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AN OVERVIEW OF BENIGN PROSTATIC HYPERPLASIA AND PROSTATIC CANCER IN MAMMALS WITH SPECIAL EMPHASIS ON MALE DOGS AND MEN WITH A PERSONAL EXPERIENCE AS A PATIENT IN BANGLADESH

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ABSTRACT

Background: Benign prostatic hyperplasia (BPH) and prostate cancer (PC) are primarily considered human diseases, but they occur spontaneously in a limited number of mammalian species. While many mammals have prostate glands, spontaneous age-related BPH is well documented in humans, dogs, and chimpanzees. BPH is non-cancerous, involving an enlarged prostate that causes lower urinary tract symptoms (LUTS), while PC involves malignant cells. Despite an unremitting increase in the number of patients presenting symptoms of BPH and PC, the viable treatment options remain relatively limited when compared to other disorders of aging. However, treatment approaches are categorized into allopathic (conventional pharmaceutical), herbal (phytotherapy), and homeopathic systems, but their comparative evaluation is very limited.

Objective: This review provides the prevalence of BPH and PC in male dogs and men, with comparative medico-surgical, herbal, and homeopathic therapies, and their combinations with benefits and side effects, with a personal case study in Bangladesh

Data sources: Databases (PubMed, Scopus, Web of Science, Google Scholar), Artificial Intelligence (AI; Copilot).

Results: Findings on BPH and PC in men and male dogs reveal striking anatomical and physiological similarities, making the dog a key natural model for human disease. BPH is highly prevalent in both species, but canine PC differs from human PC, often appearing in castrated dogs and serving as an 'androgen-independent' model, like advanced human castration-resistant PC. The multifactorial etiology of BPH explains why treatment often combines hormonal therapy, lifestyle modification, and symptom management, including surgical procedures. Medical therapy for BPH includes alpha-blockers, 5α-reductase inhibitors, or a combination of both. There are over 10 primary surgical and minimally invasive methods currently used worldwide for the treatment of BPH in men, depending on prostate volume. Most of the medicine and surgical treatments caused clear side-effects and complications, especially sexual side-effects and infertility. However, the results of any surgical procedure also depend on the method used and on whether it is performed by an experienced surgeon. Google search reveals the top 10 urologists practicing in Dhaka, some of whom are pioneers of HoLEP in Bangladesh. Of these, five randomly selected urologists consulted for BPH treatment in the different recognized hospitals, but they follow the diagnostic and treatment procedure in a similar manner, like they are targeting first the PC diagnosis by suggesting multiple tests, including PSA, USG, prostate biopsy, and MRI, without any justification to cost the patient at their specific laboratory. Similarly, they are also prescribing inappropriate drugs for BPH treatment only from a specific pharmaceutical company, even with known ineffective drugs for a hugely enlarged prostate. They have only experience with TURP surgery, whereas they have advertised on websites (Facebook) offering laser techniques to attract patients for treatment at their hospitals. Medical malpractice by specialized doctors in Dhaka is a growing concern, driven by various factors. Herbal and homeopathic medicines, mostly derived from plant sources, are widely used to manage mild-to-moderate LUTS associated with BPH in men, with variable results; their research findings have been reviewed and discussed.

Conclusion: The prevalence of BPH and PC in men is increasing globally, including in Bangladesh. Histopathological diagnosis of prostate tissues showed 82% had BPH and 16% PC, and PC accounts for over 1600 deaths in men annually in Bangladesh. BPH and PC are significant, rising health issues among older men, with BPH being far more prevalent, while PC presents a serious mortality risk due to often late-stage diagnosis. This review highlights inconsistencies in ingredient content among the marketed allopathic, herbal, and homeopathic drugs, along with the malpractice of the urologists. Quality control measures are imperative to ensure patients receive effective, safe medicines to manage BPH symptoms. The comprehensive, regular monitoring of prostate health provides the best balance between maintaining a high quality of life and ensuring that serious, progressive diseases are caught and treated early. This review serves as a valuable resource for concerned male dogs and men, offering evidence-based guidance to improve decision-making in managing BPH and prostate cancer.

Keywords: Benign prostate hyperplasia (BPH), Prostate cancer (PC), Mammals, Men, Male dogs, Risk factors, Medico-surgical therapies, Phytotherapy, Homeopathic therapy, Bangladesh

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CONTENTS

INTRODUCTION

The prostate is present in all male mammals but varies greatly in size, lobulation, and clinical relevance. Species such as marine mammals (whales and dolphins) exhibit reduced or modified prostate structures, adapted for aquatic reproduction. Rodents (rats and mice) have a complex lobular structure, making them useful as experimental models for prostate research. Horses have a compact prostate gland, less prone to disease, whereas ruminants have a small, often diffuse, rudimentary prostate. Cats are smaller, less distinct, and less likely to develop pathology than dogs. Dogs and humans have large, clinically significant prostates that are prone to BPH and PC. Considering these facts, BPH and PC are reviewed primarily in humans, with limited essential information available for dogs.

The prostate gland undergoes several growth phases; it begins as the size of a walnut (20g) between ages 20 and 30, and by age 60, it reaches approximately the size of a lemon. The prostate gland, located below the urinary bladder and surrounding the urethra, naturally enlarges over time. However, excessive growth of the prostate and the tissue surrounding it, called benign prostatic hyperplasia (BPH), can cause a range of complications. The LUTS secondary to BPH are one of the most common disorders affecting the aging man, being prevalent in about 8% of men in their 40s and 50% in men between their 50s and 60s,[1] with almost 90% of men older than 80 years.[2] LUTS describe the urinary abnormalities shared by disorders affecting the bladder and prostate, typically caused by BPH. These terms have largely replaced histologically defined 'prostatism.[3] Prostate tissue is composed of two basic elements: a glandular element composed of secretory ducts and acini, and a stromal element composed primarily of collagen and smooth muscle. Histologically, BPH is defined as benign proliferation of stromal and glandular epithelial cells within the prostate transition zone, accompanied by hyperplasia of smooth muscle and connective tissue, collectively forming a non-malignant adenoma. There are two phases of BPH progression, of which the first phase consists of an increase in BPH nodules in the periurethral zone and the second a significant increase in size of glandular nodules.[4] BPH is a non-malignant enlargement of the prostate, which results in LUTS due to obstruction and irritation of the bladder outlet.[5] BPH is a prostate adenoma characterized by the histological proliferation (hyperplasia) of stromal and epithelial cells in the transitional zone of the prostate gland. BPH may cause physical compression of the urethra and result in anatomic bladder outlet obstruction (BOO) through two distinct mechanisms: First, an increase in prostate volume, termed the static component; second, an increase in stromal muscle tone, termed the dynamic component. BOO, in turn, may present clinically with LUTS, urinary tract infections (UTIs), acute urinary retention (AUR), renal failure, hematuria, and bladder calculi.[6] Notably, two factors complicate the natural history and clinical presentation of BPH, BOO, and LUTS; first, prostate volume does not linearly correlate with the severity of BOO or LUTS; and second, progressive BPH and BOO can lead to primary bladder dysfunction, which in turn can exacerbate the severity of LUTS independently of BOO.[6] Collectively, BPH, BOO, and LUTS are associated with increased risks of mortality, depression, falls, and diminished health-related quality of life, as well as elevated costs of billions of dollars in annual health expenditure.[6] BPH is generally not considered preventable. However, modifiable factors may influence the risk of BPH and LUTS.[7] The sex steroid hormones are essential to normal prostate growth and development. Suppression of androgen-dependent prostate growth pathways with surgery or medication remains the only intervention proven to attenuate or arrest BPH progression. While androgens and genetic predisposition have important etiological roles, accumulating evidence indicates that modifiable risk factors are also associated with the development of BPH and LUTS.[7] Considering these facts, this review paper describes an overview of the BPH and PC in men and dogs, with most aspects to manage the old age disorders.

MATERIALS AND METHODS

A comprehensive literature review was conducted to examine the various aspects of BPH, including anatomy and physiology, as well as surgical management. Relevant peer-reviewed journal articles were

primarily identified through comprehensive searches of Google Scholar, PubMed, and Artificial Intelligence (AI) databases, covering publications up to April 2026. Articles were screened based on titles and abstracts, with eligible studies undergoing full-text review.

Anatomy and physiology of the prostate gland

- The normal prostate gland, a walnut-size or inverted-pyramid-shaped male accessory reproductive organ, is located just below the urinary bladder, anterior to the rectum, and encircling the proximal urethra. It measures 3-4 cm long, 4-6 cm wide, 2-3 cm thick, and weighs 18-26g.
- The prostate gland is divided into four distinct anatomical and functional zones, which include:

(a) Peripheral zone (PZ)- is the area forming the posterior and lateral sides of the gland and represents 70% of the prostatic volume, and is the area typically palpated during a digital rectal examination (DRE), where the majority (70-80%) of prostate cancers form.

(b) Central zone (CZ)- surrounds the ejaculatory ducts, representing 25-20% of the prostate volume, which usually gives rise to inflammatory processes (e.g., prostatitis).

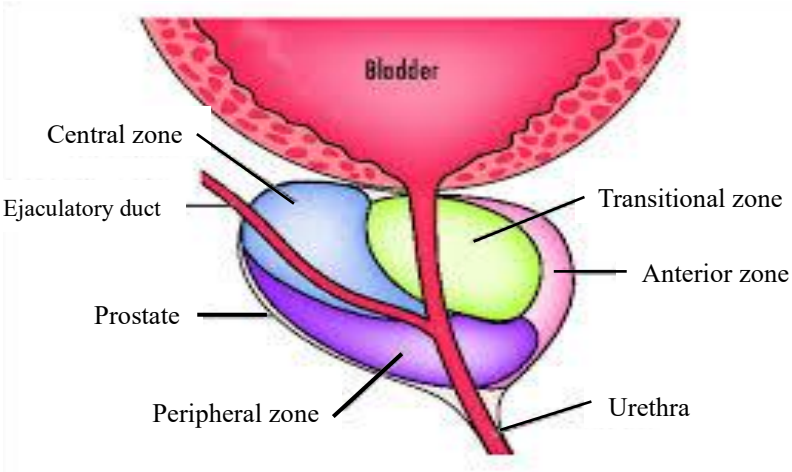

Fig. 1. Four distinct anatomical and functional zones of the prostate[1]

(c) Transition zone (TZ)- represents only 5-10% of the total prostate volume, which is the primary site of BPH, and continues to grow throughout life, and consists of two lateral lobes together with periurethral glands.

(d) Anterior fibromuscular stroma (AFS) zone- it is composed of non-granular and fibrous tissues that cover the anterior aspect of the prostate and is rarely a site of disease.[8]

- Relations of the prostate to the surrounding: (a) superior urinary bladder neck, (b) inferior- urogenital diaphragm, (c) posterior- rectum (palpable via digital rectal exam), and (d) anterior- pubic symphysis.
- Capsule- fibromuscular capsule enclosing the prostate glandular tissue.

Embryology of the prostate

The prostate gland in men originates during embryogenesis from the urogenital sinus (UGS), a derivative of the hindgut endoderm. Its development is androgen-dependent and begins around the 10^{th} to 12^{th} week of gestation. The gland develops through complex mesenchyme-epithelial interactions, where the surrounding mesenchyme instructs the urethral epithelium to form branching, glandular structures.

- Embryologically, it starts to develop by the 12^{th} week of gestation under the influence of testosterone from the testes of the developing fetus. It develops from the UGS under the influence of dihydrotestosterone (DHT).
- The primary mechanism underlying prostate development is androgen receptor signaling via DHT, which is widely distributed in the genitourinary tract.
- The prostate originates from epithelial buds formed at precise locations under the influence of paralogous homeobox (Hox) genes, the fibroblast growth factor (FGF) family, and the transforming growth factor-β subfamily.

- At birth, the prostate is a small gland containing a network of tubules and alveoli that remains quiescent until it grows rapidly during puberty.

Physiology of the prostate

The primary physiological function of the prostate gland is to produce, store, and release alkaline, enzyme-rich fluid (approximately 20-30% of semen) that enhances sperm motility, viability, and survival in the acidic vaginal environment, and to assist in ejaculation. Key physiological functions of the prostate gland are as follows:

- **Secretory functions** (Seminal fluid production): The glandular component produces a fluid rich in citrate, calcium, zinc, and proteolytic enzymes such as prostate-specific antigen (PSA), which liquefy semen after ejaculation, aiding sperm motility. The secretion contains citric acid, zinc, and prostaglandins that stabilize sperm DNA and enhance fertility.
- **Ejaculation mechanism:** The prostate contains smooth muscle fibers that contract during ejaculation, forcing prostate fluid and semen into the urethra for expulsion.
- **Urinary control**: By surrounding the urethra just below the bladder, the prostate aids in closing off the urethra during ejaculation to prevent retrograde ejaculation (semen entering the bladder).
- **Hormonal conversion:** The prostate gland converts testosterone into its more potent metabolite, dihydrotestosterone (DHT), which is crucial for prostate growth and function, via the enzyme 5α-reductase.

Structure and regulation

- Zones: Functionally, it is divided into four zones, with the peripheral zone being the site of most cancers and the transitional zone being the site of benign prostatic hyperplasia (BPH).
- Innervation: The gland is governed by the autonomic nervous system, with sympathetic input triggering ejaculation.
- Immune activity: It is an immunocompetent organ containing lymphocytes and macrophages.

Disorders of the prostate

As men age, the prostate grows and may cause potential urinary symptoms that lead to the development of BPH, prostatitis, and prostate cancer (Table 1). Each man has a prostate, and such a man is at risk for developing prostate disorders.

Table 1. Common disorders of the prostate gland in men

SN	Disorders	Description	Symptoms	Risk factors
①	Benign prostate hyperplasia (BPH)	Noncancerous enlargement of the prostate	Frequent urination, weak stream, nocturia	Age, family history
②	Prostatitis	Inflammation of the prostrate (bacterial or non-bacterial)	Pelvic pain, painful urination, fever (in acute cases)	Infection, stress, urinary tract issues
③	Prostate cancer	Malignant growth in prostrate tissue	Often asymptomatic early, later urinary issues, blood in urine/semen	Age >50, genetics, diet, lifestyle

Etiology

BPH is a noncancerous enlargement of the prostate gland characterized by the proliferation of stromal and epithelial cells, primarily in the transition zone surrounding the urethra. The exact etiology of BPH is considered a multifactorial interplay of aging, hormonal shifts, genetic, metabolic, and chronic inflammatory factors that drive the abnormal growth of prostate epithelial and stromal cells.

Key etiological factors

a. Aging

- Age is the most significant risk factor. The prostate grows throughout life, with accelerating proliferation of glandular and stromal elements after age 40.
- The histological prevalence of BPH at autopsy is as high as 50-60% for males in their 60s, increasing to 80-90% of those older than 70 years of age.[9]

b. Hormonal regulation

- Testosterone and dihydrotestosterone (DHT)- testosterone is converted to DHT in the prostate by 5α-reductase. DHT binds androgen receptors, stimulating cell proliferation and reducing apoptosis. [10,11]
- Estrogens: an age-related increase in the estrogen-to-androgen ratio may promote stromal proliferation and alter androgen receptor sensitivity.[12]
- Functional testes: Men castrated before puberty do not develop BPH, confirming that testicular androgens are necessary for its development.

c. Chronic inflammation and immune pathways

- Localized, low-grade inflammation is often present in BPH tissues, characterized by infiltrating T-cells and macrophages. This immune response releases cytokines (IL-6, TNF-α), which activate growth factors, leading to tissue remodeling and fibrosis.[11]
- Inflammatory infiltrates are commonly observed in BPH tissue, suggesting a link between immune dysregulation and disease progression.

d. Metabolic and lifestyle factors

- Metabolic syndrome (obesity, diabetes, hypertension) is associated with increased risk of BPH, possibly via insulin resistance, systemic inflammation, and higher levels of estrogen.[10]
- Dietary and lifestyle influences: high-fat diets and sedentary behavior may exacerbate risk.

e. Genetic and familial predisposition

- A family history of BPH significantly increases risk, particularly for men with affected brothers or fathers, suggesting a possible hereditary susceptibility.[10]

f. Cellular and molecular mechanisms

- **Imbalance of proliferation vs. apoptosis**- hyperplasia occurs when cell growth outweighs programmed cell death in epithelial and stromal compartments. [10]
- **Growth factors**- Transforming growth factor-β (TGF-β), fibroblast growth factors (FGFs), and insulin-like growth factors (IGFs) contribute to stromal expansion.[11]
- **Stem cell reactivation**: evidence suggests dominant prostate stem cells may re-enter the cell cycle, fueling hyperplasia.[12]

g. Urinary toxins and dysfunction

- Some theories suggest that aging-related accumulation of toxic metabolites in the urine or chronic urethral irritation might damage the prostate tissue, leading to a compensatory hyperplastic response.

Epidemiology

BPH is a highly prevalent, age-related noncancerous enlargement of the prostate, which causes lower urinary tract symptoms (LUTS) due to bladder outlet obstruction. Epidemiological key features are described.

Prevalence of BPH

BPH is prevalent in men globally, with some regional differences, including (a) high-income countries, higher detection rates due to better access to healthcare, (b) low-and middle-income countries, rapidly increasing burden, partly due to demographic shifts and improved life expectancy, and Asia and Africa-rising prevalence, but often underdiagnosed due to limited screening.[13]

- As health systems worldwide improve and life expectancy increases, the prevalence of BPH has also risen rapidly.[6]
- It has been estimated on meta-analysis that the lifetime prevalence of BPH worldwide was 26.2%, and their results indicate that nearly 1 in 4 men will suffer from BPH over their lifetime. [14]
- There were about 94.0 million prevalent cases of BPH worldwide in 2019, compared with 51.1 million cases in 2000.[15] This indicates a sharp rise in BPH prevalence, particularly in low- to middle-income countries. [16]
- In 2021, there were 112.5 million prevalent BPH cases globally, up from 50.7 million in 1990, a 122% increase.[13] The incidence is rising steadily across all regions, with the highest burden in middle socio-demographic index (SDI) regions.[13]
- Both incidence and prevalence are projected to continue increasing until at least 2035, driven by aging populations.[13,17]

Risk factors

Studies on the causes and risk factors for BPH have traditionally focused on sex hormones, genetic predisposition, and age-related changes. Still, recent studies indicate that BPH is linked to a range of modifiable factors.[18] However, several risk factors associated with it have been identified through research and can be divided into two categories: (A) Non-modifiable and (B) Modifiable (Table 2). Although non-modifiable risk factors, including age, genetics, and geography, play significant role in the etiology of BPH and BOO, recent data have revealed modifiable risk factors that present new opportunities for treatment and prevention, including sex steroid hormones, the metabolic syndrome and cardiovascular disease, obesity, diabetes, diet, physical activity, and inflammation (Fig.1).[6] These risk factors may influence the natural history of BPH and BOO across the stages of clinical progression (Fig. 2).

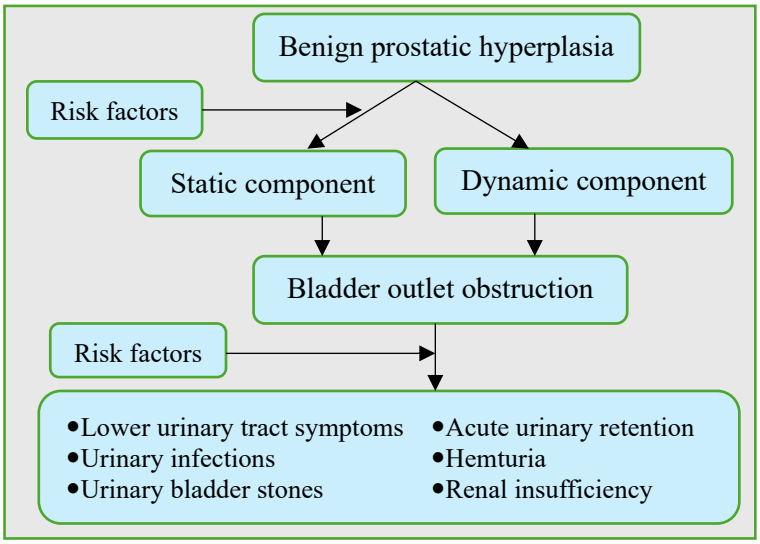

Fig. 2. Natural history of benign prostatic hyperplasia (BPH) and bladder outlet obstruction (BOO)

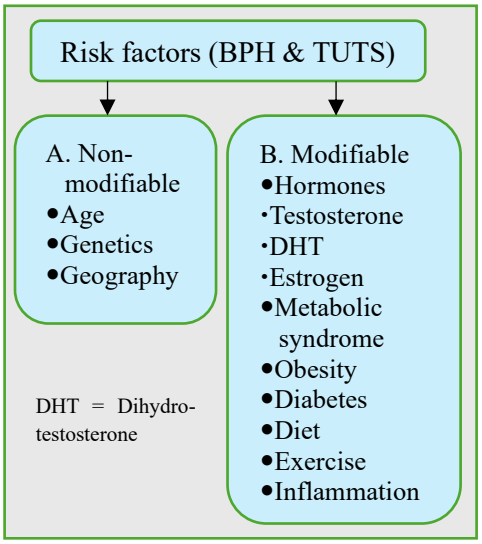

Fig. 1. Risk factors for BPH and male LUTS

(A) Non-modifiable risk factors

A non-modifiable risk factor cannot be addressed through lifestyle changes, taking medication, or other activities. The three major non-modifiable factors of BPH include:

a. Age

Age is the most significant risk factor for BPH because the condition tends to enlarge with age. BPH is

ubiquitous in aging men, with prevalence rising sharply after age 40 and affecting more than half of men over 60, and up to 80% of men by age 80.[17] The global 65-69 age group bears the highest burden, with the 40-44 and 80+ age groups showing an increasing trend.[13] Prostate gland enlargement rarely causes signs and symptoms in men younger than 40. Prevalence of BPH increases with age- affecting 50-60% of men aged 60, and over 80% of men aged 80+.[13]

b. Genetics

There have been reports of a possible genetic link to BPH. Heritability plays a significant role in BPH, with family and twin studies estimating that genetic factors contribute to 40-70% of cases. Several candidate genes and pathways (including androgen metabolism, growth factors, and inflammation) have been implicated in its development.[19-21] If a first-degree relative, such as a father, has been diagnosed with BPH, then sons are more likely to develop it as well. It seems that parents can pass along an increased risk of BPH to their male children. A study showed that 50% of men aged less than 60 years undergoing surgery for BPH had an inherited form of the disease,[22] suggesting an autosomal dominant pattern of inheritance.[23]

Men with inherited forms of BPH tend to have a larger prostate volume and an earlier age at clinical symptom onset than men with sporadic BPH.[24] Studies have identified BTN3A2 and C4A as key genetic contributors to BPH pathogenesis and have further delineated the cg14345882-BTN3A2-BPH pathogenic pathway. Additionally, the role of immune cell surface molecules and the inflammatory cytokine (interleukin [IL]-17) is a significant mediator in BPH development.[25] These findings indicate that genetic factors contribute to approximately 60% of the phenotypic variation in BPH.[26]

Genetic link to BPH in men

① Heritability

- Family and twin studies show that BPH has a strong heritable component, with genetic factors accounting for nearly half of the risk (Table 2).
- Men with a family history of BPH are more likely to develop the condition earlier and with more severe symptoms.[21]

② Candidate genes: Research highlights several gene groups:

- Androgen-related genes: variants in genes that regulate testosterone and dihydrotestosterone metabolism (e.g., SRD5A2, AR) influence prostate growth.
- Growth factor genes- alterations in FGF, VEGF, and TGF-β pathways may drive abnormal stromal and epithelial proliferation.
- Inflammation-related genes, polymorphisms in cytokine genes (IL-6, TNF-□), are linked to chronic inflammation, a contributor to BPH progression. [20]

③ Genome-wide association studies (GWAS)

- GWAS have identified multiple loci associated with prostate volume and urinary symptoms, though findings vary across populations.
- Some loci overlap with those implicated in prostate cancer, suggesting shared biological pathways.[21]

④ Epigenetics and gene regulation

- DNA methylation and microRNA regulation may influence prostate tissue remodeling.
- Epigenetic changes could explain why BPH manifests differently even among men with similar genetic backgrounds.

(c) Geography

Along with genetics, geography also plays a role in the risk of developing BPH. Men in the Western world tend to have significantly higher prostate volumes than men from Southeast Asia.[27] However, a smaller volume did not always correlate with a decreased prevalence of LUTS, because a lower prostate volume has been associated with higher mean International Prostate Symptom Score (IPSS) values in a population of 2406 Indian men compared with men in western regions.[28] However, a study has reported that men who

were born in the UK were slightly more likely to be surgically treated for BPH in comparison with those born in Australia.[5]

Table 2. Risk factors for benign prostatic hyperplasia in men

SN	Risk factors	Explanation
I.	**Non-modifiable**	
①	Age	Aging is the most significant factor, as the prostate tends to grow with age, and the likelihood of BPH increases substantially after age 40, with 50% aged 50 to over 80% by age 80.[29]
②	Genetics	While age is a risk factor for BPH in all affected patients, genetic factors may be involved in 39-72% of patients.[21]
③	Geography	BPH prevalence varies globally. Western populations report higher rates compared to Asian populations, possibly due to dietary and genetic differences.
II.	**Modifiable**	
①	Obesity	Excess body fat increases estrogen levels and insulin resistance, both of which may stimulate prostate growth. Central obesity (abdominal fat) is particularly associated with larger prostate volume.
②	Diabetes	Insulin resistance, and hyperglycemia promote prostate enlargement. Men with diabetes have higher rates of lower urinary tract symptoms (LUTS).
③	Sedentary lifestyle	Lack of daily exercise is associated with progression in LUTS, and LUTS are more prevalent in men who exercise less. Regular exercise improves hormonal balance and reduces inflammation, lowering BPH progression.
④	Dietary habits	High-fat, red meat-rich diets increase risk, while diets rich in vegetables, fruits, and omega-3 fatty acids may be protective.
⑤	Hypertension	It is associated with more urinary tract symptoms and larger prostate volume, and may decrease the effectiveness of alpha-blocker treatment.

(B) Modifiable risk factors

Metabolic syndrome (MetS)

Men with MetS generally have larger prostate gland volumes and experience faster annual growth rates of BPH than men without MetS,[30-32] as shown in Table 3.

Table 3. Comparative overview: prostate volume and BPH growth in men. [30-32]

SN	Parameter	Men with metabolic syndrome	Men without metabolic syndrome
①	Baseline prostate volume	Significantly larger (often 10-20% higher)	Smaller baseline volume
②	Transitional zone volume	Enlarged transitional zone, linked to LUTS severely	Lower transitional zone volume
③	Annual growth rate of BPH	Faster progression (~1.5-2x higher)	Slower growth
④	Risk of LUTS	Higher prevalence and severity	Lower prevalence
⑤	Mechanistic drivers	Insulin resistance, chronic inflammation, dyslipidemia, hypertension	Age-related hormonal changes only

Systematic reviews and meta-analyses indicate that MetS is strongly associated with increased prostate volume and enlargement of the transitional zone, both of which are critical markers of BPH progression. Men with MetS demonstrate a higher annual increase in prostate size, suggesting that metabolic dysfunction accelerates BPH growth.[30-32]

Metabolic syndrome, especially obesity, high blood pressure, and insulin resistance, is a risk factor for BPH. Men with diabetes, hypertension, obesity, low HDL-cholesterol levels, and high insulin levels had a

larger prostate gland than those without these conditions. Thus, prostate gland volume was positively correlated with systolic blood pressure, obesity, and fasting insulin levels, and negatively correlated with HDL cholesterol (Table 4).

Table 4. Prostate gland volume and annual BPH growth rates in men with and without metabolic syndrome and its individual components.[31]

SN	Metabolic abnormality	Categories	Prostate gland vol. (ml)	Annual BPH growth rate (ml/y)
1.	Type 2 diabetes	Men without diabetes (n=145; age 70 years)	45.0	0.928
		Men with diabetes (n=13; age 69 years)	78.0	1.385
2.	Hypertension	Men without treated hypertension (n=113; age 69 years)	44.00	0.909
		Men with treated hypertension (n=45; age 72 years)	51.0	1.060
3.	Obesity (waist measure ≥95cm)	Men with waist measure <95 cm (n=79, age 68 years)	38.5	0.834
		Men with waist measure >95 cm (n=78, age 70 years)	57.0	1.134
4.	HDL-Cholesterol	Men with high HDL-cholesterol (≥1.18mmol/l) (n=72; age 69 years)	39.0	0.780
		Men with low HDL-cholesterol (<1.18mmol/l) (n=72; age 70 years)	49.0	1.022
5.	Insulin	Men with low fasting insulin (<9 nU/ml) (n=83; age 71 years)	41.0	0.865
		Men with high fasting insulin (≥9 nU/ml) (n=69; age 68 years)	52.0	1.104
6.	Overall	Men without metabolic syndrome (n=30; age 68 years)	28.5	0.699
		Men with metabolic syndrome (n=128; age 70 years)	49.0	1.019

Insulin resistance stimulates growth factor (IGF-1) signaling, which promotes prostatic cell proliferation. Obesity and dyslipidemia cause chronic low-grade inflammation, contributing to stromal and epithelial hyperplasia. Hypertension induces vascular changes that impair prostatic blood flow, thereby exacerbating tissue remodeling. Some modifiable BPH risk factors can be addressed through lifestyle modifications, medication, and other interventions, including.

a. Obesity

Obesity can contribute to a variety of medical issues, including BPH. Research shows that higher body mass index (BMI) and central obesity increase prostate volume and the risk of LUTS, making obesity an important modifiable risk factor for BPH.[33,34] Obesity contributes to insulin resistance, chronic inflammation, and altered sex hormone metabolism- all of which promote the growth of the prostate (Table 5).[33] Men who are overweight, especially those with large amounts of abdominal fat, have a marked increase in the development of BPH. Being overweight increases intra-abdominal pressure, which increases bladder and intravesical pressure. This has the potential to cause BPH symptoms to worsen.

Table 5. Obesity-associated factors with effects on BPH, and their mechanism

SN	Factor	Effect on BPH	Mechanism
①	High body mass index (BMI)	↑ Prostate volume, LUTS severity	Increased estrogen/androgen imbalance, growth factor stimulation.[33]
②	Central obesity (waist circumference)	Stronger predictor of BPH than BMI	Insulin resistance, metabolic syndrome, chronic inflammation.[34]
③	Lifestyle factors (diet, secondary behavior)	↑ Risk of BPH	Promote obesity and metabolic dysfunction.[34]
④	Weight control	↓ Risk of BPH progression	Improves metabolic health, reduces inflammatory pathways.[33]

Adiposity, including body weight, body mass index (BMI), and waist circumference, has been reported to be associated with prostate volume across multiple study populations.[35] For example, each 1kg/m^2 increase in BMI corresponded to a 0.41 cc increase in prostate volume. Moreover, obese (BMI ≥35kg/m^2) participants had a 3.5-fold increased risk of prostate enlargement compared with non-obese (BMI <25kg/m^2) participants.[7] Obesity enhanced prostate volume (PV) growth and attenuated dutasteride-induced PV reduction.[18] It has also been demonstrated that obesity increases the risk of BPH surgery, the initiation of BPH medical therapy, and LUTS[36] and decreases the efficacy of finasteride[37] and dutasteride[18] for the treatment of BOO.

Dietary changes, exercise, and consultation with specialized physicians may help to reduce this risk factor. Ultimately, weight loss can benefit overall health, particularly in the context of BPH.

b. **Diabetes**

Diabetes is a recognized risk factor for BPH in men, particularly because it worsens LUTS and accelerates disease progression. Men with diabetes are more likely to develop BPH, experience more severe urinary symptoms, and have poorer treatment outcomes compared to non-diabetic men. [38,39]

How does diabetes contribute to BPH risk? [38,39]

- **Insulin resistance and hyperinsulinemia:** Chronic high insulin levels stimulate the prostate gland by increasing insulin-like growth factor (IGF-1) activity. This promotes the proliferation of stromal and epithelial cells in the prostate.
- **Chronic inflammation:** Diabetes is associated with systemic inflammation, which contributes to remodeling and enlargement of prostatic tissue. Inflammatory cytokines worsen LUTS severity.
- **Autonomic nervous system dysfunction:** Diabetic neuropathy affects bladder and urethral function, aggravating urinary symptoms. Leads to incomplete bladder emptying and a higher risk of urinary retention.
- **Hormonal imbalance:** Diabetes alters sex hormone metabolism (testosterone, estrogen), which influences prostate growth. Reduced androgen activity may paradoxically worsen LUTS by impairing bladder contractility.

Diabetes causes excessive glucose to remain in the bloodstream because the body has difficulty producing or using insulin, which helps convert glucose into energy. Diabetes can cause a variety of medical issues, including heart disease, vision loss, and, if untreated, death. Epidemiologic evidence suggests that diabetes significantly increases the risks of BPH and lower urinary tract symptoms (LUTS). Treating diabetes and making lifestyle changes to prevent the occurrence of diabetes can help reduce this BPH risk factor.

c. Sedentary lifestyle

A sedentary lifestyle is strongly linked to worsening BPH symptoms in men. Regular physical activity can reduce urinary problems, improve overall prostate health, and lower the risk of progression.[40,41]

Sedentary lifestyle and BPH [40,41]

- Reduced pelvic blood flow: Inactivity decreases circulation, which may impair prostate tissue health and worsen urinary symptoms.
- Obesity and metabolic syndrome: Sedentary behavior contributes to weight gain, insulin resistance, and inflammation- all factors associated with more severe BPH (Table 6).
- Hormonal imbalance: Physical inactivity can alter testosterone and estrogen balance, influencing prostate growth.
- Urinary symptoms: Men with sedentary habits often report more frequent urination, nocturia (nighttime urination), and a weak stream.
- Table 6 presents a comparative overview of sedentary and active lifestyles. [40,41]

Table 6. Comparative overview between a sedentary and an active lifestyle [40,41]

SN	Factors	Sedentary lifestyle	Active lifestyle
①	Risk BPH progression	Higher	Lower
②	Urinary symptoms	More severe (frequency, urgency, nocturia)	Reduced severity
③	Obesity/metabolic risk	Increased	Decreased
④	Inflammation level	Elevated	Lower
⑤	Quality of life	Often impaired	Improved

Exercise helps reduce inflammation and improve blood circulation, both of which are essential for maintaining prostate health. Going for a walk each day can positively affect overall health, including reducing the risk of BPH. A lack of physical exercise appears to increase the risk of developing BPH, whereas physical activity reduces it. However, physical activity, such as road biking, should be avoided because this activity can inflame or aggravate the prostate.

Increased physical activity and exercise have been consistently and robustly linked to reduced risks of BPH surgery, clinical BPH, histological BPH, and LUTS.[35,36] Moderate-to-vigorous physical activity reduced the risk of BPH or LUTS by up to 25% compared with a sedentary lifestyle, with the protective effect increasing with higher levels of activity. [42]

d. **Dietary habits**

Dietary habits play a significant role in both the prevention and management of BPH in men. Diets rich in plant-based foods, healthy fats, and antioxidants are associated with a reduced risk and milder symptoms. In contrast, daily consumption of diets high in red or processed meat, saturated fats, sugar-sweetened foods, and dairy products can increase the risk of prostate problems. Alcoholic and caffeinated beverages like coffee, tea, and soda can also increase risk due to diuretics that increase urine production.

Foods that support prostate health

- Fruits and vegetables: Rich in antioxidants (vitamin C, carotenoids, polyphenols) that reduce oxidative stress and inflammation.
- Legumes and soy: Isoflavones may modulate hormonal balance and reduce prostate enlargement.
- Nuts and seeds: Provide zinc and selenium, essential for prostate function.
- Fish (omega-3 fatty acids): Anti-inflammatory properties help reduce prostatic inflammation.
- Whole grains: Improve metabolic health by lowering risk factors such as obesity and insulin resistance.

Foods and habits that may worsen BPH

- Red and processed meat: Link to higher risk of prostate enlargement due to saturated fats and inflammatory compounds.
- High-fat dairy: May increase circulating estrogen levels and exacerbate symptoms.
- Excess alcohol and caffeine: Can irritate the bladder and worsen urinary frequency.
- Sugary and processed foods: Promote obesity and metabolic syndrome, both associated with BPH progression.

(e) Inflammation

Inflammation is part of the body's natural response to an irritating or potential threat. Chronic and acute inflammation may also contribute to the excessive growth of the prostate BPH. Chronic inflammation plays a central role in the development and progression of BPH in men. It promotes cell proliferation, tissue remodeling, and fibrosis, which worsens LUTS and accelerates prostate enlargement. Prostatic inflammation affects BPH severity in terms of prostatic enlargement, BOO exacerbation, and storage dysfunction (Fig.3).[43]

How inflammation contributes to BPH

① Pathophysiological mechanisms

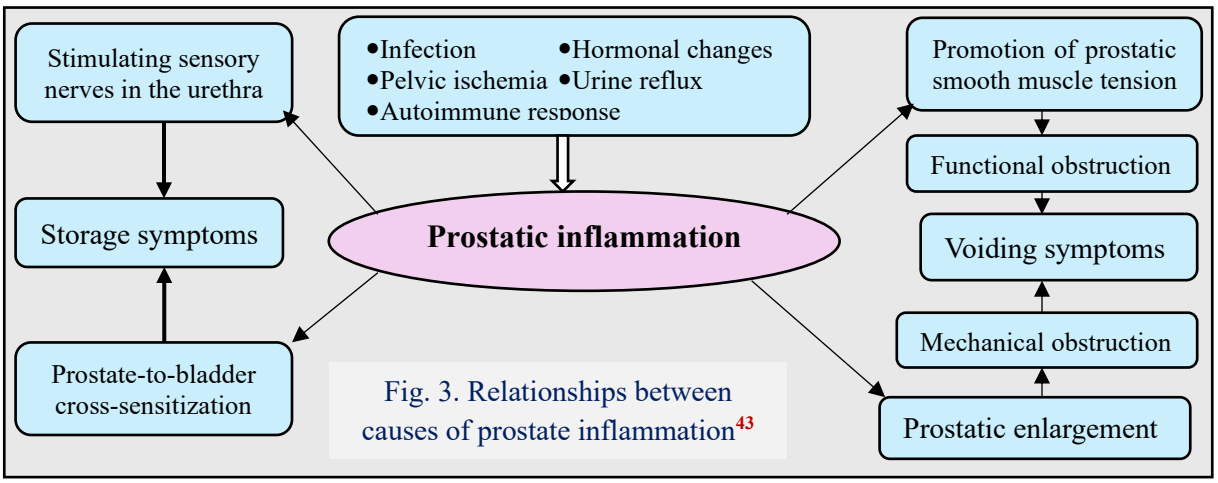

Fig. 3. Relationships between causes of prostate inflammation[43]

- **Immune cell infiltration**: Chronic inflammation recruits T cells, macrophages, and mast cells into the prostate tissue.
- **Cytokine release:** Pro-inflammatory mediators (IL-6, IL-8, TNF-α) stimulate epithelial and stromal cell proliferation.
- **Oxidative stress:** Reactive oxygen species damage tissue, leading to fibrosis and hyperplasia.
- **Angiogenesis and remodeling**: Inflammatory signaling promotes new blood vessel formation and structural changes in the prostate.
- **Fibrosis:** Collagen deposition stiffens the prostate, worsening obstruction.

② Clinical implications

- **Symptom severity**: Men with histological evidence of prostate inflammation often report more severe LUTS and higher International Prostate Symptom Score (IPSS).
- **Disease progression:** Inflammation accelerates prostate growth and increases the risk of acute urinary retention.
- **Overlap with prostatitis**: Chronic prostatitis and BPH share inflammatory pathways, which may explain symptom overlap.

Key mechanisms

- **Inflammation control**: Chronic low-grade inflammation is a driver of BPH; a diet rich in antioxidants and omega-3 fatty acids reduces it.
- **Hormonal modulation**: Plant-based diets may lower circulating androgens and estrogens, balancing prostate growth.
- **Metabolic health**: Obesity, insulin resistance, and hypertension worsen BPH; healthy diets mitigate these risks.

Table 7 presents the comparative overview of BPH without inflammation and with chronic inflammation. [43]

Table 7. Comparative overview of BPH without inflammation and with chronic inflammation. [43]

SN	Aspect	Without inflammation	With chronic inflammation
①	Prostate growth	Slow, age-related	Accelerated, driven by cytokines
②	Symptoms (LUTS)	Mild to moderate	More severe, frequent exacerbations
③	Histology	Normal hyperplasia	Immune cell infiltration, fibrosis
④	Risk of progression	Lower	Higher (retention, surgery)
⑤	Treatment response	Standard (α-blockers, 5-ARIs)	May benefit from anti-inflammatory strategies

Lifestyle changes that can increase testosterone levels in older men

Testosterone levels drop with age, but medication is not the only option. Older men can naturally support testosterone levels through regular strength training, maintaining a healthy weight, eating nutrient-dense foods, improving sleep quality, reducing stress, and ensuring adequate vitamin D intake (Table 8). These lifestyle changes are evidence-based and often more sustainable than medical interventions.[44-46]

Table 8. Key lifestyle changes for boosting testosterone. [44-46]

SN	Lifestyle factor	How to help	Practical tips
①	Strength training and exercise	Resistance training stimulates testosterone production and preserves muscle mass	Focus on compound lifts (squats, deadlifts, bench press) 2-3 times per week.
②	Healthy weight management	Excess body fat, especially visceral fat, lowers testosterone by increasing estrogen conversion.	Aim for a balanced diet and moderate calorie control.
③	Nutrient-rich diet	Zinc, magnesium, and healthy fats are crucial for hormone synthesis.	Include lean meat, eggs, nuts, seeds, leafy greens, and whole grains.
④	Vitamin D and sunlight	Vitamin D acts like a hormone, and supports testosterone regulation	Get 15-30 minutes of sunlight exposure daily or considers supplements if deficient.
⑤	Quality sleep	Poor sleep reduces testosterone and increases cortisol.	Target 7-9 hours of consistent, restorative sleep.
⑥	Stress reduction	Chronic stress elevates cortisol, which suppresses testosterone	Practice mindfulness, yoga, or breathing exercise.
⑦	Limit alcohol and processed foods	Alcohol and refined carbs can impair hormone balance.	Choose whole foods, hydrate well, and moderate alcohol intake.
⑧	Stay active daily	Sedentary lifestyle accelerates testosterone decline.	Incorporate walking, stretching, or light activity throughout the day.

Risks and considerations

- **Overtraining**: Excessive exercise without adequate recovery can reduce testosterone levels. Balance intensity with rest.
- **Extreme dieting:** Very low-fat or restrictive diets may impair hormone production.
- **Supplements:** Many 'testosterone boosters' are unproven; lifestyle changes remain the safest and most effective.
- When men are sleep-deprived, that can make a big difference in their testosterone production.
- People who have shift work, where they work at night, and their circadian rhythm gets all flipped around. Typically, testosterone peaks around 4.0 a.m., along with cortisol.
- A study was unable to find any convincing evidence that lifestyle factors have any effect on the risk of having surgical treatment for BPH, and it has been concluded that BPH is a natural part of aging for men, similar to menopause in women, and that further searching for risk factors is unlikely to prove rewarding.[5]
- A study supports independent causal roles of high waist circumference, BMI, and sedentary behavior in BPH.[47]
- Medical conditions: Diabetes, obesity, and sleep apnea can blunt testosterone response. Addressing these conditions is essential.
- For old men, consistent lifestyle habits- especially strength training, good sleep, and a nutrient-rich diet- are the most reliable ways to maintain or modestly increase testosterone. These changes not only support hormone levels but also improve overall health, energy, and longevity.

BPH in mammals

BPH is an age-related, androgen-dependent, non-cancerous enlargement of the prostate gland, and its prevalence varies in different mammal species. While nearly all male mammals possess a prostate gland, significant natural occurrences of BPH and prostate cancer have only been extensively documented in humans and dogs.

- **Humans:** The prevalence increases with age, affecting approximately 50% of men by age 60 and rising to over 80% in men over 70 years.
- **Dogs:** Spontaneous BPH is common in intact (unneutered) male dogs, with a prevalence of 16% by age 2, up to 50% by age 4-5, and present in almost 100% of intact dogs older than 7-9 years. Roughly 50% of dogs show histological signs by age 5, and 80-95% are affected by age 5-9 years. It is rarely found in castrated dogs.[48]
- **Non-human primates:** Spontaneous BPH has occasionally been reported in chimpanzees and macaques, as in humans.
- **Cats:** BPH is rare to non-existent in cats.
- **Laboratory animals:** While not natural, BPH can be induced in dogs and rats through hormonal treatment (testosterone) for study purposes.

Prostatic cancer (PC) in mammals

Prostatic cancer is one of the most common cancers in human males, yet it is rare in the animal kingdom, with dogs being the primary exception (Table 9).

- **Humans:** High incidence, particularly in developed nations, with risk increasing with age.
- **Dogs:** The dog is the only non-human species known to naturally develop high rates of prostate carcinoma, similar to humans. Spontaneous PC occurs in older dogs (typically 5+ years old), but it is generally less common than in humans, with a prevalence of about 1%. Unlike BPH, PC in dogs is often more common in castrated dogs. Canine PC is often highly aggressive, with metastasis (usually to bones) present in over 80% of cases at the time of diagnosis.
- **Cats:** Prostate tumors are extremely rare.

Table 9. Prevalence of BPH and prostate cancer (PC) in mammals

SN pecies	BPH prevalence	PC prevalence	Notes
① Humans	Very common in aging males; histologic BPH in ~50% of men by age 60, up to 90% by age 85 years.	Most common male cancer in many countries; ~1.47 million new cases worldwide in 2022.	Both conditions are major public health burdens.
② Dogs	Extremely common; >80% of intact male dogs develop BPH by age 6-7 years.	Rare compared to humans, prostate cancer occurs in <1% of male dogs, But tends to be aggressive.	Dogs are often used as models for BPH research.
③ Cats	BPH is very rare	Prostate cancer is extremely rare	Feline prostate disease is uncommon overall.
④ Non-human primates (NHP)	Age-related prostatic enlargement documented though less frequent than in human	Prostate cancer is rare but has been reported in aged primates	Useful comparative models, but the incidence is lower than in humans.
⑤ Rodents (rats, mice)	Do not naturally develop BPH; induced experimentally for research.	Spontaneous prostate cancer is rare. Transgenic models are used.	Rodents are mainly experimental model.
⑥ Other mammals	BPH is not commonly reported	Prostate cancer is extremely rare	Prostate pathology is not a significant clinical issue in these species

NHP = Non-human primates, e.g., chimpanzees, rhesus monkeys. Other mammals = horses, cattle, etc.

- **Non-human primates:** Studies of Old-World monkeys (cynomolgus macaques, rhesus macaques, baboons) have identified isolated cases of glandular hyperplasia, but significant, spontaneous, metastatic prostatic adenocarcinoma is rare in primates.

Key findings in comparative studies

- Uniqueness of humans and dogs: Only humans and dogs exhibit a high incidence of spontaneous, age-related BPH and prostatic adenocarcinoma.
- Androgen dependency: In both humans and dogs, BPH is strongly linked to androgen levels and aging.
- Metastasis rates: Canine prostate cancer is often diagnosed at a very advanced stage, with high rates of metastasis to regional lymph nodes, lungs, and bones, like aggressive, advanced, castrate-resistant, or androgen-independent prostate cancer in humans.

Key insights

- Humans and dogs are two species in which BPH is naturally common (Table 9).
- Prostate cancer is predominantly a human disease; in dogs, it occurs but is rare and aggressive, while in most other mammals, it is extremely uncommon.
- Rodents and primates are valuable for research, but their natural prevalence is low, so scientists often rely on induced or genetic models.
- The evolutionary biology of prostate disease suggests that longevity and hormonal regulation play major roles: species with longer lifespans and intact androgen signaling (such as humans and dogs) show higher prevalence.

Key differences and commonalities

- Androgen dependence: Both BPH and PC in humans and dogs are associated with androgens (e.g., testosterone), but in dogs, castration does not prevent PC and may even increase the risk.
- Species differences: While canine BPH is often used as a model for human BPH, the anatomical structures differ; canine BPH is diffuse, whereas human BPH often develops in specific transitional zones.
- Progression: In dogs, BPH is rarely a precursor to cancer, unlike in humans, where BPH is frequently found in conjunction with or preceding cancer.

Canine BPH

BPH is an almost universal, non-cancerous, age-related prostate enlargement in intact male dogs, affecting over 90% of dogs by age 9. It is driven by androgens (testosterone/DHT), causing prostate growth. It causes painless, symmetric enlargement, often leading to bloody discharge or constipation. Treatment involves castration (preferred) or medical management (finasteride, osaterone acetate) to reduce prostate size. Conversely, prostate cancer is rare, aggressive, usually in neutered dogs, and presents as painful, asymmetric enlargement.[49]

- Prevalence: Almost every intact male dog will develop BPH as they age; approximately 50% by age 4 years, and >90% by 8-9 years old. Breeds that are large in stature seem more susceptible to BPH.[50]
- **Cause and pathogenesis:** It is driven by hormonal imbalances, especially the conversion of testosterone to dihydrotestosterone (DHT) by 5α-reductase, which induces hyperplasia and hypertrophy of prostate epithelial cells> An abnormal ratio of androgens to estrogens, an increase in androgen receptors, and an increase in tissue sensitivity to androgen are all possible causes of BPH[50]

Clinical signs

- Many dogs are asymptomatic in the early stage, but can cause serosanguinous (bloody) urethral discharge, blood in urine (hematuria), and, in severe cases, ribbon-like stools (constipation) due to prostate enlargement pressing on the rectum. In 2.7% cases of BPH, urinary symptoms are present, whereas in 9.2% of cases, digestive symptoms are present. [50]
- The major causes of infertility in dogs, caused by BPH, are associated with impaired semen quality.

Hormonal imbalance, oxidative stress, biochemical changes in prostatic fluid, and hematospermia are causes of reduced semen quality in dogs with BPH. Chronic prostatitis often occurs concurrently with BPH and has an additive negative effect on semen quality and fertility. [51]

Diagnosis

- History: Most sexually intact male dogs older than six years have the disease. The mean age at diagnosis is 8.9 years for most prostatic diseases. Hematuria, urethral hemorrhage, and/or tenesmus are possible in dogs. Owners may notice stools that resemble ribbons.[50]
- Rectal palpation (digital exam) reveals that a normal prostate is painless, symmetrical, and smooth, whereas in BPH it is enlarged and abnormal.
- Other tests include prostatic radiography, prostatic ultrasonography, and prostatic biopsy.
- Transabdominal ultrasonography (best for size and echotexture) is the preferred imaging method, showing a diffuse, enlarged gland.
- Significant elevation of PSA, dihydrotestosterone (DHT), CPSE (trypsin-like enzyme), and prostate volume have also been reported in induced prostatic hyperplasia in dogs. [52]

Treatment

- The treatment of choice is castration (neutering), which leads to rapid shrinkage of the prostate.
- Treatment with the anti-androgen osaterone acetate or the 5α-reductase inhibitor finasteride is recommended to reduce prostate size and clinical symptoms and to restore fertility. [51]
- Therapeutic evaluation of osaterone acetate and finasteride found them acceptable treatments for BPH in breeding dogs, despite ongoing debate about their effects on certain characteristics. [53]
- Treatment with Finasteride and tadalafil in canine BPH, which aims to reduce prostate size. [54]
- Surgical therapy- following surgery, a 70% reduction in size results from castration.

Prostate cancer in dogs

- **Nature:** Canine prostatic carcinoma is a highly malignant, hormone-independent tumor that often metastasizes to the lungs and bones. The most common is prostatic adenocarcinoma. The average diagnosis is around 10 years old.
- **Risk factors:** Unlike BPH, this is more commonly diagnosed in castrated male dogs, making it a critical concern when an older neutered dog shows prostatic enlargement.

Clinical signs

Symptoms are more severe than BPH and include extreme pain, difficulty walking (due to bone metastasis), severe hematuria, and systemic illness like weight loss and anorexia.

- Dysuria (difficulty urinating), tenesmus (straining to defecate).
- Blood in urine
- Abdominal or back pain.
- Often diagnosed late, after metastasis.

Diagnosis

- Imaging: ultrasound shows an irregular prostate with mineralization.
- Radiographs may reveal lymph node or bone metastasis.

Treatment

- No curative therapy is available.
- **Options:** NSAIDs (like piroxicam), chemotherapy, radiation, and supportive care.
- **Surgery:** It's sometimes possible to remove the affected part of the gland if the prostate cancer is found early. However, by the time it's diagnosed, it's usually affected the whole gland and has spread around the body. Removing the whole prostate gland from a dog is not recommended because there is a high chance of complications that impact their quality of life, including lifelong urinary continence (urine licking).

Prognosis

- Poor, aggressive, fast-growing, and quick to spread. Median survival is short once diagnosed.

Differences between BPH and PC in male dogs

BPH and PC (prostatic carcinoma) in dogs are both causes of an enlarged prostate (prostatomegaly) but differ significantly in etiology, malignancy, clinical presentation, and prognosis. While BPH is a non-cancerous, age-related enlargement, prostate cancer is an aggressive, malignant neoplasm (Table 10).

Table 10. Comparative differences between Benign prostatic hyperplasia (BPH) and Prostate cancer (PC) in dogs

SN	Feature	Benign prostatic hyperplasia	Prostate cancer (Adenocarcinoma)
①	Nature	Non-cancerous, hormonal-related hyperplasia.	Malignant tumor, aggressive and invasive.
②	Metastasis	Nonde (does not spread)	Highly metastatic (lungs, bones, lymph nodes)
③	Age of onset	Middle-aged to older intact dogs (rare before 5)	Older dogs (mostly ~10 years)
④	Reproductive status	Almost exclusively in intact males.	More common in neutered male dogs.
⑤	Prostate feel	Smooth, firm, symmetrical, uniform, non-painful.	Hard, irregular, lumpy, often painful, fixed.
⑥	Urinary signs	Occasional, straining (stranguria).	Common, severe straining (dysuria), blood in urine.
⑦	Defecation	Ribbon-like stools (due to pressure)	Tenesmus (painful/strained defecation).
⑧	Imaging (US)	Symmetrical, diffuse enlargement, cyst possible.	Asymmetrical, irregular, mineralization/ calcification.
⑨	Diagnosis	History, rectal exam, response to castration	Cytology (FNA), biopsy (tissue sample)
⑩	Prognosis	Excellent; reverses with treatment/castration	Poor, very fast-growing and hard to treat.

Table 11. Comparison of Benign prostatic hyperplasia and Prostate cancer in male dogs and men

SN	Feature	Male dogs	Men
01	Prostate anatomy	Single gland, caudal to bladder, surrounds proximal urethra.	Single gland, below bladder, surrounds proximal urethra.
02	BPH prevalence	Most common prostatic disorder in intact males; nearly all unneutered dogs develop some degree with age.	Extremely common; >50% of men over 50, ~90% by age 80.
03	BPH pathophysiology	Driven by androgenic stimulation or altered androgen: estrogen ratio.	Driven by dihydrotestosterone (DHT) accumulation and aging.
04	BPH clinical signs	Often asymptomatic; hematuria, hemospermia, Hemorrhagic preputial discharge; constipation From prostate enlargement.	LUTS: weak stream, hesitancy, nocturia, and incomplete emptying.
05	BPH diagnosis	Transabdominal ultrasound, rectal examination.	Digital rectal exam, PSA, ultrasound, urodynamic studies.
06	BPH treatment	Castration (curative), medical therapy (finasteride, antiandrogens) if breeding desired.	Medical therapy (α-blockers, 5α- reductase inhibitors), minimally invasive or surgical (TURP, laser)
07	PC prevalence	Rare (~0.67%) of canine malignancies; usually adenocarcinoma.	Very common; most frequent non-skin cancer in men; 2nd leading cause of male cancer death.
08	PC pathophysiology	Aggressive, high metastatic potential (lungs, Bones, lymph nodes); not linked to castration status.	Often adenocarcinoma; multifactorial (genetics, age, hormones, environment.
09	PC clinical signs	Dysuria, hematuria, tenesmus, pain; often late-stage diagnosis.	LUTS, hematuria, bone pain (metastasis), sometimes asymptomatic early.
10	PC diagnosis	Imaging (US, CT, MRI), biopsy; often Advanced at detection.	PSA screening, MRI, biopsy, staging scans.
11	PC treatment	Limited options; surgery, radiation, chemotherapy, palliative care; prognosis poor.	Surgery (prostatectomy), radiation, androgen deprivation therapy, chemotherapy, novel immunotherapies

Key insights:

- **BPH is species-specific in presentation:** Dogs show more reproductive signs (hemospermia, discharge), while men show urinary obstruction symptoms.
- **Prostate cancer differs dramatically:** In men, it's common but often indolent; in dogs, it's rare but highly aggressive.
- **Castration effect:** In dogs, castration cures BPH but does not prevent cancer. In men, castration (androgen deprivation) is a therapy for advanced cancer, not prevention.
- **Screening gap:** Men benefit from PSA-based early detection; dogs lack routine screening, leading to late diagnosis.

Dog and human prostate cancer

Only three species, men, dogs, and lions, are believed to develop prostate cancer. Human and canine prostate glands share many functional, anatomical, and physiological features. Due to these similarities, canine PC has been proposed as a model for PC in men. The similarities between canine prostate anatomy and disease make the canine species an important model for understanding the progression of PC in men (Tables 12,13). [55]

Animal models of prostate

There are several animal models for studying prostate diseases, such as non-human primates and other species (Table 12,13), that share similarities. It is important to understand them when selecting the most suitable animal model.

Table 12. Overview of the human, non-human primates, dogs, cats, rats, and mice's prostate anatomy. [56]

SN Species	Localization	Lobulation	Shape	Relation to urethra
① Human	Behind the inferior border of the pubic symphysis and pubic arch & anterior to the rectal ampulla	A-lobular structure	Conical	Completely surrounded by the proximal urethra
② NHP	Distal end of the urinary bladder	Bilobed (cranial and caudal lobes)	Ovoid	Does not complete surrounding the urethra.
③ Dogs	Dorsal to the pubic symphysis, ventral to the rectum and caudal to the urinary bladder.	Bilobed	Ovoid	Surrounds the proximal urethra
④ Cats	Dorsal to the pubis, near the neck of the urinary bladder.	Bilobed	Ovoid	Does not surround the ventral portion of the urethra.
⑤ Rats & mice	Caudal to the urinary bladder	Four lobes (dorsal, lateral, ventral, and anterior)	Not a compact unit	Incompletely surrounding the urethra.

Table 13. Comparative aspects of human, non-human primates (NHP), dogs, cats, and rats' spontaneous prostate cancer

SN Species	Pre-malig-nant lesions	Risk factors	Incidence	Average age at diagnosis	Role of androgen	Metastases	Aggressivity	Histological classification
① Human	PIN	Age, race, family history, hormone exposure, inflammation	Variable	>65 years	Significant	Bone (lumber spine, pelvis), pelvic LNs, lungs, liver, brain	Variable	Adenocarcinoma (AC)
② NHP	NR	Age	Low	Variable	Significant	NR	NR	HIAC
③ Dogs	NR	Castration, Age	High	10 years	Independent	Bone (lumber spine, pelvis), LLN, lung	High	Ductal carcinomas
④ Cats	NR	Age?	Low	8 years	NR	LN, lung, pancreas	High	High-grade C & AC
⑤ Rats								
a. ACI/Seg	AH/DVP	Age	High	24-33 months	Independent	NR, lungs, peritoneal cavity	Variable	Cribriform AC
b. Lobund Wistar	PIN	Age	Low	26 months	ADES, then independent		Variable	Adenocarcinoma

PIN = Prostatic intraepithelial neoplasia NR = Not reported NHP = Nonhuman primates
H= Hyperplasia I= Inflammation A= Adenomas C= Carcinomas AH/DVP = Atypical hyperplasia/Dysplasia in ventral prostate

PC is a neoplasm with high genomic complexity in humans and dogs, yet it shows significant molecular similarities across these species. So far, important genes and signaling pathways have been identified and characterized in canine PC, enabling many molecular profiles to stratify the different tumor phenotypes exhibited by this neoplastic entity, especially those with high metastatic potential. [57]

Mice are an excellent option for initial studies of heterotopic tumors, while rabbits are a unique option for connecting mouse studies to canine studies using orthotopic models. However, rabbits have limitations due to their size and the prostate's complex morphology, which limit the translation of results to men. Dogs are the best preclinical model for imaging the prostate because of their similarities to the human gland, making them an invaluable resource for advanced clinical research. [58] However, when selecting a preclinical model, consider the specific research question, the imaging modality to be used, and the available resources.

Pathogenesis [59,60]

BPH develops through a complex interplay of hormonal, cellular, inflammatory, and metabolic factors that drive abnormal growth of both stromal and epithelial cells in the prostate. The condition is strongly age-related and linked to androgen signaling, chronic inflammation, and local growth factor activity. [11,43,61] It has been known that both prostate volume (≥ 30 g) and age (≥ 62 years old) are two of the factors contributing to BPH progression.

Mechanisms in BPH pathogenesis

BPH is an age-related condition characterized by the non-malignant, unregulated proliferation of epithelial and stromal cells in the prostate's transition zone, which surrounds the urethra. The pathogenesis is multifactorial, involving a disruption of the balance between cell proliferation and apoptosis (cell death), favoring cell accumulation (Fig. 4). The primary mechanisms driving BPH pathogenesis in men include:

① The androgen-dependency axis (DHT and Androgen receptor (AR)

- Androgens as a requirement: BPH does not develop in castrated men, indicating that androgens are essential for disease development.
- BPH occurs when an accumulation of androgens prevents prostate cell death and promotes cell proliferation, increasing the size of the prostate gland.
- Role of 5α-reductase: Testosterone is converted into DHT by the enzyme 5α-reductase (type 2 is the primary subtype in the prostate.
- DHT is an androgen that prevents prostate cell death and promotes their proliferation, thereby increasing the size of the prostate gland. Inhibiting DHT production can help slow or stop prostate growth.
- Androgen receptor (AR) activation: DHT has a 10-fold higher affinity for the androgen receptor than testosterone. Activated ARS in the prostatic stroma and epithelium promote growth and reduce apoptosis.
- High intraprostatic DHT: Despite declining serum testosterone levels with age, intraprostatic DHT levels remain high, driving the persistent hyperplastic growth.

② Chronic inflammation and immunological factors

Chronic inflammation is considered a central, potentially initiating factor in BPG, which includes:

- Inflammatory cell infiltration: BPH tissue shows significant infiltration of lymphocytes (CD+ T cells) and macrophages.
- Cytokine cascade: These inflammatory cells release cytokines (IL-8, IL-17, TNF-α) that stimulate fibroblast growth factor (FGF-2) and other growth factors, leading to cellular proliferation.
- Self-perpetuating cycle: Inflammation causes tissue injury, which initiates a repairing, proliferative response. This creates a 'vicious cycle' in which inflammation causes damage, triggering repair, which in turn leads to more tissue growth.

③ Stromal-epithelial interactions and growth factors

- Stromal dominance: In BPH, the prostatic stroma expands significantly due to increased fibroblast and smooth muscle cell numbers.

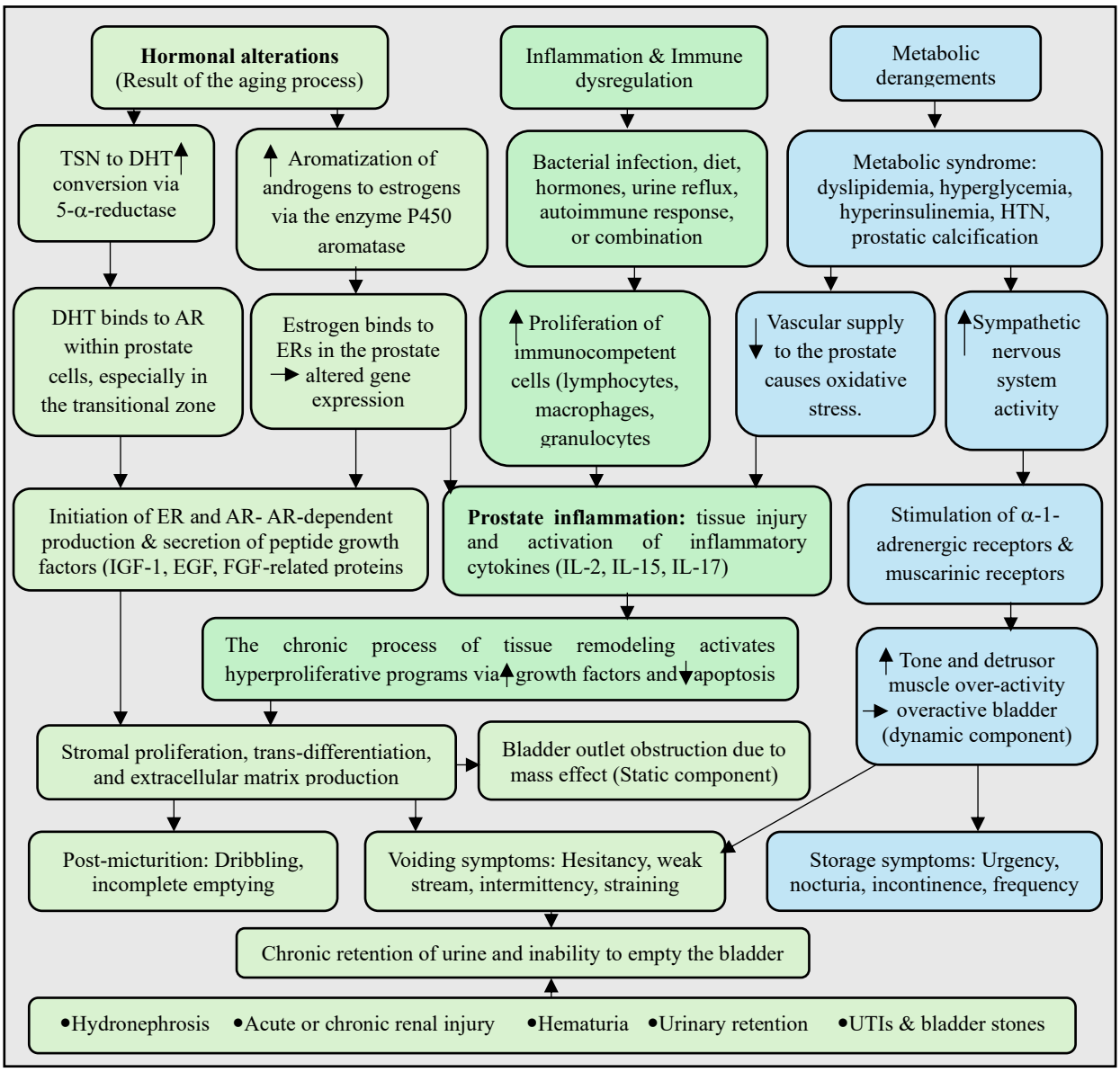

Fig. 4. Pathogenesis and clinical findings of Benign prostatic hyperplasia in men (source: www.thecalgaryguide.com)

TSN = Testosterone AR = Androgen receptor BPH = Benign Prostatic Hyperplasia DTH = Dihydrotestosterone
ER = Estrogen receptor HTN = Hypertension

- Growth factors: The prostatic stroma releases growth factors (FGF-2, FGF-7, IGF) that signal the epithelial cells to proliferate, acting via paracrine and autocrine pathways.
- TGF-β signaling: Transforming growth factor-beta (TGF-β) is involved in the differentiation of fibroblasts into myofibroblasts and contributes to tissue remodeling and fibrosis.

④ Estrogen-related pathways (estrogen/androgen imbalance)

As men age, the serum androgen-to-estrogen ratio decreases.

- Increased aromatase activity: Higher adipose tissue in older or obese men increases aromatase activity, which converts androgens into estrogens (especially estradiol).
- ER (receptors): Estrogen acts on estrogen receptors (ERα and ERβ). While ERβ can induce apoptosis,

ERα promotes stromal cell proliferation, shifting the balance towards growth.

⑤ Other contributing factors

- Metabolic syndrome/Insulin resistance: Hyperinsulinemia and high levels of insulin-like growth factor-1 (IGF-1) directly stimulate prostate cell proliferation.
- Oxidative stress (OS): Increased reactive oxygen species (ROS) in the prostate induce DNA damage and promote inflammation.
- Stem cell reawakening: Some theories suggest a 'reawakening' of embryonic signaling pathways, where stem cells in the transition zone are activated to create new glandular buds.

Clinical consequence: Static and dynamic obstruction

The cellular proliferation results in two types of obstruction:

- Static component: Actual increase in volume of prostate tissue (due to hyperplasia) that physically compresses the urethra.
- Dynamic component: Increased tone of the smooth muscle within the prostate stroma and bladder neck, which can contract and narrow the urethra, often regulated by alpha-adrenergic receptors.

The current understanding of BPH pathogenesis attributes a central role to hormones and inflammation. Emerging evidence also implicates peroxiredoxin 3 (Prdx3), autophagy, oxidative stress (OS), and proptosis as potential contributors to the onset of BPH.[62] Five key mechanisms are vital to BPH's pathophysiology: (1) Androgen signaling pathway, (2) Cellular proliferation and impaired apoptosis, (3) Static and dynamic components of prostatic obstruction, (4) Chronic inflammation, and (5) Growth factors and stromal-epithelial interactions.

① Hormonal regulation

The occurrence and progression of BPH are closely linked to hormonal factors, predominantly sex hormones, thyroid hormones, insulin-like growth factor 1(IGF-1), and insulin.[63]

BPH appears to be related to age, androgens (DHT), estrogens, and detrusor dysfunction of the bladder neck. An accumulation of DHT inhibits prostatic cell death, promotes cell proliferation, and thus increases the size of the gland. In men aged 50 years, blood testosterone levels decrease, and estrogen (as well as prolactin, luteinizing hormone, and follicle-stimulating hormone) levels rise.

Estrogen increases the number of androgen (DHT) receptors in the prostate and inhibits androgen metabolism by interfering with hydroxylation. As urinary outflow obstruction develops, the detrusor muscles of the bladder attempt to compensate by increasing pressure to expel urine, which can lead to muscle instability and worsening symptoms.

Factors that promote the accumulation of DHT and estrogens lead to symptoms of BPH and obstruction of the lower urinary tract, which, in turn, cause detrusor muscle dysfunction.

Sex hormones

Sex hormones associated with BPH primarily involve androgens (testosterone and related hormones) and estrogens. This is supported by evidence suggesting that castrated boys do not develop BPH when they age.

Age-related changes in testosterone hormone (TH), dihydrotestosterone (DHT), and estrogen balance play central roles in both BPH and prostate cancer in men. Additionally, progestogens are relevant, as progesterone receptor expression correlates positively with BPH development.[64]

a. Androgens (TH and DHT)

TH is almost exclusively synthesized from cholesterol in mature Leydig cells of the testicles (testicular testosterone) and is released into the bloodstream, where it subsequently reaches its target organs, such as the prostate. TH, which is converted to DHT by 5α-reductase in prostate tissue. It uses NADPH as a cofactor to convert TH to DHT, which is 10 times more potent than testosterone and drives prostatic growth. Both TH and DHT bind to the same receptor, the androgen receptor (AR), for their biological activities, and DHT can be produced by the reduction of TH by three types of 5α-reductase isoenzymes that have been identified

at different tissues of the adult human body, indicated by a predominant expression of SRD5α-1in the skin and liver, SRD5α-2 in the prostate, and SRD5α-3 in the skin, brain, and mammary gland.[65] Prostatic epithelial cells express the androgen receptor. Androgens are a prerequisite for embryonic differentiation to pubertal maturation, and normal development and physiological control of the prostate. Androgens help maintain the normal metabolic and secretory functions of the prostate, and they are also implicated in the development of BPH and prostate cancer. Androgens do not act in isolation, and other hormones and growth factors are involved.[66]

TH, to be maximally active in the prostate, must be converted to DHT by the enzyme 5-alpha reductase. DHT has a much greater affinity for the AR than does TH, and DHT accumulates in the prostate even when circulating concentrations of TH are low. Therefore, prostatic DHT levels may remain similar to those in young and elderly men, even though serum TH levels generally decline with age. In the prostate, the total TH level is 0.4 ng/g, and the total DHT level is 4.5 ng/g.[67] The total serum TH level is approximately 10 times higher than that of DHR.

A significant role of DHT in BPH is that the binding affinity of DHT to AR is roughly four times higher than that of TH, and in elderly men with BPH, the majority of DHT may be produced by the prostate that levels of intraprostatic DHT, the majority of DHT may be produced by the prostate. Despite a decrease in serum TH with ageing, serum or intraprostatic DHT levels can remain within normal adult ranges in elderly men. Serum DHT levels either remain constant during BPH development or are positively correlated with prostate size. The central role of DHT in the development of BPH has been further verified by the successful clinical use of finasteride (an inhibitor of SRD5α-2,3) or dutasteride (an inhibitor of SRD5α-1,2,3) in the management of BPH, showing that dutasteride @ 0.5mg/day or finasteride @ 5mg/day significantly reduces serum or intraprostatic DHT of over 70% and prostate volume of approximately 30%.[68,69]

Estrogen

Estrogen alone or in combination with androgens is involved in inducing aberrant growth and/or malignant change. Animal models have supported the canine model, where estrogens 'sensitize' the ageing dog prostate to the effects of androgens, whereas this is less clear in men. Estrogens in males are predominantly produced by the peripheral aromatization of testicular and adrenal androgens. Estrogens may have greater effects on BPH progression than androgens. Aging reduces systemic androgen levels and alters the testosterone-to-estrogen ratio, elevating estrogenic activity. This shift in the potentially adverse effects of estrogens on the prostate might be due to a shift in the intra-prostatic estrogen: androgen ratio with aging.

Estrogen, which acts through estrogen receptors (ER) alpha and beta, has been implicated in the pathogenesis of benign and malignant human prostatic tumors.[70,71] BPH is thought to originate in the transitional zone (TZ) and prostate cancer in the peripheral zone (PZ) of the prostate. Estrogen may play a crucial role in the pathogenesis of BPH via estrogen receptor beta (ERβ).

- Multiple studies have examined the associations between endogenous sex steroid hormones- testosterone, DHT, and estrogen- and BPH and LUTS. However, higher serum testosterone concentrations do not promote BPH and may even be protective. [72]
- Men who are castrated before puberty or who have an androgen-related disorder do not develop BPH.[3]

Functions of 5α-reductase

5α-reductase enzyme is naturally present throughout the body, with high activity in the prostate, liver, skin, and scalp. There are two main types of isoenzymes, e.g., type 1 (5-R1), which is expressed in the epithelial cells of the prostate, and type (5-R2), which is the major form in the prostate, primarily located in the stroma. These iso-enzymes are responsible for the proliferation of stromal and epithelial cells in the prostate transition zone.

- **Androgen conversion**: TH is converted to DHT, the main intraprostatic androgen.
- **Prostate growth promotion:** In aging men, the level and activity of this enzyme increase, leading to elevated intraprostatic DHT, which binds to androgen receptors and promotes stromal and epithelial cell proliferation (hyperplasia).
- **Disease progression**: Elevated DHT levels driven by 5α-reductase lead to increased prostate volume, resulting in lower urinary tract symptoms (LUTS), such as decreased urine stream, hesitancy, and urinary frequency.
- **Persistent androgen dependency:** Unlike other androgen-dependent tissues that downregulate, 5α-reductase remains highly active in the aging prostate, ensuring a constant supply of DHT.

Benign prostatic hyperplasia

- DHT binds androgen receptors (AR) in stromal and epithelial cells of the prostate.
- Stimulate growth factors (e.g., FGF, TGF-β),⟶ stromal proliferation, and gland enlargement.
- The androgen receptor (AR) may lead to the development of BPH via epithelial-stromal interactions, altering epithelial-mesenchymal transition and promoting stromal cell proliferation.
- Dysregulation of apoptosis in BPH leads to cell accumulation, contributing to prostate gland enlargement.
- Serum testosterone levels are reported to be lower in men aged >40 years than in healthy younger men; however, dihydrotestosterone (DHT) levels are elevated. [60]
- Patients with BPH have significantly higher levels of serum DHT than do unaffected men of similar age. This finding underlies the use of 5α-reductase inhibitors in the treatment of BPH, suggesting that the enzyme is upregulated in men with BPH.
- Explains why 5α-reductase inhibitors (finasteride, dutasteride) shrink prostate volume.

Prostate cancer

- AR signaling promotes cell survival and proliferation.
- Mutations or amplification of AR can make cancer cells hypersensitive to low androgen levels.
- Explains why androgen deprivation therapy (ADT) is the cornerstone treatment.

b. Estrogens

Age-related shift: With aging, testosterone declines, but estradiol and estrogen increase due to aromatization in adipose tissue.

BPH

- Estrogen receptor-α (ERα) activation, ⟶stromal proliferation, and inflammation.
- Estrogen has been implicated in the proliferation of prostatic stromal cells.
- Activation of estrogen receptors expressed in the prostate gland leads to aberrant glandular proliferation and inflammation.
- Estrogen receptor-β (ERβ) may have protective, anti-proliferative effects.
- BPH patients had higher serum estradiol levels or estradiol/testosterone ratios.
- An increase in the estrogen-to-androgen ratio stimulated normal prostate stromal cell proliferation, and normal prostatic epithelial cell proliferation was also stimulated indirectly by steroid action mediated by stromal cells.

Prostate cancer

- ERα promotes oncogenic signaling, angiogenesis, and epithelial transformation (Table 14).
- Dysregulated estrogen/androgen ratio contributes to malignant progression.

c. Other hormonal influences

- Progesterone: Minor role; may modulate AR activity.
- Insulin and metabolic influences: Hyperinsulinemia and metabolic syndrome increase IGF-1, enhancing the risk of both BPH and cancer.
- Chronic inflammation: hormonal imbalance fosters oxidative stress and cytokine release, creating a microenvironment favorable for neoplasia.

Table14. Comparative overview of hormone/pathway between BPH and prostate cancer in men

SN	Hormone/Pathway	Role in BPH	Role in prostate cancer
①	DHT (via AR)	Drives stromal & epithelial hyperplasia	Promotes tumor growth, AR mutations amply effect.
②	Estrogen (ERα)	Stimulates stromal proliferation and inflammation	Oncogenic signaling, angiogenesis, and malignant transformation
③	Estrogen (ERβ)	Protective, antiproliferative	Tumor-suppressive, often lost in cancer
④	Growth factors (IGF-1, VEGF, FGF)	Mediate hyperplasia	synergize with AR → invasion and metastasis
⑤	Metabolic hormones	Contribute to the prostate enlargement	Increase cancer risk via IGF-1 and inflammation
⑥	Key difference	Non-malignant hyperplasia	Cancer involves genetic instability and malignant transformation superimposed on hormonal signaling

② Growth factors

Transforming growth factors-β (TGF-β), fibroblast growth factors (FGFs), and insulin-like growth factors (IGF) promote cell survival and proliferation.

a. Epidermal growth factor (EGF)

- EGF is associated with the growth and differentiation of epithelial cells, which are abundant in prostate tissue. Inhibition of the EGF receptor reduces the proliferation of prostatic epithelial cells.
- Other growth factors implicated in BPH include transforming growth factors, vascular endothelial growth factor, bone morphogenetic protein 5, brain-derived neurotrophic factor, thyroid hormones, and others.

b. Insulin-like growth factor-1 (IGF-1)

IGF-1 is expressed in the stromal and epithelial cells of the prostate. This is true especially in patients with acromegaly, and these patients have higher prostate volume than healthy controls.

c. Fibroblast growth factor-2 (FGF-2)

FGF-2 is expressed abundantly in the prostate epithelium and stroma, which is mitogenic to the prostate, and there is an association of FGF-2 with prostate stromal proliferation.

③ Chronic inflammation

- BPH is an immunoinflammatory disease. Chronic inflammation has been implicated in the pathogenesis of BPH (Fig. 5).

a. Immune cell infiltration: T lymphocytes and macrophages are often found in hyperplastic tissue.
b. Cytokine release: IL-6, IL-8, and TNF-α drive local inflammation and stimulate growth factor pathways.
c. Oxidative stress: Reactive oxygen species contribute to DNA damage and tissue remodeling.

- Histological inflammation has been reported in 98.1% of patients undergoing transurethral resection of the prostate (TURP) for BPH with LURS.
- It has also been reported that chronic inflammation occurred in 77.6% of prostate biopsy cases, and prostate volume was significantly larger in the group with chronic inflammation than in those without it.
- Inflammatory mediators implicated in the pathogenesis of chronic inflammation in BPH include lymphocytes, monocytes/macrophages, IL-8, IL-17, and others.

④ Age-associated tissue remodeling

- Senescence: Aging cells secrete pro-inflammatory mediators (senescence- associated secretory phenotype)
- Extracellular matrix changes: Increased collagen deposition stiffens tissue, worsening obstruction.
- Microvascular changes: Arteriosclerosis and reduced perfusion may promote hypoxia and fibrosis.

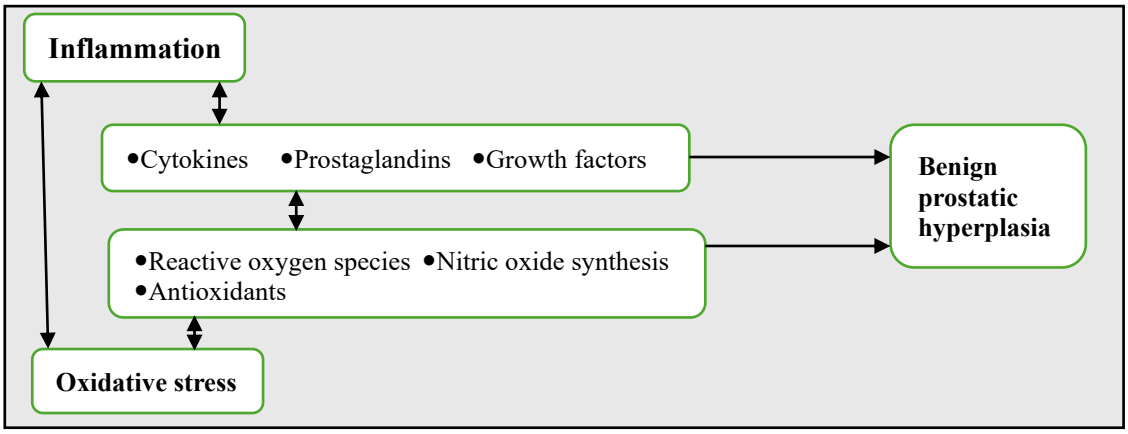

Fig. 5. Pathological mechanisms of BPH development via inflammation and oxidative stress

⑤ Metabolic and lifestyle factors

- Metabolic syndrome: Obesity, insulin resistance, and dyslipidemia are linked to increased risk of BPH.
- Diet and lifestyle: High-fat diets and a sedentary lifestyle exacerbate hormonal and inflammatory imbalances.

⑥ Race

Race is an independent risk factor for the development of BPH, and it has been reported that Caucasian men are more likely to develop BPH than their African American counterparts (9.9% vs. 4.1%, respectively). However, surgical interventions meant for severe BPH were more common in African American men. In addition, BPH has been reported to be likely heritable.

⑦ Microbiota

- The microbiota associated with prostatic enlargement includes the gut, urinary, and prostate microbiota. It has been reported that the Firmicutes/Bacteroides ratio of gut microbiota was significantly higher in patients with enlarged prostates.
- Changes in the bladder microbiota may be associated with worsening LUTS in older men.
- The urine microbiota composition of patients with BPH differed from that of the control group, consisting of Alcaligenes, Pseudomonas, Lactobacillus, Akkermansia, and Cetobacterium.
- The prostate microbiota was found in the prostatic duct. Isolates from the BPH tissue included *E. coli*, Staphylococcus, and Micrococcus spp.
- Aromatase has also been implicated in the development of BPH. It has been reported that blocking the conversion of androgens to estrogens by aromatase inhibitors appears to prevent prostatic hyperplasia.
- BPH arises from androgen-driven growth, amplified by chronic inflammation, aging-related tissue remodeling, and metabolic influences. This multifactorial pathogenesis explains why treatment often requires both pharmacological and lifestyle approaches.

Symptoms

- BPH (enlarged prostate) can make it difficult for urine and ejaculate to pass through the urethra.
- Patients with BPH present with a constellation of symptoms generally referred to as LUTS. These complex symptoms can be grouped as voiding, storage, and post-micturition symptoms (Table 15).
- Voiding symptoms include hesitancy, poor stream, intermittency, and straining; storage symptoms include frequency, urgency, urge incontinence, and nocturia; and post-micturition symptoms include a feeling of incomplete bladder emptying and terminal dribbling. (Table 15)
- Other symptoms may include hematuria, uremic features, or urosepsis.
- Urinary retention, and others, some patients may also experience erectile dysfunction, infertility, as well as a reduction in the quality of life (QoL).

Table 15. Categories of symptoms of BPH in men

SN	Category	Examples	Impact
①	Storage symptoms	Frequency, urgency, nocturia	Disrupts sleep, daily activities
②	Voiding symptoms	Hesitancy, weak stream, intermittency, and straining	Causes frustration, prolonged urination
③	Post-micturition symptoms	Dribbling, incomplete emptying	Leads to discomfort, hygiene issues

- The symptoms of BPH can be objectively assessed using validated tools, such as the International Prostate Symptom Score (IPSS). Scores of 0-7, 8-19, and 20-35 would translate to mild, moderate, and severe symptoms, respectively.
- The mechanical obstruction caused by the enlarged prostate gland and resultant stasis of urine forms a podium for recurrent urinary tract infection, prostatitis, and, by extension, chronic orchitis, which can affect optimal testicular function, sperm production, and sperm characteristics and function directly.
- Cumulative evidence indicates that infection and inflammation of the prostate are detrimental to sperm quality and male fertility.
- Men with moderate to severe LUTS are at increased risk for sexual dysfunction, including moderate to severe erectile dysfunction (ED), ejaculatory dysfunction, and hypoactive sexual desire.
- The incidence of ED in symptomatic BPH patients in the age group of 61 to 70 years has been reported as 100%, and 60% in the age group 50-60 years in Bangladesh. [73]

Complications if untreated

- Urinary tract infections (UTIs): due to incomplete emptying
- Urinary bladder stones: From residual urine
- Kidney damage: Rare but possible if obstruction is severe
- Acute urinary retention: Sudden inability to urinate, often requiring emergency care.

Diagnosis

The BPH is benign and not life-threatening. However, it can significantly impair the quality of life of affected individuals. Therefore, early diagnosis and treatment are crucial. As a man ages, the prostate grows, and a BPH diagnosis occurs when prostate enlargement has progressed enough to cause noticeable symptoms and disrupt everyday life.

Diagnosis of BPH in men involves a combination of clinical history, physical examination, laboratory tests, and specialized urological investigations. The most common methods include symptom questionnaires, digital rectal exam (DRE), urine and blood tests, PSA testing, urinary flow studies, and imaging (Table 16).

① Disease and patient history

- Relevant patient history includes fluid intake, history of sleep apnea, having diabetes mellitus, heart failure, hypertension, chronic kidney disease, or neurologic disorders, family cancer history, tobacco use, alcohol consumption, sexual history, and current medications.
- Important family history can include urethral, bladder, prostatic, or urothelial cancer. Having multiple sex partners increases the risk of prostatitis.

② Characteristics, signs, and symptoms[74]

- BPH should be considered in men with voiding difficulties or urinary incontinence.
- Voiding symptoms include urinary hesitancy, delayed bladder emptying, intermittent voiding, a weak urinary stream, and dysuria.
- Storage symptoms include urinary frequency, nocturia, urgency, enuresis, and incontinence.
- Post-urination symptoms include a sensation of incomplete voiding and urine dribbling.

Table 16. Methods of diagnosis for BPH in men

SN	Method	Purpose	Notes
①	Medical history and symptom assessment	Identifies LUTS such as weak stream, nocturia, and hesitancy.	Often uses the IPSS questionnaire
②	Digital rectal examination (DRE)	Assesses prostate size and consistency	Quick bedside test that helps rule out nodules suspicious for cancer.
③	Urine test (urinalysis)	Detects infection, hematuria, or other causes of urinary symptoms	Important to exclude differential diagnosis
④	Blood tests	Evaluate kidney function (creatinine, urea)	Ensuring no renal impairment due to obstruction
⑤	Prostate-specific antigen (PSA) test rules out prostate	Screens for prostate enlargement and cancer.	Elevated PSA can be due to BPH, prostatitis or cancer.
⑥	Urinary flow test (uroflowmetry)	Measures strength and speed of urine stream	Reduced flow suggest obstruction.
⑦	Post-void residual (PVR) urine measurement	Assesses incomplete bladder emptying.	Done via ultrasound or catheterization
⑧	Imaging (ultrasound, MRI, CT if needed)	Evaluates prostate size, bladder wall changes, hydronephrosis	Transrectal ultrasound (TRUS) is common.
⑨	Cystoscopy (in selected cases)	Direct visualization of the urethra and urinary bladder	Used if hematuria or suspicion of strictures/ tumors.

- The International Prostate Symptoms Score (IPSS) is a validated 8-item questionnaire that quantifies patients' symptoms.[75] Three questions pertain to storage symptoms (frequency, nocturia, urgency), and four pertain to voiding (feelings of incomplete emptying, weak stream, intermittency, straining). The final question assesses the patient's self-reported impact of symptoms on quality of life. It is the only symptom score that can predict significant urinary retention. An IPSS of 20 or higher, demonstrating severe lower urinary tract symptoms, has a favorable likelihood ratio of 1.5 for bladder outlet obstruction; an IPSS of less than 20 has a negative likelihood ratio of 0.8 (Table 17).[76,77]
- Many neurological conditions can cause or worsen LUTS.

Table 17. Benign prostatic hyperplasia symptom score index [76,77]

SN	Urination status	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your score
①	Incomplete emptying- It does not feel like I empty my bladder at the way	0	1	2	3	4	5	-
②	Frequency- I have to go again less than two hours after 1 finish urinating	0	1	2	3	4	5	-
③	Intermittency- I stop and start again several times when I urinate	0	1	2	3	4	5	-
④	Urgency- It is hard to wait when I've to urinate	0	1	2	3	4	5	-
⑤	Weak stream- I have a weak urine stream	0	1	2	3	4	5	-
⑥	Straining- I've to push or strain to begin urination	0	1	2	3	4	5	-
⑦	Nocturia- I get up to urinate after I go to bed until the time I get up in the morning	0	1	2	3	4	5	-
							Total AUA Symptom Score: 00	

Total score: 0-7 = Mildly symptomatic 8-19 = Moderately symptomatic 20-35 = Severely symptomatic

③ Physical examination[74]

- Physical examination focuses on the suprapubic and genital regions to exclude other causes of LUTS.
- Cardiac examination can reveal hypotension or lower extremity edema.
- Abdominal examination can reveal bladder enlargement.
- Neurologic examination can reveal sensory deficits.
- Genital examination can identify urethral discharge, phimosis, penile lesions, or meatal stricture.
- A digital rectal examination (DRE) may show features of an enlarged prostate with characteristic features suggestive of BPH, like non-tender, firm, smooth, rubbery, non-nodular, preserved median groove and lateral sulci, and an examining finger not stained with blood.
- Digital rectal examination can evaluate prostate size, consistency, and tenderness; however, the examination reliably identifies only prostates larger than 50 ml.
- The diagnosis of BPH can be made only with a prostate biopsy and histology.

④ Diagnostic testing

- The investigation would include urine microscopy, culture, and sensitivity; a comprehensive metabolic panel (CMP); a complete blood count (CBC); prostate-specific antigen (PSA); and urologic ultrasonography (kidneys, ureters, bladder, prostate volume, and postvoid residual urine volume). Baseline urodynamic studies, such as uroflowmetry, can also be performed. Retrograde cystoscopy can be carried out when indicated.
- Urinalysis should be performed to screen for glucosuria, proteinuria, hematuria, and evidence of infection, with urine culture as indicated.
- Prostate-specific antigen (PSA) testing is not required for patients with LUTS. Serum PSA is a limited predictor of prostate volume, risk of acute urinary retention, and need for surgery.
- Renal function testing is recommended only if renal insufficiency is a concern.
- Urologists sometimes perform postvoid residual testing, uroflowmetry, and transrectal ultrasonography. However, postvoid residual testing is not helpful for routine testing, with a positive predictive value of 63% and a negative predictive value of 52% for bladder outlet obstruction. Uroflowmetry is not beneficial for the initial evaluation of lower urinary tract symptoms. [77]
- Transrectal ultrasonography is more accurate than digital rectal examination at measuring prostate size. Transrectal ultrasonography is usually recommended before treatment with 5-alpha reductase inhibitors or surgery.[77] However, the evidence that prostate-size measurement before medication initiation improves outcomes is limited. [75]

Important considerations

- Differential diagnosis: Symptoms of BPH can mimic those of prostate cancer, urinary tract infection, bladder stones, or urethral stricture. Hence, multiple tests are often combined.
- PSA limitations: Elevated PSA is not specific to BPH; interpretation must consider age, prostate size, and risk factors.
- Imaging is not always required but is useful when surgical intervention is considered.
- Symptom scoring (IPSS) helps quantify severity and guide treatment decisions.

Practical guide

When evaluating a man for suspected BPH:

- Start with history plus the IPSS questionnaire.
- Order urinalysis and blood tests to exclude. infection and check kidney function. functional evaluation.
- Perform DRE to assess prostate enlargement
- Check PSA if cancer rise needs assessment.
- Do uroflowmetry and PVR measurement for
- Use imaging or cystoscopy selectively, depending clinical suspicion.

Treatment options for BPH

Treatment of BPH and PC differs significantly between men and dogs due to biological differences, though both rely heavily on managing hormone-driven prostate growth (especially DHT). Allopathic medicine (conventional), herbal (phytotherapy), and homeopathic treatments all aim to reduce prostate volume or manage cancer, with allopathy acting as the primary intervention, particularly in cancer cases.

- BPH often involves gradual, slow changes that can make it difficult to notice and may require consulting a physician for treatment. It is essential to monitor changes in urinary patterns and behaviors. Screening is particularly valuable for identifying BPH before its symptoms progress.
- The goal of treatment for BPH is to reduce LUTS, prevent disease progression, and prevent complications such as urinary retention.
- The treatment options for BPH could be categorized using the IPSS as a guide. Mild symptoms can be treated with conservative modalities, moderate symptoms with medical therapy, and severe symptoms with surgical intervention.
- Pharmaceutical targets for BPH include 5-α-reductase inhibitors (inhibition of DHT synthesis from testosterone), aromatase inhibitors (inhibition of estrogen synthesis), and α-adrenoreceptor antagonists (muscle relaxation to relieve LUTS).

Applications of three types of medical management, especially allopathic, phytotherapies, and homeopathic, are practiced for the treatment of BPH in men, which are included in this review.

① Conservative treatment

- Patients with IPSS symptoms rated as mild (0-7) may elect lifestyle modifications, depending on symptom bother.[77,78]
- Common lifestyle changes include losing weight, decreasing evening fluid intake, and decreasing total daily fluid intake or the quality of substances with bladder-irritating or diuretic properties, such as caffeinated beverages (coffee, tea, energy drinks, cola), sugary beverages (soft drinks, juices), alcoholic beverages, and fluids containing artificial sweeteners, artificial colorings, or artificial flavorings (often these substances exert diuretic and bladder-irritating effects. [78,79]
- Patients should also be advised that pelvic floor exercises- not strengthening or Kegel exercises- and maintaining a time void and regular bowel regimen to avoid constipation can also be quite impactful.[78,79]
- Lifestyle changes, since the following risk factors can contribute to BPH development, which include (a) A sedentary lifestyle, (b) obesity, (c) eating food high in sugar or unhealthy fats, (d) smoking or excessive alcohol, and (e) other unmanaged comorbidities, such as diabetes or heart disease.
- Bladder training involves incremental delayed voiding to regain bladder control as well as pelvic floor exercise or mindfulness.[77,80,82] Low-quality evidence suggests that sitting while urinating reduces post-void residual urine volume.[83] Some men will experience spontaneous improvement in symptoms over time, without therapy.[79]
- For patients with moderate to severe LUTS at baseline or symptoms refractory to conservative management, initiation of medical therapy and consideration of procedural treatment are options.[79]

② Medications

The primary medications for BPH in men include alpha-blockers (e.g., tamsulosin, alfuzosin), 5α-reductase inhibitors (e.g., finasteride, dutasteride), and phosphodiesterase-5 inhibitors (e.g., tadalafil). Each works differently-some relax prostate/bladder muscles, others shrink the prostate, and some improve urinary symptoms while also treating erectile dysfunction.

Primary medical treatment typically involves alpha-blockers or phosphodiesterase type 5 inhibitors. Alpha blockers offer rapid benefits and can be used for acute urinary retention. Combining alpha blockers and phosphodiesterase-5 inhibitors is not beneficial. For uncontrolled symptoms, 5-alpha reductase inhibitors should be started if the prostate volume is 30 ml or greater on ultrasonography. 5α-reductase inhibitors may

take up to 1 year to become fully effective and are more effective when used with α-blockers.[75]

a. Alpha blockers

- Alpha blockers are a class of drugs that work by antagonizing alpha-1 receptors in the bladder neck and prostate, which results in the relaxation of smooth muscle in these areas,[79-85] and in turn, reduced constriction of the urinary channel and lower resistance to urinary flow.[80]
- They do not shrink the prostate, but they may improve urine flow if there is a blockage.
- The five main alpha-blocker drugs include second-generation drugs (terazosin and doxazosin) and third-generation drugs (silodosin, tamsulosin, and alfuzosin). The third-generation drugs are generally well tolerated, and tamsulosin is associated with fewer side effects. Second-generation alpha-blocker drugs require dose titration owing to their antihypertensive effects.[79,86]
- The therapeutic effect of an alpha blocker starts within hours to days, although it generally takes 3 to 7 days to reach maximum effect.[80,81,84,87]

Side effect

- Common side effects include lightheadedness, dizziness, headache, nasal congestion, erectile dysfunction, and ejaculatory dysfunction or anejaculation (formerly known as retrograde ejaculation). These side effects usually accompany the therapeutic effect of the drug, are generally dose-dependent, and resolve within a few days with drug discontinuation. [86]
- Rates of ejaculatory dysfunction following use of tamsulosin, and silodosin have generally been found to be about 10-30%. Ejaculatory dysfunction caused by alpha-blockers is typically reversed after stopping the medication.
- Prostate medications such as α-blockers have been shown to decrease the quality of semen parameters, including sperm count and motility.
- Alpha-blockers and phosphodiesterase-5 inhibitors are first-line therapies. Combining these medications increases adverse effects, such as headache and muscle pain, with only a slightly added benefit. [88,89]
- Use of alpha-blockers leads to a rapid improvement in LUTS compared with placebo, as shown in 19 randomized controlled trials involving nearly 10,000 participants.[90] Symptom improvement is consistent among different alpha blockers. [87,90]
- The nonselective alpha-blockers terazosin and doxazosin lower blood pressure more than the selective alpha-1-blockers tamsulosin and alfuzosin. [91]
- Selective alpha blockers are more likely to cause ejaculatory dysfunction,[88] whereas nonselective alpha blockers are more likely to cause orthostatic hypotension. [90] A small trial suggests that taking selective alpha blockers every other day improves ejaculatory dysfunction while maintaining benefit. [92]
- Patients taking an alpha blocker, especially tamsulosin, who plan to undergo cataract surgery should be informed of the possible association risk of intraoperative floppy iris syndrome.[91] It may occur due to local smooth muscle inhibition resulting in iris prolapse at the incision site during phacoemulsification in cataract surgery. [80,81,93]
- Comparative clinical trial study on tadalafil @ 5mg/day and tamsulosin @ 0.4mg/day in patients with symptoms of LUTS due to BPH showed that both drugs were reported to be effective with some drug-related adverse effects in Bangladesh. [94]
- For patients with acute urinary retention, immediately start an alpha blocker after urinary catheterization and treat the patient for three days before attempting to remove the catheter. [77]
- Phosphodiesterase-5 inhibitors, such as tadalafil, are similarly effective when used as alpha blockers, even in patients without erectile dysfunction, based on a Cochrane review of four randomized controlled trials with 933 participants.[88] Phosphodiesterase-5 inhibitors should be a first-line option in men with coexisting BPH and erectile dysfunction.

b. 5-alpha reductase inhibitors

Testosterone is a male hormone that is converted to DHT, a more potent ligand for the androgen receptor and an arbiter of prostate growth. Inhibition of the conversion of testosterone to DHT with 5-alpha reductase inhibitors (5ARIs) can reduce prostate growth and tip the scales toward prostatic cellular apoptosis and atrophy. Atrophy is more pronounced in the glandular epithelium of the prostate, where PSA is made, as opposed to the smooth muscle stromal component of the gland.[95] The impact of 5ARIs on glandular cells results in a 50% reduction in PSA after 6 to 12 months of treatment.[82,95,96] PSA is a key predictor of treatment outcome; baseline PSA measurement is recommended for all patients considering 5ARI therapy.

Finasteride and dutasteride are the most used 6ARIs.[82,95,96] Finasteride inhibits the 5AR type II isoenzyme, while dutasteride inhibits type I and II isoenzymes (Fig. 6).[96] The clinical effect of these medications does not differ, because type II 5ATI is more commonly found in prostate tissue. Notably, 5ARIs require about three months of use before noticeable improvements in the urinary system occur, and approximately six months to reach full effect in terms of prostate volume reduction.[82,95,96] These drugs may be best for men with huge prostate glands. There is a black box warning regarding 5ARIs because they were thought to increase the risk for higher-grade prostate cancers, potentially, but were later determined to be helpful in the process of detecting these cancers.[77,82,96] These drugs are regularly used and thought to be safe.

Five-alpha-reductase inhibitors (finasteride and dutasteride) decrease serum DHT levels[97] and prevent the clinical progression of BPH and LUTS.[98] A prevention trial found that finasteride reduced the risk of incident symptomatic BPH and LUTS- the first study to suggest that BOO onset may be prevented in asymptomatic men. [37]

- 5-Alpha reductase inhibitors, such as finasteride and dutasteride, are primarily used to treat LUTS due to BPH, often as combination therapy, particularly in men with low urinary flow or large prostates on ultrasonography, based on several long-term randomized controlled trials involving more than 1,000 patients. [77]
- 5-Alpha reductase inhibitors are recommended if prostate volume is 30 mL or greater on imaging.
- 5α-reductase inhibitors have a delayed onset, and the whole effect may take up to 1 year. The benefits of 5α-reductase inhibitors persist for up to 10 years. [99,100]
- Finasteride reduces the progression of BPH at 4 years, but it does not reduce LUTS progression compared with doxazosin; combining finasteride and doxazosin reduces symptom progression. [99]

Dutasteride is a 5α-reductase inhibitor that acts on two main isoforms, types 1 and 2. These enzymes play a critical role in converting testosterone, a male hormone, into dihydrotestosterone (DHT), a more potent androgen. DHT is known to contribute significantly to the development and enlargement of the prostate.

The primary mechanism of action of dutasteride is inhibition of both isomers of 5α-reductase. By blocking these enzymes, dutasteride effectively reduces the conversion of testosterone into DHT. This reduction in DHT levels helps in managing the symptoms associated with BPH.

The high levels of DHT contribute to prostate cell growth, and by lowering DHT levels, dutasteride reduces 5α-reductase-mediated stimulation of prostate cell growth, thereby alleviating BPH symptoms.

- Dutasteride improves symptoms and reduces the risk of future urinary retention and the need for surgery.[100]
- Dutasteride is an aza-steroid medication belonging to the class of 5α-reductase inhibitors of types I and II. The enzyme 5α-reductase converts testosterone intracellularly to the more potent androgen dihydrotestosterone (DHT). A reduction of more than 90% in DHT levels is observed with dutasteride, whereas only a 70% reduction is observed with finasteride.
- The 5α-reductase is a nuclear-bound steroid intracellular enzyme primarily located in the prostatic stromal cell that converts the androgen testosterone into the more active metabolite, dihydrotestosterone (DHT). DHT is the primary androgen, playing a role in the initial development and subsequent enlargement of the prostate gland.

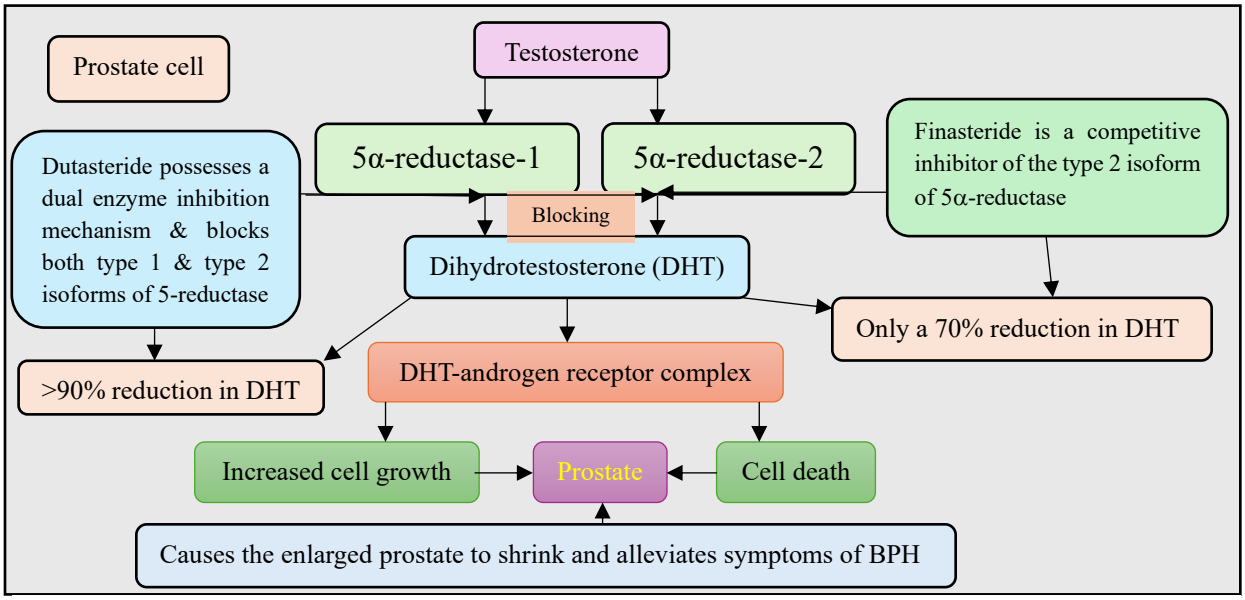

Fig. 6. Mode of action of dutasteride and finasteride

- Dutasteride works by blocking the 5α-reductase enzyme, preventing testosterone from being converted to dihydrotestosterone (DHT). Since DHT is the primary hormone that stimulates prostate growth, reducing its levels causes the enlarged prostate to shrink and alleviates symptoms of BPH.
- Combining 5-alpha-reductase inhibitors and alpha-blockers is more effective than either medication alone after more than 1 year. However, in one year or less, there is no difference. [101]
- The primary adverse events associated with 5-alpha reductase inhibitors are erectile dysfunction, decreased libido, and abnormal ejaculation, with each having one more occurrence per 100 person-years with finasteride than placebo. [99,100]
- 5-Alpha-reductase inhibitors can reduce PSA levels by up to 50%, so the physician should consider doubling PSA values when interpreting results from cancer screening. Men taking 5-alpha reductase inhibitors have delayed diagnosis of prostate cancer, slightly higher risk of high-grade cancers, and worse cancer outcomes.[77,96]
- Desmopressin appears to improve nocturia only minimally compared with placebo. [102]
- Most of the treatment options for LUTS due to BPH, both pharmacologic and surgical, are known to have significant sexual side effects and, most importantly, ejaculatory dysfunction. While ejaculatory dysfunction due to pharmacologic therapy is usually reversible on cessation of treatment, it is often permanent and irreversible.
- Hormone-mediating agents such as clomiphene citrate and antioxidant-based supplements such as vitamins C, E, and D, as well as zinc and coenzyme Q10, are widely used by most urologists.
- Some novel therapies are now used to treat BPH in a bid to mitigate the problem of infertility associated with standard conventional treatment options and thus enhance the chances of wife conception in these affected men. A notable example today is the Uro-Lift.

Side effects

- Side effects of 5ARIs vary widely across research studies, but include bothersome symptoms related to testosterone deficiency, including erectile dysfunction, ejaculatory dysfunction (reduced semen volume and thinned semen consistency), decreased libido, and possible fertility implications. [77,103]

- These drugs have the adverse effects of erectile dysfunction, hypoactive sexual desire, and ejaculatory dysfunction, including reduced, absent, or painful ejaculation, and these negatively impact fertility. [104]
- 5α-Reductase inhibitors like finasteride have been shown to reduce sperm quality even in low doses.
- These factors in patients with BPH may collectively impair sperm production and functionally result in male infertility.
- The long-term use of 5α-reductase inhibitors, while inhibiting DHT synthesis and alleviating BPH symptoms, may induce insulin resistance.[105] Concurrently, IR can trigger hyperinsulinemia, potentiating a pathological cycle that worsens BPH.
- Fig. 7 shows a proposed approach to treating BPH.

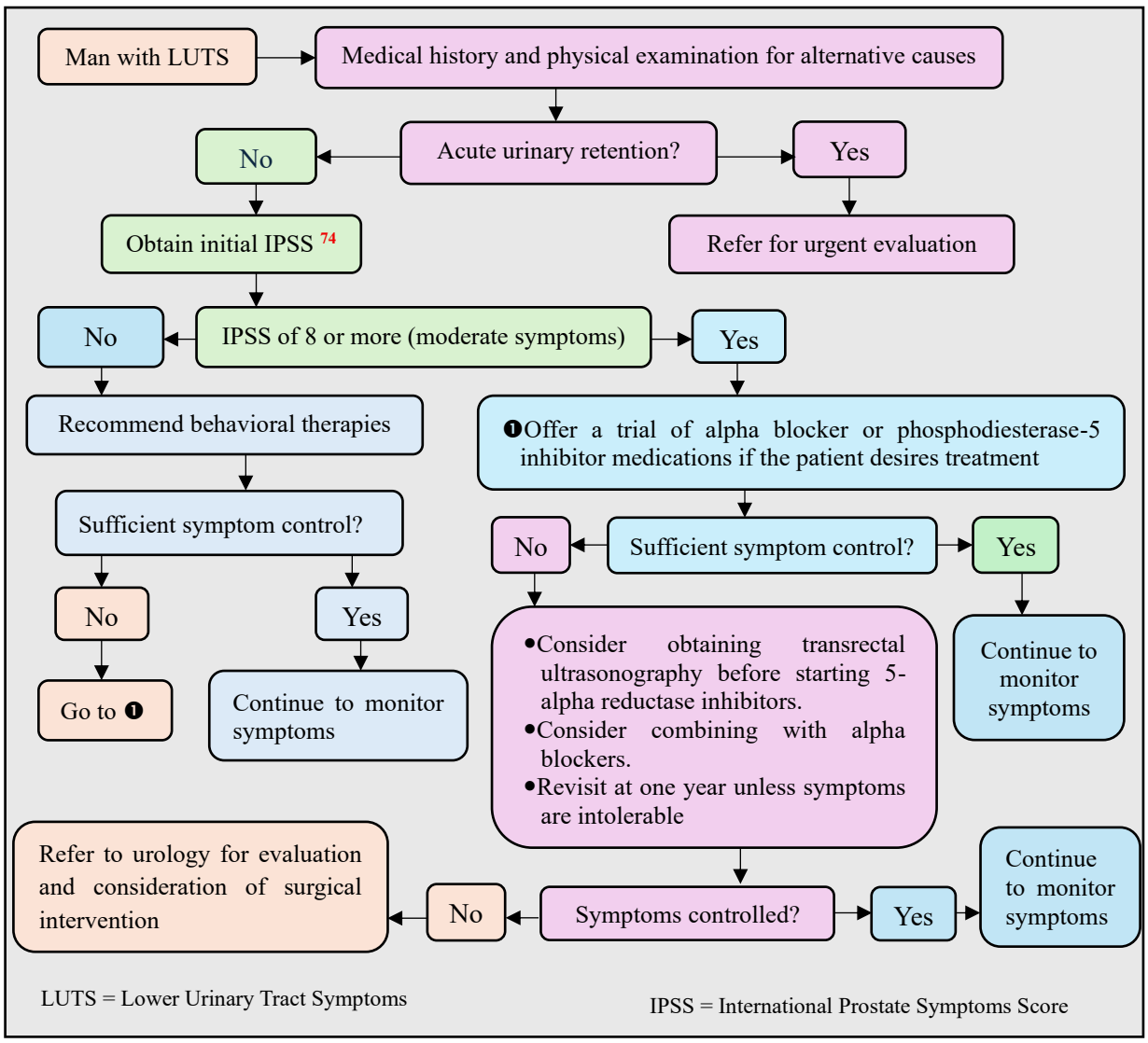

Fig. 7. Algorithm for treating urinary tract symptoms from benign prostatic hyperplasia

- Table 18 provides first-and second-line medication treatment options for LUTS of BPH.[77,79,88,89,90,99,100,101,106-108]

Table 18. Medication treatment options for LUTS of BPH [74]

Medication class	Evidence summary	Prospective	Consequences
A. First line			
① Alpha blockers	Lower IPSS by 2 to 4 points-based on 21 RCTs with more than 10,000 patients. [90]	Improvement is a class effect rapid improvements of symptoms. Low-cost	Caution with use around cataract surgery because of floppy irissyndrome. Adverse effects of orthostatic Hypotension and ejaculatory dysfunction. [90]
② Phosphodiesterase-5 inhibitors	Demonstrate similar effectiveness to alpha blockers, based on a Cochrane review of four trials with 933 patients, [88] effects are the same in patients without erectile dysfunction.	Dual effects in patients with both BPH and erectile dysfunction.	Combination with α-blockers has only a slight added benefit over either medication alone. Mild adverse effect of headache is most common. [89,90]
B. Second line			
① 5-Alpha reductase inhibitors	Lower the IPSS score by 1 to 2 points based on 14 RCTs with nearly 15,000 patients. [90] Decrease volume of prostate by 15 to 25% at six months based on on three RCTs with nearly 4,000 men. [77]	Decrease the progression of BPH over the years. Decrease the risk of urinary retention and surgical intervention. [99] Combining with alpha blockers are a more effective than either medication alone at one year.[101]	Full symptoms improvement can take up to a year. Adverse effects of erectile dysfunction, decreased libido, and abnormal ejaculation.[99,100] Decreases prostate-specific antigen value; risk of delay in diagnosis of prostate cancer.[106]
② Anticholinergics	Combination therapy with alpha Blockers lower the IPSS score by 2 points compared with alpha blockers alone, evidence from 19 RCTs with 3,631 patients, but very low certainty because of high risk of bias & heterogeneity. [107]	Combining with alpha blockers may improve quality of life but is uncertain in clinical significance. [107]	Risks of acute urinary retention, dementia, and mental status changes, especially in older populations. [108]

LUTS = Lower urinary tract symptoms BPH = Benign Prostatic Hyperplasia IPSS = International Prostate Symptom Score
RCT = Randomized controlled trial

c. Phosphodiesterase-5 inhibitors

- Treatment with phosphodiesterase-5 inhibitors helps maintain ejaculatory function and may provide additional relief of irritative symptoms, including urgency and frequency, compared with alpha-blockers and 5-alpha reductase inhibitors.[86]
- Phosphodiesterase-5 (PDE5) inhibitors increase intracellular cyclic guanosine monophosphate, causing nitric oxide-mediated relaxation of smooth muscle throughout the prostate, detrusor muscle (bladder), and urethra. [109]
- Tadalafil is the most extensively studied PDE5 inhibitor for patients with BPH and LUTS, with an average improvement in IPSS of at least 3 points. Avanafil has the shortest onset of action (15-20 minutes) in this class but is not widely used to treat BPH.[77,110]

Side effects

Side effects of PDE5 inhibitors include facial flushing, headache, back pain, dyspepsia, and the potential for blue-tinted vision; however, most of these side effects are minimal or absent at low daily doses for BPH. Well-known contradictions to PDE5 inhibitors include the use of nitrates. [77,80]

d. Beta-3 agonists and anticholinergics

- Beta-3 agonists, including mirabegron and vibegron, act via the sympathetic pathway to relax the detrusor muscle and increase bladder capacity. [77,80]

- They are indicated for patients with overactive bladder and can benefit patients with predominantly irritative LUTS, including urgency, frequency, and incontinence.
- While vibegron is available in a single dose, mirabegron is available in multiple doses and appears to provide similar therapeutic benefit. [111]
- Emerging research suggests this class of drugs may also benefit patients with BPH, but this remains an area of active investigation.[112]
- Anticholinergic medications are associated with cognitive impairment and dementia, in addition to the well-known side effects of mental fogginess or confusion.[80]
- Studies have shown that trospium, a larger quaternary amine, does not cross the blood-brain barrier and may therefore be a safer option.[111]
- Anticholinergics exert therapeutic effects within hours to days, although this can vary with short- and long-acting formulations and doses.
- Long-acting formulations tend to have fewer bothersome side effects, as these agents do not reach the high serum levels that cause unwanted effects.[77,80]
- Beta-3 agonists can be combined with anticholinergics to treat severe overactive bladder, as both agents act on the bladder via distinct, synergistic molecular pathways. [77]

Side effects

- Beta-3 agonists have very favorable side-effect profiles and little to no risk for those with dementia or cognitive impairment.[111-113]
- Both mirabegron and vibegron are contraindicated in patients with poorly controlled hypertension, although vibegron has been found clinically to pose a negligible risk of blood pressure change.
- All anticholinergics have undesirable side effects, including dry mouth, dry eyes, constipation, and potential vision changes.[80]

Combined therapy

Monotherapy with either alpha-blockers, antimuscarinics, or 5-alpha reductase inhibitors does not provide symptomatic relief for some patients with BPH; thus, treatment for these patients often involves the use of combined agents or multiple therapies. The combination therapy has proven effective across the spectrum of BPH-LUTS (Table 19). [114]

Combined therapy for BPH in men typically involves alpha-blockers plus 5α-reductase inhibitors (5-ARIs) and, in selected cases, combinations with phosphodiesterase type 5 inhibitors (PDE5i) or β3-agonists. This approach improves both symptom relief and long-term control of disease progression compared with monotherapy.[15]

Why combination therapy?

- **Alpha-blockers:** Provide rapid relief of lower LUTS by relaxing smooth muscle in the prostate and bladder neck.
- **5-ARIs:** Reduce prostate size and risk of urinary retention or surgery by blocking testosterone converted to dihydrotestosterone (DHT) conversion.
- **Combination:** Addresses both short-term symptoms and long-term progression, especially effective in men with moderate-to-severe LUTS and enlarged prostates (>40 ml).[115]
- Men with larger prostates are good candidates for this combined therapy.
- Possible drug combinations include: (a) Finasteride and doxazosin, (b) Dutasteride and tamsulosin, a combination of both drugs that is available in a single tablet, and (c) Alpha blockers and antimuscarinics.
- Both single Silodosin and the combination of silodosin + tadalafil have been reported to be effective in BPH, but the combination is significantly more effective.[116,117]
- Table 19 presents the common combination strategies for drugs for BPH in men.

Table 19. Common combination strategies for drugs for BPH in men

SN	Therapy	Mechanism	Benefits	Limitations
①	Alpha-blocker + 5-ARI	Relaxation of smooth muscle + shrinkage of the prostate	Rapid symptom relief + reduced the risk of progression, retention, and surgery	Sexual side effects (ED, decreased libido), delayed effect of 5-ARI
②	Alpha-blocker + PDE5 inhibitor (e.g., Tadalafil)	Smooth muscle relaxation + improved blood flow	Improves LUTS and erectile dysfunction simultaneously	Cost, contraindicated with nitrates
③	Alpha-blocker + Beta-3 agonist (e.g., Mirabegron)	Smooth muscle relaxation + bladder storage improvement	Useful for persistent storage symptoms (frequency, urgency)	Limited long-term data, possible hypertension
④	Triple therapy (Alpha-blocker+ 5-ARI +PDE5i)	Multi-target approach	Maximal LUTS relief + sexual function benefit	Higher risk of polypharmacy side effects

Risks and Trade-offs

- Sexual dysfunction: More common with 5-ARIs (finasteride and dutasteride)
- Hypotension/dizziness: Alpha-blockers, especially non-selective ones (terazosin and doxazosin).
- Polypharmacy concerns: Increased side effects and drug interactions with multiple agents.
- Patient selection is key: Best outcomes in men with large prostates and severe LUTS; less benefits in mild cases. Table 20 summarizes medication classes for BPH in men.
- Combining drug therapy may have more side effects than taking just one drug.
- Potential side effects may include dizziness, erectile dysfunction, weakness or fatigue, and a drop in blood pressure when moving from sitting or lying down to standing.
- Antimuscarinics may be used for patients with overactive bladder symptoms to relax the bladder muscles. Involuntary bladder muscle contractions characterize an overactive bladder. It leads to frequent and urgent need to pass urine.

Table 20. Summary of medication classes for BPH in men

SN	Class	Examples	Mechanism	Benefits	Side effects	Best for
①	Alpha-blockers	Tamsulosin, Alfuzosin Doxazosin , Terazosin Silidosin	Relax smooth muscle in prostate & bladder neck	Rapid symptom relief, improved urine flow	Dizziness, fatigue. retrograde ejaculation	Men with moderate symptoms needing quick relief
②	5-alpha reductase inhibitirs (5-ARIs)	Dutasteride, Finasteride	Block conversion of testosterone to DHT, shrinking prostate	Reduce prostate size, lower risk of urinary retention and surgery	Sexual dysfunction, decreased libido	Men with large prostates (>40 ml)
③	Combination therapy	Tamsulosin plus Finasteriode/ Dutasteride	Dual mechanism: relax + shrink	Greater symptom relief, reduced progression	Combined side effects	Men with severe symptoms and enlarged prostate
④	Phosphodi-esterase-5 inhibitors (PDE5i)	Tadalafil	Increase cGMP →relax smooth muscle	Improve urinary symptoms + erectile function	Headache, flushing, back pain	Men with BPH + erectile dysfunction
⑤	Beta-3 agonists	Mirabegron	Relax bladder muscle, increase capacity	Reduce urgency/ frequency	Hypertension, headache	Men with BPH + overactive bladder symptoms

Table 21. Most frequently used active compounds licensed in Europe in the treatment of LUTS [113]

SN	Active compound	Pharmacological effect	Dose (mg)	Administration	Speed of onset	Interaction may occur
①	Alfuzosin	α1-adrenoceptor antagonist	7.5-10	Immediately following a meal, at the same time each day, depending on the formulation.	Days	In combination with vasodilators (e.g., PDE5 inhibitors, nitrates), and other antihypertensives.
②	Doxazosin	α1-adrenoceptor antagonist	2-8 (TR)	IR: Daily once at bedtime ER: Daily once with the first meal	Days	Before cataract surgery, consultation is necessary.
③	Silodosin	α1-adrenoceptor antagonist	4-8	With a meal, at the same time each day.	Days	In the case of tamsulosin, warfarin and diclofenac
④	Tamsulosin	α1-adrenoceptor antagonist	0.4-0.8	30 minutes after the first meal	Days	Co-administration is not recommended.
⑤	Terazosin	α1-adrenoceptor antagonist	5-20 (TR)	Daily once at bedtime	Days	
⑥	Dutasteride	5α-reductase (type 1 and 2) inhibitor	0.5	Without chewing, at the same time each day.	6-12 months	In combination with strong CYP3A4 and CYP2D6 inhibitors.
⑦	Finasteride	5α-reductase (type 2) inhibitor	0.5	Without chewing, at the same time each day.	6-12 months	No drug interactions have been identified.
⑧	Alfuzosin + Finasteride	Combination therapy	10/5	Swallow 2 different tablets without chewing, after dinner	Days	ama
⑨	Tamsulosin + Dutasteride	Combination therapy	0.4/0.5	Swallow 1 tablet without chewing, 30 min after a meal, at the same time each day.	Days	ama

TR = Titration recommended IR = Immediate release ER = Extended-release ama = As mentioned above

Clinical considerations

- Alpha-blockers act quickly but do not reduce prostate size.
- 5-ARIs take months to show effect but prevent progression.
- Combination therapy is often used in men with both significant symptoms and large prostates.
- PDE5 inhibitors are beneficial if erectile dysfunction coexists.
- Beta-3 agonists are newer and mainly target storage symptoms (urgency)

Risks and Trade-offs

- Sexual side effects (erectile dysfunction, reduced libido, ejaculation issues) are associated with 5-ARIs and some alpha blockers.
- Blood pressure changes (dizziness, hypotension) can occur with alpha-blockers.
- The long-term safety of newer drugs such as PDE5 inhibitors and beta-3 agonists remains under investigation.
- Cataract surgery complications: Alpha blockers may complicate intraoperative oculoplastic procedures.

③ Antibiotics

Patients are prone to exposure to antibiotics and their attendant toxicities, some of which affect testicular function. For example, nitrofurantoin is known to have gonadotoxic effects on the testes, causing decreased sperm count and motility; erythromycin, tetracycline, and the aminoglycosides disrupt sperm production, reducing count and motility; while sulfa drugs decrease sperm count and motility and affect morphology. The multifactorial etiology explains why treatment often combines hormonal therapy, lifestyle modification, and symptom management.

Phytotherapies (Herbal therapies)

Phytotherapies are defined as treatments that use plants or substances derived from them. Numerous phytotherapies have been investigated worldwide, with variable success in treating LUTS in men with BPH (Table 22). [118]

The use of herbal medicine and alternative medicine is reported to be in up to 50% of prescriptions for BPH in Europe, along with an increased global interest in holistic medicinal approaches. The most frequently studied herbs, either in isolation or in combination, were *Serenoa repens* (54%), *Urtica dioica* (14%), *Cucurbita pepo* (14%), *Lycopene* (14%), *Pygeum africanum* (14%), and *Linum usitatissimum* (7%). These herbal-based formulations mostly improved the symptoms associated with BPH, which include International Prostate Symptom Score (IPSS), American Urological Association Symptom Index (IPSS/AUASI), Maximum urinary flow rate (Qmx), Prostate Surface Antigen (PSA), Quality of life (QoL) scores, post-voiding residual volume (PRV), and Prostate volume (PV).[119]

There are now 27 phytotherapy plants available for BPH, [120] herbal preparations, mostly derived from eight plant sources.[121] These herbal products are commercially marketed as single-ingredient products or as combinations of two or more herbs. In addition to more than 100 commercial products containing saw palmetto (*Serenoa repens*) as a single ingredient or in combination with others, there are also commercially available products. Currently, pharmacologic treatments often lead to side effects, especially sexual dysfunction, so dietary supplements (DS) containing plant-based compounds such as β-**sitosterol** (SIT) are preferred. Dietary supplements are highly accessible and widely used, but poorly regulated, so often patients are victims of fraud.

Beta-sitosterol

β-Sitosterol (SIT), a plant-derived phytosterol, is a promising nutraceutical with broad benefits, notably for cardiovascular health (lowers LDL cholesterol), diabetes (improves glucose/insulin), and cancer prevention (anti-proliferative), alongside antioxidant, anti-inflammatory, and prostate health effects in BPH (Fig. 8). [122,123]

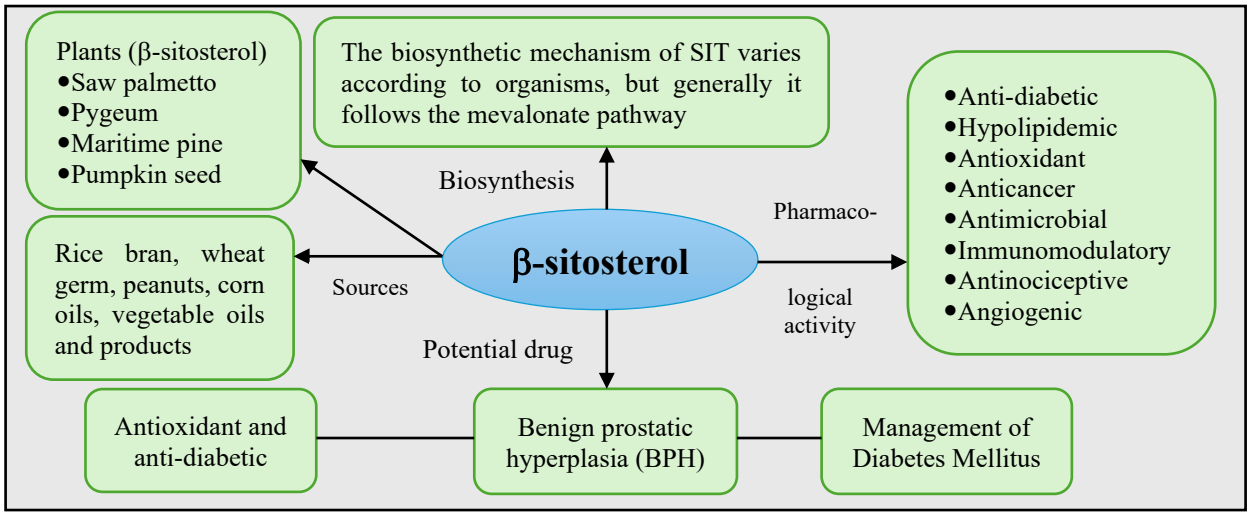

Fig. 8. Graphical introduction of β-sitosterol with sources and functions. [123]

Beta-sitosterol is found in many plants used for BPH treatment, but its concentration can vary widely depending on the plant source and the degree of extract standardization. Saw palmetto and maritime pine bark extracts often have the highest concentrations in supplements specifically formulated for BPH.

However, its efficacy for BPH is often linked to the total amount of free (non-glucosidic) beta-sitosterol in the extract. Beta-sitosterol is found in rice bran, wheat germ, peanuts, corn oils, and soybeans. The exact amount of β-sitosterol in raw plant material can vary based on growing conditions and processing methods.

Beta-sitosterol is the major plant sterol (phytosterol) in herbal supplements for prostate health, typically accounting for 42.0-78.0% of the total plant sterol content. While a healthy diet provides about 200-400 mg of phytosterols daily, the concentrations in medicinal plants can be significantly higher. The concentration of beta-sitosterol varies significantly depending on the plant source and the extraction and processing method used. The following plants are commonly used in BPH treatments and contain notable levels of beta-sitosterol.

① Saw Palmetto (*Serenoa repens*)- Extracts (often oil-based) are a primary source. Standardized saw palmetto oil can contain more than 3.0% beta-sitosterol and 85% total fatty acids.

② Maritime Pine Bark (*Pinus pinaster*)- Highly concentrated extracts from this source can have greater than 70% beta-sitosterol content in specific formulations.

③ South African Star Grass (*Hypoxis rooperi*)- Preparations derived from the corm of this plant are also a key source of beta-sitosterol for BPH treatment.

④ Stinging Nettle Root (*Urtica dioica*)- Nettle root is often used in combination with saw palmetto and is a rich source of beta-sitosterol.

⑤ African Plum Bark (*Pygeum africanum*)- The bark extract contains beta-sitosterol and is a common component in BPH phytotherapy.

⑥ Pumpkin Seeds (*Cucurbita pepo*)- Pumpkin seeds and their oil are a good dietary source of phytosterols, including beta-sitosterol.

Table 22. Beta-sitosterol concentration in major medicinal plants used in BPH in men

SN	Medicinal plants	Extract/ supplement	β-sitosterol content	Note
①	Saw palmetto (*Serenoa repens*)	Conventional oil enriched extract (e.g., Vispo™)	0.2-0.3% >3.0% of oil (up to >70% total sterols)	Saw palmetto extracts are primarily composed of fatty acids, with β-sitosterol as a key phytosterol component. Enriched extracts show superior efficacy.
②	African plum/Pygeum (*Prunus africanum*) (*Prunus domesticus* extract)	Standard extract Trade products Bark (raw) ProsmanTM β-sitosterol Docosyl ferulate	13-14% >10,000 µg/g 680 µg/g 0.431 mg/g 0.16 mg/g	Research often standardizes Pygeum extracts to total triterpenes (e.g., 14%) or total sterols (e.g., 13%). The bark itself contains about 680 µg/g. Effective in BPH caused a reduction in IPSS score, prostate volume, & serum PSA levels. [124]
③	Stinging nettle (*Urtica dioica*)	Root extract (dry) β-sitosterol	0.80-0.86g/kg 75-82%	β-sitosterol is the dominant sterol in nettle roots, followed by campesterol and stigmasterol.
④	Maritime pine bark (*Pinus pinaster*)	Conc. extracts (e.g., Apoprostat® Fort; Pycnogenol®)	>70.0% phytosterol content	This plant source is used in specific high-concentration formulations for BPH treatment in some markets.
⑤	Pumpkin seeds (*Cucurbita pepo*) Rye Pollen	Seed oil Raw seeds Extracts	44.4g/100g 384 mg/kg 0.5-1.0%	Approximately 0.038% in raw seeds
⑦	Pine/Pinus pinaster (*Hypoxis rooperi*)	Extract products	70.0%	

Key considerations

- **Standardization**: The actual concentration can vary significantly between different commercial products due to differences in harvesting, extraction, and manufacturing processes. Standardized extracts are generally recommended for consistent therapeutic effects.

- **Active component:** β-sitosterol is considered a primary active ingredient, and higher concentrations often correlate with improved efficacy in preclinical and clinical studies.
- **Dosage:** Clinical studies for BPH treatment have effectively used dosages of purified β-sitosterol ranging from 60 mg/day to 195 mg/day to improve BPH symptoms and urinary flow. A commonly mentioned effective dose is 20 mg three times per day.

High levels are also found in botanicals such as saw palmetto conventional oil contains 0.2-0.3% and enriched extract 3% β-sitosterol, rye grass pollen (contains 0.5-1.0% β-sitosterol), *Pygeum africanum* (contains 0.68mg/g or 0.068%; commercial products 13-14% β-sitosterol), stinging nettles (*Urtica dioica* contains 0.8-0.86g/kg total phytosterols of which 75-82% β-sitosterol, African star grass (*Hypoxis hemerocallidea*, previously known as *Hypoxis rooperi*) contain 74.69 µg of β-sitosterol/5mg (1.5%) of extract, or from Scots pine (*Pinus sylvestris* bark contains 2.98-4.50 mg/g) and Pica which have been found to be beneficial for BPH in men.

Beta-sitosterol (a plant-derived phytosterol) has demonstrated efficacy in improving urinary symptoms and flow measures in men with mild to moderate benign prostatic hyperplasia (BPH), but it does not significantly reduce prostate size. The dose is 60 mg twice daily; it can be reduced to 30 mg twice daily after symptoms improve. Its effects are considered clinically relevant, though generally less potent than prescription medications.

Herbal supplements intended to enhance prostate health may contain various sterols, vitamins, and minerals. Plant sterols make up an abundant ingredient component, with saw palmetto extract or its primary component, beta-sitosterol, often comprising the most abundant sterol. A precise dose/kg body weight of SIT in adults with BPH has not been established in any clinical protocols. However, based on several clinical studies, a dose of 60-140 mg of SIT is estimated to alleviate BPH symptoms. [122]

Some independent laboratories, such as Eurofins and LabCorp (formerly Covance), demonstrate a wide range, by weight, for the most common plant sterols in these supplements- campesterol, stigmasterol, beta-sterol, brassica-sterol, and human cholesterol.[125] Among these, beta-sitosterol was the major plant sterol component, accounting for 42.4-78.0% of the total plant sterol content (Table 23).

Table 23 shows that beta-sitosterol is the most prevalent phytosterol in prostate health supplements. Beta-sitosterol has been shown to inhibit the binding of the active form of testosterone, dihydrotestosterone (DHT), to the androgen receptor. DHT is the major growth factor of the prostate, and inhibition of DHT activity has been shown to slow the growth of prostate tumors and BPH.[126]

Table 23. Prostate supplement plant sterol compositions. [125]

SN	Sterol (mg)	Commercial prostate supplements (*same composition)						
		Prostagenix 3 capsules (1.391g)	Pros-T 2 soft gel (3.18g)	Prostavar Ultra 3 capsules (1.168 g)	Prosterol 3 tablets (1.129g)	PtostRX* 3 capsules (1.129g)	Super Prostate* 3 capsules (1.386g)	Vasotrexx 3 capsules (0.836g)
①	Cholesterol	<0.564	3.86	1.69	1.41	2.37	2.37	3.66
②	Campesterol	74.6	266	201	138	108	108	204
③	Stigmasterol	8.65	179	210	201	73.9	73.9	169
④	Beta-sitosterol	823	375	374	361	359	359	356
⑤	Brassicasterol	<0.564	17.3	2.22	11.1	2.2	2.2	3.37
⑥	Other	149	44.1	42.8	44.6	34	34	63.6
	Total sterols	1055.25	885.26	831.71	757.11	579.47	579.47	799.63
	Beta-sitosterol %	78.0	42.4	45.0	47.7	62.0	62.0	44.5
	Testing lab	Eurofins	LabCorp	LabCorp	LabCorp	LabCorp	LabCorp	LabCorp

The use of DS to treat BPH symptoms is questionable, and this may be due not to the efficacy of the active compound but to the quality of commonly available DS. The quality of these DS is questionable especially

because of permissible legislation.[127] The number of DS available on the market is continuously increasing, making it practically impossible to maintain quality control.

The chromatographic analysis confirmed the presence of SIT in five randomly selected DS of the local market in Romania, but also showed a considerable variability of SIT content among DS, with only one product meeting the necessary concentration to bring potential benefits in BPH (Table 24)

Table 24. Beta-sitosterol content in the randomly selected five different marketed dietary supplements

Dietary supplement	Recommended daily dose (unit)	Declared conc. of SIT (mg/unit)	Measured conc. (mg/unit)*
DS-1(320mg SP)	1	Minimum 0.32	2.98 ± 0.13
DS-2(320mg SP)	1	Minimum 0.32	4.71 ± 0.18
DS-3(320mg SP)	1	Minimum 0.32	1.27 ± 0.01
DS-4(SE)	1	130	120.12 ± 0.63
DS-5(SE)	1	025	010.67 ± 0.21

SP = Saw palmetto SE = Standard extract conc.= Concentration
*Mean ± SD (Standard deviation) SIT = Sitosterol DS = Dietary supplements

It is considered a moderately effective and well-tolerated treatment option for mild to moderate BPH symptoms such as frequent urination and poor urine flow. It improves urinary symptoms and flow measures but does not appear to reduce the actual size of the prostate.

Systematic reviews of randomized controlled trials report improvements in LUTS and urinary flow compared with placebo over short to medium durations, based on preparations derived from *Hypoxis rooperi* and various Pinus/Picea species.[128,129]

Efficacy in BPH management

Systematic reviews and randomized controlled trials consistently demonstrate that a non-glycosidic beta-sitosterol preparation significantly improves symptoms compared with placebo.

- **Symptom improvement**: Studies using the IPSS reported significant reductions, with one meta-analysis finding a weighted mean difference of -4.9 points compared with placebo on other quality-of-life measures (Table 25).

Table 25. Clinical efficacy of beta-sitosterol versus placebo against BPH in men. [128,129]

SN	Outcome	Effect versus placebo	Notes
①	Symptom scores (e.g., IPSS, AUA)	Meaningful reduction	Typically observed within 4-6 months, magnitude clinically noticeable in pooled analyses.
②	Peak urinary flow (Qmax)	Small-to-moderate increase	Improvements suggest reduced obstruction, but not equivalent to prescription alpha-blockers.
③	Post-voided residual (PVR)	Decrease	Directionally favorable; varies by studies.
④	Prostate size	No consistent change	Symptom relief without apparent reduction in volume

- **Improved urinary flow**: Beta-sitosterol has been found to significantly increase peak urine flow rate and reduce post-void residual urine volume (PVR).
- **Comparable efficacy**: Its effectiveness in improving symptoms is clinically relevant and comparable to some conventional pharmaceutical agents, such as alpha-blockers, although it may be less effective than 5-alpha reductase inhibitors like finasteride.
- **Prostate size**: Beta-sitosterol improves symptoms and flow without significantly reducing the overall size of the prostate gland itself, which is a key difference from other drug classes used for BPH treatment.
- Plant sterols exhibit dual activities that lower the availability of DHT to prostate epithelial cells: (a) They inhibit the conversion of testosterone to DHT, and (b) They induce the pool of cholesterol available to the Leydig cells; hence, less cholesterol is converted to testosterone for conversion to DHT.

Mechanism of action

The exact mechanism of action is not fully understood, but it is believed to involve the following multiple pathways:

- **Anti-inflammatory effects:** It may interfere with prostaglandin metabolism and reduce chronic inflammation in prostate tissue, a contributing factor to BPH progression.
- **Hormonal effects:** It may inhibit the 5α-reductase enzyme, which converts testosterone into the more potent dihydrotestosterone (DHT), the primary growth factor for the prostate.
- **Inhibition of smooth muscle contraction**: It directly inhibits smooth muscle contraction in the prostate, helping improve dynamic obstruction and urinary flow. [130]
- **Stromal effects:** Recent in vitro studies indicate that prostate stromal cells are inhibited without cytotoxicity, providing a biologic link to symptom relief in LUTS/BPH, independent of prostate size reduction.[130]

Safety and consideration

- It may be most appropriate for men with mild to moderate BPH symptoms who prefer a natural supplement, with beta-sitosterol content varying widely, to avoid the potential side effects of prescription medicine.
- A significant concern is the lack of standardization in commercial supplements, as beta-sitosterol content varies widely across products. This highlights the importance of choosing standardized extracts to ensure efficacy.
- DSs are usually adulterated, potentially by incorporating lower-quality extract and supplementing with exogenous plant lipid fractions rich in sterols. [131]

Efficacy of mono-herbal medicine in BPH

Supplements are not regulated the same way prescription medicines are, because herbal product quality and ingredient accuracy can vary. Supplements are not a substitute for a medical evaluation, especially if symptoms are worsening. However, the efficacy based on research of some commercial herbal preparations is described as follows:

1. Harzol (Hoyer-Madaus/Abanta Pharma, Germany)

- It contains 10 mg of phytosterols (beta-sitosterol), derived from the South African star grass (*Hypoxis rooperi*) and plant oils.
- Clinical studies indicate that Harzol is generally effective at improving LUTS, but it does not shrink the physical size of the prostate gland.
- The beneficial effects of beta-sitosterol treatment observed in the 6-month double-blind trials were maintained for 18 months, but the 18 patients who chose not to receive further therapy showed no signs of improvement.[132]

2. Cernilton (Cerniton America, Utica, Ohio)

- It is also known as Cernitin or Graminex, a derivative of several rye grass pollen (*Secale sereale*) extract that contains β-sterols used to treat LUTS associated with BPH.
- It is derived from pollen of rye, corn, and timothy grass, often processed through microbial digestion to produce water-soluble and fat-soluble fractions.
- While many trials report improvements in overall subjective LUTS in men with BPH,[133,134] evidence suggests it does not significantly improve objective measures such as urinary flow rate (Qmax) or reduce volume or prostate size compared with placebo.

3. Bazoton (Kanoldt Arzneimittel GmbH, Islanding, Germany)

- It is a phototherapeutic agent containing a dry extract of stinging nettle roots (*Urtica dioica*) used to treat BPH stages I and II.

- It helps with irritable symptoms, such as urgency, frequency, and nocturia.
- More preclinical and clinical research is warranted to identify the active constituents, assess their effects on prostate cell growth, and evaluate the product's anti-inflammatory effects in the treatment of BPH.[135]

Among the many commercial herbal products, only two have been subjected to laboratory and clinical investigations to assess their efficacy and potential mechanisms of action: extracts of the American dwarf palm tree (*Serenoa repens*) and bark of the African plum tree (*Pygeum africanum*). However, a review of the efficacy of *Seronoa repens*, *Pygeum africanum*, *Secale cereale*, and *Hypoxis rooperi* found no significant benefit of phytotherapy in the treatment of BPH. Twenty years ago, the urologic community was encouraged by trial results that suggested phytotherapy could effectively treat symptomatic BPH. Since that time, several well-designed studies have consistently shown that these agents are no more efficacious than a placebo, despite being largely safe to ingest (Table 26). [136]

Table 26. Research findings on phytotherapies in treating LUTS of BPH in men

SN	Plant name	No. of patients	Country	Comparison with	Follow-up period	Results of herbal products	Ref. No.
01.	*Serenoa repens* (Saw palmetto)	225	United States	Placebo	14 months	No significant reduction in prostate volume & LUTS	137
	Serenoa repens (Saw palmetto)	369	United States	Placebo	72 weeks	No significant reduction in prostate volume & LUTS	138
	Serenoa repens (Saw palmetto)	060	Turkey	Tamsulosin	06 months	No significant reduction in prostate volume & LUTS	139
	Serenoa repens (Saw palmetto)	070	Italy	320 mg/day	30 days	50% effective improvement of LUTS.	140
	Tadennan®	-	-	25 mg cap × 4	30 days		
02.	*Pygeum africanum* (*Prunus africana*)	263	Germany France & Austria	Placebo	60 days	Improvement of LUTS but not the residual volume rate	141
	Pygeum africanum (*Prunus africana*)	209	France	None	12 months	IPSS scores improved 35 to 38%, Qmax increased 1.63 to 2.02 mL	142
	P. africanum 25mg + *Urtica dioica* 300mg	049	Brazil	Placebo	6 months	Produced clinical & urodynamic effects similar to placebo.	143
03.	*Cucurbita pepo*	130	Germany	None	24 months	IPSS improved 4.7 points Minimum impact on sexual Function	144
	Cucurbita pepo	073	Iran	Tamsulosin	3 months	No significant differences on IPSS, prostate volume & LUTS	145
04.	*Urtica dioica*	558	Iran	Placebo	6 months	Significant differences in peak flow (4.8 mL/s), IPSS (6.6 points) residual volume (37 mL/s)	146
	Urtica dioica (Ud)	248	Iran	Prazosin	2 months	IPSS score 10.46 in 7g U. dioica compared to 2 points in the control group.	147
05.	*Epilobium angustifolium*	128	Italy	Placebo	6 months	Mean difference of IPSS score 2.5 points, residual volume 4.3 mL, but not for prostate volume.	148

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Contd. Table 26. Research findings on phytotherapies in treating LUTS of BPH in men

SN	Plant name	No. of patients	Country	Comparison with	Follow-up period	Results of herbal products	Ref. No.
06.	*Hypoxis hemerocallidea* (β-sitosterol)	200	Germany	Placebo	6 months	Mean difference, peak flow(4.1ml/s) IPSS (5.3 points), residual volume 23.8 mL, but no change in prostate.	132
	Hypoxis hemerocallidea (β-sitosterol)	177	Germany	Placebo	6 months	Mean difference, peak flow(4.5ml/s) IPSS (5.4 points), residual volume 33.5 mL, but no change of prostate.	149
07.	*Serenoa repens*- 320mg *Urtica dioica*- 120 mg *Pinus pinaster*- 5 mg	080	Italy	None	12 months	85% patients reported symptomatic improvement in LUTS. No improvement of prostate volume	150
08.	*Solanum lycopersicum Serenoa repens* Alfuzosin, lycopene, & Bromelain	250	Italy	Aluzosin	12 months	Significantly mean difference IPSS (5 points) and residual volume 23 mL compared with aluzosin control.	151
09.	*Roystonea regia* (D-004)	100	Cuba	Terazosin	6 months	More effective than terazosin in IPSS score (1.1 points), no change on prostate volume & residual volume	152
10.	*Secale cereale* Cernilton @ 750 mg daily	240	China	Secale cereale (375 mg)	4 years	Reducing IPSS mean difference 5.3 points, residual volume 11.1 mL, and peak flow 9.5mL/s	153
11.	*Linum usitatissimum* (@ 600 mg daily)	078	China	Placebo	4 months	Reduced IPSS by 6.88 points and improved peak flow by 2.7 ml/s.	154
12.	Progamet + α-blockers Control α-blockers	046 046	Italy	α-blockers	90 days	Significant reduction in IPSS, increased Q-max & improved erectile function compared with α-blocker group.	155
13.	ProstateEZE Max [*C. pepo*, *E. parviflorum*, Lycopene, *P. africanum* and *S. repens*]	032 025	Australia	Placebo	03 months	Reduction in IPSS 35% in active compared to 8% in the placebo group. Significant reduction of daytime urinary frequency in active (7.0, 5.9; 15.6%) compared to the placebo group.	156
14.	Sam palmetto, Serenoa, Permixon®, P. africanum, Tadenan®,Cernilton®, Cernitin™, & Hypoxis	-	-	Placebo	-	*P. africanum* and *Hypoxis rooperi* resulted in improvement in flow rates and symptoms while S. cereale caused improvement of symptom not flow rate compared to placebo.	157

Progamet™ (USP-Union of Pharmaceutical Sciences) derived from Prunus Africana, Urtica dioica, and Epilobium angustifolium)

Phytotherapy for BPH in men involves plant-derived herbal products that have been widely studied for symptom relief, but the evidence varies in strength and consistency (Tables 27 and 28). Table 27 presents herbal therapies for BPH in men, Table 28 shows active compounds and biological activities of medicinal plants used in the treatment of BPH, based on preclinical studies.

Table 27. Herbal therapies for BPH in men. [118,158]

SN	Herbal agents	Mechanism of action	Evidence of benefit	Safety profile
①	Saw palmetto (*Serenoa repens*)	Inhibits 5-alpha reductase, anti-inflammatory, reduces prostate growth	Mixed results: some RCTs show LUTS improvement, others show no difference vs placebo.	Generally safe, mild GI upset, headache
②	*Pygeum africanus* (African plum bark)	Anti-inflammatory, reduces prostatic fibroblast proliferation	Improves nocturia, residual urine volume, and flow rate.	Well tolerated; rare GI side effects
③	Nettle root (*Urtica dioica*)	Inhibits SHBG binding, mild anti-inflammatory	May reduce LUTS when combined with saw palmetto.	Safe, occasional allergic reactions
④	Pumpkim seed (*Cucurbita pepo*)	Rich in phytosterols, modulates bladder function	Some studies show improved frequency and urgency.	Safe, food-based, minimal adverse effects
⑤	Rye pollen extract	Anti-inflammatory, smooth muscle relaxation	Reported improvement in IPSS scores and quality of life.	Safe, rare allergy in pollen -sensitive patients
⑥	Combination polyherbal therapy	Synergistic effects across multiple pathways.	Emerging evidence suggest enhanced efficacy vs single agents.	Safety depends on formulation, generally well tolerated.

Table 28. Active compounds and biological activities of medicinal plants used in the treatment of BPH, based on preclinical studies

SN	Plant species, Drug part	Active compounds	Biological activities/ Supposed mechanism of action
①	Cucurbita pepo Seed	Polysaccharides, sterols para-aminobenzoic acid, proteins and peptides, carotenoids, γ-aminobutyric Acid; seed: fatty acids, phytosterols.	•Inhibits 5α-reductase •Decrease of DHT level •Inhibits testosterone-induced hypertrophy. •Anti-tumor
②	*Epilobium parvi-florum* *E. angustifolium* aerial parts	Polyphenols, steroids, triterpenoids, fatty acids.	•Anti-inflammatory, antioxidative, anti-proliferative, anti-microbial, analgesic, anti-androgenic activities. A =
③	Hypoxis Hemerocallidea Corm	Phytosterols: hypoxoside, rooperol, β-sitosterol, stigmasterol, stigmastanol; hypoxhemerolosides A-F, curcapicycloside, obtuside A, interjectin, Crassifoside F, acuminoside, geraniol glycoside, Vanillic acid, β-arbutin, orcinol glycoside.	•Anti-inflammatory activity. •Increase of TGF-β1 expression and protein kinase C-α activity in stromal cells.
④	*Solanum lycopersicum*	Tetraterpene carotenoids: lycopene, β-carotene, α-carotene; minerals, vitamins.	•Antioxidant activity •Decreases the expression of fruit. B=
⑤	Pinus pinaster bark	Procyanidins, taxifolin, cinnamic acid, ferulic acid, caffeic acid, benzoic acid (87,88)	•Anti-inflammatory activity. •Nitric oxide synthase (eNOS) C=
⑥	Roystonea regia fruit (oil)	D-004 extract (oleic, lauric, palmitic, and myristic acids.	•Inhibition of 5α-reductase. D =
⑦	Prunus africana Bark	Phytosterols, fatty acids, triterpenes, proanthocyanidins, atraric acid, lauric acid, myristic acid, ferulic acid, atranorin, cholesterol, N-butylbenzene sulfonamide, hydroxybenzoic, linoleic, stearic, arachidonic, behenic, lignoceric acids.	•Inhibits 5α-reductase. •Inhibition of DHT and estrogen receptors, progesterone and androgen receptors. E =
⑧	Secale cereale pollen	Carbohydrates, amino acids, proteins, phenolic compounds, sterols, triglycerides, plant pigments	•Inhibition of cyclooxygenase and the 5-lipoxygenase activity. F =
⑨	Serenoa repens fruit	Carbohydrates, sterols, flavonoids, triglycerides, fatty acids.	•Inhibits 5α-reductase. •>Inhibits the formation of DHT and some testosterone metabolites. G =
⑩	Urtica dioica root	Sterols, flavonoids, tannins, acids, minerals, lectins, polysaccharides, ceramides, monoterpenoids, fatty triterpene and phenylpropane.	•Anti-proliferative, anti-inflammatory -inhibition of COX and lipoxygenase H =

A = •Increase of CYP2D2 (78) •Decrease of CYP2E1 and CYP1A1 expression
•Decrease of cYP2B1, CYP2C6, CYP2D2, CYP3A1 protein levels
B = •Nicotinamide adenine dinucleotide phosphate oxidase. •Anticancer and anti-inflammatory activities.
C = •Activity •Reduction in malondialdehyde, increased glutathione, catalase, and peroxidase levels.
•Decrease in DHT level.
D = •Antioxidant effects. •Inhibition of phenylephrine-induced contractions in isolated rat prostate strips.
E = •Inhibits the basal growth of prostate stromal cells stimulated by EGF, IGF-1, bFGF, TPA, and PDBu.
F = •Inhibition of prostaglandin and leukotriene synthesis
•Anti-inflammatory activity decreased TNF-α and IL-6 cytokine levels.
•Decreased androgen receptor and PSA expression.
G = •Inhibit the conversion of testosterone into DHT. •Inhibition of α-receptor binding.
•Inhibits the receptor binding of androgens. •Anti-proliferative effects.
•Inhibition of eicosanoid synthesis. •Spasmolytic effects.
•Anti-inflammatory activity.
H = •Inhibits TNF activity •Stimulates T-lymphocyte activity and complement activation.
•Inhibits the binding of sex hormone-binding globulin. •Inhibits prostate growth.

- Medicinal plants and plant-derived natural products are increasingly used to treat BPH with LUTS.[113,159,160]
- Pumpkin seed (Cucurbita pepo) or its extract is widely used and contains a variety of biologically active compounds that inhibit 5α-reductase, thereby reducing circulating DHT levels. However, pumpkin can cause gastrointestinal symptoms such as indigestion and diarrhea.
- The fruit extract of the saw palmetto plant (*Serenoa repens*) may have mechanisms of action that include 5-alpha reductase inhibition and inhibition of DHT binding to androgen receptors. [96,103,161]
- Two independently conducted, placebo-controlled trials of specific saw palmetto extracts found no benefit over placebo across multiple parameters relevant to BPH and LUTS. [138,162]
- Use of saw palmetto does not improve LUTS or prostate volume compared with placebo, based on high-quality evidence from 32 long-term randomized controlled trials of 5,666 men. [163]
- Small, short-duration, low-quality studies suggest improvements in LUTS and urinary flow measurements with *Pygeum africanum*.[164]
- Beta-sitosterol, a phototherapeutic compound, appears to improve urinary symptoms and flow measures; however, its long-term effectiveness and safety are unknown. [85]
- There have been mixed results regarding the exact mechanisms of action of these supplements, and these results vary further depending on the extraction and formulation methods.
- Manufacturers of plant-derived natural products often make claims about efficacy and effects that are neither regulated nor endorsed by the drug registration authorities of the relevant country, including the U.S. FDA.

Evidence summary of herbal therapies

- Systematic reviews indicate that phytotherapy is popular due to fewer side effects than those associated with alpha-blockers or 5α-reductase inhibitors; however, clinical trial results are inconsistent.
- Saw palmetto remains the most studied, yet large RCTs (e.g., the STEP trial) found no significant benefit over placebo in moderate-to-severe LUTS.
- *Pygeum africanum* and rye pollen extract show more consistent improvements in urinary symptoms and flow rates.
- Combination therapies (e.g., saw palmetto, nettle root, and pumpkin seed) may offer synergistic benefits, though high-quality comparative trials are limited.
- Phytotherapy holds significant potential in BPH management, offering symptom relief with minimal side effects. However, a challenge of phytotherapy is that dosages can be difficult to manage. Additionally, the active ingredients of many of these herbs remain unknown.

Phytotherapies have experienced widespread global sales, partly due to the availability and popularity of health food stores. Old data from 1994 indicate that annual US sales from these stores totaled US$553 million,[165], and sales over the past three decades are likely to have increased further. Approximately one in two people used at least one dietary supplement regularly, with over two-thirds of those aged 70 or older.[166] The mechanisms of action of dietary supplements remain incompletely understood. Historically, many medications have been used for treatment before a complete understanding of their mechanism of action has been developed. Another difficulty for patients with phytotherapy is the difficulty of managing dosages. Additionally, the active ingredient for many of these substances remains unknown. However, the evidence for phytotherapy remains inconclusive, with some agents supported by more substantial evidence than others. Few patients and short-duration clinical trials for each phototherapeutic agent yielded mixed results, whereas larger, better-designed studies found no significant benefit of phytotherapy in the treatment of BPH. However, patients with mild BPH symptoms who are reluctant to take standard pharmaceutical medications may try this agent, provided that the patient understands their current limitation. Those with moderate or severe BPH should be discouraged from alternative and complementary treatments.[120] Therefore, patients considering phytotherapy as a treatment of BPH alone, but the benefits may be limited, and it appears there is a need for combination with allopathic drugs plus phytotherapy for better results.

Saw palmetto (*Serenoa repens*)

Saw palmetto, also known by its botanical name *Sabal serrulatum* (homeopathic brand drug for BPH), and there are 730 species of American palms, of which 106 species of palm have known medical uses. *S. repens* has emerged as a natural product for the treatment of prostatic disorders, particularly cancer and hyperplasia.[125] Herbal supplements containing saw palmetto extracts or its primary phytosterol, beta-sitosterol, are widely used to support prostate health. There are more than 100 varieties of saw palmetto extract on the market today, with more than 70 in the United States alone. Saw palmetto has become so popular that it ranks among the top 10-selling supplements in the United States. The various markets saw palmetto products show marked variation in content due to both variability in the extraction process and in the plant itself.[167]

The most extensively studied saw palmetto commercial product is marketed as the drug Permixon (Pierre Fabre Medicament, Castres, France), and about 14 such products have been analyzed for free fatty acid (FFA) content, esters, and glycosides.[168] The FFA content, which has been suggested as the primary source of clinical benefit, ranged from 80.7% for Permixon to 40.7% for Solaray (Nutraceutical Corp., Park City, UT, USA). Methyl and ethyl esters were noted at 16.7% Prostaurgenine (Hoyer-Madaus, Mannheim, Germany) and at 2.5% for Permixon. Permixon also had the lowest glycoside content at 6.8%, whereas Solaray had the highest at 52.15%. Therefore, variability in product content could skew the results of trials evaluating saw palmetto.[120] Table 29 summarizes data from *placebo-controlled trials of Serenoa repens*.

Table 29. Summary data from *Serenoa repens* placebo-controlled trials

SN	No. of patients Randomized + placebo controlled	Study duration (weeks)	Significant LUTS improvement vs Placebo	IPSS change	
				Saw palmetto	Placebo
①	644	4-48	Yes	N/A	N/A
②	NA*	3-107	Yes	N/A	N/A
③	085	26	Yes	-4.4	-2.2
④	093	12	No	-3.62	-3.62
⑤	225	52	No	-0.68	-0.72

Herbal supplements derived from saw palmetto and containing beta-sitosterol and other plant sterols are not considered efficacious for the treatment of prostate cancer.

Along with α-blockers and 5α-reductase inhibitors, the extract of the American dwarf palm (*Serenoa repens*) is unquestionably the most widely used for the treatment of BPH in men without FDA registration. Together with *Pygeum africanum*, an extract from the bark of the African plum tree, it is licensed in Germany, France, and other European countries for symptomatic BPH.[121]

Several mechanisms of action of *Serenoa repens* have been proposed based on *in vitro* and *in vivo* studies in animals and humans. However, the exact mechanism of action remains unclear.

Possible mechanism of action of *Serenoa repens* extract in BPH[121]

a. Anti-androgenic action through hormonal mechanisms

- Inhibition of 5α-reductase isoenzymes I and II
- Inhibition of the binding of DHT to the cytosolic androgen receptor
- Inhibition of the nuclear estrogen receptors in prostatic tissue.
- Modulation of prolactin-induced prostatic growth by receptor signal transduction

b. Anti-inflammatory effects

- Inhibition of cyclooxygenase and lipoxygenase enzymes in the eicosanoid cascade.

c. Induction of apoptosis and antiproliferative action

- Inhibition of bFGF induced prostatic epithelial proliferation

Efficacy of *Pygeum africanum* in BPH

Pygeum (*Pygeum africanum*, also known as *Prunus africanum*) is an herbal extract derived from the bark of the African cherry tree (African plum tree/ Prunus African tree). *P. africanum* of the Rosaceae family has been used in Europe under the trade name of Tadenan (Fournier, Dijon, France) and has been prescribed for BPH there for several decades.[169,170] The active compounds implicated in the treatment of BPH consist of N, N-bis (2-hydroxyethyl) benzene sulfonamide and atraric acid.[171]

Mode of action

Three proposed modes of action have been hypothesized for *P. africanum's* effect on BPH symptoms based on *in vitro* studies, which include: (a) it may inactivate androgen receptors via inhibition of nuclear translocation,[169] (b) inhibit cellular growth factors such as fibroblast and epidermal growth factor,[172] and (c) it have anti-inflammatory properties related to the inhibition of 5-lipoxygenase and consequent decrease of leukotriene production and other 5-lipoxygenase metabolites.[173]

It shows promise as a treatment for BPH and may even help with erectile dysfunction (ED), a common symptom of BPH. This herbal remedy has been around for centuries, but nowadays it is available in pill and capsule form in the supplement aisle or online.

Pygeum bark extract shows modest but significant efficacy for BPH symptoms, improving overall urinary issues, decreasing nighttime urination (nocturia), reducing residual urine, and increasing urine flow, with good tolerability and mild side effects compared to placebo, though studies are often small and varied. Reported studies have limitations, including short-term follow-up, small sample sizes, and heterogeneity (Table 30).

Table 30. Double-blind, placebo-controlled studies of *Pygeum africanum* extract for BPH in men. [174]

SN	Daily drug dose/duration	No. of patients	Residual volume	Nocturia improvement	Maximum flow	Other
①	Tadenan 75mg 60 days	50	*	*	-	Response good to poor (88%-12%)
②	Tadenan 100 mg 60 days	255	*	*	+17%	Overall 66% response
③	Tadenan 100 mg 6 weeks	120	-	78%	-	-
④	Pigenil 100mg 60 days	040	-	75%	Increased	Dysuria improved in 11/18
⑤	Tadenan 100 mg 6 weeks	57	-	10%	-	Overall 77% improvement
⑥	Tadenan 100 mg 60 days	60	23%	47%	-	-
⑦	Tadenan 100 mg 12 weeks	16	-	35%	No benefit	No evidence of benefit
⑧	Tadenan 200 mg 60 days	40	*	*	+55%	*
⑨	Tadenan 200 mg 2 months	39	-	*	+91%	*
⑩	Tadenan 200 mg 60 days	20	-	*	-	*

*Results not interpretable from the sources

Major findings on efficacy

- **Symptom improvement**: More than twice as likely to improve overall symptoms compared to placebo.
- **Urodynamic benefits**: Increases peak urine flow (by ~23%) and reduces residual urine volume (by ~24%), while reducing nighttime (nocturia) urination (by ~19%).[169]
- Sexual function: May improve erectile function, potentially by alleviating underlying BPH/prostatitis.
- **Improved quality of life**: Studies have shown improvements in IPSS and quality-of-life scores.

Mechanism of action

- The benefits of *P. africanus* are attributed to several phytochemicals (such as beta-sitosterol, pentacyclic triterpenoids, and ferulic acid esters) that work through multiple mechanisms.
- *P. africanum* extract contains compounds like phytosterols and prostaglandin that may help reduce prostate inflammation and support healthier prostatic function.
- It also contains saturated and unsaturated fatty acids, as well as phytosterols such as beta-sitosterol.
- Pygeum acts by improving prostate function, potentially by reducing inflammation and increasing prostatic secretions, thereby improving urinary flow.
- May increase prostatic secretions and improve seminal fluid, potentially more effective in men without inflammation (low IgA).
- Hormone receptors (such as DHT) potentially reduce inflammation, as indicated by cytokine studies.[175]

Considerations

- Efficacy varies by product; standardized extract (such as Tadenan) is key to consistent results, as different preparations exhibit varying biological activities.
- Many studies are small, short-term, and used varied dosages, so long-term effectiveness needs further research.
- Reviews suggest it's a useful, cost-effective option, but more large, standardized trials are needed, especially to compare it with established BPH drugs, and effects are seen within weeks to months.
- There is not enough research to draw firm conclusions about Pygeum benefits for BPH and ED or other men's health issues.

Rye pollen (*Secale cereal*)

Rye pollen extract (often branded as Cerniton,™ AB Crenelle, Engelholm, Sweden), prepared from the Swedish rye grass pollen Secale cereal, has been studied for LUTS due to BPH, with evidence suggesting modest symptom relief and improved flow metrics compared to placebo, though trials are generally small and methodologically limited.

The extract is prepared by microbial digestion of rye grass pollen, followed by extraction with water and acetone. Cernilton is composed of 60 mg of a water-soluble fraction (Cernitin T60) and 3 mg of an acetone-soluble fraction (Cernitin GBX) per tablet.

Pollen extracts have been found to contain at least 21 amino acids, as well as enzymes, coenzymes, sterols, minerals, trace elements, and all known vitamins. Cernitin GBX fraction contains phytosterols and fatty acids, including alpha-linoleic acid. [176]

- Clinical effects: Systematic review data indicate reductions in symptom scores and improvements in peak urinary flow and residual urine compared with placebo. Individual-controlled trials report improved uroflow and reduced residual urine with Cernilton compared with placebo.[133]
- Onset and durability: Benefits are typically assessed after 30 days of treatment; sustained effects beyond short- to medium-term follow-up are less certain due to limited long-term data.
- Comparators: Evidence versus standard pharmacotherapy (e.g., alpha-blockers, 5-ARIs) is sparse; most trials compare to placebo or non-pharmacologic controls.
- Safety: Generally well tolerated in trials, with low rates of mild adverse events; robust safety data are limited by small sample sizes and short durations (Table 31).

Table 31. Summary treatment outcome of rye pollen extract in BPH in men

SN	Outcome	Effect vs Placebo	Notes
①	Symptom score (LUTS/IPSS)	Modest improvement	Magnitude varies, trials are small and heterogeneous
②	Peak urinary flow (Qmax)	Improved	Reported increases in uroflow indices in controlled trials
③	Residual urine	Reduced	Decreases observed in several studies
④	Prostate size	Unclear/limited effect	Most studies focus on symptoms/flow, not volume
⑤	Adverse events	Low, mild	Generally well tolerated, limited long-term data

Mechanism of action

- Several mechanisms of action have been proposed for S. cereale, including relaxation of urethral and bladder smooth muscle via antagonism of alpha-adrenergic receptors.
- In vitro, studies have shown that the water-soluble fraction T60 inhibits the growth of prostate cancer cell lines and primary cultures from BPH specimens.[177] Additional mechanisms include induction of apoptosis in prostatic epithelial cells and anti-prostaglandin and anti-leukotriene actions by inhibiting the arachidonic acid cascade.[173,178]
- Animal studies have demonstrated a significant reduction in rat prostate size following three weeks of therapy,[179] as well as a contractile effect on the bladder and a relaxing effect on the urethra in mice and pigs. [180]

Stinging nettle (*Urtica dioica*)

Stinging nettle- typically the most common root extract- has been studied for LUTS due to BPH, with several randomized trials and a meta-analysis suggesting modest symptom improvement versus placebo. Reported benefits include reductions in IPSS and small gains in peak flow, though effect sizes vary and heterogeneity is notable across preparations and study quality (Table 32)

Table 32. Key outcomes from clinical studies on the efficacy of Stinging nettle in BPH in men

SN	Outcome	Direction of effect vs placebo	Typical magnitude	Notes
①	IPSS (symptom Score)	Improves	Small-moderate reduction	Consistent across several RCTs; variability by extract and duration.
②	Qmax (peak flow)	Improves	Small increase	Clinical relevance may be limited.
③	PVR	Mixed	Small reduction or No change	Inconsistent across trials
④	Prostate volume	No meaningful change	Minimal differences	Symptom relief without clear size detection
⑤	PSA/Testosterone	No consistent change	Neutral	Monitored in large trials
⑥	Adverse events	Similar to placebo	Mild GI or dematologic	Generally well tolerated

Proposed mechanisms

- 5α-reductase modulation and SHBG interaction: Nettle root constituents may weakly influence androgen pathways and binding proteins, potentially reducing prostatic stromal activity- mechanisms remain incompletely defined and likely less potent than conventional pharmacotherapy.
- Anti-inflammatory effects: Phytochemicals may attenuate local inflammation in the prostate and bladder neck, contributing to symptom relief without altering gland size.

Practical takeaways

- Nettle's effect sizes on IPSS and Qmax are smaller and slower than those of 5-ARIs, and it does not reduce prostate volume as 5-ARIs do.

- It is appropriate for mild symptoms or as an adjunct where expectations are calibrated.
- It is not a substitute for guideline-directed therapy in moderate-severe disease or with complications.

Comparisons of the efficacy of mono and poly-herbal drugs in BPH

Herbal formulations are widely used as alternative or complementary therapies for BPH, especially due to concerns about side effects from conventional medications. Recent research has focused on both mono-herb and polyherbal preparations, with growing evidence supporting their role in symptom relief and improvements in quality of life for BPH patients.

Combined herbal medicines (phytotherapy) are widely used worldwide, particularly in Europe and Asia, to manage mild-to-moderate LUTS in men with BPH, particularly when used in combination with standard Western medication (WM). Clinical evidence suggests that while individual herbal treatments have shown mixed results, certain poly-herbal formulations provide synergistic effects to improve maximum urinary flow rate (Qmax) and quality of life (QoL) by acting on multiple pathways simultaneously, such as inhibiting 5-reductase, reducing inflammation, and relaxing smooth muscle.

The Unani polyherbal formulation (Habb-i-muqil and Tamsulosin) efficacy in 60 men with BPH after 90 days of post-treatment showed changes in the AUA-SI from baseline of 50.4% and 49.4%, respectively. [181]

Poly-herbal combined with Western medicine in BPH

Commonly studied herbs globally include *Serenoa repens* (saw palmetto), *Urtica dioica* (nettle root), *Cucurbita pepo* (pumpkin seed), and *Pygeum africanum* (African cherry). These plants exhibit mechanisms such as 5α-reductase inhibition, anti-inflammatory effects, and modulation of oxidative stress. Clinical and preclinical findings have demonstrated improvements in symptom scores, urinary flow, and prostate volume, as well as alleviation of LUTS, though results vary by study and formulation (Table 33).

The combination of polyherbal traditional Chinese medicine (TCM) and WM for BPH has been shown to be more effective than WM alone in improving LUTS, quality of life, and reducing prostate volume. Notable combinations include Jingui Shenqi pill, Guizhi Fuling capsule, Pulean tablet, and Huange capsule, each excelling in different clinical outcomes such as symptom scores, urine flow, and prostate volume reduction.

Two herbal drugs, Hachimijiogan (Palmijihwang-hwan in Korea; Baweidihuang-wan in Chinese; HJG, Harpoon Pharm and Food Co. Ltd., Seoul, Korea) and Ryutanshakanto (Youngdamsagan-tang in Korean; Longdanxiegan-tang in Chinese; RST, Hanpoong Pharm. and Food Co. Ltd.), have been used in clinical trials. Three groups of patients with BPH, of which group 1 (n=16) received tamsulosin 0.2mg/day plus (HJG) @ 3.0g oral solution three times daily, group 2 (n=15) received tamsulosin 0.2mg/day plus (RST) @ 3.0g oral solution three times daily, and group 3 (n=8) received only tamsulosin 0.2mg/day as a placebo control. Insignificant improvement of IPSS, uroflowmetric, and QoL in all three groups, but prostate volume increased at post-treatment. However, RST has provided pain relief in patients with chronic prostatitis and chronic pelvic pain syndrome. [182]

A meta-analysis of 107 RCTs involving 11,037 patients across 16 oral polyherbal TCM formulations showed that most formulations combined with WM (alpha blockers, 5-alpha-reductase inhibitors) demonstrated superior therapeutic efficacy compared with WM alone. For clinical efficacy, Jin Gui Shen Qi pill (JGSQP, Everspring) + WM) had the highest probability (87.38%) regarding IPSS and maximum urine flow rate, while Gui Zhi Fu Ling capsule (GZFLC, Phoenix Medical) + WM was most effective (91.105 and 98.55%). Regarding the quality-of-life score and postvoid residual urine, Pulean tablet (PLA, Conba) + WM ranked first (86.71% and 91.81%). In controlling prostate volume, Huang Lian capsule HLE, BioEssence) + WM demonstrated the highest efficacy (95.65%). Additionally, among the interventions, Lingze (LZ) tablet + WM capsule exhibited the lowest incidence of adverse drug reactions (2.32%). Therefore, combining oral poly-herbal TCM formulations with WM may provide greater therapeutic benefits in the treatment of BPH than WM alone. JGSQP, GZFLC, PLA, and HLE emerged as promising treatment options for N. [183]

Table 33. Efficacy of poly-herbal drugs in BPH in men (Leisegang et al. 2022)[119]

SN	Name of drugs and composition	Dosage and durations	Control	Outcome (Intragroup % & intergroup P-value IPSS/AUASI	Qmax	PSA	QoL	PRV	PV	Ref. No.
01.	Prostate EZE MAX[C1]	Daily for 12 weeks (n = 32)	Placebo (P) (n=25)	Expt: 36% ↓*Placebo: 8% ↓p<0.05	-	Expt.: 3.6% ↓P: 21.2% ↑NA	-	-	-	156
02.	Curbicin •C. pepo seed- 80 mg •S. repens- 80 mg	Daily for 12 weeks (n = 26)	Placebo (n = 27)	-	Expt.:44.8% ↑*Placebo: 4.5% ↑ p<0.001	-	-	Expt.: 31.5% ↓*P: 5.96% ↓p<0.01	-	185
03.	Granu Fink (A) •C. pepo seed extract •Pumpkin seeds (B) C. pepo seeds	A. 1 g (n=481) B. 10g (n=475) daily for 52 weeks	Placebo (n=475)	Expt. A:28.8% Expt. B: 36.3% Placebo: 27.3%	Expt. A: 45.1% ↑B: 49.1% Placebo: 41.7%	A. 5.8% ↑B. 11.10% P 10.5%	A. 33.4% B. 36.0% P 29.2%	A. 5.3% B. 7.3% P. 3.4%	A. 7.9% B. 9.4% P. 8.9%	186
04.	Saw palmetto HB[C2]	Daily for 48 weeks (n = 21)	Placebo (n = 23)	Expt. 30.3% Placebo 18.7% NS	Expt. 25.3% Placebo 5.2% NS	Expt. 4.9% Placebo 2.7% NS	-	-	Expt. 5.8% P 0.4% NS	187
05.	•Cernitin - 378 mg •S. repens- 286 mg •Vitamin E- 100 iu	Daily for 12 weeks (n = 70)	Placebo (n = 69)	Expt. 32.7% Placebo 18.3% (p = 0.009)	Expt. 5.4% Placebo 8.3% NS	Expt. No change Placebo 36.8 NS	-	-	-	188
06.	Prostaplex[C3]	Two capsules daily for 12 weeks (n = 46)	Placebo (n = 46)	Expt. 12.0% Placebo 2.3% p <0.001	Expt. 13.5% Placebo 8.92% p < 0.001	Expt. 0.44% Placebo 12.5% NS	-	-	-	189
07.	Profluss •S. repens- 320 mg •Lycopene- 5 mg •Selenium- 50 mcg	Daily for 12 weeks (n = 45)	Placebo (n=45)	Expt. 10.0% Placebo NS Decrease p < 0.05	Expt. 12.5% ↑Placebo Increased NS	-	-	-	-	190
08.	P. africanum and U. dioica •P. africanum- 25 mg •U. dioica- 300 mg	325 mg daily for 48 weeks (n = 27)	Placebo (n = 22)	Expt. 21.6% Placebo 19.7% NS	Expt. 17.2% Placebo 13.3% NS	-	Expt. 12.5% Placebo 5.7% NS	-	-	143
09.	Progamet; USP-Union •P. Africana- 100 mg •U. dioica- 300 mg •E. angustifolium-600 mg	Daily for 90 days	α-blocker (alfuzosin)	Expt. 19 to 14 Control 16.3 to 17 p<0.0001	Expt. 13 to 16 Control 14 to 14 p <0.0001	-	-	-	-	191
10.	Habb-i-muqil[C4]	1g twice daily 90 days (n = 30)	Tamsulosin @0.4 mg/d (n = 30)	Expt. 59.44% Control. 49.43% (p<0.001)	-	Expt. 0.96 Control 2.06	Expt. 50.42% Control 41.17% (p<0.001)	-	Expt. 29.64 Control 42.23	181

[C1] = *C. pepo* seed oil- 160 mg, *E. parviflorum* 500 mg, Lycopene- 2.1 mg, *P. africanum*- 15 g, and *S. repens*- 660 mg

[C2] = *S. repens* lipoidal extract 160 mg, *U. dioica*- 80 mg, *Lemon bioflavonoid* extracts 160 mg, and β-Carotene- 190 mg

[C3] = *S. repems*- 300 mg, Curcumin- 100 mg, Pollen- 100 mg, β-Carotene- 25000 iu, Vitamin C- 1000 mg, Vitamin D- 4000 iu, Zinc- 15 mg, Alfalfa leaf conc-250 mg, Buchu leaf 150 mg, and Corn silk- 150 mg.

[C4] = *Commiphora muqul* (Muqil)-85 g, *Terminalia chebula* (halena zard, halela siya, halela kabli)- 60 g each, *Emblica officinalis* (Amla khushk)- 60 g, *Ferula persica* (sakbinaj)- 20 g, and *Bressica nigra* (khardal)- 10 g

P = Placebo IPSS/AUASI = International Prostate Symptom Score/ American Urological Association Symptom Index
Qmax = Maximum urinary flow rate PSA = Prostate Specific Antigen QOL = Quality of life PRV = post-void residual volume
PV = Prostate volume NS = Not significant

Network meta-analysis (NMA) of 72 randomized controlled trials (RCTs) involving 15 oral Chinese patent medicines in 7,800 patients showed that Jin Kui Shen Qi pills (JKSQ), Herb Deport) + Conventional Western Medicine (CWM) was the most effective approach for increasing the total efficiency ratio in men with BPH. CWM included α-blockers (e.g., doxazosin mesylates, terazosin hydrochloride, tamsulosin hydrochloride), 5α-reductase inhibitors (e.g., finasteride, eplerenone), M-receptor antagonists (e.g., tolterodine tartrate).

Huang capsule (HE, Anhui Huangshan Capsule Co. Ltd., China) + CWM was the most effective method in decreasing prostate volume, Qianlie Shutong capsule (Baoding Tianhao Pharmaceutical Co. Ltd. China) (QLSTC) + CWM was the most effective approach in decreasing residual volume, Xialiqi capsule (XLQ, Yiling Pharmaceutical) + CWM) was the most effective way in increasing maximum urinary flow rate, and

Longbisu capsule (LBS, Jiasen Ding's) + CWM was the most effective method in decreasing IPSS. To reduce adverse reactions, HE + CWM has the best efficacy. Considering both drug efficacy and safety, Ningmitai capsule (NMT; Guiyang Xintian Pharmaceutical Co. Ltd., China) + CWM would be the most ideal choice. [184]

Role of minerals and vitamins

Certain vitamins (such as D, E, and C) and minerals (such as zinc and selenium) help reduce inflammation, oxidative stress, and hormonal imbalances that contribute to BPH. While they are not standalone treatments, adequate intake of dietary fiber or supplements may help prevent and manage BPH symptoms (Table 34).

How vitamins and minerals influence BPH (Key mechanism)

- Anti-inflammatory effects: Micronutrients reduce chronic low-grade inflammation, a driver of prostate enlargement.
- Antioxidant protection: Vitamins and minerals neutralize free radicals, lowering oxidative stress in prostate tissue.
- Hormonal modulation: Some nutrients influence testosterone metabolism and dihydrotestosterone (DHT) activity, slowing hyperplasia.
- Immune support: Adequate micronutrient intake strengthens immune surveillance, reducing risk of chronic prostatic irritation.

Table 34. Comparative role of vitamins and minerals in BPH

SN	Nutrient	Role in prevention	Role in treatment	Evidence strength
①	Vitamin D	Regulates cell growth, reduces inflammation	May improve urinary symptoms, and slow progression	Moderate-strong (observational plus clinical trials)
②	Vitamin E	Antioxidant, protect prostate cells.	May reduce oxidative stress in BPH tissue.	Moderate (mixed trial results)
③	Vitamin C	Collagen synthesis, antioxidant	Supports vascular health, may reduce LUFT severity	Moderate (dietary studies)
④	Zinc	Essential for prostate function, regulates DHT	Deficiency linked to enlarged prostate; supplementation may help	Strong (prostate tissue studies)
⑤	Selenium	Antioxidant, immune support	May reduce risk of prostate enlargement and cancer	Moderate (epidemiological data)
⑥	Magnesium	Smooth muscle relaxation	May improve urinary flow and reduce LUTS	Limited but promising
⑦	Omega-3 fatty acids	Anti-inflammatory	May reduce prostatic inflammation	Moderate

Risks and considerations

- Excess supplementation (e.g., high-dose zinc or selenium) can be harmful, potentially increasing cancer risk or causing toxicity.
- Dietary source preferred: Whole foods (fish, nuts, seeds, fruits, vegetables) provide a balanced array of micronutrients with synergistic effects.
- Not a replacement for medical therapy: Vitamins and minerals may complement but not substitute for α-blockers, 5α-reductase inhibitors, or surgical interventions.
- Individual variation: Benefits depend on baseline nutritional status, genetics, and comorbidities.

Zinc

Zinc is vital for prostate health, helping maintain normal structure and regulate cellular metabolism. While the prostate accumulates high zinc levels, BPH, and especially prostate cancer, involve diminished zinc,

suggesting that adequate levels may help curb progression. Some studies suggest zinc supplementation may help reduce prostate size and improve LUTS, evidence remains mixed.[192] However, excessive zinc supplementation may increase risks for advanced prostate cancer, requiring caution.[193]

Key aspects of zinc and BPH

- **Essential function:** The healthy prostate gland has the highest concentration of zinc in the body, which aids in anti-inflammatory and antioxidant functions.
- **BPH impact:** Although zinc is generally lower in diseased prostate tissue, maintaining adequate zinc levels is crucial for protecting against further enlargement.
- **Androgen regulation:** Zinc may regulate androgen levels, reducing inflammation and inducing apoptosis (cell death) in prostate cells.
- **Mechanism of action:** Zinc influences the inhibition of cell proliferation and encourages apoptosis (programmed cell death) in hyperplastic prostate tissue.
- **Preventive effects:** Increased dietary zinc intake is associated with a 32% lower risk of BPH. Studies indicate that men with higher dietary zinc intake (e.g., >18.9 mg/day) have a significantly lower risk of developing BPH than those with lower intake.[192]
- **Potential benefits:** Zinc supplementation might improve BPH symptoms like LUTS, with some studies suggesting it may help prevent further prostate enlargement.
- **Risks of excess:** High doses of zinc supplements (>75 mg/day) are associated with a higher risk of developing advanced aggressive prostate cancer.[194]
- **Best sources:** Zinc gluconate is well-absorbed, but dietary sources like pumpkin seeds and nuts are often recommended. (Sauer et al. 2020).

Zinc deficiency is associated with BPH in more than 50% of men over 60.[195] Aging men have elevated estrogen levels, and estrogen inhibits intestinal zinc uptake. Men with BPH may have low zinc levels. Marginal zinc deficiency is common among older adults, and in men, it may worsen BPH symptoms. Research showed that supplementing with zinc resulted in a reduction in the size of the prostate gland and symptoms of BPH.

Table 35. Endogenous and exogenous factors that may contribute to low zinc status in older men [195]

SN	Endogenous factors		Exogenous factors	
	Morbidities that provoke Zn excretion	Morbidities that prevent Zn absorption	Diet	Drugs
①	Severe or persistent diarrhea.	Malabsorption syndromes, celiac disease and short bowel syndrome	Lack of Zn intake in the elderly due to restricted food choices and patterns.	Omeprazole & other proton pump inhibitor medications.
②	Inflammatory bowel disease, including Crohn's disease and Ulcerative colitis.	Gastrointestinal cancers	Presence of dietary factors that influence Zn absorption, e.g., Phytic acids.	Medications like tetracycline and quinolone antibiotics.
③	Alcoholic liver disease	-	-	Metal-chelating agents, such as penicillamine, diethylene-triamine pentaacetate (DTPA)
④	Chronic renal disease	-	-	Anticonvulsant drugs (e.g., Sodium valproate)

Further research showed that zinc inhibits 5-alpha-reductase 20 and reduces androgen receptor binding in the prostate. This effect on androgen is thought to result from zinc's ability to inhibit prolactin, which, like estrogen, increases the receptors for DHT in the prostate. Therefore, zinc not only reduces DHT production but also inhibits DHT binding to receptors.

Coffee can decrease zinc absorption by 50%, because caffeine stimulates the adrenergic nervous system

(smooth muscles of the prostate), and encourages patients with BPH to limit their intake.

Pumpkin seeds are a rich source of zinc, and this may explain their potential therapeutic benefit for BPH.

Precaution

When prescribing zinc supplements, be aware that zinc can compete with the absorption of copper, calcium, and iron. Make sure the patient does not exceed the recommended dose (30 mg daily) and does not take calcium or iron supplements with zinc.

Homeopathic medicines for prostate pathology

Homeopathic terminology[196]

X= A substance diluted in the ratio 1:10 [6x or 6D: A decimal series dilution]
C= A substance diluted in the ratio 1:100
- 200C: A substance that has undergone 200 cycles of dilution and succussion (agitation)
- CH = A Hahnemann centesimal dilution: A 1:100 dilution that is then shaken vigorously

M = A substance diluted in the ratio 1:1,000.
- 50M = A substance that has been diluted and diluted 50,000 times.
- CM = A substance that has been diluted and diluted 100,000 times.

MT = Mother tincture, identified by ∅ or Q
Potentiation: Serial dilution and shaking, extracting a formulation's vital nature.

Homeopathy shows potential as a complementary approach for managing symptoms of BPH, particularly in improving urinary flow and reducing pain, but evidence regarding a significant reduction in prostate size is mixed and limited to small-scale studies. For prostate cancer, scientific evidence on the direct efficacy of homeopathic drugs is weak or nonexistent *in vivo*, or animal studies, with no consensus on efficacy for human treatment, making it unsuitable as a replacement for conventional, evidence-based care.

Homeopathy in BPH

Research indicates that individualized homeopathic treatment can significantly improve LUTS in BPH patients, often addressing both the physical symptoms and the underlying, non-cancerous enlargement of the prostate. Fifteen homeopathic medicines have been recommended for the treatment of BPH in men with their symptoms, without any research reporting evidence of efficacy for these medicines. These are: (1) *Chimaphila umbellate,* (2) *Copaiva officinalis*, (3) *Populus tremuloloides*, (4) *Triticum repens*, (5) *Juniperus communis,* (6) *Uva ursi,* (7) *Ferrum picricum*, (8) *Sabal serrulata,* (9) *Thuja occidentalis*, (10 *Staphysagria,* (11) *Conium maculatum,* (12) *Agnus castus*, (13) *Lycopodium clavatum*, (14) *Apis mellifica*, and (15) *Causticum*.[197]

Commonly used drugs

Homeopathic medicine offers several remedies commonly used to manage the symptoms of BPH and improve the quality of life in men with an enlarged prostate. These medicines are often selected based on specific urinary symptoms, such as urgency, frequency, and weak stream, to stimulate the body's natural healing mechanisms. [198]

Key homeopathic medicines for BPH [198,199]

- ***Sabal serrulata*** (Saw palmetto): Used for frequent urination (especially at night), difficulty starting urination, and urinary retention.
- ***Thuja occidentalis****:* Frequently used for chronic prostatitis and urinary symptoms, like a weak, forked, or split stream, with a frequent, urgent need to urinate.
- ***Conium maculatum***: Effective when the prostate is hardened, often with an interrupted or slow stream, dribbling of urine, and a feeling of incomplete emptying.
- ***Chimaphila umbellata***: Used for significant urinary retention, interrupted urinary flow, weak stream, straining to urinate, and a feeling of a ball or pressure in the perineum (pelvic arb) while sitting.
- ***Staphysagria:*** Targeted for cases with a burning sensation in the urethra, urinary pressure, and an incomplete sensation of emptying the bladder.
- ***Lycopodium clavatum****:* Helpful for cases of enlarged prostate with chronic, slow urination, especially

when accompanied by digestive issues or a 'slump' in the infection.

- ***Baryta carbonica***: Often used for prostate enlargement in elderly men, particularly when accompanied by a sudden urge to urinate and dribbling.
- ***Clematis erecta***: Used when the urinary stream is interrupted, or the urine passes drop by drop (strangury).
- ***Ferrum picricum***: Indicated for prostate issues, particularly for correcting urine retention and improving the flow of urine.

The 'Sabal serrulata ∅ and individualized medicines have a significant effect on BPH, with the improvement ranging from 33.3% (weak stream) to 100% (intermittency), and of the 30 patients treated, 26 (86.7%) patients had marked improvement in IPSS BPH. [200]

Homeopathic medicines have been used to treat BPH in men with prostate volume >20 ml and PSA 4.0 ng/ml, with efficacy of 51.0% (53/27) for Thuja, 56.5% (46/26) for Sulfur, 74% (34/46) for Pulsatilla, and 54.0% (13/7) for Lycopodium. In addition, significantly ($p = 0.005$) reduced the 2.3 ml prostate volume with these drugs.[201]

BPH affected 30 patients who were treated with homeopathic drugs for 12 months, showing a significant ($p = 0.001$) reduction in LUTS from 21.60 to 12.23 units, a ~57% reduction in symptoms of bladder obstruction. However, a transabdominal pelvic ultrasonographic scan did not yield statistically significant results.[202]

Homeopathy remedies like Sabal serrulata (Saw palmetto; effective for managing urinary retention and frequent urges to urinate), *Thuja occidentalis* (particularly helpful in cases of chronic prostatitis or recurrent UTI), *Conium maculatum* (Used for cases with interrupted urinary flow and weak stream), and *Chimaphila umbellate* (Used for managing strangury, an urgent, painful need to urinate, and an enlarged prostate) have been evaluated in BPH in men and small-scale studies demonstrate the potential of these drugs to relieve symptoms and improve quality of life, but challenges such as the lack of standardized protocols and large-scale trials remain.[199]

Three patients affected by BPH based on clinical and ultrasonography, were treated with *Lycopodium clavatum* in first patient (200C, two doses for 2 consecutive days at early morning on at empty stomach), Thuja occidentalis (30C/2 days in empty stomach in early morning) in the second patient with Prostate volume 77g with PSA normal (30C/2 days), and *Arsenicum album* (200C 2 doses for two consecutive days in empty stomach in the early morning) in the 3rd patient with prostate volume 79g and PSA 7.6 ng/ml, and all three patients improved clinically and pathologically, including a reduction in prostate size.[203]

A 57-year-old male patient having BPH with 29.1 cc prostate volume and PSA 2.04 ng/ml with LUTS was treated with homeopathic medicine *Clematis erecta* 30, and LUTS started improving by the end of the first month, with significant improvement at the end of 3rd month, with prostate volume 17.4 cc. This finding highlights the usefulness of homeopathic medicines, which can not only relieve obstruction and improve bladder emptying in patients but also cause significant changes in prostate gland weight within a short period of treatment. [204]

Homeopathy offers a range of remedies tailored to individual symptom profiles in patients with BPH. Remedies such as *Sabal serrulata*, *Conium maculatum*, and *Chimaphila umbellata* have shown consistent clinical effectiveness.[205]

Combined homeopathy medicines for BPH

Several commercial homeopathic, combination, and specialized products are marketed for the management of BPH and associated LUTS in men. These products often combine multiple drugs, targeting symptoms like frequent urination, weak stream, and dribbling.

① **SBL Prostonum drops** (Sharif Homeo Pharmacy)

- **Compositions**: *Sabal serrulata*, *Chimaphila umbellata*, *Clematis erecta*, *Conium maculatum*, *Pareira brava*, and *Pulsatilla nigricans*.

② Dr. Reckeweg R25 Drops for BPH (Prostatan, Germany)

It is a German homeopathic remedy formulated to treat prostate gland disorders, including acute/chronic prostatitis and BPH. It is used to relieve symptoms like painful, frequent, or urgent urination, bladder irritation, and pain in the groin/abdomen.

Ingredients and uses

- ***Chimaphila umbellata***: Relieves pain and discomfort associated with urinary disorders and helps to reduce inflammation and improve urinary flow.
- ***Clematis:*** Helps to alleviate urinary retention and reduce inflammation. It supports healthy urinary function and relieves discomfort.
- ***Conium:*** Supports prostate health and helps relieve pain in the groin and abdomen. It helps to reduce inflammation and improve overall urinary health.
- ***Ferrum picrinicum***: Improves urinary flow, manages urinary incontinence, and improves urinary control.
- ***Pareira brava:*** Effective in managing bladder calculi, catarrh, and gravel in urine. It supports healthy urinary function and alleviates discomfort.
- ***Sabal serrulata:*** Targets prostate gland health and reduces pain and inflammation.
- ***Populus tremuloides and Pulsatilla***: Support bladder function.

③ ADEL 21 Proscenat drops (Sharif Homeo Pharmacy)

- Compositions: *Acidum sulfuricum* 6x, *Conium* 6x, *Staphysagria* 6x, *Cantharis* 12x, *Selenium* 6x, *Nasturtium aquaticum* 4x, and *Ononis spinosa* 4x.

④ Bakson formula P Tablet (Meet Homeo Pharmacy)

- Compositions: *Chimaphila umb.* 3x, *Clematis erecta* 3x, *Conium mac*. 3x, *Ferrum picricum* 6x, *Pareira brava* 3x, *Populus tremuloides* 3x, *Pulsatilla nig,* 3x, *Sabal serr.* 3x.

⑤ Blooume 28 prosan drops (Homeo Mart)

- Compositions: *Sabal serrulata* 1x, *Chimaphila umbellate* 3x, *Conium maculatum* 3x, *Bareira brava* 3x, *Ferrum picricum* 6x, and *Solidago virgaurea* 1x.

⑥ Schwabe German Sabal Pentarkan Ptk.75 (Homeomart)

- Compositions: *Sabal serrulate*- ∅ 40%, *Echinacea purpurea*- ∅ 30%, *Passiflora incamata*- 1x (10%), *Cantharis* 3x (10%), *Mercurlus bijodatus* 8x 10%, and alcoholic content 57% v/v.

⑦ Allen A42 Prostatitis drops (Dr. Reckeweg, Germany)

- Compositions: *Cedron* 3x- 1.0 ml, *Chimaphila umbellate* 3x- 0.5 ml, *Sabal serrulata* 3x - 1.0 ml, *Ferrum piccricum* 3x- 0.5 g, *Clematis erecta* 3x- 0.5 ml, *Conium maculatum* 3x- 0.75 ml, and *Pareira brava* 3x- 0.5 ml.

⑧ Bhargava Prostoral tablets (NWIL)

- Compositions: *Chimaphilla umbellata* 3x (75 mg), *Ferrum picricum* 3x (30 mg), *Hydrangea arborescens* 3x (30 mg), *Pareira brava* 6x (50 mg), *Sabal serrulata* 3x (60 mg), *Staphysagria* 3x (75 mg), and *Thuja occidentalis* 3x (80 mg).

⑨ Wheezal Dr. Farokh JM Prostex Tablets (Homeomart)

- Compositions: *Cantharis* 200, *Chimaphilla umbellata* ∅, *Conium maculatum* 1M, *Medorrhinum* 200, and *Thuja occidentalis* 30.

⑩ Dr. Bakshi B13 Prostatitis drops (Bakson Drugs and Pharmaceuticals Pvt. Ltd.)

- Compositions: *Chimaphilla umbellata* 3x, *Clematis erecta* 3x, *Conium maculatum* 5x, *Pareira brava* 2x, *Thuja occidentalis* 3x, *Pulsatilla nigricans* 3x, and *Sabal serrulata* 2x.

While a single homeopathic medicine is not effective, especially for symptomatic remedies, multiple homeopathic medicines are combined and commercially marketed by various homeopathic doctors and

pharmacies, in the hope of providing symptomatic relief for prostatic disorders in men. There seems to be no published research reports on any of these commercially available combined homeopathic medicines for BPH in men. Efficacy reports are primarily based on user reviews, traditional homeopathic use, and clinical experience in homeopathic medicine, rather than on large-scale, placebo-controlled, double-blind studies.

The homeopathic literature states that several constitutional medicines (CM) [Thuja, Sulfur, Lycopodium, *Baryta carbonica*, *Natrum muriaticum*, Tuberculinum, *Calcarea carbonica*, Carcinosin, and Staphysagria], and organopathic medicines (OM) [Sabal serrulate, Hydrangea, Chimaphilla, Solidago, Senecio, Triticum, *Ferrum picricum*, and Picric acid] have been reported to be effective in patients of BPH.

A study on the simultaneous prescription of both constitutional and organopathic medicines (BCOM) has been conducted to assess the response of patients with BPH to homeopathic treatment in 180 patients (60 per group). Overall, 85% of patients showed improvement in subjective symptoms such as frequency, urgency, hesitancy, intermittent flow, unsatisfactory urination, and a feeble stream, and a decrease in residual urine volume, but there was no reduction in prostate size. Treatment response was highest with BCOM (38.24%) compared to OM (31.62%) and CM (30.15%). [206]

It may be concluded that homeopathic medicines are used either singly, in combination, or in the BCOM formula, but the results are sometimes improvement in subjective symptoms, focusing more on quality-of-life improvements than on curative, long-term reductions.

Homeopathy: Cancer therapy

12-24% of European oncology patients and 40.4% of European integrative oncology patients use homeopathy.[207,208] Specifically, 22.8% of cancer patients have used homeopathy, but 6.4% currently use it.[209] Pediatric oncology drives integrative homeopathic treatment, including 76.5% of German parents,[210] 72.2% of Dutch parents,[211] 49.0% of the Swiss parents,[212] and 6.0% of Australian parents [211,213] used homeopathy for cancer therapy.

- Ruta 200 C and Phosphorus 1M (1000 C) inhibit N′-nitrosodiethylamine (NDEA)- induced hepatocellular carcinoma in rats and 3-methylcholanthrene-induced sarcomas in mice. Ruta is selectively cytotoxicity to glioblastoma multiforme.[214]
- Ruta 9 C dosed at 2.0 ml daily for 8 or more weeks, used to treat locally advanced solid cancers or metastatic cancers initially produced significantly improved quality of life, that elapsed by the end of the trial in 28 weeks.[215]

Homeopathy for prostate cancer

Homeopathy is not a scientifically verified cure or treatment for prostate cancer. Major health institutions state there is no reliable evidence to support its use for treating cancer, and it should not replace conventional medical treatment. [216-218]

- The antiproliferative effects of homeopathic preparations of *Sabal serrulata*, *Thuja occidentalis*, and *Conium maculatum*, *in vivo,* on PC-3 and DU-145 human prostate cancer as well as MDA-MB-231 human breast cancer cell lines have been assessed. Treatment with *Sabal serrulata in vitro* resulted in a 33% decrease in PC-3 cell proliferation to 72 hours ($p<0.01$), whereas no effect was observed on MDA-MB-231 human breast cancer cells. *Thuja occidentalis* and *Conium maculatum* had no effect on the proliferation of human prostate cancer cells. The biological effect was (a) significantly stronger in *Sabal serrulata* than in controls, and (b) specific to human prostate cancer. It has been concluded that *Sabal serrulata* should be further investigated as a specific homeopathic remedy for prostate pathology.[219]
- Despite some promising *vitro* results, other studies have found that these remedies did not alter growth or gene expression in certain cancer cells. Research concludes there is no reliable evidence that homeopathy can cure or prevent cancer, and it should not replace conventional treatment.
- Homeopathy is sometimes suggested as a complementary, palliative approach to improve the quality of life or manage the side effects of conventional prostate cancer treatments.

- Phyto MT showed intermediate cytotoxicity to HeLa cervical cancer cells and PC3 prostate cancer cells.

Carcinosin

Scientific evidence supporting the use of the homeopathic drug Carcinosin as a standalone treatment for cancer in humans is currently limited. Existing research primarily comprises laboratory studies using cancer cell lines and animal models that suggest potential anticancer activity, but these findings have not been replicated in large-scale human clinical trials.

Scientific evidence summary

Research into Carcinosin and cancer treatment has primarily been limited to laboratory and animal studies rather than high-quality human clinical trials.

a. Laboratory and animal studies: Several *in vitro* and animal studies (especially on mice and human cancer cell lines in a lab setting) suggest that Carcinosin and other potentized homeopathic drugs may have some effects:

- Studies have indicated that Carcinosin 200 C can induce apoptosis (programmed cell death) in certain cancer cells and modulate cancer-related gene expression in laboratory settings.
- Research in mice with induced liver cancer showed that Carcinosin 200, alone or combined with Chelidonium 200, had a considerable ameliorative or protective effect against the carcinogen-induced damage, suggesting potential as a supporting palliative measure.[220]
- Homeopathic medicines Carcinosin, Apis, and Thuja, at different strengths, were evaluated for their anticancer activity in vivo against Ehrlich Ascites Carcinoma (EAC) cells in Swiss Albino mice, using EAC fluid (tumor) weight and EAC cell count as activity parameters. Results showed that Carcinosin's survival time is proportional to its potency, and the observed findings also support the validity of the animal model for anticancer evaluation. Apies and Thuja did not show promising results for increasing survival time.[221]
- A murine trial of the BPHRF (Prasanta Banerji Homeopathic Research Foundation) medications *Conium maculatum* (hemlock) 200 CH, *Thjua occidentalis* (Thuja, Arbor vitae) 200 CH, *Phytolacca decandra* (Phyto; poke root) 200 CH, Carcinosin (primarily derived from cancerous breast tissue) 200 CH, daily at 0.1 ml/10g body weight, found that Carcinosin 200 CH resulted in the longest survival and the least adverse effects. [222]

b. Human clinical evidence: High-quality controlled human clinical trials demonstrating Carcinosin's efficacy in treating cancer are lacking.

- A review of published literature on homeopathy found insufficient evidence to support clinical efficacy.
- Homeopathic breast cancer treatment varies based on the cancer subtype in women (Table 36). [223]
- *Serenoa repens* (Saw palmetto) displays caspase-independent cytotoxicity in human prostate cancer cells, effective when other homeopathic treatments are ineffective.[214]

Table 36. Homeopathic breast cancer treatment varies based on the cancer subtype [223]

SN	Homeopathic remedies	Types of cancer, %				Efficacy results	
		Ductal cancer	Breast cancer	Infiltrating cancer	Metastasis	Types of efficacy	Percentage
①	Calc-Carb	16	10	14	1	Cure	14
②	Carcinosin	20	06	18	5	Prevented	41
③	Conium M	02	02	02	1	Palliated	14
④	Phytolacca	01	07	0	0	Improved	31
⑤	Thuja	10	07	08	2	Total	100
⑥	Biochemical salt	03	03	02	3		
⑦	Others	03	14	03	4		

- Existing human studies tend to focus on the feasibility of integrating homeopathy into supportive care to improve patients' quality of life and manage side effects from conventional treatments (like hot flashes or chemotherapy-induced neuropathy), rather than a primary cure for cancer itself.
- Homeopathic complexes, including Conium maculatum, Sabal serrulate, Thuja occidentalis, and Carcinosinum, can reduce the incidence of prostate cancer *in vivo* by 23% and tumor volume by 38% compared with untreated groups.[224]

Important considerations

- Lack of scientific consensus: Homeopathy is a controversial system of care. The high dilutions involved, often beyond the Avogadro number (meaning no molecules of the original substance remain), lead to no scientifically verified plausible mode of action for the remedies in conventional medical terms.
- Lack of regulation: Homeopathic remedies are largely unregulated, and their claims of efficacy have not been scientifically verified for cancer treatment.
- Complementary vs. primary treatment: Current research suggests that homeopathy's potential role may be limited to support or palliative care, and there is no evidence that it can change the natural history or progression of cancer.
- Table 37 presents the comparison of the efficacy of allopathic, herbal, and homeopathic medicines in BPH in men.

Table 37. Comparison of the efficacy of allopathic, herbal, and homeopathic medicines in BPH in men

SN	Feature	Allopathic	Herbal (Phytotherapy)	Homeopathic
①	Approach	Evidence-based, pharmacological, and surgical	Natural plant extracts, anti-inflammatory	Individualized / Constitutional
②	Main goal	Rapid relief, prostate shrinkage, cancer removal	Mild-moderate symptom management	Symptom management, and prostate gland reduction
③	Evidence	Strong (High-level trials)	Mixed (Some trials show benefit)	Limited (Mostly small-scale studies)
④	Onset	Days/Weeks (alpha-blockers)	Weeks/Months	Weeks/Months
⑤	Side effects	Sexual dysfunction, libido loss, Dizziness, infertlity	Generally, rare, mild gastro-intestinal discomfort.	Generally considered non-toxic
⑥	Scientific evidence	Strong, FDA-approved.	Mixed/Moderate (depends on extract)	Limited (highly debated)
⑦	Common agents	Tamsulosin, Finasteride, Dutasteride	Saw palmetto, Pygeum, Pumpkin seed	Sabal serrulate, Conium, Thuja etc.

The effectiveness of herbal and homeopathic medicines is often debated because they lack large-scale, standardized clinical trials compared with allopathic medicines, though many patients report symptomatic relief.

Conclusions

While some studies show promising results, they are often small-scale (7.6 ng/ml) or lack long-term, large-scale, randomized, placebo-controlled trials. However, homeopathic remedies may serve as a complementary, safe, non-invasive option for symptomatic management in BPH, but should not replace standard medical care or cancer screening for prostate cancer.

③ Surgical intervention

Surgical interventions for BPH range from traditional methods like transurethral resection of the prostate (TURP) to newly developed, minimally invasive techniques, including laser therapies (HoLEP, GreenLight), water vapor therapy (Rezum), prostatic urethral lift (UroLift), and aquablation, all aiming to improve urine flow by removing or shrinking prostate tissue. The choice of surgical method depends on

prostate size and patient health, and the desired balance between efficacy and side effects profile, such as sexual dysfunction.

Although each surgical method for BPH has advantages and disadvantages compared to others, the ideal technique may differ for each patient. While selecting the process, the patient's factors and priorities should be reviewed, and the urologist and the patient should decide together. In Bangladesh, there is no choice for BPH patients because urological surgeons are mainly trained with only the oldest method of TURP. Factors that affect the choice of surgical method include the patient's age, comorbidities, use of anticoagulant agents, prostate volume, previous surgeries, the presence of simultaneous stones in the bladder, and prostate cancer accompanying BPH.[225]

- Indications for surgical intervention may include failure of lifestyle interventions and medical therapy, a desire to avoid daily medications, intolerable adverse effects, or signs of poor control such as renal insufficiency, urinary retention, recurrent urinary tract infections, or recalcitrant gross hematuria.
- Of men who are treated for LUTS from BPH, approximately 1% patients with LUTS require surgery.[226]
- Most of the surgical interventions used in BPH management, if they open the urinary channel, can also damage the bladder neck, further worsening the occurrences of sexual dysfunction.[227]
- Decisions about specific surgical or minimally invasive surgical therapies should involve shared decision-making regarding procedural risks, which are likely to include sexual adverse effects, procedure effectiveness, and retreatment risk.

Surgical intervention is the most effective treatment for BPH, with approximately 100,000 procedures performed annually in the United States.[228] Surgical methods for BPH can be divided into three types according to their treatment principles: (a) Resection methods (resection of prostate tissue piece by piece), (b) Vaporization methods (vaporization of excessive prostate tissue), and (c) Enucleation methods (peeling the enlarged prostate from the prostate capsule) (Table 38).

Table 38. Classification of different endoscopic surgical methods of benign prostatic hyperplasia.[229]

SN Surgical methods with abbreviations	Energy source	Techniques/ Procedure
A. Resection methods		Resecting the enlarged prostate adenoma with monopolar or bipolar resection loop, piece by piece.
a. Monopolar transurethral resection of prostate (M-TURP)	Monopolar	
b. Bipolar transurethral resection of prostate (B-TURP)	Bipolar	
B. Vaporization methods		Vaporizing the enlarged prostate adenoma with side-firing laser fiber. or mushroom-like bipolar electrode.
a. Diode laser vaporization of prostate (DioLVP)	Diode laser	
b. Potassium titanyl phosphate laser vaporization of the prostate (KTP LVP)	KTP laser Green light	
c. Bipolar vaporization of the prostate (Bipolar VP)	Bipolar	
C. Enucleation methods		Peeling the entire prostate adenoma from prostrate capsule using end-firing laser fiber or designed bipolar loop, then morcellating the adenoma with a shaver.
a. Thulium laser enucleation of prostate(Thulium LEP)	Thulium laser	
b. Holmium laser enucleation of the prostate (HoLEP)	Holmium laser	
c. Diode laser enucleation of the prostate (Diode LEP)	Diode laser	
d. Bipolar enucleation of the prostate (Bipolar EP)	Bipolar	

Classification of surgical interventions for BPH

The main classifications are minimally invasive surgical therapies (MIST), and invasive surgical therapies (conventional surgeries)

I. Minimally invasive surgical therapies (MIST)

These procedures generally involve no external incision and are often performed in an outpatient setting, sometimes under local anesthesia. They typically offer faster recovery but may have a higher retreatment rate compared to more invasive options. They are often suitable for men who have smaller to moderate-sized prostates or those who are high-risk for traditional surgery.

A. Mechanical therapies

① Prostatic urethral lift (UroLift)

Involves placing small, permanent implants to pull the enlarged prostate lobe away, compressing the tissue to open the urinary channel without cutting or removing tissue.

② Temporary implantable nitinol device (iTind)

A temporary, stent-like device is inserted to expand the urethral lumen, thereby causing pressure necrosis of adjacent tissue over time; the device is removed after a few days to weeks.

B. Thermo-ablative therapies

① Transurethral microwave therapy (TUMT)

- Uses a transurethral probe to deliver heat (microwave energy) through a catheter to heat and ablate the prostate tissue, causing necrosis.
- TUMT uses microwave-induced heat to produce coagulative necrosis in prostatic tissue. This microwave radiation is delivered via an intraurethral antenna, which, when properly positioned, can heat targeted regions of the prostate.
- TUMT has been shown to improve symptoms and sustain this effect but remains inferior to TURP in its efficacy. [230]

② Water vapor thermal therapy (Rezum)

Uses radiofrequency to create thermal energy in a jet of water vapor and injects controlled doses of steam to destroy excess prostate tissue, which then causes the enlarged targeted prostate tissue to undergo necrosis and shrinkage.

C. Other MIST

① Prostatic arterial embolization (PAE)

A radiologic procedure that blocks the blood flow to the prostate with microscopic particles, causing the gland to shrink from lack of blood flow.

II. Invasive surgical therapies

These are traditional surgical procedures, some requiring an external incision (open surgery) and others performed endoscopically (through the urethra). They are often reserved for moderate-to-severe symptoms or very large prostates and are associated with excellent, durable outcomes.

A. Transurethral surgery (endoscopic/electrosurgical procedures)

These procedures are performed in the operating room by inserting instruments through the urethra (transurethral). They are considered moderate to severe BPH symptoms and typically require regional or general anesthesia in the operating room by inserting instruments through the urethra (transurethral) to remove or modify the obstructing tissue.

① Transurethral resection of prostate (TURP)

Historically, it has been considered the ‘gold standard’ for BPH surgery, using a heated electrical wire loop inserted through the urethra to trim away excess prostate tissue blocking the urethra. It can be performed using both monopolar and bipolar energy, with bipolar technology reducing the risk of complications like TUR syndrome.

② Transurethral incision of the prostate (TUIP)

- Instead of removing tissue, this procedure involves making one or two small incisions in the prostate and bladder neck to widen the urinary channel. It is suitable for small prostates and may preserve normal ejaculation.
- Either an electrocautery device or a laser is used to incise the prostate tissue from the bladder neck down to the verumontanum. This incision allows the crowded circumferential band of hypertrophied tissue to separate, and the bladder outlet is ‘opened up.’

- TUIP is typically recommended for men with minor prostatic glands (<30 ml).
- The presence of a large median lobe is a relative contraindication, as it may cause persistent obstruction if incised.
- Bilateral TUIP may be performed, but with a greater risk of ejaculatory dysfunction compared with a single midline incision.
- Bilateral TUIP may be performed, but with a greater risk of ejaculatory dysfunction compared with TURP. Outcomes relating to IPSS have been shown to be similar between TUIP and TURP, but with decreased improvement in peak flow rates. [231]

B. Prostate laser surgery

Laser procedures use high-energy to remove or vaporize excess tissue and are suitable for a wide range of prostate sizes, including large glands, and for patients on anticoagulant therapy. Uses various types of lasers (Holmium, Thulium, GreenLight) to ablate (vaporize) or enucleate (cut and remove) excess tissue.

① Photo-selective vaporization of the prostate (PVP, GreenLight Laser)

Use a laser to vaporize the overgrown prostate tissue, effectively 'melting' it away to enlarge the urinary channel.

② Holmium laser enucleation of the prostate (HoLEP)

Use a laser to enucleate (pee away) the entire obstructive adenoma, pushing it into the bladder, where it is then broken and removed.

③ Holmium laser ablation of the prostate (HoLAP)

HoLAP is a safe and effective procedure for the treatment of enlarged prostates <40 ml. Due to high recurrence rates. HoLAP should be avoided in prostates >40 ml. [232]

④ Thulium laser enucleation of the prostate (ThuLEP)

The thulium laser is a safe and highly effective procedure compared to other procedures, such as HoLEP and TURP, in terms of blood loss, speed of tissue resection, catheterization time, hospital stay, drop in hemoglobin, PSA, and versatility of prostate resection. [233]

C. Open or Robotic Surgery (Simple prostatectomy)

These approaches are generally reserved for men with severely enlarged prostates (typically >80 grams), or when there are complicating factors like bladder stones or damage.

① Open prostatectomy

Performed through an external incision in the lower abdomen. This procedure involves removing the inner, obstructing part of the prostate (the adenoma) while leaving the outer capsule intact.

② Laparoscopic or Robotic-assisted simple prostatectomy

A minimally invasive simple prostatectomy using small abdominal incisions, and a camera generally leads to a shorter hospital stay than open surgery.

③ Robotic-assisted simple prostatectomy

Utilizes a robotic system to guide the surgeon's instruments with enhanced precision, associated with less blood loss and fewer complications.

④ Transurethral water-jet ablation (Aquablation therapy)

Aquablation (AquaBeam® Procept BioRobotics) is a novel technique for treating LUTS secondary to BPH. It involves robotic-assisted hydrodissection of prostate tissue with high-velocity saline under transrectal ultrasound guidance.

Classification by energy source or method

① Electrosurgical- TURP, TUIP Transurethral electrovaporization
② Laser- PVP (GreenLight), HoLEP, HoLAP, Thulium laser procedures
③ Thermal or Water-based- TUMT, Rezum (water vapor), Aquablation (waterjet)
④ Mechanical or Implant- UroLIft, iTind
⑤ Embolization- PAE (blocking blood flow)

Descriptions of some surgical procedures for BPH

Transurethral resection of prostate (TURP)

TURP is the most common surgical procedure for urinary obstruction caused by BPH. It involves removing obstructing prostate tissue through the urethra using a resectoscope, without external incisions. TURP is a minimally invasive surgery where a surgeon inserts a resectoscope (a thin tube with a camera and an electrical wire loop) through the penis into the urethra to shave away excess prostate tissue. It is primarily performed for BPH when medications fail, or symptoms are severe.

Transurethral resection of the prostate (TURP), a practice established in the 1930s, is traditionally accepted as the gold standard of surgical treatment for benign prostatic obstruction (BPO). The advent of the laser in the 1990s has repeatedly challenged this historical standard, leading to the emergence of a variety of new surgical methods.[234] Until the 2000s, TURP was still used as an effective treatment, but its use has since declined, while the use of lasers for BPO treatment has significantly increased. [235]

There are two types of transurethral resection of the prostate (TURP), which include (a) Mono TURP and (b) Bipolar TURP, and Table 39 shows differences between the two methods.

Table 39. Differences between Monopolar TURP and Bipolar TURP in men

SN	Features	Monopolar TURP	Bipolar TURP
1.	Electrical current path	Travels from the instrument, through the patient's body is connected to a grounding pad on the skin.	Stays contained between the two lips of the instrument.
2.	Irrigating fluid	Uses a hypotonic, non-conductive fluid like distilled water or glycine.	Uses a standard isotonic saline solution which is safer to absorb.
3.	Bleeding	Higher risk of bleeding during and after surgery.	Better coagulation of blood vessels and less bleeding.
4.	Surgery details	Current can sometimes damage surrounding tissues.	Current is more contained, leading to a clear view for the surgeon.
5.	Outcomes	May result in higher post-operative blood loss.	Often results in a shorter hospital stay and catheterization time.
6.	Symptom improvement	Similar long-term improvement in urinary systems, though some studies suggest B-TURP may remove more tissue.	Similar long-term improvement in urinary symptoms.

The wire loop cuts and cauterizes tissue, relieving obstruction and improving urine flow.

Indications

① Moderate to severe LUTS due to BPH: (a) Difficulty starting urination, (b) Weak urine stream, (c) Frequent urination (especially at night), and (d) Incomplete bladder emptying.

② Complications of BPH include recurrent urinary retention, bladder stones, or kidney damage.

How the procedure works

- Instrument: A resectoscope (about 12 inches long, 0.5 inches wide) with a camera, irrigation system, and wire loop.
- Technique: The surgeon trims the obstructing tissue, simultaneously sealing the blood vessels to minimize bleeding.
- Duration: Typically, 60-90 minutes.
- Hospital Stay: Usually 1-2 days, with a catheter left in place temporarily.

Benefits:

- Effective relief of urinary symptoms in most patients
- Quick recovery compared to open surgery
- No external incision (done through the penis)
- Considered the gold standard method for BPH

Side effects and complications

- Common: Temporary bleeding, infection, retrograde ejaculation (semen flows into the bladder), urinary urgency.
- Less common: Urethral stricture, bladder neck contracture, or need for repeat surgery.
- Rare but Serious: TUR syndrome (fluid absorption leading to electrolyte imbalance).
- Short-term: Bleeding, infection, temporary difficulty urinating.
- Long-term: Retrograde ejaculation (semen enters bladder instead of exiting).
- TURP syndrome (rare): absorption of irrigation fluid causing electrolyte imbalance.
- TURP is unsuitable for patients who cannot discontinue anticoagulation for surgery.
- TURP is the primary treatment for LUTS from BPH that is uncontrolled despite medical therapy for average-sized prostates (30 mL to 80 mL).
- Although TURP is the most effective treatment option, risks include traumatic, bleeding, incontinence, adverse sexual effects, and cases of ejaculatory duct obstruction post-TURP have been reported.[236]
- It has been reported that ejaculatory dysfunction occurs in up to 65.0% of post-TURP patients, of which about 50% have retrograde ejaculation.[104]
- Based on a meta-analysis of 20 RCTs with up to five years of follow-up: 70% reduction in symptoms by IPSS, 69% improvement in quality of life.[236]
- Monopolar TURP is a risky procedure because of the likelihood of severe complications such as massive bleeding or transurethral resection syndrome.[237]
- Bipolar TURP is an impressive and secure technique that is correlated with a distinctly shorter catheterization time, shorter hospital stays, less decrement in the levels of serum sodium, and is comparable to monopolar TURP in terms of efficacy by attention to IPSS IIEF-5 scores.[238]
- TURP has a morbidity rate of 11.1%, and complications of this procedure include transurethral resection (TUR) syndrome, retrograde ejaculation, and urinary stress incontinence. [239,240]
- TURP was the primary endoscopic treatment of BPH and is still widely used, but it usually causes adverse effects on sexual function, including primary retrograde ejaculation.[241]

The main complications of TURP include hemorrhage requiring a blood transfusion (occurring in 2% of cases in a meta-analysis), stress urinary incontinence or permanent lifelong leakage associated with increased abdominal pressure (0.6% or less), postoperative urinary retention (4.5-6.8%), need for retreatment (0.5%), temporary postoperative dysuria and urinary urgency (0-38%), urethral stricture (4.1%), and transurethral resection syndrome (TURS). [241-244]

TURS typically presents with neurologic symptoms of confusion, nausea, vomiting, hypertension, vision changes, and bradycardia. The incidence of TURS has decreased dramatically with the use of bipolar electrodes, which enable the use of iso-osmolar irrigate (normal saline). Additionally, using bipolar electrodes poses a lower risk of hemorrhage, as the technology facilitates better hemostasis.

Sexual dysfunction with retrograde ejaculation is the main risk and occurs in about two-thirds to three-fourths of patients.[245,246] The risk is lower if only parts of the prostate are removed and certain areas are preserved.[247,248] The effects of transurethral resection on erectile function vary, as some studies show it may improve sexual function. In contrast, others have shown that it can impair erections if the resection is too extensive and perforates the capsule or extends into or beyond the peripheral zone of the prostate (near the neurovascular bundles that facilitate erection).[241,249,250]

Conclusions

TURP remains the standard surgical option for BPH when medications fail or symptoms are severe, offering reliable relief but with notable side effects.

Laser vaporization of the prostate (LVP)

LVP, also called Photo-selective vaporization of the prostate (PVP), is a minimally invasive surgical

technique used to relieve urinary obstruction caused by BPH. It employs high-energy laser light to precisely remove excess prostate tissue, restoring urine flow while minimizing bleeding and recovery time. Several laser-based techniques use concentrated light to generate intense heat and vaporize prostate tissue.

Photo-selective laser vaporization (PVP)

This method, often known as Green-light™ laser therapy, uses high-powered diode lasers to vaporize and melt away excess prostate tissue, thereby sealing blood vessels and minimizing blood loss, making it a safe option for men on blood thinners (Table 40).

- Green-light laser (potassium titanyl phosphate, KTP) that is highly absorbed by hemoglobin but not by water, allowing vaporization and removal of prostatic tissue with adequate hemostasis.

Key concepts

- Indication: Moderate to severe urinary symptoms due to BPH (weak stream, urgency, nocturia, incomplete emptying).
- Mechanism: A cystoscope is inserted through the urethra; a laser fiber delivers concentrated light energy that vaporizes obstructing prostate tissue.
- Laser type: The GreenLight system (532 nm wavelength) is commonly used; its energy is selectively absorbed by hemoglobin, allowing precise tissue removal with excellent hemostasis.
- Goal: Improve urine flow, reduce symptoms, and avoid complications of untreated obstruction (e.g., recurrent infections, bladder damage).
- Table 40 shows the comparison of photo-selective laser vaporization (PVP) with other related methods

Procedure steps

① Preparation: Patient under anesthesia; cystoscope inserted via. urethra.
② Laser application: The surgeon directs the laser to vaporize the obstructing tissue layer by layer.
③ Tissue removal: Unlike TURP, no tissue is sent for pathology- tissue is vaporized.
④ Catheterization: Often shorter duration than TURP; many patients are catheter-free within 24 hours
⑤ Recovery: Typically, outpatient or short hospital stay.

Table 40. Comparison of photo-selective laser vaporization (PVP) with other related methods

SN	Feature	Photo-selective vaporization of the prostate (PVP)	Transurethral resection (TURP)	Holmium Laser enucleation (HoLEP)
①	Invasiveness	Minimally invasive	Moderately invasive	Minimally invasive
②	Bleeding risk	Very low (laser seals vessels)	Higher	Low
③	Hospital stays	Short/outpatient	1-3 days	1-2 days
④	Catheter time	<24 hours typical	2-3 days	1-2 days
⑤	Tissue retrieval	None (vaporized)	Yes	Yes
⑥	Suitability	Best for small-moderate prostates	Standard option	Suitable for large prostates

Advantages

- This method can be used to treat gigantic prostate glands that are not amenable to other current procedures and usually require an open surgical approach.
- It is a virtually bloodless procedure, suitable for patients on blood-thinning therapy.
- Rapid symptom relief with improved urinary flow. Similar IPSS scores compared with TURP.
- Lower risk of TUR syndrome (no irrigation fluid absorption)
- Systematic review of 45 RCTs comparing LPV of the prostate to TURP found no significant difference in symptoms; LPV of the prostate leads to fewer transfusions and shorter hospital stays.

Limitations and risks

- No tissue sample for pathology (cannot rule out incidental prostate cancer)
- Durability: Effective in the long term, but some patients may need retreatment.

- Side effects: Temporary burning, urgency, or retrograde ejaculation.
- Not ideal for very large prostates (>80-100 g), where HoLEP may be superior.

Clinical perspective

Laser vaporization has become a widely accepted alternative to TURP, especially for patients at high bleeding risk or those preferring a faster recovery. It balances efficacy with safety, though the lack of tissue retrieval remains a drawback.

Thulium laser vapo-resection (ThuVARP)/vapo-enucleation (ThuVEP)

- ThuVARP and THuVEP are minimally invasive surgical techniques for BPH that combine vaporization and enucleation, offering precise tissue removal with reduced bleeding and a shorter recovery time compared to traditional TURP.
- The thulium laser simultaneously cuts and vaporizes tissue, and the resected pieces can be removed and examined for cancer cells, which is not possible with pure vaporization methods.

Core concepts

a. Energy source: Thulium: YAG laser (wavelength ~2013 nm) with continuous-wave emission, allowing smooth cutting and coagulation.

b. Techniques:

- ThuVARP (Vapo-resection): Layer-by-layer vaporization and resection of prostate tissue, like TURP but with laser energy.
- ThuVEP (Vapo-enucleation): Enucleation of entire adenoma lobes using laser dissection, followed by morcellation.

c. Target group: Men with moderate-to-severe LUTS due to BPH, including large prostates (>80 g).

- Table 41 presents the comparative overview of ThuVARP (Vapo-resection), ThuVEP (Vapo-enucleation), and TURP.

Table 41. Comparative overview of ThuVARP (Vapo-resection), ThuVEP (Vapo-enucleation), and TURP (Gold standard)

SN	Feature	ThuVARP (Vapo-resection)	ThuVEP (Vapo-enucleation)	TURP (Gold standard)
①	Technique	Vaporization + Resection	Enucleation + Morcellation	Resection with electrocautery
②	Best suited for	Small-medium prostates	Large prostates (>80 ml)	Small-medium prostates
③	Hemostasis	Good, continuous coagulation	Excellent, minimal bleeding	Moderate
④	Catheterization time	Short	Short	Longer
⑤	Hospital Stay	Reduced	Reduced	Longer
⑥	Functional outcome (IPSS/Qmax)	Comparable to TURP	Comparable or superior to TURP	Established benchmark
⑦	Complications	Lower risk of TUR syndrome; some irritative symptoms	Low bleeding, rare transfusion	TUR syndrome, higher bleeding risk
⑧	Durability	Good mid-term outcomes	Strong long-term durability	Long-term proven

Advantages

- Reduced bleeding risk due to strong coagulative properties.
- Shorter hospital stays and catheterization compared to TURP.
- Applicability to large prostates (ThuVEP especially)
- No risk of TUR syndrome (no glycine irrigation needed).
- Comparable symptom relief (IPSS, QoL scores) to TURP and HoLEP
- Generally, it preserves sexual function.

Limitations and risks

- Learning curve: ThuVEP requires advanced surgical skills, like HoLEP
- Operative time: Can be longer in very large prostates
- Post-operative irritative symptoms: Dysuria and urgency may occur transiently
- Equipment cost: Laser systems and morcellators are expensive.

Transurethral water vapor thermal therapy (WVTT)

WVTT, commonly known as Rezum® therapy, is a minimally invasive treatment for BPH that uses convective radiofrequency-generated water vapor to ablate excess prostate tissue, improving urinary symptoms while preserving sexual function.

Mechanism of action

- Technology: Radiofrequency energy converts sterile water into vapor at ~103 ^{0}C.
- Delivery: Vapor is injected trans-urethrally into the prostate tissue via a specialized device.
- Effect: Thermal energy causes immediate cell necrosis; over the course of weeks, the body resorbs the treated tissue, reducing prostate volume.
- Target: Effective for lateral lobes, median lobe, and prostates up to ~80 ml.

Procedure

- It can be performed in a doctor's office with local anesthesia or light sedation, avoiding the need for general anesthesia to numb the urethra and prostate to make them more comfortable during the surgery.
- A surgeon inserts a small needle to inject water vapor into the transitional zone (lateral and median lobes) of the enlarged prostate in up to 15 different sites for up to 9 seconds each.
- Controlled, 9-second doses of high-temperature steam (heated to approximately 103 ^{0}C or 217 ^{0}F) are injected into the enlarged prostate tissue.
- The steam diffuses throughout the prostate tissue but does not cross the surgical capsule into the peripheral zone.
- The steam condenses into water, releasing energy that causes the targeted prostate cells to die (apoptosis) and tissue necrosis.
- The body naturally clears dead cells over time; as dead cells are shed, prostate volume decreases, and urine flow improves.
- Over the next 4 to 6 weeks, the ablated tissue shrinks, enlarging the prostate lumen.

Clinical outcomes

- Symptom relief: Significant improvement in IPSS and quality of life within 3 months, sustained up to 5 years in studies.
- Flow rate: Increase in maximum urinary flow (Qmax)
- Durability: Retreatment rates are relatively low (~4 to 5% at 5 years).
- Sexual function: Minimal impact on erectile function; lower rates of retrograde ejaculation compared to TURP.
- Table 42 shows the comparison of water vapor thermal therapy (WVTT) with other related therapies

Table 42. Comparison of water vapor thermal therapy (WVTT) with other related therapies

SN	Feature	WVTT (Rezum)	TRUP	HoLEP	Medical therapy
①	Invasiveness	Minimally invasive, office/outpatient	Invasive surgery	Endoscopic laser surgery	Non-invasive
②	Anesthesia	Local or light sedation	General/Spinal	General/Spinal	None
③	Recovery	Short, catheter 3-5days	Longer, catheter 5-7 days	Similar to TURP	Immediate
④	Sexual side effect	Low risk	High risk of retrograde ejaculation	Moderate	Variable
⑤	Durability	Good (5+ years)	Excellent	Excellent	Limited, progression common

Safety and Risks

- Common transient effects include dysuria, hematuria, urgency, and frequency (which resolve in 2-4 weeks).
- Complications: Rare; may include urinary retention, infection, or the need for retreatment.
- Contraindications: Very large prostates (>80-100 ml), active infection, or inability to tolerate

catheterization. Previous radiation treatment or fibrosis of the prostate (due to a prior procedure for BPH) are relative contraindications for this procedure.

Advantages

- The primary advantages of WVTT are that it can be performed in the office under local anesthesia, it generally preserves ejaculatory function, and it can be used in prostates with a median lobe.
- Because the procedure is short (typically 10-15 minutes), the patient is usually discharged the same day.
- It preserves sexual function, erectile and ejaculatory function in most men. However, the side effects that can affect sexual life are very low.
- Best suited for men with moderate to severe LUTS due to BPH who want a minimally invasive option with preservation of sexual function, and those at high surgical risk.

Disadvantages

- Healthcare providers may not recommend the Rezum method if the patients have: (a) Kidney function complications, (b) A urethral implant, and (c) a huge prostate (>80 grams).
- Not ideal for very large prostates, retreatment risk slightly higher than TURP/HoLEP.
- The initial injection of steam often causes prostatic edema, so an indwelling Foley catheter or intermittent catheterization is required for a few days postoperatively.
- Mild burning in the urination in the first days, pain or discomfort while peeing or ejaculating, peeing more than usual, or having more urgent urination, blood in pee (hematuria) or semen (hematospermia), the penis does not release semen when it reaches sexual climax (dry ejaculation), narrowing of the urethra (urethral strictures), and bladder stones.
- Complications of WVTT include dysuria, hematuria, urinary frequency and urgency, hemato-spermia, and urinary tract infection.[251,252] These symptoms are typically mild to moderate and resolve within three weeks.
- Ejaculatory dysfunction has also been reported in 2.4% of 136 men, which is less than with TURP but more than with prostatic urethral lift,[251] effective, and patient

Conclusion

WVTT is increasingly recognized as a safe, effective, and patient-friendly alternative to traditional surgical approaches for BPH, bridging the gap between medical therapy and invasive surgery.

Transurethral electro-vaporization of the prostate (TUVP)

TUVP is a minimally invasive surgical technique for BPH that uses high-voltage electrical current to vaporize obstructive prostatic tissue, thereby relieving urinary symptoms. Table 43 compares TUVP with other related surgical techniques for BPH.

Table 43. Comparison of TUVP with other related surgical techniques for BPH

SN	Technique	Mechanism	Advantages	Limitations
①	Transurethral electro-vaporization of the prostate (TUVP	Electrical vaporization of tissue	Less bleeding, shorter catheterization, minimally invasive	Limited long-term data compared to TURP
②	Transurethral resection of prostate (TURP)	Mechanical resection with electrocautery	Gold standard, long-term efficacy	High risk of bleeding, TUR syndrome
③	Laser vaporization (e.g., GreenLight)	Laser energy vaporizes tissue	Minimal bleeding, suitable for anticoagulated patients	Higher cost, requires specialized equipment
④	Open prostatectomy	Surgical removal via incision	Effective for very large prostates	More invasive, longer recovery

Key features of TUVP

- Purpose: To alleviate LUTS caused by BPH, such as weak stream, hesitancy, nocturia, incomplete emptying, and retention.

- Mechanism: A resectoscope with an electrode delivers electrical energy that vaporizes prostate tissue, creating a cavity and reducing urethral obstruction.
- Anesthesia: Performed under general or spinal anesthesia.
- Outcome: Improved urine flow and symptom relief without the need for open surgery.

Benefits of TUVP

- Reduced intraoperative bleeding compared to TURP
- Shorter hospital stays and catheterization time
- Minimally invasive with quicker recovery
- Effective symptom relief for small to medium-sized prostates

Risks and Considerations

- Complications: Dysuria, hematuria, urinary tract infection, or temporary irritative symptoms.
- Durability: Long-term outcomes are less well established than with TURP.
- Patient selection: Best suited for moderate prostate enlargement; very large prostates may require TURP or open surgery.
- The results are well maintained in the 5-year follow-up, with low reoperation rates.[253]

Conclusions

- TUVP is often considered when patients desire a minimally invasive option with reduced bleeding risk, especially those with comorbidities or anticoagulation. However, TURP remains the benchmark for long-term efficacy, and laser techniques are increasingly popular for their safety profile.
- Different prostate vaporization techniques offer varied trade-offs between safety (especially for bleeding-prone patients), recovery time, and long-term durability. The primary differences lie in the type of energy used (laser vs. bipolar plasma/steam), the method of tissue removal, and specific patient outcomes (Table 44).

Table 44. Differences among the prostate vaporization techniques in men

SN	Features	Photo-selective laser vaporization (PVP)	Bipolar plasma vaporization (BPVP)	Water vapor therapy (Rezum)	Trans-urethral resection of the prostate (TURP)
1.	Energy source	Laser (KTP or LBO)	Bipolar electrical energy	Steam (water vapor)	Monopolar/Bipolar electrocautery loop
2.	Tissue for Pathology?	No (tissue is vaporized /destroyed	No (tissue is vaporized)	No (tissue shrinks over time)	Yes (tissue is resected /removed)
3.	Bleeding risk	Very low	Low	Very low	High (complications)
4.	Catheterization time	Shorter	Shorter than TURP/ HoLEP	Short (managed at home for few days)	Longer
5.	Hospital stay	Shorter (often out-patient/day case)	Shorter	Outpatient procedure	Longer
6.	Recovery time	Generally faster early recovery time	Faster recovery time	Faster recovery time (return to normal activity within days)	Longer
7.	Long-term efficacy	Comparable to TURP, but potentially higher reintervention rate	Comparable to TURP	Symptom involvement over weeks/months	Excellent, considered gold standard
8.	Susceptibility for anticoagu-lants	Ideal for patients on blood thiners	Suitable	Suitable	High bleeding risk, requires stopping meds.
9.	Prostate size	Suitable for a wide range, but may have longer operation for large prostate glands	Effective for small-to-medium prostate glands	Generally for small-to-medium prostate glands	Suitable for 30-80 mL

Transurethral prostate convective water vapor thermal therapy (WVTT)

WVTT, like the Rezum™ system and similar treatments, is a minimally invasive procedure that uses

sterile water vapor (steam) to shrink enlarged prostate tissue, causing LUTS from BPH by delivering precise heat energy, improving urine flow, and BPH symptoms. A device delivers radiofrequency-heated water vapor (steam) into the prostate, ablating obstructive tissue, shrinking the gland, and improving urine flow while preserving sexual function, making it an effective, quick alternative to surgery, often done outpatient with local anesthesia. The convective heat from the vapor creates targeted cell death (ablation) in the obstructing tissue, leading to shrinkage and long-term symptom relief, with low retreatment rates.

How it works (The Science of Steam)

① Energy generation: A device creates steam from sterile water using radiofrequency energy.
② Convective delivery: The steam, carrying stored thermal energy, is delivered directly into the obstructing prostate tissue via a cystoscope.
③ Ablation: As the steam condenses back into water, it releases its energy, causing targeted cell death (necrosis) in the hyperplastic tissue.
④ Tissue shrinkage: The body naturally reabsorbs the treated tissue, shrinking the prostate and opening the urethra.

Key benefits:

- Minimally invasive: Performed through the urethra, avoiding incisions.
- Preserves functions: Excellent safety profile for erectile and ejaculatory function compared to traditional surgery (TURP).
- Quick procedure: Takes minutes to complete.
- Outpatient/Office setting: Can often be done without general anesthesia.
- Treats All Zones: Can address median lobe enlargement, a challenge for other methods.
- RCT with 197 patients comparing water vapor thermal therapy with control therapy found a mean reduction in IPSS of 11.2 points compared with 4.3 points ($p<0.0001$).
- Preservation of erectile and ejaculatory function. IPSSs remain improved up to 36 months.

Ideal candidates

- Men with moderate to severe LUTS due to BPH.
- Often effective for large prostates that other treatments struggle with.

Potential side effects

- Temporary painful or frequent urination, blood in urine/semen, or decreased ejaculation volume.
- Rarely, urinary tract infections or a temporary inability to urinate.
- No direct high-quality comparative studies between water vapor thermal therapy and TURP.
- Possible high retreatment rate.

C. Simple prostatectomy

- Removal of prostatic obstruction using an open, laparoscopic, or robotic method.
- Minor RTC compared simple prostatectomy with TURP in patients with prostate volume>80 mL and found that prostatectomy was no slower and was more effective and may be safer in this population.[254]
- It can be performed on large (>80 mL) prostates when a transurethral approach cannot accommodate their size. Remove more prostatic tissue than TURP.

Consequences

- The most invasive treatment, Open prostatectomy, has an increased risk of bleeding and transfusions.
- Robotic prostatectomy has increased operative times and a steeper learning curve. The complication rate is like that of TURP.

Transurethral incision of the prostate (TUIP)

TUIP is a minimally invasive surgical option for men with small-to-moderately enlarged prostates and bothersome urinary symptoms due to BPH. It involves making one or two small cuts in the prostate and bladder neck to relieve obstruction without removing tissue.

Purpose

- Indication: Men with BPH, especially those with smaller prostates (<30 g) and significant LUTS.
- Goal: Relieve obstruction by widening the bladder neck and urethral passage.
- Fertility consideration: Often preferred in younger men concerned about preserving ejaculation and fertility.

Procedure

- A resectoscope is inserted through the urethra.
- The surgeon makes 1-2 incisions at the bladder neck and prostate tissue using either electrocautery or laser.
- These cuts reduce pressure on the urethra, improving urine flow.

Benefits

- Less invasive than TURP (transurethral resection of the prostate)
- Shorter operative time and hospital stay.
- Lower risk of retrograde ejaculation compared to TURP.
- Effective for mild to moderate BPH symptoms.
- Table 45 presents the comparison between TUIP and TURP

Table 45. Comparison between TUIP and TURP

SN	Feature	TUIP	TURP
①	Prostate size suitability	Small (<30 g)	Moderate to large (>30 g)
②	Tissue removal	No tissue removed, only incisions	Tissue resected and removed
③	Hospital stay	Shorter	Longer
④	Retrograde ejaculation	Lower risk	Higher risk
⑤	Durability	May require repeat procedure	More durable, long-term relief
⑥	Bleeding risk	Lower	Higher

Risks and complications

- Temporary urinary retention or infection.
- Possible need for repeat procedure if symptoms recur.
- Rare bleeding compared to TURP.
- Less effective in men with large prostates.
- It is still associated with about a 35% risk of ejaculatory dysfunction and can lead to irreversible ejaculatory dysfunction.
- Lack of extensive, high-quality studies with long-term outcomes.

Conclusions

- TUIP is best suited for younger men with smaller prostates who want symptom relief while minimizing risks to sexual function.
- It is less invasive than TURP but may not provide lasting relief in larger prostates.
- For men with significant obstruction and larger prostates, TURP or other modalities (laser incision, thermal therapy, or Urolift) for teaching or patient education?

Bipolar transurethral enucleation of the prostate (BTUEP)

BTUEP is a minimally invasive endoscopic surgery that removes obstructive prostatic adenoma within the capsule, offering a size-independent alternative to TURP and open prostatectomy for BPH.

Key points

- Definition: B-TUEP uses bipolar energy to enucleate the adenoma through the urethra, mimicking open simple prostatectomy but without external incisions.
- Indication: Effective for large prostate (>80 ml), but also applicable for small prostates (30-80 ml) as an alternative to TURP.
- Technique: The adenoma is dissected from the surgical capsule using bipolar current, then morcellated and removed transurethrally.

- Advantages: Lower bleeding risk, shorter catheterization, reduced hospital stay, and applicability across prostate sizes.
- Limitations: Requires advanced surgical expertise and specialized equipment.

Surgical technique

① Endoscopic access via the urethra. ② Identification of the surgical capsule and anatomical landmarks
③ Enucleation of adenoma using bipolar energy (like peeling the gland from its capsule).
④ Morcellation of tissue fragments inside the bladder.
⑤ Hemostasis is achieved with bipolar coagulation.

Clinical outcomes

- Symptom relief: Comparable to TURP and HoLEP with significant improvement in IPSS.
- Flow rates: Sustained improvement in Qmax (urinary flow)
- Complications: Lower transfusion rates, reduced risk of TUR syndrome (since bipolar energy uses saline irrigation) (Table 46).
- Re-treatment rates: Very low, like HoLEP.
- In a small RCT of 240 patients with prostates >80 mL, those who underwent BTEP had less anemia and greater symptom improvement at 24 months than those who underwent TURP. 37
- Removes more prostate tissue, has less blood loss, and shorter indwelling catheter time, and can treat a large prostate (Table 46)[255]

Table 46. Comparison of B-TUEP with other related techniques of BPH surgeries

SN Feature	TURP (Monopolar/ (Bipolar)	B-TUEP	HoLEP (Laser enucleation)	Open simple prostatectomy
① Prostate size suitability	Best for 30-80 ml	Any size, > 80 ml	Any size	>80-100 ml
② Bleeding risk	Moderate	Lower	Very low	Higher
③ Hospital stays	2-3 days	1-2 days	1-2 days	5-7 days
④ Catheterization time	2-3 days	1-2 days	1-2 days	5-7 days

Risks and Considerations

- Transient stress incontinence may occur postoperatively but usually resolves.
- Urethral stricture or bladder neck contracture are rare but possible.
- Surgeon expertise is critical- outcomes depend heavily on skill and experience.

Conclusion

B-TUEF is a versatile, safe, and effective surgical option for men with BPH across all prostate sizes. It combines the durability of open surgery with the minimally invasive benefits of endoscopy, making it a strong alternative to TURP and HoLEP in centers with experience.

Laser surgeries for BPH

Laser surgeries for BPH are minimally invasive procedures that use laser energy to remove or shrink prostate tissue, relieving urinary obstruction. The most established technique is Holmium Laser Enucleation of the Prostate (HoLEP), which is highly effective for large prostates and offers durable results. Laser surgery for BPH offers significant advantages over traditional surgery, such as reduced bleeding, shorter hospital stays, and a quicker recovery (Tables 47 and 48).

- HoLEP uses a holmium laser to remove the entire obstructive prostate adenoma, often considered a 'size-independent' gold standard. It provides tissue for histological analysis.
- GreenLight PVP uses a high-power laser to vaporize prostate tissue, creating a large cavity. This technique is often ideal for smaller to medium-sized prostates and is known for minimal blood loss.
- ThuLEP/ThuVAP (Thulium laser) is like HoLEP/PVP, but uses a thulium laser, which offers higher precision and efficacy in enucleation or vaporization, often with faster operating times.

Table 47. Comparison of different types of laser surgeries for BPH in men

SN	Method	Technique	Best for	Advantages	Limitations
①	Holmium Laser enucleation of of the Prostate (HoLEP)	Laser enucleates and removes obstructive tissue	Small to very large prostates	Removes more tissue than other methods; durable long-term relief; low retreatment rates	Requires specialized training; longer operative time
②	Photosensitive Vaporization (PVP/GreenLight Laser)	Vaporizes tissue using high-powered laser	Small to medium prostates	Less bleeding; shorter hospital stay; quicker recovery	Less effective for very large prostates; higher retreatment rates
③	Thulium Laser Enucleation (ThuLEP)	Similar to HoLep but uses thulium laser	Medium to large prostates	Precise cutting; reduced bleeding; comparable to HoLEP	Less widely available. long-term data still evolving.

Table 48. Comparing treatment options for BPH in men (*prostatelasercenter.com/bph/treatment-compariosn/)*

SN	Categories/requirements/side-effects	Laser focal therapy	TULSA-PRO*	TURP/ GreenLight	UroLift	Rezum
①	Minimally invasive	Yes	Yes	No	Yes	Yes
②	Low blood loss	Yes	Yes	No	Yes	Yes
③	Relatively low risk of retrograde ejaculation	Yes	Yes	No	Yes	Yes
④	Get to keep the prostate urethra	Yes	Yes	No	Yes	Yes
⑤	Requires general anesthesia	No	Yes	Yes	No	No
⑥	Results in the removal of excess tissue	Yes	Yes	Yes	No	Yes
⑦	Requires a surgical device to be inserted into the penis	No	Yes	Yes	Yes	Yes
⑧	Real-time image guidance during ablation	Yes	Yes	N/A	N/A	No

Holmium laser enucleation of the prostate (HoLEP)

Holmium laser ablation of the prostate (HoLAP), officially known as Holmium laser enucleation of the prostate (HoLEP), is a minimally invasive surgical procedure for BPH that uses a holmium laser to precisely 'peel out' obstructing prostate tissue through the urethra, creating a wide channel for urine flow, offering durable, potentially one-time solution with minimal bleeding and short recovery, suitable for all prostate sizes. The removed tissue is then morcellated (cut and flushed out) without incisions, using normal saline to eliminate the risk of TUR syndrome.

Historically, TURP has been considered the 'gold standard' for treating LUTS due to BPH. Contemporary literature indicates that HoLEP was developed in 1998 as a highly effective and safe surgical management for BPH in men, often considered a new 'gold standard' for its long-lasting outcomes, lower bleeding risk, and shorter hospital stays compared to traditional methods such as TURP.[256] A scope is inserted through the urethra, and the laser is used to peel the tissue away, which is then removed from the bladder via a separate instrument. This approach is practical for men with BPH, even for very large prostates, and is associated with less bleeding compared to traditional surgery. Laser-based endoscopic enucleation of prostate (EEP) is an efficient, safe, and feasible procedure even in very large prostates (PV>175, >200, and > 300 mL), with a retreatment rate of 0-1.3% in all studies involving prostate size ≥ 175 mL.[257]

What HoLEP involves

- Technique: A holmium laser is used to enucleate (peel away) obstructive prostate tissue, which is then removed from the bladder using a morcellator.[258]
- Goal: Relieve bladder outlet obstruction caused by enlarged prostate tissue.
- Duration: Typically, 2-3 hours, depending on prostate size.
- Hospital stays: Many patients are discharged within 24 hours; some procedures are performed on an outpatient basis.

Procedure

- HoLEP can be performed under general anesthesia and often requires an overnight hospital stay.
- The surgeon inserts a surgical instrument called a resectoscope through the urethra.
- The resectoscope includes a camera that allows the surgeon to view the prostate gland.
- The instrument inserts a laser into the resectoscope. It pulses laser beams into the prostate to cut the tissue that's blocking the flow of pee (a process called enucleation).
- Then they seal up the blood vessels with the laser.
- Then remove the laser from the resectoscope and replace it with a morcellator. This device suctions out the prostate tissue left behind in the bladder and removes it from the body.
- The surgeon will send pieces of prostate tissue to the lab for analysis to check for any abnormalities, such as prostate cancer.
- Once the tissue removal is complete, the surgeon removes the resectoscope and places a urinary catheter.

Systematic reviews

Multiple systematic reviews comparing HoLEP to other BPH surgeries, primarily TURP, including bipolar technologies, highlight several advantages and some trade-offs.[259-260]

a. Efficacy and long-term outcomes

- Symptom improvement: HoLEP provides significant and durable improvement in LUTS, maximum urinary flow rate (Qmax), and post-void residual (PVR) volume. Long-term follow-up studies (up to 10 years) show sustained symptom relief in about 75% of patients.
- Tissue removal: HoLEP typically removes more prostatic tissue than TURP, leading to a very low risk of repeat procedure for recurrent BPH symptoms (<1.0% recurrence rate reported in some long-term studies). The removed tissue can also be analyzed for incidental prostate cancer.
- Size-independence: HoLEP is effective for prostates of all sizes, making it a suitable option even for gigantic glands (80- 100mL), where traditional TURP may be less effective or require a more invasive open prostatectomy.
- Table 49 shows the comparison of HoLEP with other surgical procedures of BPH in men.

Table 49. Comparison of HoLEP with other procedures

SN	Features	HoLEP ()	TURP (Transurethral resection)	Open prostatectomy
①	Tissue removal	Complete enucleation, Suitable for large prostates	Partial resection, less effective for very large prostates	Complete removal, but invasive
②	Bleeding risk	Lower (laser cauterizes vessels)	Moderate	Higher
③	Hospital stay	Short (often <24 hours)	2-3 days	5-7 days
④	Catheter duration	Shorter (often <24 hours)	2-3 days	Longer
⑤	Recovery	Faster return to normal activities	Moderate	Slow
⑥	Durability	Long-lasting, low retreatment rates	Higher retreatment risk	Durable but invasive

b. Safety and recovery

- Reduced bleeding: HoLEP is associated with significantly less blood loss and a lower blood transfusion rate compared to TURP and open prostatectomy, making it safer for men on anticoagulant or antiplatelet therapy.
- Faster recovery: Patients undergoing HoLEP benefit from shorter hospital stays and reduced catheterization times. Many can go home on the same day or within 24 hours.
- Complications: HoLEP has a favorable safety profile with a low risk of serious complications. The main risk factor is transient urinary incontinence, which typically resolves within a few weeks to months.

c. Trade-offs

- Operative time: HoLEP procedures may have longer operative times than TURP, particularly during a surgeon's learning curve.
- Sexual function: The procedure causes permanent retrograde ejaculation (semen flows into the bladder during orgasm) in most men, which does not affect orgasm sensation but can impact fertility. Newer procedures like aquablation may offer better ejaculation.

Advantages

- Effective for all sizes: HoLEP removes more tissue than TURP, making it effective even for very large prostates (>100 g).
- Minimally invasive: No external incisions are needed, leading to faster recovery.
- Low bleeding: The laser coagulates blood vessels during treatment, significantly reducing blood loss and transfusion risk.
- Durability: Long-term studies show low retreatment rates comparable to those of open surgery.
- Safer irrigate: Uses normal saline, preventing dilutional hyponatremia (TUR syndrome)
- Tissue examination: The removed tissue can be sent for pathology to check for cancer.
- Power settings: Recent meta-analysis (2025) found that both low-power (20-50 W) and high-power (80-power (80-100 W) HoLEP were effective, with similar outcomes. Low power may be more cost-effective and versatile.

Risks and considerations

- Temporary urinary incontinence (common but usually resolves within weeks).
- Retrograde ejaculation (loss of semen during ejaculation, not harmful but affects fertility).
- Rare complications: Urethral stricture, bladder injury, or persistent irritative symptoms.
- Learning curve: HoLEP requires specialized training, and outcomes depend on the surgeon's expertise.

Risks and potential complications

- Possible risks include injury to the prostate, urethra, or bladder.
- There is a risk of infection or urinary incontinence.
- Urinary bladder overactivity symptoms may take several months to improve.
- Lower risk of transurethral reaction syndrome.
- Risks and potential complications depend on the surgeon's level of expertise.
- Higher risk of dysuria, retention, and repeat procedure compared with TURP.
- It has been shown to have similar risks of ejaculatory dysfunction as TURP.
- Lack of extensive, high-quality studies with long- term outcomes.

Practical guidance

- Patient selection matters: HoLEP is preferred for large prostates (>80-100 g), while GreenLight PVP is often chosen for smaller glands or patients on anticoagulation.
- Durability vs. Convenience: HoLEP offers the most complete tissue removal and the lowest retreatment rates, but PVP may be quicker with less bleeding risk.
- Local expertise: The availability of trained surgeons and equipment often determines which procedures are offered.

Conclusions

- HoLEP is best suited for men with moderate-to-severe BPH, especially large prostates or those at higher bleeding risk, and is increasingly favored over TURP or open surgery.
- Advantages include minimal invasiveness, durability, safety, and effectiveness across prostate sizes.
- Limitations require experienced surgeons; some sexual side effects are common.
- Choice of technique depends on prostate size, patient comorbidities, and local expertise.

Minimally invasive surgical treatments

Minimally invasive treatment options for BPH include the prostatic urethral lift procedure, water vapor thermal therapy, WVAT, Optlume® BPH, and temporary implantation of a nitinol device (Table 50).[261-263]

Prostatic urethral lift (UroLift® system)

The prostatic Urethral Lift (PUL), often known as the UroLift System, is a safe, minimally invasive procedure for BPH with LUTS that uses tiny permanent implants to lift and hold enlarged prostate tissue away from the urethra, creating a wider channel for urine flow without cutting, heating, or removing tissue. Uro-lift is a mechanical intervention that widens the anterior prostatic urethra by retracting the lateral lobes of the prostate using nitinol and stainless-steel implants.[264] It preserves sexual function (no erectile/ejaculatory issues). It offers quick recovery, making it great for younger men. However, it is less suitable for very large prostates or significant median lobes; however, studies show durable results and low retreatment rates in appropriate candidates.

Ideal patients for Uro-Lift

- Uro-Lift is FDA-approved for men older than 45 who have a prostate not too small or not too large (within 30-80 ml), with lateral lobes enlarged but no median lobe enlargement.[2]
- Men who wish to avoid medication side effects (like sexual dysfunction) and are averse to traditional surgery.[264] Value quick recovery and sexual function preservation.
- Fig. 9 shows a suggested pathway for determining whether patients are suitable candidates for the Uro-lift procedure. [265]
- Patients' selection criteria for Uro-lift are restricted to men >50 years old, prostate volume of 20-70 ml on ultrasound, IPSS >12, Q_{max} <15 ml s-1, and postvoid residual volume of <350 ml. [266]

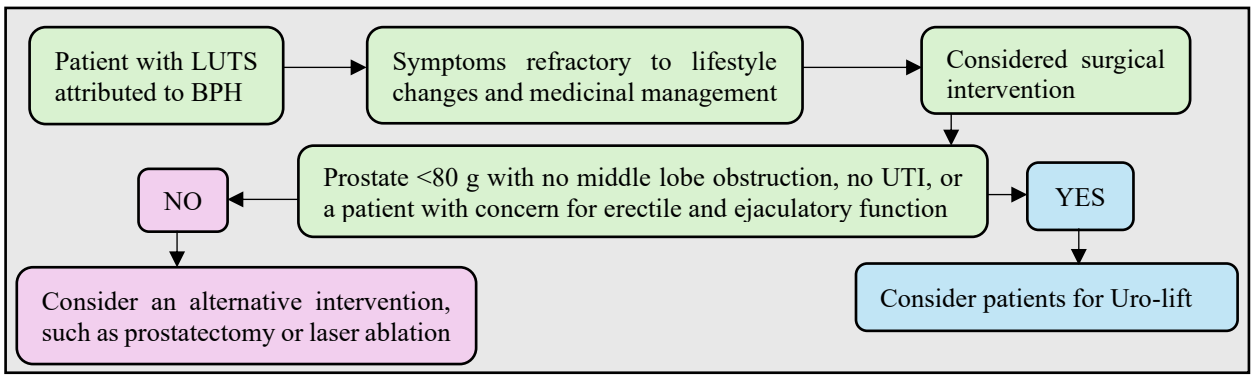

Fig. 9. Suggested pathway to Uro-lift for patients with LUTS secondary to BPH.[265]

Table 50. Comparison of UroLift system with other related BPH surgeries

SN	Feature	UroLift System	TURP (Resection)	Laser (HoLEP)/GreenLight	Medical therapy
①	Invasiveness	Minimally invasive	Moderately invasive	Moderately invasive	Non-invasive
②	Hospital stay	None (outpatient)	1-2 days	1-2 days	None
③	Sexual side effects	Rare	Common (retrograde ejaculation)	Common	Variable
④	Symptom relief	Moderate, rapid	Strong, durable	Strong, durable	Mild-moderate
⑤	Durability	5-7 years (may need retreatment)	Long-term	Long-term	Variable
⑥	Ideal candidates	Small-moderate prostates, no median lobe	Larger prostrate	Larger prostates	Early/mild symptoms

Limitations of Uro-Lift

- Uro-Lift is not recommended for men with a prostate larger than 100 ml and a history of urinary retention.[266]
- Prostates with an enlarged median lobe or prostate volume greater than 80 cc are not well suited for this treatment, which highlights the importance of diagnostic cystourethroscopy and prostate imaging (ultrasonography or cross-sectional imaging) to determine candidacy for the procedure.[241]
- It is also contraindicated in men with urinary tract infection (UTI), certain urethral conditions, urinary incontinence due to an incompetent sphincter (i.e., one that does not fully close), current gross hematuria, or known nickel, titanium, or stainless-steel allergies.
- It is necessary to begin by excluding any significant risk of prostate cancer by clinical examination, PSA testing, and MRI scanning if necessary.

Pre-operation examinations

Firstly, we need to evaluate the general health and take vitals- like temperature, pulse, and blood pressure, and secondly, tests or procedures to help determine the size of the prostate and the severity of the BPH.

a. Urine flow test- This test measures the speed and strength of the pee stream and measures the amount of pee.

b. Postvoid residual volume test- This test measures how much pee is still in the bladder after voiding.

c. Ultrasonography- A provider will take images of the prostate.

- Urinalysis (urine test)- A urine test evaluates how pee looks, as well as any chemicals that indicate bacteria in the urine (urinary tract infection; UTI). If an infection is present in the urine, it must be treated before the operation.

d. If the patients are taking aspirin, anti-inflammatory drugs, and certain herbal supplements, they should stop taking them at least six hours before the operation.

e. It is a good idea to wear clothes (hospital gowns) that are easy to take off during and after the operation.

f. Some surgeons use local, spinal, or general anesthetics. In contrast, some surgeons use a short period of intravenous sedation (propofol and midazolam) as a day case, making the procedure quick and painless with rapid recovery. [261,267]

g. A family member or friend should accompany them during the operation so that they can drive home after the operation.

Procedure

- Uro-lift is undertaken by implanting permanent monofilament implants under transurethral endoscopy to displace the lateral prostatic lobes to reduce urethral obstruction.
- The urologist places a urinary catheter to drain urine from the bladder.
- The device (guided by a cystoscope-miniature camera) is inserted into the urethra through a catheter, and the device then pushes the prostate tissue away from the urethra.
- A needle is then used to implant the device, which keeps the prostate tissue away from the urethra permanently. The implants are made of stainless steel, sutures, and a special metal called Nitinol, which has super-elasticity and shape memory. Typically, four to six implants are placed into the prostate, depending on the size and severity of side effects.
- A small, unblind RCT of 91 patients comparing prostatic urethral lift with TURP found greater preservation of ejaculatory function with prostatic urethral lift (100% vs. 61%; $p<0.0001$), but less improvement in total urinary tract symptoms. [268]
- It can be performed with local anesthesia, preserving erectile and ejaculatory function.

Post-operative care

- Paracetamol, ibuprofen, or naproxen can be prescribed for the first few days post-procedure.
- A broad-spectrum antibiotic is prescribed for three days post-operation
- Patients should also continue their alpha-blocker or 5α-reductase inhibitor for at least 2 weeks

postoperatively.

Advantages

- Minimally invasive- no cutting, heating, or removal of any prostate tissue.
- Rapid symptom relief, better than reported for medications.
- UroLift is superior to TURP in terms of recovery time and ejaculatory function.[264]
- Preserving sexual function helps avoid sexual side effects like erectile dysfunction or retrograde ejaculation, common with other BPH treatments. Retrograde ejaculation is when semen flows backward into the bladder instead of out through the penis.
- Day surgery- Often performed as an outpatient procedure (typically takes 30-60 minutes), allowing same-day discharge, and return to regular activity in days, not months.

Limitations and side effects

- The UroLift system procedure is not perfect, but it is better than pharmaceutical interventions. [267]
- Not for everyone; it may not be suitable for very large prostates (over 80g), those with a large median lobe (tissue growing into the bladder), or those with clotting disorders or antiplatelet/anticoagulation medications.
- Durability- benefits last year, but symptoms can return as BPH progresses, potentially requiring retreatment.
- Some increased urge to void and pelvic discomfort, which typically resolve within 2 to 4 weeks after the procedure.
- Trial data show the retreatment rate is 13.6% at five years (i.e., 2-3 per year; [269]), whereas the TURP retreatment rate is 1-2% per year.[267]
- Studies indicate that fewer than 14% of people who undergo UroLift require additional treatment after 5 years.
- Urologists may not be able to perform a Uro-lift in case of a huge prostate, a long urethra, and problems with urinary retention that prevent the urinary bladder from emptying when urinating.
- Other complications may include: (a) needing to pee more often, (b) Pain or discomfort when urinating, (c) Blood in urine (hematuria), and (d) Urinary tract infection. [270]
- Complications are generally temporary and include dysuria (25-53%), hematuria (16-75%), pelvic pain (3.7-19.3%), and need for post-operative catheterization (20-100%).[271] In addition, mal-positioned implants can lead to bladder irritation or the growth of bladder stones, which require another surgical procedure to manage.[272]
- Prostate cancer screening following a UroLift operation showed a significant increase in PSA from 1 month to 1 year (2.47-1.85 ng/ml) during the investigation period, compared with the preoperative median of 1.60 ng/ml. However, no prostate cancer was detected in patients with suspicious PSA trends. [273]

Outcome assessment of the Uro-Lift

No BPH treatment is without some discomfort or difficulties, or the expected symptoms following any endoscopic manipulation. Many men have minimal discomfort after UroLift treatment, though some will report pelvic discomfort, much like after a set of prostatic biopsies. Assessment is usually based on the accepted patient outcomes metrics of the IPSS, quality of life scores, and flow rates, as follows: [267]

a. A third of patients do ‘very well’- all are very happy.

b. A third of patients do ‘well’- the patient is satisfied and certainly happier than they were on drugs, and the patients are doing better in terms of flow rate.

c. A third of patients do not find the treatment effective, often due to:

- Some need for removal/repositioning of implants
- About a third of this group (±10% overall) requires more invasive treatments, such as bladder neck incision (BNI), TURP, or HoLEP. The need for more invasive treatment becomes evident within the first few weeks of the post-UroLift system procedure.

- These are men to consider for urodynamic testing.
- Table 51shows the comparison of minimally invasive surgical therapies for symptomatic BPH [263]

Table 51. Comparison of minimally invasive surgical therapies for symptomatic BPH [263]

SN	Parameters	Water vapor thermal ablation	Prostatic urethral lift (Uro-lift)	Optilume® BPH	Temporarily implanted nitinol device (iTind™)
①	Availability of published data	5 years	5 years	12 months	12 months
②	Recommended Prostate size	30 to 100 cm3	30 to 80 cm3	30 to 60 cm3	25 to 75 cm3
③	Suitable for obstructive median	Yes lobes	No	No	No
④	Symptom relief	Improvement in 2 to -4 Weeks, duration to 5 yrs	Improvement in 2 weeks; durable to 5 years	Improvement in 3 months, sustained at 12 months	Improvement in 3 months, sustained at 12 months
⑤	Retreatment rate	4.4% at 5 years	13.6% at 5 years	Not available	6.5% at 2 years

Most men undergoing PUL require ongoing medical and/or surgical management for BPH.[274] Patients undergoing UroLift were discharged from recovery in 97% of cases, with 29% discharged with indwelling or intermittent catheterization. The rate of 30-day complications was 18%, with 89% graded Clavien I-II. Unplanned emergency room or clinic visits within 30 days of the procedure occurred in 14% and 17% of men, respectively, with 4% requiring hospital readmission. In follow-up, α-blockers and/or 5α-reductase inhibitors were continued or initiated post-operatively for 44% of men; 20% of men required repeat surgical intervention at a mean of 19.2 months, consisting of repeat PUL (30%), TURP (28%), or thulium laser enucleation (18%). Overall, 53% of men needed medication and/or repeat surgery for BPH following PUL, and this was independent of age, race, prostate volume, intravesical prostate protrusion, baseline IPSS and QOL, stricture, number of implants used, or a history of urinary retention. [274]

Transurethral microwave therapy (TUMT)

TUMT is a minimally invasive outpatient procedure that uses microwave energy to heat and destroy excess prostate tissue, relieving urinary obstruction in men with BPH. It is generally reserved for patients with moderate symptoms who are poor candidates for surgery.

Key features of TUMT

- Mechanism: A catheter with a microwave antenna is inserted into the urethra. Controlled microwave energy heats prostate tissue, causing coagulative necrosis and shrinkage.
- Setting: Performed on an outpatient basis, usually under local anesthesia or mild sedation.
- Duration: Typically, 30-60 minutes.
- Recovery: Patients can go home the same day; a temporary urinary catheter is often required for 3-7 days.

Advantages

- Minimally invasive: No surgical incision, lower risk compared to TURP or open prostatectomy.
- Safety: Suitable for men with significant comorbidities who cannot undergo major surgery.
- Symptom relief: Improves lower urinary symptoms (frequency, urgency, weak stream).
- Reduced bleeding risk: No cutting of tissue, so bleeding complications are rare.

Limitations and risks

- Efficacy: Symptom improvement is less pronounced and less durable compared to TURP. Retreatment rates are higher.
- Catheter dependence: Temporary catheterization is common due to post-procedure swelling.
- Side effects: Burning sensation, urinary urgency, hematuria, or urinary tract infection.
- Not ideal for very large prostates (>80 ml): Effectiveness decreases with larger prostate size.
- Cochrane systematic review of six RCTs comparing transurethral microwave therapy with TURP found

similar reduction in urinary symptoms, with transurethral microwave therapy having fewer significant adverse effects (number needed to treat = 8.95% Cl, 7 to 11) but with a higher risk of retreatment in one year (number needed to harm = 12; 95% Cl, 7 to 25; relative risk = 0.2; Cl, 0.09 to 0.43).[275]

- Outpatient procedure, Lower risk of erectile and ejaculatory dysfunction, strictures, incontinence, and blood transfusions compared with TURP.
- High retreatment rate compared with TURP (relative risk= 7.07; 95% Cl, 1.94 to 25.82) (Table 52)
- Increased risk of acute urinary retention (relative risk = 2.61; 95% Cl, 1.05 to 6.47).

Table 52. Comparison of TUMT with other related BPH surgical treatments

SN	Feature	TUMT	TURP (Gold standard)	HoLEP/GreenLight
①	Invasiveness	Minimally invasive	Moderately invasive	Minimally invasive
②	Symptom relief	Moderate	Strong, durable	Strong, durable
③	Hospital stay	Outpatient	1-3 days	Outpatient or 1 day
④	Catheterization	3-7 days common	1-2 days	1-2 days
⑤	Bleeding risk	Very low	Moderate	Very low
⑥	Retreatment rate	Higher	Low	Low
⑦	Best for	Frail patients, comorbidities	Fit patients needing durable relief	Wide range, including large prostates

Clinical role

- Indicated for: Men with moderate LUTS due to BPH, especially those unfit for surgery.
- Not first-line: Considered when medical therapy fails, but surgery is too risky.
- Long-term outcomes: Provides symptom relief but often requires repeat treatment or transition to surgical options later.

Transurethral (Robotic) water-jet ablation (TWJA)

TWJA (Aquablation) is a minimally invasive, heat-free surgical option for men with BPH, offering precise tissue removal with reduced risk of sexual side effects compared to traditional techniques. Guided by real-time ultrasound and endoscopic imaging, the system maps the prostate and directs the water jet with millimeter precision. Unlike TURP or laser procedures, this procedure does not use heat or cautery, minimizing collateral damage to surrounding structures (Table 53).

Place in therapy

Aquablation is positioned as an alternative to TURP or laser surgery for men with moderate-to-severe LUTS due to BPH, especially those: (a) Concerned about sexual side effects, (b) With large or irregularly shaped prostates, and (c) Seeking a robotically standardized procedure.

Table 53. Comparison of evidence and outcome of TWJA (aquablation) with other methods

SN	Features	Aquablation	TURP (Gold standard)	Laser (HoLEP/GreenLight)
①	Mechanism	Heat-free water jet	Monopolar/Bipolar Electrocautery	Laser vaporization/ enucleation
②	Precision	Robotic, ultrasound guided	Surgeon dependent	Surgeon dependent
③	Sexual side effects	Lower risk of retrograde ejaculation	High (up to 65-75%)	Moderate
④	Symptom relief (IPSS)	Comparable to TURP	Excellent	Excellent
⑤	Prostate size suitability	Small to very large (>80-100 cc)	Best <80 cc	Best <100 cc
⑥	Hospital Stay	Short (often <24 hours)	1-2 days	1-2 days
⑦	Learning curve	Shorter (robot assists)	Moderate	Strep

How it works

① Patient under anesthesia; a transurethral probe is inserted.

② Ultrasound mapping creates a 3D image of the prostate.
③ Robotic guidance ensures consistent, reproducible tissue removal.
④ High-pressure water jet ablates targeted tissue in minutes
⑤ Hemostasis is achieved with minimal cautery if needed.

Advantages

- Heat-free- less collateral damage
- Effective for large prostates
- Shorter operative time and hospital stay
- Robotic precision- reproducible outcomes
- Lower rate of sexual dysfunction

Limitations and Risks

a. TWJA is considered not medically necessary as a treatment of BPH for individuals meeting the following criteria:

- International Prostate Symptom Score (IPSS) of ≥12.
- Failure or inability to tolerate maximally titrated medical therapy (α1-adrenergic antagonists, 5α-reductase inhibitors, or combination medication therapy) over a trial period of no less than 3 months.
- Imaging shows the prostate gland volume is greater than 30 ml and less than or equal to 80 ml.
- The individual does not have any of them: active treatment for urinary tract infection, active treatment for prostatitis, or known or suspected prostate cancer.

b. Availability and cost: Requires a specialized robotic system, not widely accessible.
c. Bleeding risk: Slightly higher than laser techniques; may need adjunctive cautery.
d. Long-term data: Still emerging compared to TURP/HoLEP.
e. Training: Surgeons need familiarity with robotic workflow.

- Cumulative adverse events occurred in 25.9% of the water-jet ablation group vs. 41.5% of the TURP group ($p<0.02$). [276]

Transurethral needle ablation (TUNA)

TUNA is a minimally invasive procedure for BPH that uses radiofrequency energy delivered through needles inserted into the prostate to shrink obstructing tissue and relieve urinary symptoms. It is typically performed under local anesthesia on an outpatient basis and offers an alternative to more invasive surgeries like TURP.

Key features of TUNA

Use of a special catheter that incorporates needles to deliver low-level radio-frequency power to a localized area of the prostate.

a. Mechanism: Radiofrequency energy generates heat, causing thermal necrosis of targeted prostate tissue. The treated tissue later resorbs, reducing urethral compression.
b. Procedure:

- Performed via a cystoscope inserted through the urethra.
- Two needles are deeply inserted into the prostate tissue.
- It takes about 1 hour; tissue resorption occurs over ~30 days.

c. Setting: Outpatient, usually under local anesthesia.
d. Target group: Men with moderate BPH symptoms who prefer minimally invasive options or are poor candidates for major surgery.

- A systematic review of 4 RCTs comparing transurethral needle ablation with TURP (450 patients) found a smaller improvement in IPSS scores (mean difference = 3.9; 95% CI, 1.27 to 6.63) with transurethral needle ablation (Table 54). [277]
- Reduced risk of blood transfusions, strictures, and incontinence compared with TURP. (Table 54)

Advantages

- Outpatient procedure, quick recovery.
- Lower risk of bleeding compared to TURP.
- Preserves sexual function better than resection in many cases.

Table 54. Comparison of TUNA with other related BPH surgical therapies

SN	Feature	TUNA	TURP	Laser ablation	Medical therapy
①	Invasiveness	Minimally invasive	Moderately invasive	Minimally invasive	Non-invasive
②	Anesthesia	Local	Spinal/general	Local/Spinal	None
③	Hospital stays	Outpatient	1-3 days	Outpatient/Short stay	None
④	Symptom relief	Moderate	Strong	Strong	Mild-moderate
⑤	Durability	Less durable, retreatment possible	Long-lasting	Long-lasting	Requires ongoing use
⑥	Complications	Lower risk of bleeding retrograde ejaculation is less common	Higher bleeding risk, retrograde ejaculation	Variable	Drug side effects

- Suitable for patients with comorbidities who cannot tolerate major surgery.

Limitations and risks

- Efficacy: Symptom relief is less robust than with TURP or other therapies; retreatment rates are higher.
- Delayed effect: Tissue resorption takes weeks, so improvement is gradual.
- Durability: Long-term outcomes show higher recurrence rates than with TURP.
- Complications: Possible urinary tract infection, transient dysuria, or urinary retention.

Clinical context

- TUNA is best suited for men with moderate BPH symptoms, smaller prostate volumes, and those seeking a balance between efficacy and safety.
- It is less favored today than newer minimally invasive techniques (e.g., Rezum, UroLift), but it remains an option when these are unavailable or contraindicated.

Prosthetic arterial embolization (PAE)

PAE is a minimally invasive, image-guided procedure used to treat bothersome urinary symptoms in men with BPH. It works by reducing blood flow to the prostate, causing it to shrink and relieving obstruction.

Indication

- Men with moderate-to-severe LUTS due to BPH, especially those who are poor surgical candidates or wish to avoid traditional surgery.
- Table 55 shows the comparison between PAE and TURP in the treatment of BPH in men

Procedure

- Performed by an interventional radiologist using fluoroscopy or CT angiography.
- Tiny particles are injected into prostatic arteries to block the blood supply.

Advantages

- Minimally invasive, no general anesthesia required.
- Lower risk of sexual side effects (retrograde ejaculation, erectile dysfunction) compared to TURP or open surgery. Shorter recovery time

Table 55. Comparison between PAE and TURP in the treatment of BPH in men

SN	Feature	PAE (Prostatic artery embolization)	TURP (Transurethral resection of prostate)
①	Invasiveness	Minimally invasive, catheter-based	Endoscopic surgery
②	Anesthesia	Local plus sedation	Spinal or General
③	Hospital stay	Often outpatient or 1 night	2-3 nights
④	Symptom relief	Significant, but slightly less than TURP in most trials.	Strong, durable relief
⑤	Sexual side effects	Rare (low risk of retrograde ejaculation (RE)	Common (RE up to 65-75%)
⑥	Complications	Minor (UTI, transient hematuria, groin hematoma	Bleeding, TUR syndrome, strictures
⑦	Durability	Good medium-term (3-5 years data)	Long-term proven (>10 years)

Limitations

- Technically demanding due to variable prostatic arterial anatomy.

- Not universally available, it requires specialized centers.
- Long-term durability of outcomes is still under study.
- A Cochrane review of six RCTs and two observational studies comparing prostatic arterial embolization with TURP found no clear differences in IPSS or quality of life, and no significant adverse events. Not currently recommended because of worse symptom outcomes compared with other available procedures.[278]

Risks and challenges

- Technical difficulty: Arterial anatomy varies; risk of non-target embolization (e.g., bladder, rectum)
- Complications: Post-embolization syndrome (pelvic pain, dysuria, low-grade fever), rare ischemic injury.
- Evidence base: Randomized controlled trials show PAE improves IPSS, and quality of life, but TURP remains superior in maximum urinary flow rate (Qmax) improvement.

Practical considerations

- Ideal candidates: Men with large prostates (>80 mL), high surgical risk, or those prioritizing preservation of sexual function.
- Not suitable for: Patients with severe arterial disease, uncorrectable coagulopathy, or very small prostates.
- Outlook: PAE is gaining acceptance as an alternative, especially in centers with strong interventional radiology expertise. Ongoing trials are refining patient selection and long-term outcomes.

Prognosis

- The American Urological Association recommends using the IPSS to follow improvement and progression. [77]
- Despite lower urinary symptoms from BPH affecting approximately two of every three men 50 years or older, only one-third of affected men seek treatment, and only a small number require procedural interventions. [249]
- BPH is associated with a four times higher prostate cancer risk and a three times higher bladder cancer risk. Prostate cancer screening guidelines are not affected by the presence of BPH. [279,280]

Conclusions

- PAE offers a promising, less invasive option for BPH management. particularly for men who want to avoid surgery or preserve sexual function. However, TURP remains the gold standard for maximum symptom relief and long-term durability.
- Several minimally invasive surgical procedures have fewer adverse effects than TURP, but many lack high-quality data or have higher retreatment rates. However, many minimally invasive surgical therapies are office-based procedures that do not require general anesthesia or discontinuation of anticoagulation.
- For small-sized prostates (<30 mL), TURP or the minimally invasive transurethral incision of the prostate should be considered. [231]
- For large-sized prostates (>80 mL), simple prostatectomy is recommended over TURP. Bipolar transurethral enucleation of the prostate or holmium laser enucleation of the prostate are less invasive alternatives to prostatectomy. [281]

Simple prostatectomy: Robotic or open approach

Robotic simple prostatectomy generally offers less blood loss, shorter hospital stays, and faster recovery compared to open surgery, but open prostatectomy remains effective, especially for very large prostates or where robotic expertise/resources are limited. The choice depends on patient factors, prostate size, surgeon experience, and hospital availability. Table 56 presents a comparative overview of robotic and open simple prostatectomy.

Procedure

- These procedures involve a surgical incision and opening the prostate either from its anterior surface or through the bladder (after opening the bladder too).

Table 56. Comparative overview between robotic and open simple prostatectomy

SN	Feature	Robotic simple prostatectomy (RASP)	Open simple prostatectomy (OSP)
①	Surgical approach	Minimally invasive, small incisions, robotic Arms controlled by surgeon	Large lower abdominal incision, direct manual removal
②	Blood loss	Significantly reduced; lower transfusion rates	Higher risk of bleeding; transfusions more common
③	Hospital stay	Shorter (2-3 days typical)	Longer (5-7 days typical)
④	Post-operative pain	Less pain due to smaller incisions	More pain, slower mobilization
⑤	Recovery time	Faster return to normal activity	Slower recovery, longer convalescence
⑥	Complications	Lower rates of infection, wound issues	Higher risk of wound infection, hernia, long catheterization
⑦	Functional outcomes	Comparable urinary symptom relief; some studies suggest better continence recovery.	Effective symptom relief, but higher Morbidity.
⑧	Prostate size suitability	Excellent for large prostate (>80-100 g)	Traditionally preferred for very large prostate (>100 g)
⑨	Surgeon factor	Requires robotic expertise and access to technology	Widely available; less dependent on advanced equipment
⑩	Cost	Higher (robotic systems, consumables)	Lower upfront cost

- The surgeon peels out the hyperplastic tissue (transitional zone) from within the peripheral zone of the prostate, similar to what is done in holmium laser enucleation of the prostate.
- Advances in robotic surgery have improved visualization of the operative field, reduced blood loss, enabled smaller incisions, shortened hospitalization, and improved recovery.
- Depending on the surgical approach (extraperitoneal, transvesical, or transperitoneal), patients typically remain hospitalized for 1 to 3 days and have a Foley catheter for 5 to 10 days postoperatively.
- The single-port robotic platform has enabled some surgeons to do prostatectomies as same-day surgeries and remove the catheter 3 days later. [278]

Key evidence

- Robotic advantages: Meta-analyses show RASP reduces blood loss, transfusion rates, and hospital stay compared to OSP.
- Open surgery risks: OSP is associated with higher rates of bleeding, infection, and longer recovery.
- Functional outcomes: Both approaches provide excellent relief of LUTS due to BPH, with similar long-term efficacy.
- Limitations: Robotic surgery requires specialized equipment and trained people; cost and access may be limiting factors.

Risks and considerations

- Robotic: Higher cost, limited availability in resource-constrained settings, steep learning curve.
- Open: Greater morbidity, longer recovery, but may be more practical where robotic systems are available.
- Patient factors: Age, comorbidities, prostate size, and prior surgeons should guide the choice.
- Surgeon experience: Outcomes depend heavily on the surgeon's skill with either technique.

Complications

- The main complications are retrograde ejaculation and hemorrhage requiring blood transfusion. Stress incontinence, erectile dysfunction, bladder neck contracture, and transient urinary urgency and frequency with urge incontinence, which is seen after many procedures for BPH.[279,280]
- Whether performed open or robotically, it is a definitive and durable treatment.
- Radical prostatectomy after HoLEP is feasible, safe, and ontologically sound when performed by experienced surgeons in specialized centers. [282]

Conclusions

If robotic expertise and resources are available, robotic simple prostatectomy is generally preferred for its safety and recovery advantages. However, open surgery remains a reliable option- especially in large

prostates or settings where robotic systems are not accessible.

Comparative efficacy of BPH surgery

Transurethral resection of the prostate (TURP) remains the gold standard for BPH surgery, but laser therapies (HoLEP, GreenLight), minimally invasive thermal/electro-vaporization techniques, and open/simple prostatectomy each have distinct advantages and trade-offs depending on prostate size, patient comorbidities, and desired outcomes (Table 57).

TURP is the gold standard operative treatment in mild to moderate enlargement of the prostate (30-80 mL). However, in large prostates, TURP has a higher rate of morbidity, complications, and repeated procedures. This is due to the development of transurethral resection syndrome (TURS) when the TURP procedure is prolonged. Moreover, many complications caused by the TURP procedure include sexual dysfunction, retrograde ejaculation, recurrent urinary retention, and urethral stricture. [283,284]

Randomized controlled trials comparing vaporization, resection, and enucleation of the prostate using monopolar, bipolar, or various laser systems (holmium, thulium, potassium titanyl phosphate, or diode) as surgical treatments for BPH in men. Eight endoscopic surgical methods for BPH appeared to be safer than monopolar TURP. Among these treatments, enucleation methods showed better Qmax and IPSS values than vaporization and resection methods.[229]

Table 57. Comparison of office-based procedures for BPH, compared with transurethral resection

SN	Treatment	Trans-urethral resection of the prostrate	Prostatic urethral lift procedure	Water vapor thermal therapy	Temporary inserted nitinol device
1.	Surgery type	Cytoscopic electric excision	Cystoscopic placement of suture to open the urethra	Cystoscopic application of steam to ablate the prostate	Cystoscopic placement of a temporary urethral stent
2.	Operating setting	Operating room	Office	Office	Office
3.	Anesthesia	General or spinal	Local, sometimes with sedation	Local, sometimes with sedation	Local, sometimes with sedation
4.	Ideal prostrate size	≤80 ml (sometimes a bit larger)	≤80 ml with no median lobe enlargement	≤80 ml (sometimes a bit larger)	<75 ml, with no median lobe enlargement
5.	Contraindi-cations	Anticoagulation Elevated bleeding risk Narrow urethra	Large median lobe High bladder neck Allergy to implant	Fibrotic gland (due to prior procedure for prostatic hyperplasia or radiation	Large median lobe Large gland Fibrotic gland
6.	Advantages	Historical gold standard Widely accessible	Preserves sexual function	Preserves sexual function	Preserves sexual function
7.	Postoperative catheter time	1-3 days	None (some cases)	3-7 days	None
8.	Durability	Good	Poor	None	None
9.	Erectile dysfunctions	Unknown	None	None	None
10.	Unique Complications	Electrolyte abnormalities (transurethral resection syndrome)	Expected retreatment Bladder stones	Transient retention from prostate edema	Dislodgement or migration

A systematic meta-analysis of the comparative effectiveness and safety of TURP, HoLEP, and Rezum for BPH found that both HoLEP and TURP significantly improved IPSS and Qmax. In contrast, Rezum improved symptoms to a lesser extent than TURP and HoLEP. Rezum preserved sexual function, especially ejaculation, significantly ($p<0.001$) better than TURP and HoLEP. [285]

The enucleation technique allows standard HoLEP (S-HoLEP) to be used on all prostate sizes with reasonable safety, efficacy, and durability. Accordingly, it is the recommended standard therapy for the

management of BPH in large prostates. However, currently, the use of S-HoLEP is still considered suboptimal due to a steep learning curve, prolonging the procedure, causing higher intraoperative bleeding, and increased complications.[284,286,287] Moses' laser technology, developed by Lumenis, splits the laser beam into two. The first energy wave separates the water by forming a bubble cavity, and the second wave transfers laser energy directly from the bubble cavity to the target. These mechanisms were believed to increase the efficacy of the HoLEP procedure. [286,288]

Moses HoLEP (M-HoLEP) showed superiority compared to standard HoLEP, especially M-HoLEP, which significantly provided shorter enucleation time, shorter hemostasis time, and shorter laser use time. M-HoLEP had a significantly lower postoperative PVR and a significantly higher complication rate than S-HoLEP. However, there were no safety issues in M-HoLEP compared with S-HoLEP.[287]

Success rates for S-HoLEP, TURP, and PVP were 67.6%, 65.4%, and 34.1%, respectively, and the S-HoLEP and TURP groups did not differ significantly. Regression analysis revealed that prostate volume ≥ 50 mL and bladder outlet obstruction index (BOOI) of ≥40 were independent factors predicting S-HoLEP success.[289]

The TriNet X, a third-party database, was used to investigate the incidence of surgical reintervention following PUL, TURP, and PVP procedures in male patients aged 18-100 years with BPH from 2015 to 2019, and have found that the highest reintervention rates were for PUL of 16.1% at four year of follow-up, compared with 7.8% and 7.5% for those who had TURP and PVP, respectively.[290] The cumulative procedure rate for UroLift at four years was twice that of TURP and PVP. UroLift might be a suitable option for those who desire symptomatic relief from BPH with minimal erectile and ejaculatory side effects in appropriate patients. However, the re-procedure rate should be considered when selecting a surgical treatment modality for men with BPH.[290]

Table 58 presents the comparison of operating room-based surgeries other than transurethral resection for BPH.[241] Table 59 shows the summary of comparative efficacy of the major surgical options for BPH in men, and Table 60 presents the comparative evaluation of major surgical therapies for BPH in men.

Table 58. Comparison of operating room-based surgeries other than transurethral resection for BPH[241]

SN	Treatment	Photo-selective vaporization of prostrate	Holmium laser enucleation of the prostate	Simple prostatectomy	Robotically controlled water jet treatment
1.	Surgery type	Cytoscopic laser Vaporization	Cytoscopic laser excisions	Abdominal excision	Cytoscopic water jet ablation
2.	Operative setting	Operating room	Operating room	Operating room	Operating room
3.	Anesthesia	General or spinal	General or spinal	General or spinal	General or spinal
4.	Ideal prostrate aize	≤100 ml (sometimes larger)	≤250 ml	>80 ml, with or without concomitant Pathology+	≤150 ml
5.	Contraindi-cations	Prior radiation	Not available	Anticoagulation, elevated bleeding risk	Anticoagulation, elevated bleeding risk
6.	Advantages	Excellent hemostasis Small caliber scope	Size-independent Durable results	Done under vision (robotic) Durable results	Preserve sexual function 1-5 days
7.	Postoperative catheter time	1 day	1 day	5-10 days	
8.	Durability	Good	Excellent	Excellent	Unknown
9.	Erectile Dysfunction	Rare	Unknown	Unknown	None
10.	Unique Complications	Obstruction from sloughed tissue Passage	Bladder injury from morcellator	Risks of surgical incision Risks of intra-abdominal surgery	Unknown

Table 59. Summary of comparative efficacy of the major surgical options for BPH in men

SN	Method	Best for	Mechanism	Advantages	Risks/Limitations
①	Transurethral Resection of Prostrate (TURP)	Moderate size prostates	Resection of obstructing tissue via resectoscope	Long-standing Gold standard, effective for symptom relief	Bleeding, retrograde ejaculation, TUR syndrome
②	Open/Robotic Simple Prostatectomy	Very large prostate (>80-100 g)	Enucleation of adenoma via open or robotic approach	Best for massive glands, durable relief	More invasive, longer recovery, higher bleeding risk
③	Laser Therapies (HoLEP, Green-Light, PVP)	Small to very large prostates	Laser vaporization or enucleation	Less bleeding, safe for anti-coagulated patients, durable	Steeper learning curve, transient irritative symptoms
④	Prostatic Urethral Lift (UroLift)	Small-moderate prostates, men desiring sexual preservation	Implant retract lobes to open urethra	Minimally invasive, preserves ejaculation	Less effective for very large prostates or median lobe, risk of needing repeat surgery.
⑤	Water Vapor Therapy (Rezum)	Small-moderate prostates	Steam ablation of tissue	Office-based, preserves sexual function	Delayed symptom relief, transient irritative symptoms
⑥	Aquablation	Moderate-large prostates	Robotic waterjet resection	Precise, shorter operative time	High bleeding risk, availability limited.
⑦	Transurethral Vaporization/ Incision (TUVP/TUIP)	Small prostates (< 30g)	Vaporization or incision of of the bladder neck	Shorter procedure, less bleeding	Less durable relief, not for large glands

Table 60. Comparative evaluation of major surgical therapies for BPH in men

SN	Therapy	Best prostate size	Symptom relief	Bleeding risk	Retreatment rate	Hospital stay
①	TURP	30-80 mL	High	Moderate	Low	2-3 days
②	HoLEP	Any size, >100 mL	Very high	Very low	Very low	1-2 days
③	GreenLight PVP	<80 mL	Moderate-high	Very low	Moderate	Outpatients
④	Thermal/Electro-vaporization	<60 mL	Moderate	Low	High	Outpatients
⑤	Open/Robotic prostatectomy	>150 mL	Very high	High (open) Moderate (Robotic)	Very low	5-7 days (open) 2-3 days (robotic)

Decision factors

- Prostate size: TURP for moderate, HoLEP or open /robotic prostatectomy for very large glands.
- Comorbidities: Laser therapies are safe for patients on anticoagulants.
- Sexual function preservation: UroLift and Rezum are preferred if avoiding retrograde ejaculation is a priority.
- Durability vs. invasiveness: TRUP and HoLEP offer long-term relief but are more invasive than office-based therapies.

Risks and trade-offs

- Bleeding and transfusion risk: Higher in TURP and open surgery.
- Retrograde ejaculation: Common after TURP and laser procedures, less with UroLift/Rezum.
- Urinary incontinence: Rare but possible, especially with enucleation procedures.
- Retreatment rates are higher with minimally invasive therapies than with TURP/HoLEP.

Practical guidance

- Mild-moderate symptoms: Consider minimally invasive (UroLift, Rezum).

- Large prostates (>80 g): HoLEP or Simple prostatectomy
- Patients on anticoagulation: Laser therapies (HoLEP, GreenLight)
- Sexual preservation priority: UroLift or Rezum

Key Considerations and Risks

- Patient comorbidities: Anticoagulated patients benefit from laser therapies.
- Prostate size: Larger prostates favor HoLEP or open /robotic approaches.
- Durability vs Invasiveness: TURP and HoLEP offer long-term relief; minimally invasive options trade durability for safety.
- Resource availability: Advanced lasers and robotics may not be accessible in all centers.

Surgical management of BPH is highly individualized. TURP remains the benchmark, but HoLEP and minimally invasive therapies are increasingly favored for specific patient groups. The decision should balance prostate size, comorbidities, and patient preference.

In practice, TURP remains the benchmark, but HoLEP is increasingly preferred for large prostates due to superior safety and durability. GreenLight PVP is excellent for fragile patients, while open/robotic prostatectomy is reserved for very large prostates.

Conclusion of BPH therapy

Several options exist for the medical management of BPH, and choices are influenced by indications, efficacy, and side effects (Fig. 10).[78]

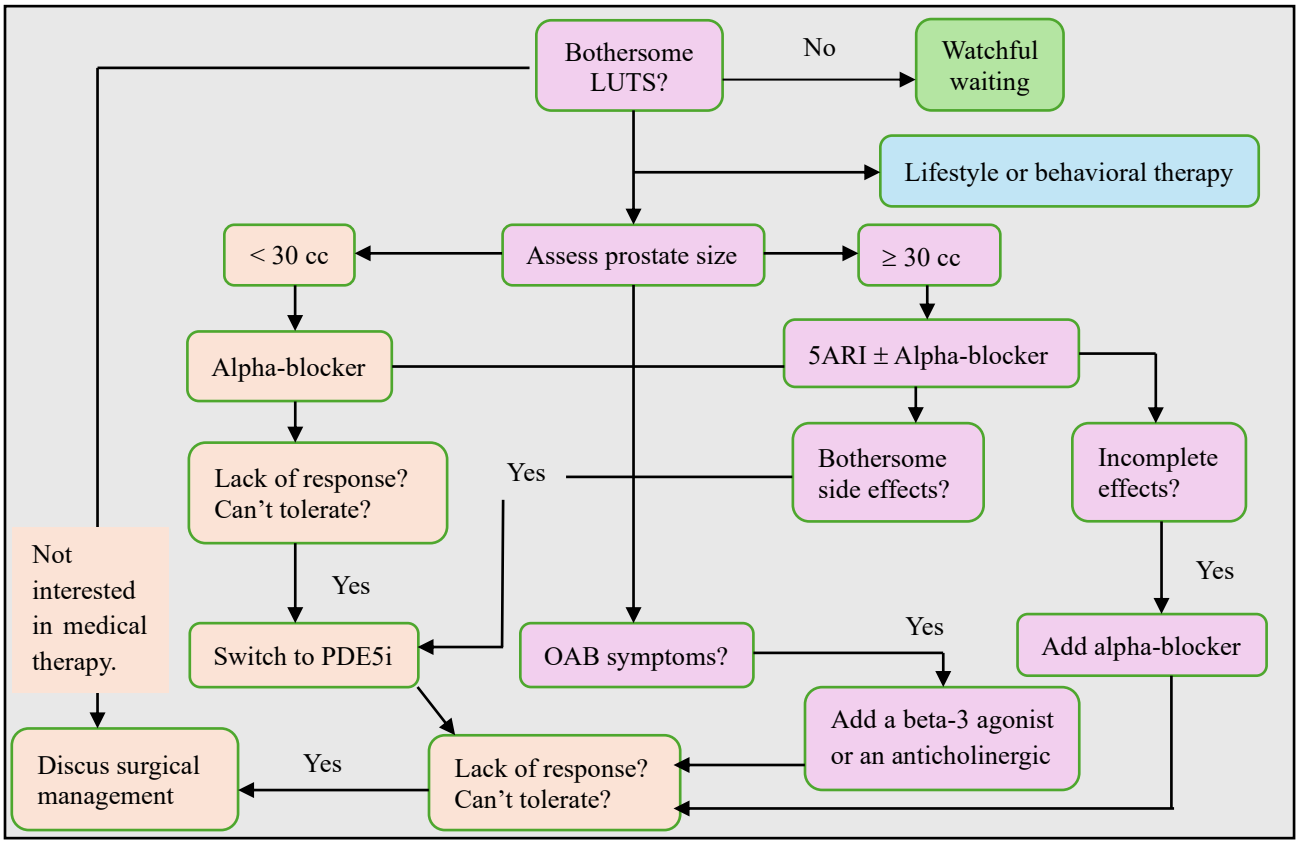

Fig. 10. Algorithmic approach to medical management of benign prostatic hyperplasia.
5ARI = 5-alpha reductase inhibitors; LUTS = Lower urinary tract symptoms; OAB = Overactive bladder
PDE5i = Phosphodiesterase-5 inhibitor

Prostate cancer

BPH and prostate cancer are distinct conditions that often coexist in aging men. While they share risk factors such as age and hormonal changes, BPH itself does not directly cause prostate cancer. However, men with BPH may undergo more frequent urological evaluations, which can increase prostate cancer detection tests.

- BPH: Non-cancerous enlargement of the prostate gland, common in men over 50. It causes LUTS such as weak stream, nocturia, and incomplete emptying.
- Prostate cancer: Malignant growth of prostate cells, the most common cancer in men worldwide. It ranges from indolent tumors to aggressive disease.

Relationship between BPH and Prostate cancer

- No direct causal link: Current evidence suggests BPH does not increase the risk of developing prostate cancer. The two conditions can coexist because they share common risk factors (aging, genetics, hormonal influences) (Table 61)
- Detection bias: Men with BPH often undergo PSA testing, biopsies, or imaging, which may lead to higher detection rates of prostate cancer.
- Inflammation hypothesis: Some studies propose that chronic inflammation in BPH tissue may contribute to carcinogenesis, but findings remain inconclusive.

Table 61. Role of shared risk factors between BPH and prostate cancer

SN	Factor	Role in BPH	Role in prostate cancer
①	Age	Prevalence rises after 50 years	Strongest risk factor
②	Hormones (Testosterone/DHT)	Drives prostate enlargement	Fuels cancer growth
③	Genetics/Family history	May predispose to BPH	Increases cancer risk
④	Lifestyle/Environment	Obesity, diet, metabolic syndrome	Same influences linked to cancer

Clinical implications

- Symptom overlaps: Both conditions can cause LUTS, making differentiation challenging.
- Screening: PSA elevation can occur in both BPH and cancer, complicating diagnosis.
- Counseling: Patients should be reassured that BPH is not precancerous, but vigilance is still needed, given overlapping risk factors.

Key takeaways for practice

- BPH and Prostate cancer: They are separate diseases, though they often coexist.
- Shared risk factors explain coexistence: Age, hormones, and genetics drive both conditions.
- Clinical vigilance is essential: Men with BPH should be monitored but not assumed to be at higher cancer risk solely due to prostate enlargement.

Prostate cancer is one of the malignancies that affects men of all racial and ethnic groups and leads to higher rates of mortality in men globally, mainly belonging to a lower socioeconomic status, due to late detection of the disease.[291]

Prostate cancer remains the most common cancer among men, and it is often slow growing. However, it can be aggressive, diagnosed via PSA tests, digital rectal exams, MRI, and biopsy, with treatment depending on stage (active surveillance, surgery, radiation for localized; hormonal therapy, chemo for advanced). A malignant tumor in the prostate gland, which can spread (metastasize), and most cases are low-grade and slow growing, but some are aggressive, which may lead to cancer death.

Etiology

Prostate cancer is a multifactorial disease that arises from a complex interplay of genetics (hereditary predisposition), hormonal regulation, and environmental factors. The risk factors related to prostate cancer

include family risk, ethnicity, age, obesity, and other environmental factors.[291] More than 50% of prostate cancer risk is attributed to genetic factors, old age, and high risk in Black men. [292]

① Genetic and hereditary factors

- Family history increases risk: men with a first-degree relative affected have a 2-3x higher risk.
- Specific gene mutations (e.g., BRCA1/2, HOXB13) are linked to aggressive disease.
- Ethnic differences: African American men have the highest incidence and mortality, while Asian men have the lowest.

Men with close family lineage are at a 50% risk of developing prostate cancer, as compared to men with no family history of prostate cancer. Specific gene mutations in hereditary prostate cancer have been reported, and it has been shown that patients with these mutations have an increased risk of the disease.[293] Gene mutations are a prevalent cause of cancer. Candidate genes for prostate cancer predisposition are genes that partake in the androgen pathway and metabolism of testosterone. The development of the prostate epithelium and prostate cancer cells relies on androgen receptor signaling and testosterone.[294] The identification of cancer biomarkers and the targeting of specific genetic mutations can inform the development of targeted treatments for prostate cancer. Biomarkers for targeted treatment include tumor DNA biomarkers, general DNA biomarkers, and general biomarkers.[295] About 5.5% of the prostate cancer-affected men had detectable mutations in DNA repair genes such as ATM, BRCA1, and BRCA2.

Cancer occurs because of changes in the DNA sequence due to mutations such as point mutations, single-nucleotide polymorphisms (SNPs), and somatic copy number alterations (SCNAs).[296] Mutations can cause prostate cells to become cancerous by inactivating tumor suppressor genes and activating oncogenes.[297] This often leads to uncontrolled cell division. Mutations in genes can be passed on from generation to generation or acquired by an individual. Acquired mutations usually occur during DNA replication in the nucleus.[298] The common genes used as biomarkers for prostate cancer are BRCA genes, HOX genes, the ATM gene, RNase L (HPC1, Iq22), MSR1 (8p), and ELAC2/HPC2 (17p11).[291]

② Hormonal influences

- Androgens (testosterone, dihydrotestosterone) play a central role in prostate growth and carcinogenesis.
- Estrogens may also contribute via paracrine and intracrine signaling within the prostate.

③ Environmental and Lifestyle factors

a. Diet: High intake of red meat, dairy, and saturated fats is associated with increased risk; diets rich in vegetables, soy, and fish may be protective.

- Several **modifiable risk factors** have been well established, although several **dietary factors** have been investigated in the past decade. Greater intakes of dairy products, meat, and fat, and of total energy, and lower intakes of tomato products, lycopene, selenium, and vitamin E have all been linked to higher prostate cancer risk.
- Excessive consumption of milk and milk products may be linked to an increased risk of benign prostatic hyperplasia (BPH) due to their high saturated fat content and hormone content. Studies suggest that high dairy product intake can increase inflammation and prostate enlargement, exacerbating BPH symptoms like urinary urgency and frequency. However, some research also points to a positive association between high dairy product intake and an increased risk of prostate cancer, though evidence is mixed.

Dairy products are a significant source of calcium; dietary calcium could influence prostate cancer development by lowering the concentration of 1,25-dihydroxyvitamin D3[1,25(OH)2D3], a hormone thought to protect against prostate cancer. These results support the hypothesis that dairy products and calcium are associated with a greater risk of prostate cancer. A significant positive trend in milk product consumption with prostate cancer, but not in calcium, in the Netherlands. Three case-control studies- in the United States, Greece, and Japan- found no significant association between dietary calcium and prostate cancer risk. In contrast, a Serbian case-control study observed a statistically significant inverse trend for calcium and prostate cancer. The Greece study, however, did observe a positive nonsignificant association

for milk and dairy product intake and risk of prostate cancer. The evidence for an association between calcium intake and prostate cancer risk, although suggestive, remains conflicting and limited.

b. Obesity and metabolic syndrome: Linked to more aggressive disease.

c. Sunlight/Vitamin D exposure: Lower levels may increase risk.

d. Carcinogens: Occupational exposures (e.g., to cadmium, pesticides) have been implicated.

Epidemiology

a. Global burden

Prostate cancer is the second most common cancer in men worldwide, with incidence strongly influenced by age, genetics, and lifestyle factors, with 1466680 new cases and 396792 deaths in 2022.[292] Previously, it was estimated 1,276.106 new cases of prostate cancer resulted in about 358,989 deaths worldwide in 2018, with a higher prevalence in developed countries,[299] which indicates an increase in the prevalence of prostate cancer in men globally. Approximately 1.5 million new cases of prostate cancer are diagnosed annually worldwide, of which 75% of patients present with cancer localized to the prostate, which is associated with a 5-year survival rate of nearly 100%. Prostate cancer has been estimated to have 299010 new cases and 35250 deaths in 2024 in the United States.[292] The most common type of prostate cancer is adenocarcinoma (≥99%), and the median age at diagnosis is 67 years.[292]

b. Regional variation

- High incidence in developed countries, including North America, Europe, and Australia.
- The low incidence in Asia and Africa, especially in rural China, suggests environmental and dietary influences.

c. Age factor

- Prevalence rises sharply with age. Autopsy studies show latent prostate cancer in ~5%of men under 30, increasing to >50% in men over 80 (Table 62).

d. Screening impact

- Widespread use of PSA testing in the late 1980s-1990s led to a spike in incidence, followed by a decline in mortality (>40% since 1991) due to earlier detection and improved therapies.

Table 62. Summary of role factors in the etiology/epidemiology of prostate cancer in men

SN	Factor	Role in etiology/epidemiology
①	Age	Strong risk factor: prevalence rises with age.
②	Genetics	BRCA1/2, HOXB13 mutations; family history double risk.
③	Ethnicity	Highest in African American men; lowest in Asian men.
④	Hormones	Androgens drive growth; estrogens may modulate risk.
⑤	Diet & Lifestyle	High-fat diet, and obesity increase risk; a plant-based diet is protective.
⑥	Screening	PSA testing increased incidence but reduced mortality.

Prostate cancer is a disease of aging men with strong genetic and hormonal underpinnings, but its global distribution highlights the importance of environmental and lifestyle factors.

Signs and Symptoms

Prostate cancer often develops silently, with early stages showing few or no symptoms. When signs do appear, they usually involve urinary changes, sexual dysfunction, or pain due to advanced disease.

Major signs and symptoms

① Urinary symptoms

- Difficulty starting or stopping urination
- Frequent urination, especially at night (nocturia)
- Pain or burning sensation during urination (less common)
- Weak or interrupted urine stream
- Urgency or inability to empty the bladder fully

② Sexual and reproductive symptoms

- Erectile dysfunction (difficulty achieving or maintaining an erection (Table 63).
- Painful ejaculation
- Reduced semen volume

③ Pain and discomfort

- Persistent pain in the lower back, hips, or thighs (suggests spread beyond the prostate)
- Pelvic discomfort or pressure

④ Advanced disease symptoms (Table 63).

- Blood in urine (hematuria) or semen
- Unexplained weight loss
- Bone pain (common when cancer spreads to bones)
- Fatigue and general weakness

Table 63. Symptom overview of prostate cancer in men

SN	Category	Common symptoms	Notes
①	Urinary	Weak stream, nocturia, urgency, incomplete emptying	Open mistaken for BPH
②	Sexual/Reproductive	Erectile dysfunction, painful ejaculation, low semen	May overlap with age-related changes
③	Pain/Discomfort	Pelvic pain, lower back/hip pain	Suggest local or metastatic spread
④	Advanced disease	Hematuria, bone pain, weight loss, fatigue	Usually indicates late-stage cancer

Diagnosis

Prostate cancer diagnosis in men relies on a combination of screening, clinical evaluation, imaging, and biopsy, with magnetic resonance imaging (MRI), with the biopsy being the definitive test. Early cancers are often asymptomatic, so detection depends heavily on proactive screening with PSA blood tests and digital rectal exams. There is no single, specific test for prostate cancer; however, the following tests are used for the diagnosis of prostate cancer in me.

Steps in diagnosis

① Medical history and physical examination

a. History: Family history of prostate cancer, urinary symptoms (frequency, hesitancy, weak stream), or systemic signs, including bone pain in advanced disease (Table 64)

Table 64. Key differences between BPH and prostate cancer in men

SN	Feature	BPH (Benign)	Prostate cancer (Malignant)
①	Nature	Non-cancerous enlargement	Uncontrolled growth of cancer cells
②	Onset	Gradual with aging	Can be slow or aggressive
③	Symptoms	Mostly urinary	Urinary + Possible pain, blood, etc.
④	Risk of spread	Does not spread	Can spread to bones, lymph nodes
⑤	PSA level	Mildly elevated	May be significantly elevated
⑥	Treatment	Medication, surgery	Surgery, radiation, hormone therapy

b. Digital rectal examination (DRE)

- Physician palpates the prostate via the rectum to detect nodules, asymmetry, or induration.
- Limitation: Detects only posterior and lateral abnormalities; sensitivity is modest.
- A gloved finger is inserted into the patient's rectum to assess the enlargement, nodularity, asymmetry, or induration, which may suggest BPH or prostate cancer. However, it is subjective, examiner-dependent, and less sensitive for detecting small or anterior lesions.
- DRE remains a simple, low-cost tool for assessing prostate enlargement, but its accuracy is limited compared to modern imaging and PSA testing. It is most useful as part of a combined diagnostic approach rather than a standalone test (Table 65).

Table 65. Comparison among the DRE, PSA, and ultrasound/MRI tests to diagnose BPH in men

SN	Aspects	DRE	PSA	Ultrasound/MRI
①	Cost	Very low	Moderate	High
②	Invasiveness	Mild discomfort	Blood test	Non-invasive imaging
③	Accuracy for size	Moderate, examiner-dependent	Not size-specific	High accuracy
④	Cancer detection	Limited sensitivity	Good for early detection	Excellent with mpMRI

mpMRI = Multiparametric magnetic resonance imaging

② Screening tests

a. Prostate-specific antigen (PSA)

- The PSA test remains the cornerstone of prostate cancer screening.[300] Needs PSA is a glycoprotein secreted by the epithelial cells of the prostate gland. It is usually found in semen but can also be detected in the bloodstream.[301]
- Blood samples are collected to measure PSA levels, which are analyzed at a PSA cutoff of 4 ng/ml. PSA levels above four ng/mL suggest that the patient needs further testing.[302]
- PSA is prostate gland-specific and not prostate cancer-specific; therefore, prostate-specific antigen levels can indicate benign pathologies such as BPH and prostatitis and not prostate cancer, and men who do not have prostate cancer have also been reported to have elevated PSA levels.
- Free PSA is a type of PSA found in the bloodstream that is not bound to proteins. Measuring free PSA levels alongside total PSA helps distinguish between BPH and prostate cancer. A lower ratio of free PSA to total PSA (e.g., below 10%) may indicate a higher risk of prostate cancer, whereas a higher ratio (e.g., above 25%) suggests benign conditions like prostatitis or BPH. The test is typically ordered for men with moderately elevated PSA levels (e.g., 4-10ng/ml) to guide further diagnostic decisions.

b. DRE + PSA combination: Increases detection rates compared to either test alone.

③ Imaging studies

a. Transrectal ultrasound (TRUS): Guides biopsy; limited sensitivity for cancer detection.

b. Multiparametric MRI (mpMRI)

- Provides a detailed visualization of suspicious lesions.
- Used increasingly before to target sampling and reduce unnecessary biopsies.
- Bone scan/CT/PET: Reserved for staging in suspected advanced disease.

④ Prostate tissue biopsy

a. TRUS-guided biopsy: Standard approach, multiple cores taken.

b. MRI-targeted biopsy: Improves accuracy by sampling suspicious lesions.

c. Histopathology: Confirms cancer and assigns Gleason score (grading aggressiveness)

- A prostate tissue biopsy is usually performed to confirm the presence of cancer.[303] Any man at risk of prostate cancer should have a magnetic resonance imaging (MRI) of the prostate performed before obtaining a prostate biopsy.[304] This serves to minimize complications such as LUTS, hematuria, and temporary erectile dysfunction. Furthermore, the number of biopsy cores obtained is linked to a higher risk of complications such as rectal bleeding, hematospermia, bleeding problems, and acute urine retention.[305] However, the benefits and drawbacks of radiogenomics as compared with actual prostate cancer peril stratification management have been reported.[306]
- A biopsy is a medical procedure in which a thin hollow needle is used to collect small tissue samples from the prostate gland for microscopic examination.
- The biopsy can be performed through the skin between the anus and scrotum or through the rectal wall, known as trans-rectal biopsy.[307]
- The prostate gland is usually located using imaging techniques such as MRI and transrectal ultrasound

(TRUS). A TRUS is a small probe inserted into the rectum of a patient. The probe emits sound waves that go through the prostate gland and produce echoes. The probe then detects and interprets the echoes, and a computer system converts them into a black-and-white image of the organ.[308]

- An MRI scanner produces detailed images of body tissues using a strong magnetic field and radio waves.[309] MRI positive results can be used for specifically targeting abnormal areas of the prostate gland during a biopsy.[310]
- Tissue samples of biopsy are studied microscopically, and biopsy results are usually reported as follows:

·Negative for prostate cancer, there were no cancer cells detected in the biopsy samples.
·Positive for prostate cancer, there were cancer cells detected in the biopsy samples.
·Suspicious, abnormal cells present but may not be cancer cells.[311]

- Table 66 presents the different tests used for the difference between BPH and prostate cancer in men[312]

Table 66. Difference between BPH and prostate cancer in men[312]

SN	Test	Findings in BPH	Findings in prostate cancer
①	Digital Rectal Exam (DRE)	•Typically feels a smooth, symmetrical, and rubbery enlargement. •The gland feels soft and elastic, just bigger than it should be.	•Typically feels hard nodules, lumps, or irregularities. •If the gland feels rock-hard, asymmetrical, or fixed in place, it raises a red flag for malignancy.
②	Prostate-Specific-Antigen (PSA)	• Generally, levels under 4ng/ml care considered normal, though this varies by age. •BPH produces higher PSA, which is Associated with the volume of prostate tissues.	•Cancer cell 'leak' more PSA into the blood than healthy cells. •A rapid rise in PSA or a very high level can indicate cancer.
③	Transrectal Ultrasound (TRUS)	•TRUS is excellent for measuring the volume of the prostate. •It can clearly show the transition zone enlargement typical of BPH. •Measure post-void residual urine in the bladder.	•Standard ultrasound is not very specific for cancer. •While some tumors appear as dark (hypoechoic) spots, many are invisible. •Its main role is to guide a biopsy needle.
④	Multiparametric MRI (mpMRI)	•MRI can look at the density of cells and blood flow. •Detect the organized, swirling nodules of BPH.	•Cancerous tissue often has restricted water diffusion and increased blood flow compared to BPH •Distinguish between the chaotic, dense growth of cancer.
⑤	Cellular level	•BPH involve hyperplasia (more normal cells)	•Cancer involves neoplasia (abnormal, invasive cells
	Progression	•BPH progresses locally. It gets bigger and squashes the urethra and bladder.	•Cancer can metastasize, spreading through the Lymph nodes to bones and lungs
	Impact on health	•Untreated BPH damages the kidneys and bladder function due to retention and back-pressure	•Untreated cancer threatens life by organ failure and systemic spread.
⑥	Biopsy factor*	•BPH: Normal glandular tissue, perhaps signs of inflammation or hyperplasia	•Cancer: Gleason pattern of cells- disorganized structures that confirm cancer.
⑦.	Treatment Options	•Medications: Alpha-blockers or 5-α reductase inhibitors are often the first line. •Transitional surgery (TURP), is effective, it carries risks like bleeding and sexual dysfunction, and incontinence.	•Treatment depends on the stage. •It may involve active surveillance, radiation, or radial prostatectomy. •The safer alternative: Prostatic artery embolization, and Echolaser

*When PSA levels are high or the MRI looks suspicious, a biopsy is the only way to know for sure. Small samples of tissue are taken and examined under a microscope

⑤ Staging and risk stratification

- TNM classification: Tumor size, lymph node involvement, metastasis.
- Gleason score + PSA levels: Used to categorize low, intermediate, or high-risk disease.

•Nomograms: Help predict progression and guide treatment decisions.
•Table 67 shows the comparative overview of different tests used for the diagnosis of prostate cancer

Table 67. Comparative overview of different tests used for the diagnosis of prostate cancer

SN	Step	Purpose	Limitations
①	History & DRE	Detects palpable abnormalities	Misses small/anterior tumors
②	PSA test	Screening and monitoring	False positives from BPH/prostatitis
③	Imaging (MRI/TRUS)	Localize suspicious lesions	Cost, availability, operator-dependence
④	Biopsy	Confirms diagnosis, grading	Invasive, risk of infection/bleeding
⑤	Staging tests	Assess spread	Used mainly in advanced cases

Key considerations
•Overdiagnosis risk: Many prostate cancers are indolent; not all require immediate treatment.
•False positives: Elevated PSA may lead to unnecessary biopsies.
•Bangladesh context: PSA and biopsy are widely available in Dhaka, but access to mpMRI may be limited; clinicians often rely on PSA + TRUS biopsy for diagnosis.
Conclusions
The pathway to diagnosing prostate cancer begins with PSA and DRE, proceeds to imaging if suspicious, and is confirmed only by biopsy.

Prostate cancer in Bangladesh

Histopathological examination of 2917 prostate tissue samples was tested, of which 637 (16%) cases were diagnosed as prostate cancer, 3221 (82%) BPH, 53 (1.35%) chronic prostatitis, and three cases of rare diseases like lipid storage disease in Bangladesh (Table 68). Among prostate cancer cases, the majority (95%) were prostatic adenocarcinoma, followed by 3.0% prostatic intraepithelial neoplasia (PIN), 1.0% squamous cell carcinoma, and 1.0% as primary transitional cell carcinoma (TCC). The highest rate of prevalence of prostate cancer was reported in the 71-80 years age group (48.35%), followed by 18.05% in the 61-70 years age group (Table 68). The ratio between BPH and malignant prostate cancer was about 5: 1.[313]

Research on BPH and prostate cancer in men in Bangladesh

Pathological changes in the prostate gland occur commonly with advancing age, including inflammation, atrophy, hyperplasia, and carcinoma, and a change in volume is also evident. A study was conducted on 70 post-mortem human prostates collected from the unclaimed dead bodies that were examined in the Department of Forensic Medicine, Dhaka Medical College, Bangladesh. The results were divided into three age groups: Group A (10-20 years), Group B (21-40 years), and Group C (41-70 years), of which the Mean ± SD volume of prostate was 7.68 ± 3.64 cm^3, 10.61 ± 3.99 cm^3, and 15.40 ± 6.31 cm^3, respectively. The age group over 40 years had a significantly larger prostate size only in the aging male population. [314]

Research studies indicate that while BPH is the most common prostate disease in Bangladeshi men over 40, the incidence of prostate cancer remains relatively less common but still significant, with around 1600 deaths annually and an age-adjusted death rate of 3.07 per 100,000 men.[315] A study found that 98% of symptomatic, old patients were diagnosed with BPH, while only 2.5% were found to have prostate cancer.

Key findings highlight a high prevalence of BPH, with studies showing a benign-to-malignant ratio of approximately 5:1. PSA levels are used for screening, and a lower free PSA-to-total PSA ratio indicates a higher risk of malignancy. Histopathological examination of biopsy samples is required for confirmation. Table 68 presents an overview of the BPH and prostate cancer in men in Bangladesh

Table 68. Overview on the BPH and prostate cancer in men in Bangladesh

SN	Condition/ Disease	Key findings	Name of study institution	Surgical method used	Ref. No.
01.	Benign Prostatic Hyperplasia (BPH)	Ultrasonography studies in BD show ~45-50% prevalence of prostate enlargement in men over 40, Prevalence rises sharply with age, affecting the majority of men over 60 (Table 69)	Chattogram Medical College Hospital	Transurethral Resection of the Prostate (TURP)	315
02.	BPH and Prostate Cancer	Ultrasonography, DRE and PSA ≤ 4ng/ml 198 BPG patients examined, of which 97.5% had BPH and 2.5% had prostate cancer on histo-pathological examination. It indicates that prostate cancer is not rare in men with PSA level ≤4 ng/ml (Table 70)	SirSalimulla Medical College Mitford Hospital, Dhaka Medical College & Hospital, NIKDU, BSMMU Hospital, Dhaka	TURP	316
03.	Prostate Cancer	WHO data published in 2020 Prostate cancer deaths in BD reached 1664 (0.23%) of the total deaths. The age-adjusted death rate is 3.07 per 100,000 of the population ranks BD #173 in the World	WHO Global Cancer Observatory report	-	317
04.	Prostate Cancer	Cancer registry data from NICRH (Dhaka) highlights prostate cancer as a moderate but rising contributor to male cancer cases.	A total of 89 prostate cancer has been recorded in men patients.	-	318
05.	BPH and Prostate Cancer	In a group of 681 LUTS patients, researcher assessed total PSA, free PSA and prostate volume, which has significantly correlated with both total and free PSA. Prostate cancer become more heterogeneous, which may cause false positive and false negative results. In symptomatic patients, PSA has a high sensitivity and a low specificity for the detection of prostate cancer.	Review article		319
06.	BPH and Prostate Cancer-PSA and Prostate Volume (PV) assessment	A total of 110 men aged ≥ 50 with BPH underwent transabdominal USG, PSA and prostate biopsy. Malignancy was confirmed in 15.45% patients, who had significantly higher mean PSA (25.48 ± 11.62 ng/ml) and larger PV (57.4 ± 16.2 ml). PSA >10 ng/ml had high specificity (94.6%) and accuracy (89.1%), while combining PSA >10 With PV Grade III/V increased specifically to 97.8%.	BIRDEM General Hospital, Dhaka	-	320
07.	Survey on Prostate cancer	Approximately 34% patients aged 46-50 years cancer, with 82%, has no genetic relationships.	Outdoor and indoor patients of hospitals (Name not mentioned)	-	321
08.	Lipid peroxi-dation and antioxidant of cancer patients	Oxidative stress markers malondialdehyde was found to have significantly increased, antioxidant erythrocyte reduced glutathione and superoxide dismutase were significantly reduced, whereas glutathione S-transferase activity was significantly increased in prostate cancer patients compared to the control group.	Inpatient and outpatient Department of Urology, BIRDEM General Hospital, BSMMU, and Dhaka Medical College Hospital, Dhaka.	-	322
09.	Clinicopatho-logic pattern the prostate diseases	Histological diagnosis of prostate diseases & Gleason grading and scoring of the biopsies of 220 patients were studied (Table 73). The rate of incidental prostate cancer detected in surgical specimens removed from clinically presumed BPH appears to be rising (Table 73).	National Institute of Kidney Diseases and Urology, Bangladesh	TURP, TRUS, DGCB TP & RP	323

Contd. Table 68. Overview on the BPH and prostate cancer in men in Bangladesh

SN	Condition/ Disease	Key findings	Name of study institution	Surgical method used	Ref. No.
10.	USG and Histological diagnosis	USG and histological evaluation of 50 BPH patients, aged 50-89 years with urinary symptoms. Nodular hyperplasia (NH 88%), NH with chronic prostatitis (2%), and adeno-Carcinoma (8%) of prostate have been diagnosed (Table 75)	Sir Salimullah Medical College and Mitford Hospital, Dhaka	-	324
11.	Free and Total PSA Ratio in Diagnosis of BPH & Prostate cancer (PC)	Prostatic problems of 288 patients in Rajshahi were diagnosed based on free/total PSA. PC was detected significantly higher from 80 years, while BPH was between 60 and 80 years. The overall accuracy of total PSA were significantly lower (61.45%) than that of free/total PSA (91.67%) (Table 76).	Outpatients and indoor patients, Department of Urology, Rajshahi Medical College Hospital, Bangladesh Study period from July 2019 to June 2020.	-	325
12.	Free PSA in Diagnosis of Prostate Cancer (PC)	Urology outpatients and inpatients (n=350) were selected for the study of TURS, PSA, and DRE. Histopathology of prostate biopsy detected 95 prostate cancer patients, 82 with PSA >4ng/ml, and 85 patients had f/t PSA ratio ≤0.16. Total PSA and f/t PSA ratio may help detect PC early and distinguish BPH from PC. (Table 8)	Outpatients and inpatients, Department of Urology, Rajshahi Medical College Hospital, Bangladesh Study period from April 2021 to March 2022.	-	326

TURP = Transurethral Resection of the Prostate
TP = Total prostatectomy
TRUS =Transrectal ultrasound
RP = Radical prostatectomy
DGCB = Digital guided core biopsy

Table 69. Clinical studies on BPH with pre-and post- operative volumes of prostate measured by abdominal ultrasonography in Chattogram Medical College Hospital in Bangladesh (n=157)[315]

SN	Age-wise prevalence		Occurrence of symptoms		Pre-and post-operative prostate volumes			
	Group yrs.	No. (%)	Types	No. (%)	Size (cc)	Pre-operative	After enucleation	P value
①	41-50	27 (17)	Urgency	154 (98.0)	<20	09 (05.73)	18 (11.46)	0.464
②	51-60	37 (24)	Dribbling	150 (96.0)	21-40	34 (21.66)	38 (24.20)	
③	61-70	60 (38)	Hesitancy	143 (91.0)	41-60	31 (19.75)	45 (28.66)	
④	>70	33 (21)	Acute retention	134 (85.0)	61-80	30 (19.11)	43 (27.39)	
⑤			Dysuria	127 (81.0)	81-100	21 (13.38)	11 (07.01)	
⑥			Palpable bladder	116 (74.0)	>100	32 (20.38)	02 (01.27)	

Table 70. Frequency of prostate cancer in 198 patients with BPH and PSA level d" 4ng/ml in Bangladesh[316]

SN	Age-wise prevalence		Micturition		Lab investigation		Types of disease	
	Group yrs	Frequency (%)	Types	Frequency (%)	Prostate (g)	Frequency (%)	Diagnosis	Frequency (%)
①	<60	046 (23.1)	Poor stream	187 (94.4)	<40	123 (63)	Malignant	005 (02.5)
②	60-70	100 (50.0)	Dysuria	152 (76.8)	>40-60	030 (15)	BPH	193 (97.5)
③	>70-80	042 (21.2)	IC voiding	165 (83.3)	>60	045 (22)	Total	198 (100)
④	>80	010 (05.1)	Frequency	171 (86.4)	PSA (ng/ml)			
⑤			Urgency	140 (70.7)	<2	063 (321.8)		
⑥			Nocturia	149 (75.3)	2-4	135 (68.2)		

Table 71. Histopathological diagnosis of prostate cancer in BPH patients in Bangladesh[313]

SN	Diag-nosis	Overall No. of cases	+ve %	Cancer-wise No. of cases	+ve %	Age-wise prevalence (years) 41-50 No. of cases	+ve %	51-60 No. of cases	+v %	61-70 No of cases	+ve %	71-80 No. of cases	+ve %	81-90 No. of cases	+ve %	>90 No. of cases	+ve %
①	ADC	606	15.48	606	95.13	18	02.98	67	11.06	106	17.49	301	49.67	102	16.83	12	01.98
②	SCC	007	00.18	007	01.10	01	14.29	04	57.14	002	28.58	-	-	-	-	-	-
③	TCC	005	00.14	005	00.79	-	-	-	-	002	40.00	003	60.00	-	-	-	-
④	PIN	019	00.48	019	02.98	04	21.05	05	26.32	005	26.32	004	21.05	01	05.26	-	-
⑤	CP	053	01.35	-	-	-	-	-	-	-	-	-	-	-	-	-	-
⑥	Others	003	00.08	-	-	-	-	-	-	-	-	-	-	-	-	-	-
⑦	BPH	3221	82.29	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Total	3914	100	637	100	23	03.61	76	11.93	115	18.05	308	48.35	103	16.17	12	01.88

ADC = SCC = TCC = PIN= Prostatic intraepithelial neoplasia CP = Chronic prostatitis

Table 72. Prostate volume and PSA trends in BPH and malignant prostatic diseases in men in Bangladesh[320]

SN	Variable	BPH (n=93) No. (%)	Malignant (n=17) No. (%)
	A. Age (years) Mean ± SD	67.1 ± 9.0	70.5 ± 7.8
	B. Symptoms		
①	Burning sensation	47 (50.54)	11 (64.71)
②	Increased frequency	93 (100)	17 (100)
③	Dribbling of urine	80 (86.02)	15 (88.24)
④	Fever	23 (24.73)	01 (05.88)
⑤	Hesitancy	75 (80.65)	15 (88.24)
⑥	Urgency	87 (93.55)	15 (88.24)
⑦	Urinary retention	74 (79.57)	15 (88.24)
	C. Prostate volume (PV): USG		
①	Grade I (20-30 g)	35 (37.63)	02 (11.76)
②	Grade II (31-50 g)	39 (41.94)	05 (29.41)
③	Grade III (51-80 g)	16 (17.20)	08 (47.06)
④	Grade IV (>80 g)	03 (03.23)	02 (11.76)
⑤	PV ml: Mean ± SD	44.8 ± 18.5	57.4 ± 16.2
	D. PSA trends: (ng/ml)		
①	0-5	76 (81.72)	04 (23.53)
②	5.1-10	12 (12.90)	02 (11.76)
③	>10	05 (05.38)	11 (64.71)
④	Mean ± SD	6.42 ± 3.15	25.48 ± 11.62

E. Diagnostic accuracy of key predictors, %

SN	Parameters	PSA >10ng/ml	PV Grade III/IV	PSA >10 ng/ml + PV Grade III/IV
①	Sensitivity	64.7	58.8	47.1
②	Specificity	94.6	79.6	97.8
③	PPV	68.8	34.5	80.0
④	NPV	93.3	91.3	91.3
⑤	Accuracy (%)	89.1	76.4	89.1

PPV = Positive predictive value (PV) NPV = Negative PV

Table 73. Clinicopathologic pattern of prostate cancer at a tertiary care teaching hospital in Bangladesh[323]

SN	Biopsy procedures	No. of patients	Cancer +ve No. (%)
①	TURP biopsy cases	160	14 (08.75)
②	Digital guided core biopsy	040	25 (62.50)
③	TRUS core biopsy cases	010	08 (80.00)
④	Total prostatectomy	008	07 (87.50)
⑤	Radical prostatectomy	002	02 (100)
	Total	220	60 (100)

Contd. Table 73. Clinicopathologic pattern of prostate cancer at a tertiary care teaching hospital in Bangladesh[323]

SN	Diagnosis	Patients No. (%)	PSA (ng/ml)	Positive No. (%)
①	Adeno-carcinoma	060 (27.27)	4-1540 3.0	59 (98.33) 01 (01.67)
②	BPH	148 (67.27)	4-8	07 (04.72)
③	BPH + CP	007 (03.18)	4-10	02 (28.57
④	CP	005 (02.27)	8	01 (20.00)
	Total	220 (100)		70 ()

SN	Gleason GG	Gleason scoring	No. (%)	Prognostic value
①	Group -1	3 + 3 = 6	13 (21.67)	WDA
②	Group- 2	3 + 4 = 7	17 (28.33)	MDA
③	Group- 3	4 + 3 = 7	10 (16.67)	MDA
④	Group- 4	4 + 4 = 8	18 (30.00)	PDA
⑤	Group- 5	(4+5) = 9 (5+4) = 9 or (5+5) = 10	02 (03.33)	PDA

CP = Chronic prostatitis WDA = Well-differentiated adenocarcinoma
MDA = Moderately differentiated adenocarcinoma
PDA = Poorly differentiated adenocarcinoma

Table 74. Biochemical and oxidative stress in prostate cancer patients in Bangladesh[322]

SN	Variables	Cancer patients (n=207)	Healthy control (n=200)
①	PSA (m=ng/ml)	44.54 ± 35.50**	03.06 ± 00.49
②	MDA (nmol/ml)	13.23 ± 02.20**	06.67 ± 01.37
③	GSH (µmol/g of Hb)	01.74 ± 00.89*	02.51 ± 00.77
④	GST (nmol/ml/min)	101.03 ± 10.90	98.62 ± 10.23
⑤	SOD (iu/ml)	111.84 ± 12.60	159.79 ± 19.44

PSA = Prostate-Specific Antigen MDA = Malondialdehyde
GSH = Erythrocyte reduced glutathione GST = Glutathione S-transferase
SOD = Superoxide dismutase

Table 75. Comparison between transabdominal ultrasonography of enlarged prostate and histopathological examination.[324]

SN	Population tested Age in years	Patients No. (%)
①	50-59	16 (32)
②	60-69	20 (40)
③	70-79	08 (16)
④	80-89	06 (12)
	Total	50 (100)

SN	Types of clinical features symptom	No. (%)
①	Incom. emptying	45 (90)
②	Frequency	42 (84)
③	Intermittency	40 (80)
④	Urgency	38 (76)
⑤	Weak stream	35 (70)
⑥	Straining	33 (66)
⑦	Nocturia	30 (60)

Contd. Table 75. Comparison between transabdominal ultrasonography of enlarged prostate and histopathological examination.[315]

USG diagnosis of prostate

SN	USG findings	No. (%)
①	BPH	47 (94)
②	PC	03 (06)
	Total	50 (100)

SN	Histopathological diagnosis HF	No. (%)
①	NHP	44 (88)
②	NHCP	02 (04)
③	ACP	04 (08)
	Total	50 (100)

Comparison between USG & HP diagnosis

SN	USG	Histopathology BPH	Cancer	Total
①	BPH	46 (92)	1 (2)	47 (94)
②	Carcinoma	00 (00)	3 (6)	03 (06)
	Total	46 (92)	4 (8)	50 (100)

Validity test results

SN	Validity test	%
①	Sensitivity	100
②	Specificity	75
③	Accuracy	98
④	PPV	97
⑤	NPV	100

Table 76. Application of free/total PSA ratio in the diagnosis of BPH and prostate cancer in men in Bangladesh[319,326]

a. Age-wise prevalence of patients at RMCH, Rajshahi

SN	Age (yrs)	BPH10	BPH11	Total	PC10	PC11	Total
①	<60	15 (08.0)	010 (04.0)	025 (05.59)	0	05 (05.0)	05 (02.62)
②	60-69	81 (42.0)	115 (45.0)	196 (43.84)	23 (24.0)	20 (21.0)	43 (22.51)
③	70-80	81 (42.0)	110 (43.0)	191 (42.73)	42 (44.0)	40 (42.0)	82 (42.93)
④	>80	15 (08.0)	020 (08.0)	035 (07.83)	31 (32.0)	30 (32.0)	61 (31.94)
	Total	192 (42.95)	255 (50.05)	447 (42.95)	96 (50.26)	95 (49.74)	191

b. Comparison of duration of LUTS (n=288)

SN	Duration (months)	BPH10 (n=192)	BPH11 (n=255)	Total	PC10 (n=96)	PC11 (n=95)	Total (n=191)
①	<5	004 (02.0)	140 (55.0)		23 (24.0)	06 (06.0)	29 (15.18)
②	5-10	115 (60.0)	00 (39.0)		65 (68.0)	37 (39.0)	102 (53.40)
③	>10	073 (38.0)	00 (06.0)		08 (08.0)	52 (55.0)	060 (31.41)
	Total	192 ()	255 ()		96 (50.26)	95 (49.74)	191
Mean ± SD		09.36 ± 4.36	-		06.28 ± 2.54	-	

c. Comparison of signs and symptoms

SN	Signs and symptoms	BPH10 (n=192)	BPH11 (n=255)	Total 447	PC10 (n=96)	PC11 (n=95)	Total 191
①	Low back pain	15 (08.0)	15 (06.0)	30 (00.67)	46 (48.0)	20 (21.0)	66 (34.55)
②	Weight loss	50 (26.0)	26 (10.0)	76 (17.00)	31 (32.0)	40 (42.0)	71 (37.17)
③	Hematuria	0	02 (01.0)	02 (0.45)	04 (04.0)	21 (22.0)	25 (13.10)
④	No targeted signs	127 (66.0)	212 (83.0)	339 (75.84)	15 (16.0)	14 (15.0)	29 (15.18)

d. Association of TURS findings

SN	TURS	BPH10 (n=192)	BPH11 (n=255)	Total (n=447)	PC10 (n=96)	PC11 (n=95)	Total (n=191)
①	Hypoechoeic	012 (06.0)	189 (74.0)	201 (44.97)	77 (80.0)	70 (74.0)	147 (76.96)
②	Isoechoeic	180 (94.0)	066 (26.0)	246 (55.03)	19 (20.0)	19 (20.0)	038 (19.90)

e. Association of DRE findings

SN	DRE	BPH10 (n=192)	BPH11 (n=255)	Total 447	CP10 (n=96)	CP11 (n=95)	Total (n=191)
①	Positive	008 (04.0)	05 (02.0)	013 (02.91)	73 (76.0)	80 (84.0)	153 (80.10)
②	Negative	184 (96.0)	250 (98.0)	434 (97.09)	23 (24.0)	15 (16.0)	038 (19.90)

f. Association of volume of prostate

SN	Prostate volume (ml)	BPH10 (n=192)	BPH11 -	Total -	PC (n=96)	PC -	Total -
①	<50	108 (56.0)	-	-	69 (72.0)	-	-
②	≥50	084 (44.0)	-	-	27 (28.0)	-	-
Mean ± SD		46.6 ± 8.7	-	-	42.2 ± 7.1	-	-

g. Accuracy of free and total PSA

SN	Serum PSA (ng/ml)	BPH 10 (n=192)	BPH11 (n=255)	Total (n=447)	PC10 (n=96)	PC11 (n=95)	Total (n=191)
x.	**Free PSA**						
①	>0.934	108 (56.25)	060 (23.53)	168 (37.58)	73 (76.04)	70 (73.68)	143 (74.87)
②	≤0.934	084 (43.75)	195 (76.47)	279 (62.42)	23 (23.96)	25 (26.32)	048 (25.13)
	Total	192	255	447	96 (50.26)	95 (49.74)	191
y.	**Total PSA**						
①	>4	96 (50.00)	139 (54.51)	235 (52.57)	81 (84.38)	82 (86.32)	163 (85.34)
②	≤4	96 (50.00)	116 (45.49)	212 (47.43)	15 (15.63)	13 (13.68)	028 (14.66)
	Total	192	255	447	96	95	191

Studies at Rajshahi Medical College Hospital (RMCH) show that the free/total PSA (f/t PSA) ratio is a significantly more accurate diagnostic tool than total PSA (tPSA) alone for differentiating prostate cancer (PC) from BPH in men over 50, particularly within the 4-10ng/ml 'gray zone.' A lower f/t PSA ratio indicates a higher risk of malignancy, helping reduce unnecessary biopsies. (Islam et al. 2023).

Diagnostic accuracy: The f/t PSA ratio has higher sensitivity, specificity, and positive predictive value for the diagnosis of PC than tPSA alone, which often overlaps with BPH (Table 9).

Optimal Cutoff value: Research indicates that using a percentage of fPSA, often at a cutoff of 0.16 (16%), shows strong potential for differentiating cancer from BPH, with greater overall accuracy than tPSA.

- **BPS vs. PC**: While total PSA is often elevated in both conditions, a lower proportion of fPSA (lower f/t ratio) is reported in malignant cases.
- **Target populations:** The tests are critical for men over 50 in the region presenting with LUTS, with PC significantly higher in patients aged 80 and above, whereas BPH is most common between 60-80 years.
- **Reducing biopsies**: The f/t PSA ratio helps reduce unnecessary invasive biopsy procedures by better distinguishing BPH cases from PC within the 4-10 ng/ml tPSA range (Table 76).

Contd. Table 76. Application of free/total PSA ratio in the diagnosis of BPH and prostate cancer in men in Bangladesh[319]

h. Comparison of F/T PSA ratio (%)

SN	Components	Total PSA10	Total PSA11	F/T ratio10	p-value PSA 10	F/T ratio11
①	Sensitivity	84.37	86.32	87.50	0.691568	89.47
②	Specificity	50.00	45.49	93.75	0.000226	96.08
③	PPV	45.76	37.10	87.50	0.000203	89.47
④	NPV	86.48	89.92	93.75	0.5215186	96.08
⑤	False +ve	54.23	62.90	12.50	0.000001	10.53
⑥	False -ve	13.51	10.08	06.25	0.000001	03.92
Overall accuracy		**61.45**	**56.57**	**91.67**	**<0.011**	**94.29**

Current evidence does not support the idea that BPH directly turns into prostate cancer.

Prostate cancer treatment options[327,328]

Prostate cancer treatment in men ranges from careful monitoring for slow-growing disease to aggressive interventions like surgery, radiation, and systemic therapies for advanced stages. The choice depends on cancer stage, risk group, age, health status, and patient preference.[327]

① Expectant management (observational)

a. Active surveillance

- Regular PSA tests, digital rectal exams, and biopsies.
- Treatment only if cancer shows signs of progression.
- Best for low-risk, localized cancers in younger/healthy men.

Active surveillance is a structured program that employs monitoring and expected intervention as the main techniques for managing prostate cancer. The criteria for active surveillance typically incorporate recommendations informed by disease characteristics, comorbidities, life expectancy, side effects, and patient preferences.[329] The PSA level, clinical progression, or histologic progression is used as a prostate cancer trigger point.[330]

The advantages of active surveillance include preservation of erectile function, reduced treatment costs, avoidance of unnecessary treatment for indolent cancers, and maintenance of quality of life and normal activities. Its disadvantages include the likelihood of cancer metastasis before treatment, missed opportunity for a complex therapy with side effects for larger and aggressive cancers, reduced chances of preservation, mostly after surgery, increased anxiety in patients, and frequent medical checks.[331]

b. Watchful waiting

- No routine testing; focus on symptom management.
- Often used in older men or those with serious comorbidities

② Surgery

Radical prostatectomy (open, laparoscopic, or robotic assisted)

- Remove the prostate gland and surrounding tissue.
- Suitable for localized cancer in men with >10-year life expectancy.
- Risks: Urinary incontinence, erectile dysfunction.

Radical prostatectomy

Radical prostatectomy (RP) is the surgical removal of the entire prostate gland (and often the seminal vesicles) to treat localized prostate cancer in men. It is the most effective robotic-assisted surgery, aimed at maximizing cancer control while minimizing side effects such as urinary incontinence and erectile

dysfunction.

Indications

- Localized prostate cancer (confined to the prostate, no spread to distant organs)
- Fit and healthy patients who can tolerate major surgery.
- Sometimes considered in locally advanced disease if combined with other therapies.

Surgical approaches

a. Open radical prostatectomy

- Retropubic (lower abdominal incision)
- Perineal (incision between scrotum and rectum)

b. Minimally invasive

- Laparoscopic radical prostatectomy
- Robotic-assisted laparoscopic prostatectomy (the most common today) offers precision and faster recovery.

- Table 77 presents the comparison of Radical prostatectomy with other treatments

Benefits

- Complete removal of cancerous prostate tissue
- Provides pathological staging (helps determine the exact cancer extent)
- Long-term cancer control in localized disease.

Risks and side effects

- Urinary incontinence (leakage, usually improves over time)
- Erectile dysfunction (due to nerve damage; nerve-sparing techniques reduce risk).
- Surgical risks: bleeding, infection, injury to nearby organs.
- Other complications: urethral narrowing (stricture) and lymphocele if lymph nodes are involved.

Table 77. Comparison of Radical prostatectomy with other treatments

SN	Treatment	Best use case	Prostatectomy	Consequence
①	Radical prostatectomy	Localized cancer, fit patients	Removes prostate, accurate staging	incontinence, erectile dysfunction
②	Radiotherapy	Localized or locally advanced	Non-surgical, outpatients	Bowel/urinary irritation, long-term fatigue
③	Active surveillance	Low-risk localized cancer	Avoids side effects	Risk of progression, anxiety
④	Hormone therapy	Advanced/metastatic cancer	Slows progression	Hot flashes, bone loss, metabolic effects

Key decision points

- Age and health status: Younger, healthier men benefit most.
- Cancer stage and grade: Surgery is most effective for localized disease.
- Patient preference: Balancing cancer control with quality of life (continence, sexual function).
- Availability of expertise: Robotic surgery is increasingly available worldwide, including South Asia, but access may vary.

Radical prostatectomy is available in tertiary hospitals in Dhaka and other major cities, often via open surgery, though robotic-assisted techniques are emerging in select centers. The patient should weigh oncological outcomes versus side-effect risks and discuss with a urologist experienced in prostate cancer surgery.

RP is the procedure of medically removing the prostate gland by open and/or laparoscopic surgery.[322] The procedure requires making small incisions on the abdomen or via the perineum. Radical prostatectomy, a surgical option that involves the removal of the prostate and nearby tissues, is used in connection with radiation therapy for the treatment of low-risk prostate cancer. Salvage radical prostatectomy is usually recommended to patients with local recurrence in the absence of metastases after undergoing external beam

radiation therapy, brachytherapy, or cryotherapy. Patients younger than age 70 with organ-confined prostate cancer, with a life expectancy higher than 10 years, who have little to no comorbidities, are best suited for radical prostatectomy. There are a few complications associated with this procedure, which include incontinence and erectile dysfunction arising from surgical damage to the urinary sphincter and erectile nerves.[333]

In recent decades, RP has undergone transformative changes, moving from open surgery, with significant morbidity, to minimally invasive and robot-assisted techniques. These advances have improved surgical precision, reduced blood loss, and accelerated functional recovery. Key enhancements, such as the 'Veil of Aphrodite,' hood-sparing, and Retzius-sparing approaches, aim to preserve neurovascular structures vital for continence and sexual function, addressing the persistent challenge of balancing oncological control with quality-of-life outcomes. Single-port (SP) robotic platforms represent the latest frontier, offering various access routes, including extraperitoneal, transvesical, and transperitoneal routes, to further reduce incisional morbidity. Ongoing innovations in robotic systems, augmented imaging modalities, and personalized surgical planning are likely to refine prostate cancer care and enhance both survival and post-treatment quality of life.[334]

③ Radiation therapy

Radiation therapy is a cornerstone treatment for prostate cancer in men, used either as a primary option or alongside surgery and hormone therapy. The two main approaches are external beam radiation therapy (EBRT) and brachytherapy (internal radiation), each tailored to cancer stage, risk group, and patient health.

- External beam radiation therapy (EBRT): High-energy beams are directed at the prostate (Table 78)

Table 78. Key approach to radiation therapy

SN	Type	Method	Indications	Advantages	Limitations/Side effects
①	External beam radiation therapy (EBRT)	High-energy X-ray or protons directed at prostate from out-side the body.	Localized or locally advanced prostate cancer; often combined with hormone therapy for high-risk cases.	Non-invasive, outpatients, precise targeting with modern techniques (IMRT, IGRT, proton therapy)	Urinary irritation, bowel changes, fatigue, erectile dysfunction
②	Brachytherapy (internal radiation)	Radioactive seeds or temporary implants placed inside/near prostate	Low-to intermediate-risk localized cancer; sometimes combined with EBRT for higher-risk disease.	Delivers high dose directly to prostate, shorter treatment course.	Urinary obstruction, irritative symptoms, risk of seed Migration.
③	Combination Therapy	EBRT + Brachy-therapy ± Hormone therapy	High-risk or bulky localized disease	Improves local control	Increased side effects compared to single modality

- Brachytherapy: Radioactive seeds implanted directly into the prostate.
- Often combined with hormone therapy for intermediate/high-risk disease.
- Side effects: Bowel irritation, urinary symptoms, and sexual dysfunction.

Radiation therapy is regarded as one of the most effective therapies that kills prostate cancer cells using high radiation. Radiation is delivered to cancerous cells using various techniques, such as brachytherapy (the use of seeds placed in the body) and external-beam therapy (where the energy is projected through the skin), to the cancerous sites. Radiation therapy aims to deliver high-energy radiation or particle beams directly to the prostate without affecting normal tissues, and these doses are based on the level of prostate cancer. This treatment is considered an acceptable therapy for patients unsuitable for surgical procedures.[335] Various techniques of radiation therapy are described below:

a. Brachytherapy

Brachytherapy includes the direct placement of radioactive sources into the prostate gland with the aid of seeds, injections, or wires under the guidance of transrectal ultrasound. This often involves two techniques:

low-dose and high-dose rates. The low-dose rate refers to the permanent implantation of seeds in the prostate tissue, with a significant risk of leakage into surrounding organs.

Brachytherapy can be completed in a day or less. There is a minimal risk of incontinence in patients without a previous transurethral resection of the prostate (TURP). Erectile function is also not affected.
Its disadvantages are usually a requirement for general anesthesia, acute urinary retention risks, and persistent irritative voiding symptoms.[336]

b. External beam radiation therapy (EBRT)

EBRT is a commonly used treatment technique that involves delivering high-dose X-ray beams to the prostate. It delivers higher prostate radiation doses with less emission to surrounding tissues. Radiation therapy is an effective intermediate-risk and high-risk prostate cancer treatment when used together with androgen deprivation therapy (ADT).[337] It is a suitable therapy for attenuating the metastatic potential of cancer cells.

This technique is more advantageous than surgical therapy. It can treat early stages of cancer, and it is associated with fewer risks such as bleeding, myocardial infarction, pulmonary embolus, urinary incontinence, and erectile dysfunction. It can also relieve symptoms such as bone and joint pain.[332]

Side effects of radiation include urinary urgency and frequency, erectile dysfunction, dysuria, diarrhea, and proctitis. [338]

When radiation therapy is used

- Primary treatment for localized prostate cancer (alternative to radical prostatectomy.
- Adjuvant or salvage therapy after prostatectomy if cancer recurs or margins are positive.
- Combined with androgen deprivation therapy (ADT) for intermediate-and high-risk cancers.
- Palliative therapy for advanced disease to relieve symptoms (e.g., bone pain).

Side effects and risks

- Urinary: frequency, urgency, burning, and obstruction
- Bowel: diarrhea, rectal bleeding, and proctitis
- Sexual: erectile dysfunction, reduced semen volume
- General: fatigue, skin irritation (rare with modern EBRT)

Advances improving outcomes

- Image-guided radiation therapy (IGRT): improves precision by tracking the prostate
- Intensity-modulated radiation therapy (IMRT) allows dose sculpting to spare the bladder/rectum.
- Proton therapy: reduces radiation to surrounding tissues.
- Hypofractionation: fever, higher-dose session with similar efficacy.

Practical considerations for men in Bangladesh

- Availability: EBRT is widely available at tertiary cancer centers in Dhaka; brachytherapy is less common but is offered at select institutions.
- Decision-making: Choice depends on cancer stage, PSA, Gleason score, comorbidities, and patient preference.
- Follow-up: Regular PSA monitoring post-treatment is essential to detect recurrence early.

④ Cryotherapy [339,340]

Cryotherapy for prostate cancer is a minimally invasive treatment that destroys cancer cells by freezing them with argon gas probes, typically used for localized disease or recurrence after radiation. It offers a prostate-sparing option but carries risks such as erectile dysfunction and urinary incontinence (Table 79).

What cryotherapy involves

- Mechanism: Thin needles (probes) are inserted into the prostate under ultrasound guidance. Argon gas freezes the tissue, followed by helium gas warming cycles. This freeze-thaw process kills cancer cells.

This method involves the use of surgical insertion of cryoprobes into the prostate under ultrasound guidance. It involves freezing the prostate gland to -100 to -200 °C for approximately 10 minutes.

- Protection: A warming catheter is placed in the urethra to prevent freezing damage.
- Absorption: Dead tissue is naturally reabsorbed by the body.

Indications

- Primary treatment: For men with localized prostate cancer confined to the gland, especially when surgery or radiation is not suitable.
- Salvage therapy: Often used when cancer recurs after radiation therapy.
- Partial cryotherapy: Can target only part of the prostate (focal therapy) in select cases.

Benefits

- Minimally invasive: Shorter hospital stays and recovery compared to open surgery.
- Replicable: Can be repeated if cancer returns.
- Prostate-sparing: Avoids complete removal of the gland.

Risks and side effects[341]

- Erectile dysfunction: The most common long-term complication
- Urinary incontinence: Less frequent but possible.
- Pelvic pain or swelling: Usually temporary.
- Urethral/rectal injury: Rare due to modern imaging guidance.
- Lower risk of major bleeding compared to surgery.

Table 79. Comparison of cryotherapy with related treatments of prostate cancer in men

SN	Treatment	Mechanism	Best use case	Key risks/limitations
①	Cryotherapy	Freezing prostate tissue	Localized cancer, recurrence post-radiation	Erectile dysfunction, incontinence
②	Radical prostatectomy	Surgical removal of prostate	Healthy men with localized cancer	Longer recovery, risk of impotence/incontinence
③	Radiation therapy	High-energy beams	Localized or advanced disease	Bowel/bladder irritation, recurrence risk
④	Active surveillance	Monitoring only	Low risk, slow-growing cancer	Risk of progression

Practical consideration

- Not first-line for all patients; usually reserved for those unsuitable for surgery/radiation, or with recurrence.
- Advances in technology (better imaging and precise probes) have reduced complications compared with earlier cryotherapy methods.
- Follow-up: PSA monitoring and imaging are essential after treatment to detect recurrence.

Conclusions

Cryotherapy is a niche but valuable option for men with localized or recurrent prostate cancer, balancing minimally invasive treatment with notable risks of sexual dysfunction.

⑤ Radium-223 therapy

The radium-223 dichloride (Xofigo®) is a targeted radiopharmaceutical used in men with metastatic castration-resistant prostate cancer (mCRPC) that has spread to the bones but not to visceral organs. It improves overall survival, reduces skeletal-related complications, and provides pain relief, making it a key option in the management of advanced disease. Administer an intravenous injection once every 4 weeks for 6 cycles. An outpatient procedure requires radiation safety precautions but minimal isolation (Table 80).

Mechanism of action

- Radium-223 dichloride is an alpha-emitting radionuclide.
- Mimics calcium and selectively binds to areas of increased bone turnover (sites of metastases).

Its ability to mimic calcium allows radium-223 dichloride to be selectively absorbed by the cancer cells in bone tissue. This technique has been reported to have a considerable impact on the survival and recovery

of metastatic prostate cancer patients, leading to delayed onset of bone fracture and pain.[342]

- Alpha particles deliver high-energy radiation over a very short range, causing double-stranded DNA breaks in nearby cancer cells while sparing surrounding healthy tissue.

Indications

① Approved for: (a) Men with mCRPC and symptomatic bone metastases, and (b) No known visceral metastases (e.g., liver, lung).

② Typically used after or alongside androgen deprivation therapy (ADT), and other systemic agents (e.g., abiraterone, enzalutamide).

Clinical benefits

- Survival: The ALSYMPCA Phase III trial showed a median overall survival improvement of ~3.6 months compared with placebo.
- Quality of life: Reduces bone pain, delays skeletal-related events (fractures, spinal cord compression).
- Safety advantage: Lower myelosuppression risk compared to beta-emitting agents.

Side effects

- Common: Nausea, diarrhea, vomiting, and fatigue.
- Hematologic: Anemia, thrombocytopenia, neutropenia (generally mild compared to chemotherapy).
- Precautions: Avoid patients with poor bone marrow reserve; monitor blood counts regularly.

Table 80. Comparison of Radium-223 with other related therapies

SN	Therapy	Target/Mechanism	Key benefit	Limitations
①	Radium-223	Alpha emitter, bone metastasis	Survival + Pain relief, bone specific	Not for visceral mets
②	Zoledronic acid/ Denosumab	Bone resorption inhibitors	Prevent fractures, reduce skeletal events	No survival benefits
③	Abiraterone/ Enzalutamide	Androgen signaling inhibitors	Prolong survival, systemic control	Resistance develops
④	Docetaxel/ Cabazitaxel	Chemotherapy	Survival benefits, systemic control	Higher toxicity

Key considerations

- Best suited for: Patients with symptomatic bone metastases, no visceral disease, and adequate marrow reserve.
- Combination therapy: Can be used sequentially with hormonal agents but is not recommended concurrently with chemotherapy due to marrow toxicity.
- Patient counselling: Radiation safety (bodily fluids may contain trace radioactivity), monitoring of blood counts, and management of GI side effects.

Conclusions

- Radium-223 is a bone-targeted alpha therapy that improves survival and quality of life in men with advanced prostate cancer with bone metastases. It is distinct from other systemic therapies because of its selective bone action and relatively favorable safety profile.

⑥ Hormone therapy (androgen deprivation therapy, ADT)

Hormone therapy (androgen deprivation therapy, ADT) is a cornerstone in managing advanced and recurrent prostate cancer. It works by lowering or blocking testosterone, the main driver of prostate cancer growth, and is used both as primary treatment in advanced disease and in combination with other therapies.

Key concepts of ADT

- Target: Androgens (mainly testosterone and dihydrotestosterone) stimulate prostate cancer cell growth.
- Goal: Reduce androgen levels or block their action to slow tumor progression.
- Indication: Commonly used in advanced, metastatic, recurrent, or high-risk localized prostate cancer.

- Reduces testosterone to slow cancer growth.
- Methods: (a) LHRH agonists/antagonists (injections), and (b) Orchiectomy (surgical removal of testicles)
- Used for advanced or recurrent cancer, often with radiation.
- Side effects: hot flashes, bone thinning, metabolic changes.

Prostate cancer can either be classified as androgen sensitive or androgen insensitive, which is an indicator of testosterone stimulation and the possible treatment option (Table 81).[343] Hormonal therapy is also known as androgen deprivation therapy (ADT). This technique is applied in the treatment of advanced and/or metastasized prostate cancer. Its therapeutic mechanism is based on the blockage of testosterone production and other male hormones, preventing them from fueling prostate cancer cells. Therefore, significantly decreased male hormone levels inhibit androgen action on the androgen receptor.[344]

ATD has been associated with acute and long-term side effects, such as hyperlipidemia, fatigue, hot flashes, flare effect, osteoporosis, insulin resistance, cardiovascular disease, anemia, and sexual dysfunction.[345]

Table 81. Types of hormone therapy for prostate cancer in men

SN	Method	Mechanism	Examples	Notes
①	Surgical castration (orchiectomy)	Removes testes- immediate drop in testosterone	Bilateral orchiectomy	Permanent, cost-effective, but irreversible
②	LHRH agonists	Initially surge then suppress pituitary stimulation →↓ testosterone	Leuprollde, Goserelin	Flare effect requires anti-androgen cover
③	LHRH antagonists	Directly block pituitary → Rapid ↓ testosterone	Degarelix, Relugolix	No flare, faster suppression
④	Anti-androgens	Block the androgen receptor binding	Bicalutamide, Enzalutamide	Often combined with LHRH therapy
⑤	Androgen synthesis inhibitors	Block adrenal/testicular androgen production	Abiraterone with prednisone	Used in castration resistant disease

a. Flutamide

Flutamide is a type of drug that is nonsteroidal and pure antiandrogenic, lacking hormonal agonist activity. Flutamide is an anti-androgen in the androgen-dependent accessory genitals. Treating prostate cancer with flutamide and luteinizing hormone-releasing (LHR) agonists has produced promising results.

Flutamide is known to result in hepatic dysfunction. However, a study on antiandrogen therapy (AAT) in combination with flutamide indicated that flutamide could be successful when performing regular hepatic function testing during treatment periods (104 Iguchi et al. 2020).[346]

b. Chlormadinone acetate (CMA)

CMA is an oral steroidal anti-androgen that has demonstrated anticancer activity. Chlormadinone is also used to treat BPH; it decreases testosterone level, PSA level, and prostate volume, slowing the progression of prostate cancer.[347]

Clinical use

- Castration-sensitive prostate cancer (CSPC): ADT alone or combined with radiation /chemotherapy.
- CSPS: Cancer progresses despite low testosterone; newer agents (enzalutamide, abiraterone, apalutamide) are added.
- Intermittent ADT: Cycles of treatment and breaks to reduce side effects while maintaining disease control.

Benefits

- Tumor shrinkage and symptom relief (e.g., bone pain)
- Improved survival when combined with radiation in high-risk localized disease.
- Disease control in metastatic settings.

Risks and side effects

- Metabolic: Weight gain, insulin resistance, increased risk of diabetes.
- Cardiovascular: Higher risk of heart disease.
- Bone health: Osteoporosis, fractures
- Sexual health: Loss of libido, erectile dysfunction.
- Other: Hot flashes, fatigue, anemia, and cognitive changes.

Practical considerations

- Monitoring: PSA levels, testosterone, bone density, metabolic profile.
- Supportive care: Calcium/vitamin D, exercise, cardiovascular risk management.
- Decision-making: Balance between disease control and quality of life.

Summary

- ADT is not curative but remains essential in prostate cancer management.
- It is often first-line systemic therapy, used alone or in combination with radiation, chemotherapy, or novel agents.
- The choice of method depends on disease stage, patient comorbidities, and treatment goals.

⑦ Chemotherapy

Chemotherapy uses anticancer drugs to kill or inhibit (slow) the growth of cancerous cells. Chemotherapy for prostate cancer is mainly used in advanced or metastatic diseases, especially when hormone therapy is no longer effective. The most common chemotherapeutic drugs for prostate cancer are docetaxel (Taxotere) and cabazitaxel, which can prolong survival and relieve symptoms, but chemotherapy is not typically used for early-stage prostate cancer.[348]

When chemotherapy is used

- Not standard for early-stage prostate cancer: Surgery, radiation, and hormone therapy are preferred.
- Advanced/metastatic disease: Chemotherapy is considered when cancer has spread beyond the prostate (Table 82).
- Hormone-resistant cases: Used when androgen deprivation therapy (ADT) stops working.
- Symptom relief: Can reduce pain and improve quality of life in late-stage disease.

Table 82. Common chemotherapeutic drugs

SN	Drug	Typical use	Key notes
①	Docetaxel (Taxotere)	First-line chemo for metastatic castration-resistant prostate cancer (mCRPC)	Improves survival, often combined with ADT
②	Cabazitaxel (Jevtana)	Second-line after docetaxel failure	Shown to extend survival in resistant cases
③	Mitoxantrone	Palliative use	Improves symptoms but not survival
④	Estramustine	Sometimes combined with other agents	Limited use due to side effects
⑤	Carboplatin	Less commonly	Used in select cases or clinical trials

a. Docetaxel

Docetaxel (Beizray, Docivyx, Taxotere) is regarded as the first-line standard therapy for prostate cancer cells that are castration-resistant. It is an antimicrotubular agent that binds to β-tubulin, inhibiting microtubule depolymerization, thereby suppressing mitotic cell division and inducing apoptosis.[349] CYP3A is a key enzyme in the activation of docetaxel. The development of docetaxel resistance has been associated with relapse, attributed to increased upregulation of the multidrug resistance (MDR) 1 gene, which encodes P-glycoprotein. [350]

b. Cabazitaxel

Cabazitaxel (Jevtana) is a semi-synthetic anti-neoplastic agent derived from needles of various yew species (Taxus) and is usually sold under the name Jevtana. Cabazitaxel is a second-generation therapy designed to overcome docetaxel resistance.[344]

Side effects include hypotension, bronchospasm, renal failure, neurotoxicity, fatigue, alopecia, and generalized rash/erythema. There are also reports of diarrheal deaths related to cabazitaxel therapy, resulting in electrolyte imbalances and dehydration.[350]

c. Enzalutamide

Enzalutamide is a second-generation AR inhibitor that was recognized as one of the chemotherapeutic drugs for prostate cancer in 2012. This drug focuses on the androgen pathways and has functions such as: (a) competitively inhibiting the binding of androgen to the androgen receptor, (b) inhibiting nuclear translocation and recruitment of cofactors, and (c) inhibiting the association of the activated androgen receptor. Enzalutamide targets androgens, including testosterone and dihydrotestosterone. Its therapeutic mechanism includes: (a) Competitive inhibition of androgen binding to the androgen receptor, (b) Inhibition of nuclear translocation and co-factor recruitment, and (c) Inhibition of the binding of DNA with activated androgen receptor.

The side effects of enzalutamide include fatigue, asthenia, diarrhea, and vomiting.[351]

How chemotherapy works

- Mechanism: Drugs circulate in the bloodstream and target rapidly dividing cancer cells.
- Administration: Usually given intravenously in cycles (every 3-4 weeks)
- Combination therapy: Often paired with hormone therapy to enhance effectiveness.

Benefits

- Prolongs survival in advanced prostate cancer.
- Reduces symptoms such as bone pain.
- Improves quality of life when hormone therapy alone is insufficient.

Risks and side effects[352]

- **Bone marrow suppression**: Chemotherapy affects rapidly growing stem cells in the bone marrow. As a result, there are fewer red and white blood cells and blood platelets.
- **Nerve damage**: Chemotherapy drugs can also damage nerves in the fingers and toes, leading to peripheral neuropathy. This can cause numbness and tingling in the fingers and toes. Peripheral neuropathy is more common with docetaxel and cabazitaxel.
- **Allergic reactions:** Both docetaxel and cabazitaxel can cause allergic reactions. Steroid medicines such as prednisolone can help prevent these reactions.
- Fluid buildup: Docetaxel and cabazitaxel can cause fluid retention, especially in the lower legs. Typically prescribe daily steroid medicine to help prevent this side effect.
- General: Fatigue, hair loss, nausea, vomiting, diarrhea, loss of appetite, fever, mouth sores, pain, constipation, lowered immunity (risk of infection)
- Monitoring required: Regular blood tests and supportive care are essential.

Summary

- Chemotherapy is not curative for prostate cancer but plays a vital role in advanced, hormone-resistant cases.
- Docetaxel is the cornerstone drug, with cabazitaxel as a second-line option.
- The main goals are survival extension and symptom relief, not early-stage treatment.

⑧ Targeted and Novel Therapies

Targeted and novel therapies for prostate cancer now extend well beyond traditional androgen deprivation, incorporating next-generation androgen receptor inhibitors, PSMA-targeted approaches, immunotherapy, and precision medicine guided by molecular biomarkers. These advances are reshaping care for both localized and advanced disease, offering survival benefits and improved quality of life (Table 83).

a. Androgen receptor pathway inhibition (ARPI)

- Abiraterone: Blocks CYP17A1 enzyme, reducing androgen production. Recently expanded use in earlier-stage disease with survival benefits (86% alive at 6 years vs. 77% with standard therapy).

- Enzalutamide, Apalutamide, Darolutamide: Potent AR antagonists used in metastatic hormone-sensitive and castration-resistant prostate cancer (mHSPC, mCRPC).
- Novel strategies: Combination with chemotherapy (docetaxel) or radiotherapy for synergistic effects.

b. PSMA-targeted therapies

- Radioligand therapy (RLT): 177Lu-PSMA-617 delivers beta radiation directly to PSMA-expressing cells. Shown to improve survival in mCRPC.
- PSMA-directed antibodies and CAR-T cells: Under investigation for resistant disease.
- PSMA PET imaging: Enhances staging and guides therapy selection.

c. Immunotherapy

- Checkpoint inhibitors (PD-1/PD-L1, CTLA-4): Limited efficacy alone, but trials explore combinations with ARPI, PARP inhibitors, or radiotherapy.
- Sipuleucel-T (Provenge): Autologous dendritic cell vaccine approved for asymptomatic/ minimally symptomatic mCRPC.
- Emerging strategies: Personalized neoantigen vaccines and bispecific T-cell engagers.

d. DNA damage response (DDR) targeting

- PARP inhibitors (Olaparib, Rucaparib): Effective in patients with BRCA1/2 or other homologous recombination repair mutations.
- Combination approaches: PARP inhibitors with ARPI or immunotherapy to overcome resistance.

e. Novel systemic and precision approaches

- Radiopharmaceuticals: Radium-223- Alpha emitter targeting bone metastases, improving survival and reducing skeletal events.
- Biomarker-driven therapy: Genomic profiling (e.g., BRCA, ATM, mismatch repair genes) guides targeted treatment.
- Epigenetic modulators and novel kinase inhibitors: Early-phase trials exploring histone deacetylase inhibitors and PI3K/AKT pathway blockers.
- Combination therapy paradigms: Integration of ARPI, PARP inhibitors, and immunotherapy tailored to molecular signatures.

Table 83. Comparative overview of targeted and novel therapies for prostate cancer in men

SN	Therapy class	Key agents	Target/Mechanism	Clinical use	Novelty/Advances
①	ARPI	Abiraterone, Enzalutamide, Apalutamide, Darolutamide	Androgen receptor signaling	mHSPC, mCRPC, now earlier stages	Expanded indications, better survival
②	PSMA-targeted	^177Lu-PSMA-617, PSMA antibodies, CAR-T	PSMA antigen	Advanced/ metastatic disease	Imaging+ therapy integration
③	Immunotherapy strategies	Sipuleucel-T, PD-1/PD-L1 inhibitors	Immune modulation	mCRPC	Combination emerging
④	DDR targeting	Olaparib, Rubcaparib	DNA repair defects	BRCA/HRR-mutated PCa	Precision medicine approach
⑤	Radiopharma-Ceuticals	Radium-223	Bone metastases	mCRPC with bone involvement	Alpha emitter specificity
⑥	Emerging agents	Epigenetic drugs, P13K/AKT inhibitors	Molecular pathways	Clinical trials	Novel targets under study

⑨ Abiraterone

Abiraterone acetate (Zytiga®) is a potential androgen biosynthesis inhibitor used in men with advanced

prostate cancer, particularly metastatic castration-resistant prostate cancer (mCRPC) and, increasingly, high-risk metastatic hormone-sensitive disease. It is used to treat prostate cancer that has metastasized to other parts of the body.[353] It prolongs survival, delays disease progression, and improves quality of life when combined with prednisone (Table 84).

Mechanism of action

- Abiraterone inhibits CYP17A1, a key enzyme in androgen biosynthesis.
- This blocks testosterone production in the testes, adrenal glands, and prostate tumor tissue.
- Unlike standard androgen deprivation therapy (ADT), which reduces testicular testosterone, abiraterone suppresses extra-gonadal androgen sources.

Clinical indications

- Metastatic castration-resistant prostate cancer (mCRPC): (a) Approved for use after progression on ADT, and (b) Effective both pre- and post-docetaxel chemotherapy.
- Metastatic hormone-sensitive prostate cancer (mHSPC): STAMPEDE and LATITUDE trials showed a significant survival benefit when added to ADT in high-risk patients.
- Non-metastatic high-risk disease: Investigational use in trials, showing promise in delaying progression.

Administration

- Dose: 1000 mg orally once daily (four 250 mg tablets).
- Co-administered with prednisolone (5-10 mg daily), prevents mineralocorticoid excess (hypertension, hypokalemia, fluid retention).
- Taken on an empty stomach (food increases absorption unpredictably).

Benefits

- Improved overall survival in both mCRPC and mHSPC.
- Delayed disease progression and reduced skeletal-related events.
- Better symptom control (pain, fatigue)
- Oral administration is more convenient than chemotherapy.

Adverse effects

- Mineralocorticoid-related: Abiraterone is associated with high upstream CYP17A mineralocorticoids, with concomitant side effects including edema, hypertension, fatigue, and hypokalemia.[354]
- Hepatic toxicity: Elevated liver enzymes; requires monitoring.
- Other: Fatigue, diarrhea, and joint pain.
- Drug interactions: CYP3A4 substrate- caution with strong inhibitors/inducers.

Table 84. Comparative status of abiraterone with related therapies in men

SN	Therapy	Mechanism	Key use	Survival benefits	Side effects
①	Abiraterone	CYP17A1 inhibition	mCRPC mHSPC	Significant OS gain	Mineralocorticoid excess, liver toxicity
②	Enzalutamide	Androgen receptor Inhibitor	mCRPC mHSPC	Similar to OS gain	Fatigue, seizures, falls
③	Docetaxel	Chemotherapy (microtubule inhibitor)	mHSPC mCRPC	OS gain, especially high volume disease	Neutropenia, neuropathy
④	ADT alone	Suppresses testicular testosterone	First-line	Limited in advanced disease	Hot flashes, osteoporosis

Summary

- Abiraterone is now a standard of care in advanced prostate cancer, often used upfront with ADT in high-risk metastatic cases.
- Requires prednisolone co-administration and liver/blood pressure monitoring.
- Offers survival and quality-of-life benefits, but careful patient selection and monitoring are essential.

⑩ Combined therapy

Combination therapy is a strategy that was developed to treat castration-resistant prostate cancer and other forms of prostate cancer. Combination therapy with currently used treatment options for prostate cancer could successfully increase a patient's lifespan and suppress tumors. Amongst all the available treatment strategies available for metastatic prostate cancer, androgen deprivation therapy (ADT), also called hormonal therapy, has more potential combination treatment compared to other therapeutic strategies for prostate cancer,[355] and approved and currently ongoing clinical trials with ADT treatment include ADT with radiation therapy, which often treats high-risk patients to delay or prevent the disease from progressing to castration-resistant prostate cancer (CRPC); (ii) ADT and chemotherapy, which in several clinical studies has shown to increase patient survival but results in adverse side effects and sometimes death,; and (iii) immunotherapy and ADT, which has reported to increase patient survival by 8.5 months (Table 85).[356]

Each treatment is associated with severe side effects such as toxicity and reduced leukocyte and erythrocyte counts, which lead to fatigue, hair loss, peripheral neuropathy, erectile dysfunction, incontinence, metastasis, and, lastly, developing resistance to the initial treatment.[291] Prostate cancer continues to develop resistance to different conventional treatment options.[357] The discovery of new cost-effective chemotherapeutic agents with little or no side effects and higher efficacy is necessary. [358]

Table 85. Comparison of different treatment options for prostate cancer in men

SN	Treatment option	Best for	Key benefit	Main risks/Side effects
①	Active surveillance	Low risk localized	Avoids overtreatment	Anxiety, and delayed intervention
②	Radical prostatectomy	Localized, fit patients	Potential cure	Incontinence, erectile dysfunction
③	Radiation therapy	Localized/intermediate	Non-surgical option	Bowel/urinary issues
④	Hormone therapy (ADT)	Advanced/recurrent	Slows progression	Bone loss, metabolic effects
⑤	Chemotherapy	Metastatic resistant	Extends survival	Fatigue, infection risk
⑥	Targeted/Immunotherapy	Genetic/advanced cases	Precision treatment	Cost, limited eligibility

Key considerations

- Stage and Risk group: Determines whether surveillance, local therapy, or systemic therapy is appropriate.
- Patient age and health status: Older men may benefit more from watchful waiting than from aggressive treatment.
- Quality of life: Side effects (urinary, sexual, bowel) must be weighed against the survival benefit.
- Genetic testing: Increasingly important for guiding targeted therapies.

Precision medicine for prostate cancer

Precision medicine classifies diseases using genome sequencing to identify patients with tumors harboring actionable targets, thereby enabling more informed and accurate treatment decisions. Mutations in the BRCA1 and BRCA2 genes render men with mCRPC eligible for treatment with either rucaparib or olaparib, and other prostate cancer genes that have responded well to olaparib include ATM, CDK12, CHECK2, CHECK1, PALB2, PP2R2A, and RAD54L.

Cancer patients affected with BRCA mutations who received prostatectomy or radiotherapy developed metastasis and had shorter survival as compared with patients who did not have mutations of the BRCA gene. Prostate cancer patients with specific mutations in the BRCA gene (c.4211C >G) showed sensitivity to ADT as well as radiotherapy, making the treatment more effective.[359] Mutations that make it difficult to treat or design effective CRPC therapies include F876L, which alters the ligand-binding pocket of the AR. Similarly, the W741L/C mutation promotes specific AR binding, thereby shifting AR into its active conformation. Such mutations pose obstacles to the design of effective treatments for CRPC.[360]

Treatment and management of prostate cancer

- Surveillance, prostatectomy, and radiotherapy are recognized as the standard treatments for stage I-III prostate cancer patients.

- Androgen ablation by surgical or pharmacological castration can bring about lasting remission in all stages IV and high-risk stage III patients, and first-generation antiandrogens such as flutamide and bicalutamide can aid in this case.
- In stage IV, castration resistance, characterized by genomic mutations in the androgen receptor, develops, and the prognosis is poor.[361] Table 86 summarizes prostate cancer treatment options and their adverse effects.

Table 86. Standard prostate cancer treatment options and potential adverse effects[362]

SN	Treatment options	Disease progression	Potential adverse effects
①	Active surveillance	Localized	Illness uncertainty
②	Radial prostatectomy	Localized	Erectile dysfunction, and urinary incontinence
③	External beam radiation	Localized and advanced disease	Urinary urgency and frequency, dysuria, diarrhea, and proctitis, erectile dysfunction, and urinary incontinence
④	Brachytherapy	Localized	Urinary urgency and frequency, dysuria, diarrhea, and Proctitis, erectile dysfunction, and urinary incontinence
⑤	Cryotherapy	Localized	Erectile dysfunction, urinary incontinence, and rectal pain and fistula.
⑥	Hormonal therapy	Advanced	Fatigue, hot flashes, flare effect, hyperlipidemia, Insulin resistance, cardiovascular disease, and anemia, Osteoporosis, erectile dysfunction, and cognitive deficits
⑦	Chemotherapy	Advanced	Myelosuppression, hypersensitivity reaction, gastrointestinal upset and peripheral neuropathy.

Prevention

The highest prevalence of prostate cancer has been reported in developed countries where there is prostate cancer awareness and where prostate-specific antigen (PSA) testing is a prevalent screening practice.[363] The reports of PSA tests indicated that high prevalence in Australasia (111.6 per 100,000) and the USA (97.2 per 100,000) in the year 2012.[364] Globally, prostate cancer is predicted to increase to approximately 1.5 million new cases and 499,000 deaths by the year 2030 because of the exponentially growing population of men who will be 65 years and older.[365]

Conclusions

BPH is not just an individual health issue but a growing global public health challenge. With aging populations worldwide, the prevalence and burden will continue to rise, especially in low-and middle-income regions. Early detection, lifestyle interventions, and improved access to treatment are critical to managing this trend.

Prostate cancer is one of the leading causes of death in men globally, and mutated genes, proteins, and pathways associated with an increased risk of prostate cancer development can be used as biomarkers for the disease, which provide information on the stage and cause of cancer. The localized prostate cancer is usually treated by active surveillance, surgery (prostatectomy), and radiation therapy, depending on the risk of progression, whereas advanced (metastatic) prostate cancer is usually treated with hormone therapy, targeted therapy, chemotherapy, and newer targeted protein degraders (drug resistance is a challenge). Biomarkers can also give specifications on the type of treatment required for cancer. The current treatments available for prostate cancer are beneficial to only a few patients and present numerous side effects that eventually affect the quality of life of most patients. Chemotherapy, radiotherapy, and hormonal treatment have adverse side effects, including drug resistance, which remains a setback to anticancer treatment. Medicinal plant fractions and compounds, genetic material encapsulated in target-specific nanocarriers with controlled release, and targeted therapies based on cellular pathways appear to be promising alternatives for prostate cancer treatment.

Currently used prostate cancer treatments have serious adverse effects; therefore, new research is focusing on alternative treatment options, such as the use of genetic biomarkers for targeted gene therapy,

nanotechnology for controlled, targeted treatment, and further exploration of medicinal plants for new anticancer agents.

Prognosis

Approximately 75% of patients present with cancer localized to the prostate, which is associated with a year survival rate of nearly 100%. Approximately 10% of patients present with metastatic prostate cancer, which has a 5-year survival rate of 37%.

Experience as a BPH patient with a hugely enlarged prostate in Bangladesh

BPH treatment in Bangladesh is widely available, ranging from medical management to advanced minimally invasive surgical procedures (Google search report). However, I have visited at least six of the top 10 urologists, based on Google search results, at leading hospitals for BPH treatment, and their diagnostic and treatment methods are not considered satisfactory (Tables 87 and 88 and Photos 1-12).

Urologists and Hospital-wise outcome of diagnosis and treatment of BPH with allopathic medicines

Google search reveals different advertisements for urologists and concerned hospitals, including 'Top 10 Urologist Specialist Doctors in Dhaka,' of which five urologists were selected for diagnosis and treatment of BPH, randomly followed one by one due to their unsuccessful attempt to treat the hugely enlarged prostate gland, and their method of diagnosis and treatment results are described (Tables 87 and 88).

① Comfort Diagnostic Center (Pvt) Ltd., Dhanmondi, Dhaka

The LUTS associated with BPH were first diagnosed on 8 December 2010 at the Comfort Diagnostic Center, Dhaka, and the urologist recommended serum PSA, prostate USG, uroflowmetry, and prescribed

Table 87. Transabdominal ultrasonography (USG) findings of the prostate gland and urinary bladder

SN	Date of test	Name of Hospital	Age of patient	UGC features of the prostate Size: L × B × AP	Volume	MCC	Pre-void	PVR	Photo No.
1.	07.10.2017	BMCH, Dhanmondi	65yrs	62 × 70 × 63 mm	143 cc	-	-	70 cc	1,2
2.	26.01.2019	INMAS, Mymensingh	65 yrs	-	276cc	344 ml	-	217	3
3.	24.02.2019	Comfort, Dhanmondi	65 yrs	6.3 × 6.6 × 7.2 cm	158ml	210ml	-	58	4,5
4.	11.02. 2024	ISDIC, Dhamondi	72 yrs	55 × 70 × 56 mm	115 cc	222 cc	-	56 cc	6,7
5.	04.11.2025	-Ditto-	73 yrs	84 × 74 × 79 mm	260 cc	-	106 ml	13 ml	8,9
6.	14.04.2026	DCIMCH, Shyamoli	75 yrs	7.28 × 7.29 × 8.07 cm	224.2 cm2	187.9 cm2	187.93 ml	17.9 ml	10-12

BMCH = Bangladesh Medical College Hospital INMAS = Institute of Nuclear Medicine and Allied Sciences ISDIC = IBN Sina Diagnostic Diagnostic and Imaging Center DCIMCH = Dhaka Central International Medical College and Hospital

L × B × AP = Length × Breath/Width × Anteroposterior/Height) = L × B × AP × 0.52 (or 0.523)

Normal size of the prostate = 15-25 grams, < 30 ml/ 30 cm^3 (1cc = 1g)

MCC=Maximum cystometric capacity Pre-void volume (Full bladder) PVR= Post-void residual Normal PVR value = < 25 cc

Photo 1. Hugely enlarged prostate (Vol. 142.6 cc) detected at BMCH

Photo 2. PVR (Post-void residual) 78.638 cc detected at BMCH

Photo 3. Hugely enlarged prostate with volume 276 cc and PVR 217 ml detected at INMAS, Mymensingh in 2019.

Photo 4. Hugely enlarged prostate with volume 158 cc detected at Comfort Hospital, Dhaka, in 2019.

Photo 5. PVR (Post-void residual) 58 cc detected at Comfort

Photo 6. Hugely enlarged prostate with volume 115 cc detected at INB Sina Diagnostic & Imaging Center (ISDIC), Dhaka in 2024.

Photo 7. PVR (post-void residual) 56 cc detected at ISDIC, Dhaka in 2024.

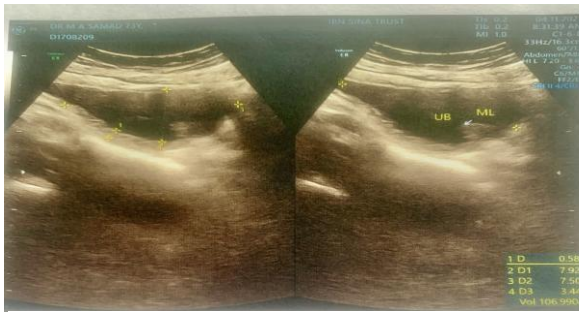

Photo 8. Hugely enlarged prostate with volume 115 cc detected at INB Sina Diagnostic & Imaging Center, Dhaka in 2025

Photo 9. PVR (post-void residual) volume 13 cc detected at ISDIC, Dhaka in 2025.

Photo 10. Hugely enlarged prostate with volume 224.3 ml detected at the Dhaka Central Int Medical College & Hospital.

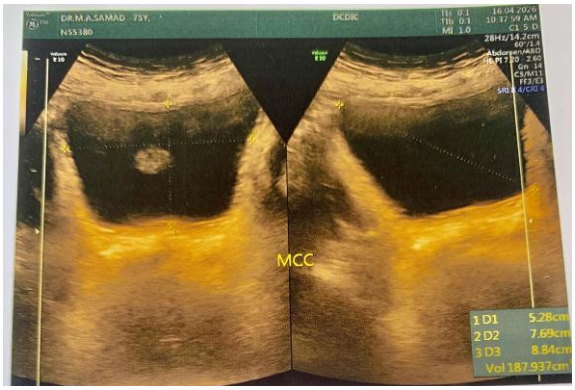

Photo 11. MCC (Maximum cytometric capacity) volume 187.9 ml of the urinary bladder detected at the DCIC&H, Shyamoli in 2026

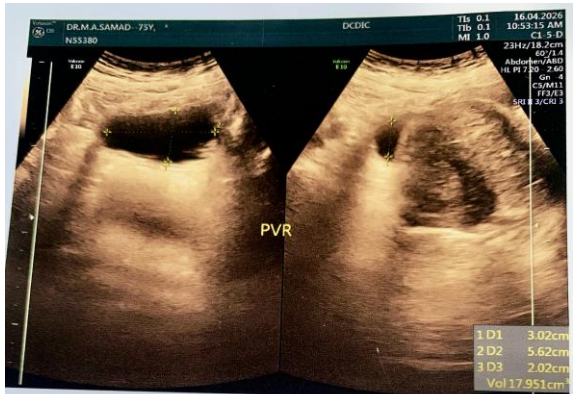

Photo 12. Post-void residual (PVR) volume 17.9 ml detected at the DCIMC&H, Syamoli in 2026

=

Uromax® (Tamsulosin hydrochloride) 0.4 mg orally daily. Uromax® was found ineffective against BPH with a hugely enlarged prostate (Table 87) based on LUTS and PSA results (Table 87 and 88). On the second visit on 21.5.2011, the urologist suggested a prostate biopsy, which was not an appropriate test for the patient, and accordingly avoided doing it. On the third visit on 24.02.2019, the urologist suggested USG of the prostate again, and the USG reports showed a hugely enlarged prostate with median lobe protruding within the bladder cavity with volume 158 and PVR 58 cc. Whereas the urologist mentioned a prostate size of 276 ml, a PVR of 217 ml, and a DRE test showing a huge prostate BPH, a small 1 cm^3 nodule in the apical region of the prostate, and accordingly suggested MP MRI of the prostate. The conclusion of the MRI report is, 'MP-MRI features of this enlarged prostate are unlikely to have any malignancy and fall in PI-RADS category-2.' PS-2 = A PI-RADS score of 2 on prostate MRI indicates a low probability that clinically significant prostate cancer is present. It often represents BPH, including prostatitis and scarring. A biopsy is generally not recommended for a PI-RADS-2 lesion. [366]

The urologist misguided the BPH patient:

- The urologist was only prescribed Uromax® for a hugely enlarged prostate that was not the appropriate treatment, but it was necessary to prescribe a combination of dutasteride plus tamsulosin hydrochloride product, as a result, prostate size increased.
- The urologist held the patient from 8 December 2010 to 26.02.2019 period, without any appropriate treatment, and only suggested different unnecessary diagnostic tests like prostate biopsy, MRI, and repeatedly others.
- The urologist should inform the patient that he is only experienced in applying TURP for prostate sizes of less than 80 grams, but not the hugely enlarged prostate that requires HoLEP surgery, which is beyond his expertise. Under these circumstances, the urologist's responsibility was to refer the case to a urologist experienced in HoLEP, but he didn't.

② Bangladesh Medical College and Hospital (BMCH), Dhanmondi, Dhaka

One of my medical doctor friends who was working as an academician at the BMCH informed me that he has booked a cabin for a patient with arrangements for a prostate operation with one of the top 10 urologists in Dhaka. Accordingly, 1 went to the hospital with all preparations on 7 October 2017. The urologist suggested some tests, including uroflowmetry, PSA, and USG of the prostate. Uroflowmetry was normal; PSA 8.62 ng/ml; prostate volume 143 cc; PVR 70 ml (Tables 87 and 88, Photos 1 and 2). Instead of a surgical operation for the enlarged prostate, he prescribed three categories of drugs: (a) Prostaid® 500 mg (herbal) daily for 2 months, (b) Urimax®/Prostacin D® 1 capsule daily, and (c) Cap. Urodart® 1 capsule daily for six months (Table 88). He suggested contacting after six months, and if the prostate size shrinks by less than 80 g, then he could use the TURP method for surgery, as he was not trained in any other method

of surgery to use in a hugely enlarged prostate >80g. Accordingly, an appointment was made to see the urologist after six months at five pm at the ISDIC, but the urologist did not come to his chamber to see any patients until 8.30 pm. As a patient, I left the hospital without waiting any longer to see the doctor.

Comments on the doctor's activities in Dhaka

- The urologist prescribed drugs for BPH in men with Uromax® (Tamsulosin hydrochloride =TH) / Prostacin D® (TH + dutasteride), and Cap Urodart® (dutasteride). It appears to be the same drug from different companies, because Prostacin D® contains both TH and Dutasteride, whereas Uromax® and Urodart® are sold separately (Table 88).

Table 88. Personal experience on diagnostic and treatment procedures for the BPH of a hugely enlarged prostate by different urologists in Bangladesh

SN	Date	Name of Hospitals	Application of diagnostic methods							Prescription	Results
			ESR1 mm1st hr	DRE	PSA2 (ng/ml)	USG (prostate) Volume	PVR	Prostate biopsy (PB)	MRI		
1.	24.11.2010	Comfort, Dhaka	45	-	10.07	-	-	-	-	-	-
	08.12.2010	Comfort, Dhaka	-	-	8.26	-	-	PB3	-	Uromax®	Unsatisfactory
	21.05.2011	Comfort, Dhaka	-	-	-	-	-	-	-	-	-
	25.06.2012	Comfort, Dhaka	-	-	7.44	-	-	-	-	-	-
	24.02.2019	Comfort, Dhaka	23	SN	5.79	158 cc	58 cc	-	PS-2	-	-
2.	07.10.2017	BMCH, Dhaka	-	-	8.62	143 cc	70 ml	-	-	Prostaid + Urimax®/ Prostatin D® + Urodart®, but drugs+	LUTS improved
3.	26.01.2019	INMAS	-	-	-	276 cc	217	-	-	-	-
4.	11.02.2024	ISDIC, Dhaka	25	-	10.7	115 cc	56 cc	-	-	-	-
5.	02.09.2024	United Hospital	-	HDNM	-	-	-	-	-	Uromax® + Trevox®	Unsatisfactory
	25.09.2024	United Hospital	-	-	9.89	-	-	PB3	MRI	-	-
	04.11.2025	ISDIC, Dhaka	28	-	9.21	260 g	13 ml	-	-	-	-
6.	09.11.2025	Labaid SP	-	80g*	-	S	-	-	-	-	Not continued
7.	16.04.2026	DCIMCH	-	-	-	187.93	17.9 ml	-	-	Uromax-D®, Pronor®	Not used

BMCH = Bangladesh Medical College and Hospital INMAS = Institute of Nuclear Medicine & Allied Sciences, Mymensingh
ISDIC = Ibn Sina Diagnostic & Imaging Center Labaid SP = Labaid Specialized Hospital Pronor® = Finasteride
DCIMCH = Dhaka Central International Medical College & Hospital, Shyamoli, Dhaka Uromax® = Tamsulosin hydrochloride + Dutasteride
SN = Small nodule in the apical region of the prostate on DRE HDNM = Hard deforming nodule in the middle
PS-2 = A PI-RADS score of 2 on prostate MRI indicates a low probability that clinically significant prostate cancer is present. It often represents BPH, including prostatitis and scarring. A biopsy is generally not recommended for a PI-RADS-2 lesion.[366]
1ESR= Erythrocyte sedimentation rate, Reference value: 0-10 2Reference value <4.0 ng/ml) drugs+ = Withdrawal LUTS reappear
3PB = Prostate biopsy suggested but not done.
S = USG and uroflowmetry tests were suggested because the urologist did not believe the test report of ISDIC, but they were not done.

- This is the normal practice of specialist doctors practicing in different private hospitals, especially at night, because most of them are working at government hospitals and different medical colleges during the day. Most of the doctors encouraged patients to see them in the private hospital's chamber from evening to night, and they couldn't keep the scheduled time for each patient. This is not only for the urologists but also for the other specialists.
- On 21.08.2023, I also made an appointment to see a specialist doctor at Lab-aid Hospital, Dhanmondi at 4.0 pm, but the doctor didn't come to see the enlisted patients in time, and at 8.0 pm I left the hospital without seeing the doctor. Similarly, I also made an appointment at Uttara Crescent Hospital on 23.08.2023. The receptionist asked me to report at 6.0 pm. When I reached the reception, the receptionist asked me to pay BDT 2000/- as an advance for the first-visit fee before seeing the doctor, and I immediately paid the amount. Then I came to know that more than 100 patients were waiting to see the doctor, and at 11.30 pm, the receptionist allowed five patients at a time to the doctor's chamber, and the doctor used some seals that were made with the trade name of drugs, and he was using such seals on the prescription paper without performing any diagnostic tests, he also made such malpractice on my prescription along with suggested for some diagnostic tests. He then asked me to report on 30.08.2023 with test results in the evening without any further appointment. Accordingly, I went to see the doctor on

time, but the doctor's chamber was closed. I then learned from the hospital's main desk that the doctor had canceled the program scheduled for that date and time to see patients. This doctor sees patients at this hospital only one night a week and earns at least BDT 2 lac per visit from 100 patients, without providing appropriate services.

- The system of medical services to get appropriate specialized treatment from a specialist doctor has become highly complicated in Bangladesh, especially in Dhaka. Accordingly, transabdominal USG was performed on five occasions in four different hospitals for assessment, and the results are summarized in Table 87. The USG prostate volume varies from 115 to 276 cc across different imaging centers (Photos 1-12).

③ United Hospital, Dhaka

The United Hospital Ltd. (now renamed Continental Hospital PLC) is a private hospital in Gulshan-2, Dhaka, Bangladesh, considered one of the city's high-end private hospitals. Considering this, an appointment with a urologist (Senior consultant) was made on 2 September 2024, and upon arrival, I paid BDT 2000/- before seeing the doctor. I introduced the hugely enlarged prostate to the urologist, but he said you have a hydrocele, then I asked him, 'How do you diagnose hydrocele?' Then he said, 'ignore it.' Then I became astonished by his diagnosis of hydrocele. Then he mentioned on the prescription sheet, 115g prostate volume with a hard deforming nodule on the middle lobe of the prostate. Then he prescribed (a) Cap Tamsulosin 0.4 mg (Uromax®) and (b) Tab Levofloxacin (Trevox®) 500 mg daily. I informed him that I had discarded Uromax® in 2010 due to ineffectiveness; moreover, it is not appropriate to prescribe Uromax® in a hugely enlarged prostate, but he did not change his decision. In addition, he suggested testing total PSA after three weeks of taking prescribed drugs. After three weeks, the total PSA was tested on 25 September 2024, and the result was 9.80 ng/ml, compared with 11.7 ng/ml on 11 February 2024, indicating no significant change.

On the second visit on 26 September 2024, on payment of BDT 2000/- in advance, he again prescribed Cap Uromax® and suggested uroflowmetry, PVR, biopsy, and MP MRI of the prostate with contrast. I informed the urologist that all these tests have already been done with a hugely enlarged prostate. If you get the same findings, what will you do with the test results? He said if he can diagnose prostate cancer, then he will start chemotherapy. Then I asked him what would happen with my hugely enlarged prostate if I started chemotherapy? He had no answer for it.

Comments

- The diagnosis of a hugely enlarged prostate was confirmed with different tests conducted at different hospitals since 2010, and now requires appropriate surgical intervention. Instead of surgical intervention, the urologist showed interest in repeating all these same tests again to reconfirm the enlarged prostate, which might be due to commercial interests or a lack of specialist knowledge on appropriate surgical knowledge and devices.
- The urologist was considered the BPH patient with a hugely enlarged prostate during the patient's first visit, and he ignored that the patient had been suffering from BPH for 14 years and had been treated by different urologists.
- The Urologist might have trained on TURP surgery, which he applies to patients with sudden urinary obstruction associated with less than 80g prostate volume. Experienced urologists who serve medical professionals following medical ethics should apply HoLEP for a hugely enlarged prostate or refer to the appropriate urologist who is trained to perform HoLEP surgery for the hugely enlarged prostate.
- The urologist prescribed Uromax® even in the second visit, with no efficacy in either LUTS or PSA level, which indicates some abnormalities and biasness to the manufacturing company.
- The Urologist was unable to manage appropriate methods of diagnosis and treatment of a hugely enlarged prostate because, after that, I came to know from the website, 'Best urologist in United Hospital Ltd., Dhaka: No doctors found.'[367]

④ Experience at LABAiD Specialized Hospital, Dhanmondi, Dhaka

I had been suffering from BPH with a hugely enlarged prostate with a volume that varied from 115 to 276 ml, depending on the different hospital USG reports, and the local urologist commonly used traditional TURP surgery up to prostate size <80 grams, but laser surgery HoLEP would be required for a hugely enlarged prostate (Tables 47,49); accordingly, on a Google search it appears as, 'HoLEP surgery is available at Labaid Specialized Hospital, Dhanmondi Dhaka. It is offered through the Department of Urology as a modern, minimally invasive surgical procedure for BPH or an enlarged prostate.[368] In addition, Prof. Dr. Md. Jahangir Kabir, A pioneer in laparoscopic and laser urology (HoLEP) in Bangladesh, or advanced laser surgery, based on 2025-2026 data. [369.] Accordingly, I made an appointment with the HoLEP surgeon, Chief Consultant Urologist at Labaid Specialized Hospital, Dhanmondi, Dhaka, on 3.11.2025 for HoLEP surgery for an enlarged prostate.

- On arrival at the Hospital, the receptionist asked to deposit BDT 1500/- to see the Chief Consultant. Accordingly, I did it. After waiting at least three hours, when I met with the urologist and did a Google search, I came to know that you are doing HoLEP surgery for hugely (>80g) enlarged prostates, and I need to do it for my hugely enlarged prostate. The urologist replied that HoLEP is not a good surgical option for a large prostate without complications, and he suggested applying TURP surgery (Table 39).
- When I informed him that my prostate volume was 260 g and PVR 13 ml as per the USG report made by Ibn Sina Diagnostic and Imaging Center, he directly replied that he did not believe these findings of the report, and suggested to repeat two tests in their laboratory, including Uroflowmetry and USG. In addition, he mentioned in the prescription sheet, 'DRE shows 80-gram benign prostate', which is not possible to detect prostate volume in grams on DRE examination. This indicates that the urologist firstly hides in the website advertisement that he is a pioneer for HoLEP in Bangladesh, secondly, he used the DRE test to detect prostate volume, thirdly, it is not ethical for a specialist surgeon not to believe test results conducted in another hospital and needs to test in their hospital.
- I was only visited by this Urologist to determine whether possible to do HoLEP for a hugely enlarged prostate or not, but he made the case complex to delay earning money from the patient, and suggested in the prescription (a) keep motion loose, (b) take vegetables, fruits, and Isabgol powder, and 1.5 to 2 liter drinking water every day, for which I was ready to see him with payment of BDT 1500/-

⑤ Experience as a BPH patient at the Advanced Center of Kidney and Urology (ACKU), Dhaka

The hospital authority (ACKU) has introduced the Thulium LASER for Prostate surgery (THULEP) on its website, stating that it is the first in Bangladesh, and has a Holmium LASER for kidney surgery by RIRS or Mini PCNL.[370] Accordingly, I made an appointment on 15 April 2026 to see the Urologist, ACKU, to determine whether it would be possible to use the laser HoLEP surgical operation for the hugely enlarged prostate or not. After waiting at least four hours, I was able to see the urologist, and in my first introduction, I directly asked the urologist whether it would be possible to use laser HoLEP surgery for my hugely enlarged prostate or not? He replied that the HoLEP machine is not working and needs parts to be repaired before it can be used. I then realized that the advertisements on the website and the hospitals' actual status differ across all hospitals in Dhaka. However, the urologist assured me that he could use bipolar TURP (Table 39), which would also work similarly well as HoLEP. Then he made a prescription with (a) Cap. Uromax D® (Tamsulosin + dutasteride)1 capsule daily and (b) Tab. Pronor 5® (finasteride) 2 tablets daily. In addition, he has suggested uroflowmetry and USG of the KUB, MCC, and PVR; if the findings of these tests are favorable, he could proceed with surgical intervention.

Accordingly, USG and uroflowmetry tests were completed on 16 April 2026 before noon, and then both reports were produced for the urologist. After observing the report, he disagreed to process the Bipolar TURP that he had verbally agreed to during the first visit. Then, I informed him that you have prescribed two drugs, dutasteride and finasteride, to a single patient, which is pharmacologically non-ethical.

Comments

- All five visited urologists for the treatment of a hugely enlarged prostate in different hospitals in Dhaka dealt with in similar ways, they don't have either appropriate updated knowledge of medical treatment options or any modern laser surgical intervention, although they dealt with the patient as a new one and suggested the same different diagnostic tests and prescribed ineffective drug Uromax® for a hugely enlarged prostate. It indicates that, in a commercial manner, dealing with patients without adhering to medical professional ethics and prescribing ineffective drugs biased toward a particular company may be driven by commercial interests, as approximately 42 pharmaceutical companies market the same drug.[371]
- I also informed the urologist, ACKU, that I have been taking Sasolin D® (Tamsulosin hydrochloride, that relaxing the bladder neck muscles) and dutasteride (may work by shrinking the prostate) for six months after comparative trials of all the similar composition drugs available in the local market. Although the urologist prescribed Uromax D® (Tamsulosin hydrochloride + dutasteride) and finasteride (Pronor 5® tablet). We can see the results on Google search on, 'Is it ethical to prescribe both finasteride and dutasteride simultaneously in a BPH patient?' Answer: Prescribing both finasteride and dutasteride simultaneously for BPH is generally not considered ethically sound or clinically standard practice. Both medications belong to the same class- 5-alpha-reductase inhibitors (5-ARIs)- and work through similar mechanisms, meaning the combination offers no established benefit over monotherapy while increasing risk (Fig. 6).

Summary: Urological practices in Dhaka

- It appears from this review that all the urologists visited for treatment of BPH at different hospitals dealt with the patients in a commercial rather than adhering to medical professional ethics, which are a set of moral principles and standards, including 'respect for autonomy, beneficence, non-maleficence, and justice' that guide healthcare providers to prioritize patient well-being, dignity, and trust. These core values ensure competent care, confidentiality, informed consent, and equitable treatment regardless of background.[372,373]
- Table 88 shows that all the urologists prescribed tamsulosin hydrochloride from only one pharmaceutical company, whereas 42 companies supply this product in the local market,[371] indicating possible unethical drug prescribing in Bangladesh.
- All tests required for the diagnosis of PBP require laboratory testing, especially in pathology, biochemistry, and imaging centers, except DRE, which is performed by the urologists themselves, but their findings vary widely. The urologist of the Comfort center detected a huge prostate BPH, a small 1cm^3 nodule on the apical region of the prostate on 24 February 2019. The Urologist of the United Hospital detected a 115-gram prostate volume with a hard deforming nodule in the middle lobe on 02 September 2024. The urologist of Labaid detected 80 grams of prostate volume without any nodules on 9 November 2025. Whereas the USG report of ACKU shows echogenicity is homogenous with an intact capsule on 16 April 2026. This indicates that the urologists detected and recorded findings on DRE beyond the test detection capability.
- Currently, there are no medical treatment options other than Tamsulosin hydrochloride and dutasteride, which are extensively prescribed in BPH patients without considering their side effects. Dutasteride is generally well tolerated, but it can cause several side effects, including erectile dysfunction, lower sex drive (libido), breast tenderness, breast enlargement, difficulty ejaculating, dizziness, mood changes, and lower sperm count. More serious side effects include an increased risk of prostate cancer and birth defects.[374] Dutasteride has been reported to be associated with a small but statistically significant increase in the development of high-grade prostate cancer (Gleason score 8-10) in some men. The trials showed that the long-term daily use (>4 years) of finasteride (5 mg) and dutasteride in men aged 50 years was associated with a small but statistically significant increased risk of high-grade prostate cancer, and to

emphasize that these drugs are not approved for the prevention of prostate cancer.[375] High-grade prostate cancer is an aggressive type of prostate cancer that grows and spreads more quickly than low-grade prostate cancer. However, the earlier reports showed that dutasteride has reduced the risk of incident prostate cancer detected on biopsy and improved the outcomes related to BPH.[376] In another report, it has also been reported that there was no increased risk for Gleason 7-10 or Gleason 8-10 prostate cancers in men taking dutasteride over control groups. [377] More recently, it has been reported that dutasteride was not associated with a lower risk of prostate cancer than finasteride in patients with BPH, suggesting the safety of finasteride and dutasteride concerning the risk of prostate cancer.[378] However, further research is needed to determine whether dutasteride is associated with high-grade cancer in BPH patients.

Efficacy of herbal and homeopathic medicines in BPH

BPH is considered a chronic old age disorder that requires long-term treatment, where common allopathic medicine interventions such as 5α-reductase and α-blockers are associated with adverse events. Therefore, effective, safe, and affordable herbal and homeopathic medicines for long-term management require investigation and development.

There are hundreds of commercial herbal products for BPH globally, mostly marketed as over the counter (OTC) supplements. While dozens of individual botanical ingredients are used, the market is dominated by a few key ingredients, often sold in poly-herbal combinations. There are over 100 websites alone advertising and selling Phyto-therapeutic products (herbal remedies) for BPH in men in the US and Europe. User ratings for commercial herbal products targeting BPH are highly mixed, with many men reporting moderate relief of LUTS, particularly when using combinations of herbs, while clinical studies often show results like placebos. Considering these facts, over 20 user-rated herbal products manufactured in the USA and marketed globally were selected for clinical evaluation in BPH (prostate volume 115-276 cc), from 2019 to 2026 (Photo 13).

Photo 13. Commercial herbal products used for clinical trials for BPH with prostate volume 115 to 276 cc.

1. Saw Palmetto 3X Formula (Havasu Nutrition, USA)
- Saw Palmetto blend- 500 mg
- Stinging Nettle Leaf powder- 360 mg
- Pumpkin seed extract- 160 mg

2. Men's Prostate Formula (GNC, USA)
- Saw palmetto extract- 500 mg
- Stinging Nettle leaf powder- 360 mg
- Pumpkin seed extract-160 mg

3. Prostonic Ultra (Herb Tonic, USA)
- Saw palmetto powder- 600 mg
- Vitamin B6- 5 mg
- Pumpkin seed powder- 60 mg
- Cayenne pepper powder- 5 mg
- Gravel root powder- 5 mg
- Parshmallow root powder- 5 mg
- L-glutamic acid HCl- 70 mg
- L-glycine- 30 mg
- Zinc oxide- 50 mg
- Copper gluconate- 0.5 mg
- *Pygeum africanum* bark extract- 300 mg
- Burdock seed powder- 5 mg
- Goldenseal root powder- 5 mg
- Juniper berry powder- 5 mg
- Parsley leaf powder- 5 mg
- L- alanine- 70 mg
- Beta-sitosterol- 300 mg

4. SP+ Soft gel (Saw palmetto plus, GO Supps, USA)
- Saw palmetto oil-320 mg+
- Pumpkin seed oil 260 mg+
- Cranberry seed oil- 15 mg+

5. Ultra Prostate Formula (Life Extension, USA)
- Saw palmetto CO_2 extract (fruit)- 320 mg
- Stinging nettle extracts (root)- 240 mg
- Pumpkin oil (seed)- 200 mg
- Beta-sitosterol- 180 mg
- Phospholipids- 160 mg
- Pygeum extract (bark)- 100 mg
- ApresFlex® Indian frankincense extract- 70 mg
- Graminex® Flower Pollen Extract™ and NAX™ paste (from rye)- 63 mg
- HMRlignan™ Norway spruce and Flax lignan seed extract- 20.15 mg
- Lycopene (Lyc-O-Mato® natural tomato extract)- 10 mg
- Boron (boro-organic glycine)- 3 mg

6. EZ Prostate™ (ENterpRise, USA)
Proprietary blend: 1000 mg
- L-lysine HCL
- Apple Cider Vinegar fruit-
- Garcinia cambogia powder
- Tongkat All extract root
- Horny goat weed plant extract
- Cinnamon bark extract
- Wild yam root extract
- Bitter melon fruit extract
- Raspberry ketones
- Others- Gelatin capsule, rice powder, magnesium stearate, vegetable grade

7. Prosta Vive (Pelican Vitamins, USA)
- Vitamin E - 13 mg
- Vitamin B6 - 2 mg
- Zinc oxide - 12 mg
- Selenium- 55 mg
- Copper- 4 mg
- Magnesium- 50 mg
- Sodium (sea salt)- 70 mg
- Vitamin E- 13 mg
- Vitamin D3- 59 mcg
- Vitamin B6- 2 mg
- Saw palmetto - 200 mg
- Pygeum africanum- 100 mg
- Plant sterol complex- 50 mg
- Tongkat Ali- 100 mg
- Ashwagandha- 250 mg
- Panax ginseng- 50 mg
- Fenugreek- 500 mg
- Raspberry juice powder- 50 mg
- Soursop- 50 mg
- Green tea- 50 mg
- Cat's claw (U. tomentofa) bark-30mg
- Broccoli crown- 30 mg
- Tamato powder- 30 mg
- Maitake fruit- 10 mg
- Reishi fruit– 10 mg
- Shiitake fruit- 10 mg
- Maca root (Peruvian plant)- 250 mg
- Nettle root (Urtica dioica)- 30 mg
- Artichoke (leaves) extract- 300 mg
- Cordyceps powder- 250 mg
- Boron- 5 mg
- Proprietary blend- 200 mg

8. Pygeum 4000 mg (Carlyte New, USA)
- *Pygeum africanum* bark extract- 4000 mg

9. Beta-Sitosterol (Horbaach, USA)
Cardio Sterol™ esters complex (1200 mg per serving), which includes Beta-sitosterol (roughly 810-1110 mg), along with Campesterol, Stigmasterol, and others.

10. Beta-Sitosterol (Natures Craft, USA)

11.Prostadine™ (Prostate complex, GMP, USA)
- Saw palmetto extract
- Iodine
- Nori Yaki Extract powder
- Wakame extract
- Pygeum africanum bark
- Pumpkin seed extract
- Kelp powder
- Bladderwrack powder
- Pomegranate extract
- Shilajit
- Beta-sitosterol
- Zinc

Observed Side effects: Dry mouth, dizziness, headache, tiredness, and drowsiness.

12. Now® Clinical Strength Prostate Health (Now Foods, USA)
- Saw palmetto extract (berry)- 320 mg
- Beta-sitosterol phytosterols)- 850 mg
- LYC-O-MATO® Lycopene-10 mg
- Zinc (Zinc BI glycinate)- 15 mg
- Selenium (Selenium glycinate)- 70 mcg
- Pumpkin seed oil- 1 g (1000 mg)
- Quercetin (Quercetin dihydrate)-200 mg
- Turmeric root extract- 100 mg
- Green tea extract (leaf)- 100 mg
- Pomegranate extract (fruit)- 100 mg
- LinumLife® complex (Flaxseed lignan extract)- 25 mg
- Lycopene (LyC-O-MATO® Tomato extract- 25 mg
- Trans-resveratrol (Japanese knotweed extract)- 10 mg
- Vitamin D_3 (Cholecalciferol)- 10 mcg

Locally produced herbal products

1. Prostaid® (Radiant Pharma. Ltd.)
- Saw palmetto oil- 160 mg
- Pygeum bark oil- 1.7 mg
- Korean ginseng- 3.3 mg
- Zinc sulfate monohydrate- 33.1 mg
- Copper gluconate 2.0 mg

Stock: Currently not available.

2. Urocin™ (Trust (Unani) Ltd.)
- Punarnava (*B. diffusa*) extract- 500 mg

3. Uripam™ Softgel (Square Pharma)
- Saw palmetto- 160 mg
- Pygeum bark oil- 1.7 mg
- Korean ginseng extract- 3.3 mg
- Zinc sulfate monohydrate- 33.1 mg
- Copper gluconate- 2.0 mg

4. Urican capsule (Drug Int. Ltd.)
- Cranberry (Vaccinium macrocarpon)

5. Himalaya Uricare (Bangladesh)
- Cyperus, Shila Jeet, Didymo carpus, Pasanabheda, Little ironwood

Herbs used for the treatment of BPH

The following herbs and herbal ingredients are used for BPH in Bangladesh
- Saw palmetto (*Serenoa repens*)
- Pumpkin seeds (*Cucurbita pepo*)
- Pygeum bark (*Pygeum africanum*)
- Stinging nettle root (*Urtica dioica*)
- Korean ginseng (*Panax ginseng*)
- Soy isoflavones (*Glycine max*)

Herbal products highlighted on Facebook
- Ikkuk gondha (*Hygrophila spinosa*)
- Wasila Urocare tonic (Facebook)
- Uro-herb Plus
- Wasila Uro-care Tonic
- Miftahul Food
- Organic Mart

While sometimes used in traditional practices for urinary issues, there is no established medical evidence that these herbs can cure or effectively treat an enlarged prostate (BPH).

Differences in herbal products used for the treatment of BPH and male sexual stimulation (aphrodisiacs)

Herbal products for BPH and male sexual stimulation (aphrodisiacs) differ significantly in their therapeutic targets, active ingredients, and intended effects, though they occasionally overlap in promoting overall male vitality. BPH remedies focus on reducing prostate size and improving urinary flow, while sexual stimulation products aim to enhance libido, stamina, and erectile function.

① Functional focus and targets
- BPH herbal products: These are designed to treat LUTS associated with an enlarged prostate. They focus on reducing prostate inflammation and slowing tissue growth (anti-proliferative effects).
- Sex stimulation products: These aim to improve libido, increase stamina, enhance erectile quality, and decrease mental or physical fatigue.

② Common herbal ingredients (BD)

a. Medicinal herbs for BPH in BD

- Saw palmetto (*Serenoa repens*)
- Pumpkin seeds (*Cucurbita pepo*)
- Pygeum bark (*Pygeum africanum*)
- Stinging nettle root (*Urtica dioica*)
- Korean ginseng (*Panax ginseng*)
- Soy isoflavones (*Glycine max*)

b. Herbs for sex stimulation in BD

- Maca root
- Shilajit
- Tongkat Al
- Safed musli
- Myristica fragrans
- Gokshura (*Tribulus terrestris*)
- Ashwagandha
- Horny goat weed (Epimedium)
- Local blends like Shokti+
- Pinax Ginseng (Korean/Red)

Efficacy of herbal drugs in BPH

- Most herbal drugs appear to target symptom relief (LUTS) rather than significantly shrinking the prostate.
- While some herbal extracts show promising results in mild to moderate BPH patients, they are not approved by the FDA and not recommended by the American Urological Association (AUA) due to inconsistencies in research and lack of long-term safety data.
- Herbal drugs and phytotherapy can offer modest relief for mild to moderate LUTS caused by an enlarged prostate; they are not generally considered effective for a hugely enlarged prostate. However, it has helped to improve the quality of life when used alongside allopathic and homeopathic medicines.

BPH and Aphrodisiacs in Bangladesh

BPH and erectile dysfunction (ED/Aphrodisiacs) are distinct, differ in etiology and clinical presentation, but both are common male disorders that often coexist as conditions, particularly in aging men, with a significant overlap in treatment approaches (such as PDE5 inhibitors) and a high prevalence of ED (up to 80%) in patients with symptomatic BPH (Table 89). Target population: BPH products are usually for men over 50-60 years old, while sexual stimulants are marketed to a broader age range of married men, often targeting those in their 30s and 40s. Herbal medicines are used for both, yet their efficacy is variable, and side effects can be significant.

Table 89. Comparison of etiology, symptoms, treatment, including herbal drugs, between BPH and erectile dysfunction (aphrodisiacs) with side effects in men

SN Feature	Benign prostatic hyperplasia (BPH)	Erectile dysfunction (ED/ Aphrodisiacs)
① Definition	Non-cancerous enlargement of the prostate The gland presses on the urethra.	Inability to achieve/maintain a firm enough for sexual intercourse
② Etiology	Age-related prostate enlargement due to hormonal changes (testosterone, DHT, estrogen imbalance); risk factors include aging, family history, diabetes, obesity, cardiovascular disease.	Multifactorial: vascular (atherosclerosis, hypertension, diabetes), neurologic (spinal cord injury, neuropathy) hormonal (low testosterone), psychogenic (stress, depression), lifestyle (smoking, alcohol).
③ Common symptoms	Frequent urination, weak/slow urine stream, hesitancy, nocturia, incomplete emptying, dribbling.	Failure to initiate or maintain an erection, reduced libido, or keeping an erection firm enough for sexual intercourse.
④ Primary target	Prostate gland (reducing enlargement)	Libido, blood flow, nerve stimulation.
⑤ Conventional treatment	Alpha-blockers (e.g., Tamsulosin), 5α-reductase inhibitors (dutasteride), PDE5 Inhibitors (Tadalafil), and surgery.	PDE5 inhibitors (sildenafil/viagra, tadalafil), vardenafil, avanafil, and hormone (androgen) therapy, vacuum devices, penile implants, and surgery
⑥ Herbal treatment	Saw palmetto, Pumpkin seed oil, Stinging nettle root, Pygeum africanum, Rye pollen Beta-sitosterol,	Maca root, Ashwagandha, Horny goat weed, Shokti+ Panax Ginseng, Tribulus terrestris, Ginkogo biloba, Eurycoma longifolia (Tongkat Ali), Yohimbine.[1]
⑦ Side effects (Medication)	α-blockers: Dizziness, ejaculatory issues, 5-ARIs: Reduced libido, erectile dysfunction.	Headaches, flushes, congestion & runny nose, body aches & pains, indigestion, dizziness, vision changes.
⑧ Side effects (Herbal)	Stomach upset, headache (generally well-tolerated).	Generally safe, but may cause insomnia, hypertension, or nervousness (especially Ginseng).

[1]Some herbal sexual stimulants (e.g., Yohimbe) may cause serious cardiovascular side effects. Patients with BPH should be cautious, as certain herbs can worsen urinary symptoms or interact with prescribed medications.

Sex stimulating herbs and products

1.Duratab™ (Ibn Sinha)- *Myristico fragrant* (Jaitrik)- 66,67 mg, *Mabiya carinata* (Sand lizord)- 66.67 mg, *Argyria speciosa* (Samundar surkh)- 33.33 mg, *Calcinated silver* (Bhasma of silver)- 16.67 mg, *Crocus sativus* (Jafran)-

16.67 mg, Bezorar stone (*Johor mohra*)- 8.33 mg, Costorium (*Junde bedostor*)- 8.33 mg, and Piper bettle (*Pan pata*)- QS Uses: Premature ejaculation, sexual weakness, and depression.

2. Super Viga Sprays 10 million (Natural Maca extract for men) (Bbazar)

3. ManUp Swalpa Chandroday Makardwaj Tablet (Unani formulation)

- Makardhwaj (purified gold, mercury, sulfur)
- Karpura (camphor)
- Shuddha Jaiphal (nutmeg)
- Kali mirch (black pepper)
- Lata kasturia
- Kumari (aloe vera)/Karpasa (cotton) juice
- Medical supervision required: Contains heavy metals; must only be taken under strict medical supervision.

4. Maca Root capsules

- Brands: NatureLife Labs, NOW Foods, Force Factor, New Leaf, and Agobi
- *Lepidium meyenii* (often called Peruvian Ginseng)

5. Himalaya confide (CannaMeds India)

Each tablet contains:

- Ashvagandha (Withania somnifera): 78 mg
- Kokilaksha (Asteracantha longifolia): 38 mg
- Vanya kahu (Lactuca serriola): 20 mg
- Svarnavanga: 20 mg
- Vriddhadaru (Argyreia speciosa): 38 mg
- Jeevanti (Leptadenia reticulata): 38 mg
- Shaileyam (Parmelia perlata): 20 mg

6. Himalaya Tentex Royal Capsule (India)

- Kokilaksha (Asteracantha longifolia): 145 mg
- Vatada (Prunus amygdalus/Almond): 126 mg
- Sunishannaka (Blpharis edulis)- 115 mg
- Kumkuma (Crocus sativus/Saffron): 14 mg
- Gokshura (Tribulus terrestris): 100 mg
- Processed in: Musali (Curculigo orchioides) and Nagavalli (Piper betel)

7. Himalaya Tentex Forte Tablets (India)

- Ashvagandha (Withania somnifera)
- Shilajit
- Mucuna pruriens
- Saffron (Crocus sativus)
- Anacyclus pyrethrum
- Bombax

8. Prime Test Testosterone Booster (Made in USA)

Supplement facts and ingredients:

- Horny goat weed extract: Known for supporting libido and energy.
- Tongkat Ali root extract: Used to improve testosterone production.
- Other potential ingredients: Often include Tribulus terrestris, Nettle extract, and Boron

9. Ultrahot herbal capsules

- The name of the manufacturing Company is not available, which is required to ensure product safety.

a. Ultrahot (Made in Japan)

- Epimedium (Horny goat weed)
- Shilajit
- Yohimbine

b. Ultrahot (Made in Malaysia: Facebook)

- Tongkat Ali (Eurycoma longifolia)
- Maca peruviana (root)
- Ginseng extract, Zinc, and L-arginine (Sahanti Care)

- Lazada, Malaysia: This item is non-returnable, and warranty is not available.

Side effects: Ultrahot (contains Yohimbine, Tongkat Ali, and Epimedium), potential side effects include increased heart rate, insomnia, anxiety, dizziness, and potential interactions with cardiovascular conditions. Moreover, formulations may have a high-risk profile due to non-standardized ingredients.

10. Ginseng capsule 500 mg

- About 16 pharmaceutical companies in the Bangladesh market sell Ginseng capsules under different names (medex.com.bd). Composition: Extract of Panax ginseng equivalent to 500 mg dry root powder.[379]

Mechanism of action: Act as aphrodisiacs, increasing testosterone levels, improving blood circulation (vasodilation), or acting as stimulants for libido. These are marketed as libido boosters, energy enhancers, or stamina products to treat erectile dysfunction and low sexual desire. These products often work by improving circulation (vasodilation), increasing nitric oxide levels, boosting natural testosterone, and reducing stress.

Side effects: Ginseng side effects are generally mild. It has been reported to cause: nervousness, insomnia, headaches, dizziness, upset stomach, skin reactions, and allergic reactions. In addition, Ginseng could interact with other medicines, like digoxin, morphine, blood thinners, diabetes medications, diuretics, and antihypertensive drugs.[380]

Overlap and warnings

- Conflicting effects: Some conventional BPH remedies (and some herbs) can lower libido and cause ED, which is the opposite of sexual stimulator products.
- Safety warning: Many sexual stimulator herbal products in Bangladesh may be unregulated, and some have been found to contain undeclared synthetic compounds (like sildenafil analogs).
- Concurrent use: While some herbs (such as pumpkin seed) can be used alongside conventional medicine, combining multiple herbal products without a doctor's guidance may lead to toxicity.

Evaluation of homeopathic medicines in BPH

Homeopathic medicines, like other medicines, have been used to manage BPH, and some reports have shown a significant reduction in LUTS, with over 50% improvement in IPSS/AUASI scores. However, the efficacy of medicinal management of BPH, including homeopathic medicines, depends mainly on the volume of the prostate and single or multiple drugs used (Table 90).

Table 90. Evaluation of homeopathic drugs in BPH associated with LUTS

SN	Name of medicines	Strength & dose	Efficacy on LUTS
A. Mono-homeopathic medicine			
1.	*Sabal serrulate*	∅	Treatment alone is not effective
2.	*Thuja occidentalis*	200, 1M, CM	Partially effective for a short period
3.	*Conium maculotum*	200, 1M	Has effective action within 15 to 30 minutes in nocturia and obstruction.
4.	*Lycopodium clavatum*	200, 1M, CM	Treatment alone is not effective
5.	Carcinocin	200, IM	Efficacy is not evaluated, but it is supposed to prevent prostate malignancy.

B. Combined homeopathic medicines

① R25 Prostatan (Pharmazeuilische, Germany)

Ingredients: •Chimaphila umbellate D3 1g •Clematis vitalba D3 1g •Conium D5 1g •Ferrum picrinicum D4 1g •Pareira brava D2 1g •Papulus tremuloides D3 1g •Pulsatilla D3 1g •Sabal serrulatum •Ethanol/Aqua purificata 37 vol % alcohol

Dose and duration: 10-15 drops 3 times daily, mixed with water; daily intake of 22 ml; 5 vials. Along with tamsulosin, it relieves LUTS, but LUTS reappear on withdrawal of the drugs.

② Prostomum drops (SBL, India)

Ingredients: •Sabal serrulate 2x HPI •Clematis erecta 3x HPI •Pulsatilla nigricans 3x HPI •Chimaphila 3x HPI •Conium maculatum 3x HPI •Pareira brava 3x HPI •Excipients qs •Alcohol content 60% v/v

Dose and Duration: As directed R25, but no favorable observations were made like R 25.

③ R 41 forte N (Pharmazeuilische, Germany)

Indication: Impotence drops:

Ingredients: •Acidum phosphoricum D8 0.25 g •Agnus costus D6 0.5 g •China D8 0.5 g •Conium D30 0.25 g •Damlana D6 0.5 g •Lecithinum D6 1g •Panax ginseng D6 1 g •Phosphorus d8 0.5 g •Procainum hydrochloricum D3 1 g •Sepla D30 0.25 g •Tocopherylis ocetas D6 1 g •Yohimbinum hydrochloricum D4 0.5 g •Ethanolum, Aqua purificata

A combination of homeopathic medicines (especially constitutional and organopathic/targeted remedies) is more effective than a single remedy for managing BPH symptoms. This observation shows there are no known mono- or poly-homeopathic medicines that could cure the hugely enlarged prostate.

OVERALL CONCLUSION

The BPH is a noncancerous enlargement of the prostate that does not directly cause or turn into prostate cancer (PC). While both are common in aging men, they share similar LUTS and elevated PSA levels. BPH typically affects the inner transition zone, whereas cancer often affects the outer, peripheral zone. They can coexist, requiring an accurate diagnosis and treatment. All five urologists consulted for BPH treatment in the different recognized hospitals in Dhaka treated the BPH patient by using the same technique, like they are targeting first the PC diagnosis by suggesting multiple tests, including PSA, USG, prostate biopsy, and MRI, without any justification to cost the patient at their specific laboratory. Similarly, they are also

prescribing drugs for BPH treatment only from a specific pharmaceutical company, even with known low-effective drugs. They have only experience with TURP surgery, whereas they have advertised on websites (Facebook) offering laser techniques to attract patients for treatment at their hospitals. Medical malpractice by specialized doctors in Dhaka is a growing concern driven by systemic issues, a lack of accountability and regulatory oversight, the commercialization of healthcare and ethical issues, weaknesses in the healthcare system, poor patient-doctor communication, and challenges in legal redress. These factors collectively create an environment where specialized doctors may neglect standards of practice, resulting in preventable injuries, disabilities, and deaths. Over 8,00,000 Bangladeshi patients travel abroad annually for treatment, spending over US$ 5 billion, driven by a lack of trust in the local healthcare system, desire for advanced technology, and better service quality abroad. Each year, approximately 6.1 million people in Bangladesh fall below the poverty line due to the unbearable burden of medical expenses. All sectors, including healthcare, are grappling with a profound crisis in which political unrest has intersected with poor governance and corruption, leaving people in severe need of care without adequate support. The system, plagued by a lack of stewardship, needs major reforms to become a functioning public service.

ETHICAL APPROVAL

Ethical approval was not required, as the review relied solely on publicly available data.

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