Research Prioritization Topic Brief: Comparative Effectiveness of Lifestyle Changes, Diet Modification, Behavioral Interventions and Phytotherapy on the Clinical Symptoms of Benign Prostatic Hyperpaslia (BPH)

Assessment of Prevention, Diagnosis and Treatment Options

PCORI Scientific Program Area:
Comparative Effectiveness Research
Communication and Dissemination

Executive Summary

PCORI-proposed Comparative Research Question: Comparative effectiveness of lifestyle changes, diet modification, behavioral interventions, and phytotherapy on the clinical symptoms of benign prostatic hyperplasia (BPH).

Brief Overview of the Topic: BPH is another name for an enlarged prostate due to proliferation of tissue in the prostate. Mild BPH is often managed without the use of prescription medications or procedures. Recommended lifestyle changes include: increasing physical activity; modifying diet to avoid excessive alcohol consumption; avoiding highly seasoned and irritative foods; and regulating fluid intake, especially in the evenings. The most widely available and commonly used phytotherapy for BPH is saw palmetto or *Serenoa repens*. There is heterogeneity in the quality of over-the-counter saw palmetto products available. The American Urological Association does not recommend specific lifestyle changes, diets, behavioral interventions, or phytotherapy in their 2010 guidelines because there is insufficient evidence to support any particular intervention.

Impact on Health and Populations: BPH increases in prevalence as men age. At least 50% of men aged 40 and older have BPH. Men of all races are affected by BPH, although clinical diagnosis is most prevalent among white men.

Assessment of Current Options: Previous trials, indicate only weak or no evidence of the effectiveness of phytotherapy compared with placebo. No study was identified that included dietary modification (other than supplements), behavioral interventions or lifestyle changes such as physical activity and weight loss[1,2] and measured the effect of these interventions on

BPH outcomes. The prescription medications and procedures used to treat moderate and severe BPH can be associated with undesirable side effects.

Likelihood of Implementation of Research Results in Practice: Patients, providers and guideline developers are open to effective alternatives to prescription medications and procedures.

Durability of Information: There are no major ongoing studies related to the interventions of interest or other interventions for mild BPH. The results are likely to be relevant for at least several years.

Topic 1: Comparative effectiveness of lifestyle changes, diet modification, behavioral interventions and phytotherapy on the clinical symptoms of BPH

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2. Introduction:

Benign prostatic hyperplasia (BPH) is another name for an enlarged prostate due to proliferation of tissue in the prostate. BPH leads to an obstruction of the bladder and lower urinary tract symptoms. A definitive diagnosis of BPH is based on histology, or review of a specimen of the prostate by a pathologist. A histologic confirmation of BPH is required for diagnosis because men can experience lower urinary tract symptoms independent of BPH.[3] Symptoms include increased frequency of urination, need to urinate at night, hesitancy, urgency, and weak urinary stream. Treatments are selected based on the severity of the lower urinary tract symptoms.[4] Some men are treated for BPH based on symptoms without histological confirmation, prompting some experts to differentiate histologically confirmed BPH versus symptoms associated with BPH including lower urinary tract symptoms, benign prostatic enlargement or bladder outlet obstruction.[5]

BPH affects men exclusively, because only men have a prostate. The prevalence of BPH increases with age. Around 10% of men in their 30s have BPH compared with 80–90% of men in their 90s. Obesity, metabolic syndrome, diabetes, poor diet, and insufficient physical activity are risk factors for BPH.[2,6]

Treatment options for BPH include watchful waiting, lifestyle changes including diet and behavioral interventions, prescription medications, and surgical procedures.[4] Individuals who are not at risk of acute urinary retention are often offered watchful waiting, lifestyle changes,

and phytotherapy as first-line treatments to relieve their urinary symptoms.[7] Prescription medications and surgical procedures are recommended for individuals with moderate and severe BPH.[4] The American Urological Association examinedevidence on phytotherapy in its guidelines but does not recommend phytotherapy for the treatment of BPH.[4]

Recommended lifestyle changes include: increasing physical activity; modifying diet to avoid excessive alcohol consumption; avoiding highly seasoned and irritative foods; regulating fluid intake, especially in the evenings; and examining if other prescribed medications are contributing to the symptoms.[4]

Phytotherapy is the use of herbs or plants to treat disease. Several phytotherapies have been examined in pre-clinical and clinical studies to relieve lower urinary tract symptoms associated with BPH. The most widely available and commonly used phytotherapy for BPH is saw palmetto or *Serenoa repens.*[7] Saw palmetto extract is available at drug and grocery stores without a prescription. There is heterogeneity in the quality of the products available.[8] The American Urological Association guidelines specifically mention that saw palmetto and stinging nettle (*Urtica dioica*) are not recommended, but that ongoing trials at the time of the 2010 guideline may provide evidence that could change the recommendations.[9]

Prescription medications to treat BPH include two main classes: alpha-adrenergic blockers (alpha blockers) including alfuzosin, doxazosin, prazosin, silodosin, tamsulosin and terazosin), and 5-alpha-reductase inhibitors (5-ARIs) including finasteride dutasteride. Alpha blockers and 5-ARIs can be used in combination.[4]

Procedures to treat BPH aim to decrease the size of the prostate. These include ablation with a needle, microwave thermotherapy delivered through a catheter and minimally invasive or open surgical procedures to remove tissue. Surgery is recommended after medications fail to relieve symptoms or when patients have severe voiding symptoms, or if BPH has induced renal insufficiency, recurrent infections, bladder stones or bleeding.[4]

Current sources of information on treatment options for BPH

- Foundations and institutions have information for patients on the diagnosis and treatment options for BPH. These include the National Institute of Diabetes and Digestive and Kidney Diseases,[10] Urology Care Foundation (the foundation of the American Urological Association),[11] Mayo Clinic[12] and Google.[13]
- There are no specific dietary plans that can be administered by a nutritionist for BPH, other than a healthy diet.
- No formulation of saw palmetto or other phytotherapy has been approved by the Food and Drug Administration (FDA). No specific formulation is recommended in the information created for patients from these organizations.

3. Symptoms and Patient-Centered Outcomes:

Lower urinary tract symptoms are the most common symptoms of BPH. These include increased frequency of urination, urgency, need to urinate at night, hesitancy, and weak urinary stream. BPH can progress to include urinary retention, infections, obstruction, stones, and acute renal failure.[6]

BPH is associated with erectile dysfunction and ejaculatory problems in up to 70% of patients[14,15] and depression in up to 20% of patients.[14,16] Five percent of men who undergo surgery for BPH experience long-term impotence afterwards.[17,18] The medications to treat BPH are also associated with erectile dysfunction, ejaculatory dysfunction, and decreased libido. However, tadalafil, one of the treatments for erectile dysfunction, is also approved for the treatment of BPH.[19,20]

Quality of life is decreased among men with BPH.[21] Treatment is associated with improved quality of life.[22]

Some men are first diagnosed with BPH after a prostate-specific antigen (PSA) test for prostate cancer. These men may ask their doctor about their risk for prostate cancer because of their enlarged prostate.

4. Impact/Burden of the Condition:

The prevalence of BPH increases with age. Around 8% of men aged 31 to 40 have BPH, compared with 40 to 50% aged 51 to 60, and over 80% of men older than age 80.[6] The prevalence of BPH is increasing and is likely related to the increasing number of older individuals in the population. [6]

The prevalence of BPH does not differ by race, location or income, but there are differences in the clinical diagnosis. Based on a survey of men seen at 60 community centers, black men are less likely than white men to report a clinical diagnosis of BPH, although black men are more likely to have surgery for their BPH.[23] However, a study of health professionals who underwent prostatic surgery found no difference in the prevalence of BPH between black, white and Asian men.[24] Based on the 2001-2008 National Health and Nutrition Examination Surveys, the prevalence of BPH did not differ between black, white and Hispanic men nor between those who lived in urban and rural areas. However, there were differences in the clinical diagnosis of BPH by race and socioeconomic status. Men who are white, with higher incomes and who use health care for other conditions are more likely to receive a diagnosis and treatment.[25] Despite the relatively equal prevalence of BPH among different racial groups, most studies that have examined treatments and outcomes have included predominately white patients.[26]

Costs of BPH, including both direct and indirect costs, were estimated at US$3.9 billion in 2006. As the population is composed of more individuals that are older, the prevalence of BPH and costs of treatment will increase.[26] There are variations in the costs of the different diagnostic strategies and treatments for BPH.[27]

5. Evidence Gaps:

We searched for systematic reviews on strategies to treat BPH produced by the Agency for Healthcare Research & Quality's Evidence-based Practice Center and the Cochrane Collaboration. On April 24, 2015 an Evidence-based Practice Center published a research protocol to examine medications to treat lower urinary tract symptoms associated with BPH.[28] Fifteen Cochrane reviews were identified of which five were relevant to the topic. We identified the research questions, findings and the evidence gaps identified in the relevant reports. The American Urological Association relied on these and other sources to produce management recommendations for its members.[4]

Newer Medications for Lower Urinary Tract Symptoms (LUTS) Associated with Benign Prostatic Hyperplasia (BPH)

Research Protocol – Apr. 24, 2015

This protocol aims to compare recently evaluated and approved medications with other FDA-approved medications or placebo. Comparisons to other interventions, including phytotherapies, diet or behavioral changes will not be included. The new medications include the alpha-blocker silodosin, the anticholinergics oxybutynin, fesoterodine, darifenacin, tolterodine tartrate, tolterodine and solifenacin, the beta-3 adrenoceptor agonist mirabegron, the phosphodiesterase-5 (PDE-5) inhibitors tadalafil, sildenafil, avanafil and vardenafil, and adjunctive/combination treatment with a newer medication. This topic was nominated by the American Urological Association.[29] A 2004 review conducted by an Evidence-based Practice Center focused on surgical and other procedures to treat BPH. No Evidence-based Practice Center reports or protocols were directly related to the specific topic of this brief.[30]

***Serenoa repens* for benign prostatic hyperplasia**[31]

Editorial Group: Cochrane Urology Group Published Online 12 DEC 2012, Assessed as up-to-date 27 JAN 2012.

Objective:

"This systematic review aimed to assess the effects and harms of Serenoa repens in the treatment of men with LUTS consistent with BPH."

Conclusions:

"The update of this review included 32 randomized controlled trials involving 5666 men. Serenoa repens is widely used in Europe and the US to treat lower urinary tract symptoms associated with BPH. Our conclusion that Serenoa repens, even at escalating doses, is not superior to placebo, is based on two high quality, clinical trials, one with a follow-up of six years."

Evidence Gaps:

"We do not know if our conclusions are generalizable to proprietary products of Serenoa repens, such as Permixon® or Prostagutt® forte. Non-standardization is a long-recognized problem of phytotherapeutic products, and that includes Serenoa repens. Future research needs are that randomized controlled trials using branded Serenoa repens have a follow-up of at least one year, are methodologically sound, well powered, use validated, symptom-scale scores, and most importantly, have a placebo arm."

Lycopene for the prevention of prostate cancer[32]

Editorial Group: Cochrane Urology Group, Published Online: 9 NOV 2011, Assessed as up-to-date: 24 AUG 2011.

Objective:

"To determine whether lycopene reduces the incidence of prostate cancer and prostate cancer-specific mortality. Secondary objectives include changes in PSA levels, prostate symptoms and the nature of adverse events associated with lycopene use.

Although this review's primary outcome was prostate cancer, the secondary outcomes included common symptoms of BPH."

Conclusions:

Three RCTs, with a total of 154 participants were included in this review.

"The findings of this systematic review conclude that there is insufficient evidence to either support, or refute, the use of lycopene for the prevention of prostate cancer. Similarly, there is no robust evidence from RCTs to identify the impact of lycopene consumption upon the incidence of prostate cancer, prostate symptoms, PSA levels or adverse events.

It is also worth noting that the RCTs included in this systematic review relied on lycopene to be administered to men as supplements. Previous research has suggested that any beneficial effects from lycopene may be related to the antioxidants in the diet, rather than as supplements. Similarly, it may be the overall effect of a range of micronutrients rather than one which produces the benefit. Best estimates have suggested that the average daily intake ranges from 3.7 to 6.5 mg per day. It should be noted that the men who participated in the included studies received between 15 to 30 mg supplements of lycopene, without demonstrable improvement in primary and secondary outcomes."

Evidence Gaps:

The evidence gaps focused on prostate cancer as the primary outcome.

The increased number of men in the community consuming complementary and alternative medicines for the prevention of prostate cancer, and the current lack of high quality evidence, both support the call for a well-designed, high methodological quality, randomized controlled trial to investigate the effectiveness lycopene for the prevention of prostate cancer. Such a trial should account for prostate cancer diagnosis, mortality, changes in PSA levels, adverse events, and cost-effectiveness.

Cernilton for benign prostatic hyperplasia[33]

Editorial Group: Cochrane Prostatic Diseases and Urologic Cancers Group, Published Online: 27 JUL 1998, Assessed as up-to-date: 30 MAR 1998. In 2011, the authors indicated that they will not update the review.

Objective:

To evaluate the effects of Cernilton, a rye-grass pollen extract, versus placebo or active control on urinary symptoms in men with BPH. The main outcome was improvement in urologic symptom scale scores. Secondary outcomes included changes in peak and mean urine flow, residual urine volume, prostate size and side effects associated with the use of Cernilton.

Conclusions:

Four low-quality trials were included. The available evidence suggests that Cernilton is well tolerated and modestly improves subjective urologic symptoms for up to 24 weeks. Cernilton was not demonstrated to improve urinary flow measures compared to placebo. The long-term effectiveness and safety of Cernilton and its ability to prevent complications from BPH are not known.

Evidence Gaps:

"Future trials should be of sufficient size and duration to detect important differences in outcomes including urologic symptom scale scores (e.g., IPSS), mean and peak urine flow, voided volume, prostate size, residual urine volume, development of acute urinary retention or need for surgical intervention. Studies are needed to compare Cernilton, a-blockers, 5a-reductase inhibitors and other phytotherapeutic agents such as Serenoa repens. Studies should also use standardized doses of Cernilton products that have been analyzed for purity and potency by an independent laboratory to ensure the quality of the product."

Beta-sitosterols for benign prostatic hyperplasia[34]

Editorial Group: Cochrane Urology Group, Published Online: 26 JUL 1999, Assessed as up-to-date: 18 MAY 1999.

Objective:

"This systematic review aimed to assess the effects of beta-sitosterols (B-sitosterol) on urinary symptoms and flow measures in men with of benign prostatic hyperplasia (BPH)."

Conclusions:

Five hundred nineteen men from four randomized, placebo-controlled, double-blind trials, (lasting 4 to 26 weeks) were assessed. "The available evidence suggests that B-sitosterols are well tolerated and improve urologic symptoms and flow measures. B-sitosterols may be a useful pharmacologic treatment option for men with mild to moderate BPH, particularly men

who would like to avoid or are at increased risk for adverse effects from alpha-blockers or surgical intervention. The long term effectiveness and safety of B-sitosterols and their ability to prevent complications from BPH are not known."

Evidence Gaps:

Additional placebo and active-controlled studies (alpha-blockers, 5a-reductase inhibitors and other phytotherapeutic agents such as Serenoa repens) are needed. "These trials should utilize standardized extracts with known concentrations of B-sitosterols. Future trials should be of sufficient size and duration to detect important differences in outcomes including urologic symptom scale scores (e.g., IPSS), peak and mean urine flow, prostate size, residual urine volume, development of acute urinary retention or need for surgical intervention."

Pygeum africanum for benign prostatic hyperplasia[35]

Editorial Group: Cochrane Urology Group, Published Online: 26 JAN 1998, Assessed as up-to-date: 25 NOV 1997.

Objective:

"To investigate the evidence whether extracts of Pygeum africanum (1) are more effective than placebo in the treatment of Benign Prostatic Hyperplasia (BPH), (2) are as effective as standard pharmacologic BPH treatments, and (3) have less side effects compared to standard BPH drugs."

Conclusions:

A total of 18 randomized controlled trials involving 1562 men met inclusion criteria and were analyzed. "The overall standardized effect size and the summary improvement in global symptoms, nocturia, peak urine flow and residual urine volume suggests that Pygeum africanum is effective in men with symptomatic benign prostatic hyperplasia. This benefit is of modest size and appears to be clinically significant. Pygeum africanum is well tolerated and costs less than most prescription medications. A standardized preparation of Pygeum africanum, may be a useful treatment option, at least in the short term, for men with lower urinary symptoms consistent with benign prostatic hyperplasia."

Evidence Gaps:

"Additional placebo-controlled trials are needed as well as studies that compare Pygeum africanum to active controls that have been convincingly demonstrated to have beneficial effects on lower urinary tract symptoms related to BPH. Future trials should be of sufficient size and duration (e.g. > 6 months) to detect important differences in clinically relevant endpoints and use standardized urologic symptom scale scores."

6. Ongoing Research:

We searched ClinicalTrials.gov, NIH Reporter and PCORI's website to identify ongoing research.

ClinicalTrials.gov results

A total of 353 studies were found when we searched the listed condition to contain "benign prostatic hyperplasia." Sixteen studies were identified when we limited the search to interventions of interest (search terms included diet, dietary, supplement, phytotherapy, complementary medicine, CAM, behavioral, lifestyle, natural, palmetto, exercise, physical activity).

- Seven studies were not relevant.
  - Four studies did not include the correct population. One study is currently enrolling healthy males by invitation only to examine the pharmacokinetics of a drug combined with high fat diet (NCT02529800, estimated completion in October 2015). Another examined pelvic floor exercises and biofeedback among men who had undergone a procedure to treat prostate cancer or benign prostate disease (NCT00632138). Another compared health care provider knowledge of the digital rectal exam (NCT02278679). Another examined the effect of a vaccine in prostate cancer patients (NCT01194960).
  - Three studies did not include the interventions of interest. One compared tamsulosin versus placebo (NCT02245490). Another included a device placed during surgery (NCT01294150). Another study compared two BPH prescription medications combined with lifestyle advice, but the lifestyle advice was not described (NCT01294592).
- Two relevant studies of saw palmetto that were not conducted in the United States were listed as unknown status (NCT01021267; NCT00497939).
- The seven other relevant studies were also listed as completed.
  - NCT00037154: Saw Palmetto Extract in Benign Prostatic Hyperplasia
    - The study compared 160 mg twice a day of the herbal extract versus an identical placebo among men who had discontinued all other medications to treat BPH. The participants were seen in clinic every 3 months for 1 year.
    - The primary outcome was change in the American Urological Association Symptom Index score.

- The study results were reported in the New England Journal of Medicine in February 2006. The authors concluded: *In this study, saw palmetto did not improve symptoms or objective measures of benign prostatic hyperplasia.*[36]

- NCT01604811: Exploratory Study of L.S.E.S.r. (LipidoSterolic Extract of Serenoa Repens)(PERMIXON® 160 mg Hard Capsule) Versus Tamsulosine LP Activity on Inflammation Biomarkers in Urinary Symptoms Related to BPH (Benign Prostatic Hyperplasia) (PERMIN)
  - The study compared lipidosterolic extract of *Serenoa repens (*saw palmetto) with the prescription medication tamsulosin for 90 days.
  - The primary outcomes were change from baseline in urine and serum inflammation biomarkers.
  - No study results were posted and no links to publications were provided. The primary completion date was October 2013.
- NCT00797394: Efficacy of Natural Extract 2007RD01 Combined With Saw Palmetto in Benign Prostatic Hyperplasia Patients Compared to Saw Palmetto.
  - The study compared oral administration of one capsule containing a combination of 250 mg of 2007RD01 (a natural extract) and 160 mg of saw palmetto lipidic extract plus inactive fillers, twice a day between meals to oral administration of one capsule containing 160 mg of saw palmetto lipidic extract plus inactive fillers, twice a day between meals.
  - Primary outcome: Absolute and relative (%) change in International Prostate Symptom Score (IPSS) between baseline and end of study at 90 days.
  - Study last updated in April 2011. No results or links to publications are available. The estimated completion date was July 2010.
- NCT02313233: Research on Benefit of Umooze as Add- on Therapy in Benign Prostatic Hyperplasia
  - The study compared Umooze with a cornstarch placebo. Umooze is Astragalus radix extracts and soy extracts.
  - The original primary outcome was the International Prostate Symptom Score (IPSS) measured at 56 days. The protocol was amended to include four primary outcomes, including the IPSS measured at 56 days and after 12 months and quality of life measured at the same time points.
  - The Umooze group had a decrease in IPSS of 3.39 points at day 56 compared with a 5.94 decrease in the placebo group, indicating that the placebo group had a greater decrease in severity, although no p-value was provided. There

were no serious adverse events in either group and 2 other adverse events in each group. No publications of the study results were provided.

- NCT00416390: Lycopene in Treating Patients With Prostate Cancer or Benign Prostatic Hyperplasia
  - The study compared a once daily oral lycopene supplement with placebo for three weeks.
  - There were six primary outcomes focused on the uptake of lycopene from prostate biopsy samples and serum samples.
  - A published study reported that lycopene concentrations in the prostate biopsy and serum were greater ($p<0.05$) in the lycopene than placebo group.[37]
- NCT00861588: Effects of Isoflavone in Patients With Watchful Waiting Benign Prostate Hyperplasia
  - The study compared 40 mg of soy isoflavones (Soylife 25) capsule (once daily) versus placebo for 1 year.
  - The primary outcomes were discontinuation due to an adverse event and improvement in the urine flow rate by at least 2ml/sec.
  - The study results were published and found that there were borderline statistically significant differences ($p=0.05$) at year 1 between groups for urine flow. The flow rate did not improve by at least 2ml/sec. The study stated that there were no differences in adverse events and no serious adverse events. Six participants in the isoflavones group withdrew because of adverse events compared with 3 participants who received placebo.[38]
- NCT02244320: Observational Study in Patients With Functional Benign Prostatic Hyperplasia Symptoms Who Switched From Phytotherapy to ALNA® (Tamsulosin)
  - "The objective of the observational study -was to investigate the switch from phytotherapy to tamsulosin after at least 4 weeks of phytotherapy and still presented with a symptom sum score of ≥ 8 points (International Prostate Symptom Score (IPSS))."
  - There were two primary outcomes. One related to change in the IPSS and the other related to quality of life.
  - The study was last updated in September 2014. It was started in September 2002 with a primary completion date of May 2003. No study results were posted and no links to publications were provided.

NIH Reporter results

A search of NIH Reporter for "benign prostatic hyperplasia" OR "BPH" resulted in 72 studies. No study tested an intervention of interest in humans or animals with BPH. No relevant studies included humans.

Three studies were related to the topic, but included only animals.

- 5R01DK087962-04: Biomarkers of obesity, prostate tissue inflammation, and BPH progression
- 5R01DK087806-05: Cholesterol and prostate health
- 5K01DK098277-03: Mechanisms of fatty acid metabolism in prostate differentiation and disease

PCORI-funded projects

One funded study was identified related to benign prostatic hyperplasia. The methods project related to heterogeneity assessment.[39] The methods were applied to a National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) funded trial to compare two prescription medications (NCT00021814).

7. Likelihood of Implementation of Research Results in Practice:

The urology community has a history of testing non-prescription treatments for BPH. Based on some, but not all trials, some urologists prescribe these treatments to their patients. The willingness to prescribe these treatments along with the American Urological Association's interest in including these treatments in their guidelines suggests that the results of PCORI-funded research will be implemented into practice.

8. Durability of Information:

There were no ongoing human studies funded by NIH on this topic. All of the trials identified in ClinicalTrials.gov were completed. The studies identified in ClinicalTrials.gov found no difference between phytotherapy and its comparison, borderline statistically significant differences or did not report results. It is quite possible that the studies that did not report results in ClinicalTrials.gov or publications did not find any evidence of effectiveness.

Based on the lack of ongoing studies and the input of our experts, the results of funded research are likely to have an impact for at least several years.

9. Potential Research Questions:

- Research need: Over-the-counter supplements, including phytotherapy, are not held to the same standards of product consistency by the FDA as prescription products. A previous study has found heterogeneity among the saw palmetto products available to the consumer. Saw palmetto is one of the most commonly used products by consumers, yet the Cochrane review included only two high quality studies to make its inference that there was no difference between saw palmetto and placebo.
  Research question: *What is the comparative effectiveness of specific phytotherapy preparations compared with prescription treatments, such as alpha blockers, on patient-relevant BPH outcomes?*

- Research need: Previous studies have examined specific supplements or components of the diet, but no studies on dietary patterns exist.
  Research question: *Are there particular dietary patterns that alter the progression of BPH?*

- Research need: There are no studies on the effectiveness or efficacy of exercise on BPH or its symptoms.
  Research question: *What is the independent effect of physical activity on patient-relevant BPH outcomes, after accounting for changes to body composition and obesity-associated conditions like metabolic syndrome?*

- Research need: There are numerous trials on phytotherapy as a treatment for BPH but the majority of them were rated as low quality by the Cochrane reviewers.
  Research question: *What is the best way to communicate research findings to patients when there is conflicting evidence but the majority of evidence is rated by methodology experts as low quality?*

10. Conclusion:

BPH affects over 50% of men aged 40 and older. Despite the use of over the counter products as a treatment for BPH, the evidence from the majority of trials and systematic reviews indicates that the products were tested in clinical studies that were too small or had design flaws, resulting in unknown effectiveness of these products. There is no evidence on the effectiveness of dietary, lifestyle or behavioral changes as treatments for BPH. Evidence on these potential treatments is likely to be incorporated into society treatment guidelines.

APPENDIX

Methods

Literature search:

From December 2015 to February 2016, we conducted a literature review to identify evidence-based research around the effectiveness of lifestyle changes, diet modification, behavioral interventions and phytotherapy on the clinical symptoms of BPH. We used PubMed, Google Scholar and the Cochrane Database of Systematic Reviews to identify systematic reviews, meta-analyses and research reports and the most current reviews. We also searched the websites for government agencies, such as the CDC, the NIH and relevant professional associations (American Urological Association, European Urological Association, National Kidney Foundation), and patient advocacy groups as likely to contain relevant material on the current prevalence and available treatment services as well as any references or sites suggested by our experts.

Clinical trials and NIH Funding Announcements:

In January 2016, we conducted a search on clinicaltrials.gov, the NIH reporter and PCORI for open clinical trials related to the topic. We used the broad search terms “Benign Prostatic Hyperplasia”, “BPH” and “phytotherapy”; “diet”;”dietary”;”supplement’;”complementary medicine”;”CAM”;” behavioral”;” lifestyle”;”natural”;”palmetto”;”exercise”;”physical activity”. The results are described

References for topic: Comparative effectiveness of lifestyle changes, diet modification, behavioral interventions and phytotherapy on the clinical symptoms of BPH

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