eur Urology 2018. 74(6): p. 816-824.

[48] Wu B, et al., Cost of care for patients with metastatic castration-resistant prostate cancer initiating on docetaxel versus oral targeted therapies in the United States. Journal of Clinical Oncology, 2018. 36(30, suppl.): p. 88

[49] Mottet N., Cornford P., van den Bergh R.C.N., Briers E., De Santis M., Fanti S., Gillessen S., Grummet J., Henry A.M., Lam T.B., Mason M.D., van den Kwast T.H., van den Poel H.G., Rouvière O., Schoots I.G., Tilki D., Wiegel T.; members of the EAU–EANM-ESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Edn. presented at the EAU Annual Congress Amsterdam 2020. ISBN: 978-94-92671-07-3. Publisher: EAU Guidelines Office. Place published: Arnhem, The Netherlands. https://uroweb.org/guideline/prostate-cancer/

[50] Gandaglia et al Structured Population-based Prostate-specific Antigen Screening for Prostate Cancer: The European Association of Urology Position in 2019 found at https://www.europeanurology.com/article/S0302-2838(19)30347-1/pdf

[51] https://www.europarl.europa.eu/doceo/document/E-8-2017-007165-ASW_EN.html

[52] European Initiative on Breast Cancer https://healthcare-quality.jrc.ec.europa.eu.

[53] Mottet N., Cornford P., van den Bergh R.C.N., Briers E., De Santis M., Fanti S., Gillessen S., Grummet J., Henry A.M., Lam T.B., Mason M.D., van den Kwast T.H., van den Poel H.G., Rouvière O., Schoots I.G., Tilki D., Wiegel T.; members of the EAU–EANM-ESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Edn. presented at the EAU Annual Congress Amsterdam 2020. ISBN: 978-94-92671-07-3. Publisher: EAU Guidelines Office. Place published: Arnhem, The Netherlands. https://uroweb.org/guideline/prostate-cancer/

[54] Wirth, et al. The European Prostate Cancer Centres of Excellence: A Novel Proposal from the European Association of Urology Prostate Cancer Centre Consensus Meeting, Eur Urology 76 (2 019) 179 – 18 6

[55] Valdagni, Van Poppel et al, Prostate Cancer Unit Initiative in Europe: A position paper by the European School of Oncology, Critical Reviews in Oncology/Hematology, 2015.

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EUROPA UOMO
The Voice of Men with Prostate Cancer in Europe

European Alliance for Personalised Medicine

Publication: April 2020

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