

# Lifestyle factors, benign prostatic hyperplasia, and lower urinary tract symptoms

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## Purpose of review

Although age, genetics, and sex steroid hormones play prominent roles in the cause of benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS), recent epidemiological studies suggest that modifiable lifestyle factors also contribute substantially to the pathogenesis of these conditions.

## Recent findings

Lifestyle and metabolic factors associated with significantly increased risks of benign prostatic hyperplasia and lower urinary tract symptoms include obesity, diabetes, and meat and fat consumption. Factors associated with decreased risks include physical activity, moderate alcohol intake, and vegetable consumption. Factors for which no clear risk patterns have emerged include lipids and smoking. Randomized clinical trials of lifestyle alterations – such as weight loss, exercise, and diet – for the prevention or treatment of benign prostatic hyperplasia and lower urinary tract symptoms have yet to be performed.

## Summary

Lifestyle factors present a novel opportunity for the prevention and treatment of benign prostatic hyperplasia and lower urinary tract symptoms. Although clinical trials of lifestyle modifications have not yet been undertaken, promotion of healthy lifestyle alternatives within the context of standard benign prostatic hyperplasia and lower urinary tract symptoms treatment algorithms is potentially beneficial.

## Keywords

benign prostatic hyperplasia, diabetes, exercise, lower urinary tract symptoms, obesity

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## Introduction

Etiological models of male lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH) are evolving rapidly. Previous paradigms have focused on age, genetics, and sex steroid hormones as the primary components driving LUTS and BPH pathogenesis. However, recent epidemiological studies have revealed that, to a large extent, lifestyle factors associated with metabolism – including obesity, blood glucose, exercise, and diet – also contribute substantially to the development of these conditions [1]. These observations are important because they suggest the existence of modifiable pathways for BPH and LUTS that offer novel targets for prevention and treatment. However, no randomized trials have as yet been performed.

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## Lifestyle factors and definitions of benign prostatic hyperplasia and lower urinary tract symptoms

The most notable development in the epidemiology of BPH and LUTS in recent years is the recognition that

modifiable lifestyle factors substantially influence the natural history of these conditions (Table 1). A persistent challenge in designing and interpreting population-based studies of urinary symptoms in men, however, is case definition. The most common cause for male urinary symptoms is BPH. BPH has many different definitions in the literature: histological analysis, radiologically determined prostate enlargement, diminished urinary flow rates, history of noncancer surgery of the prostate, patient-reported history, and physician diagnosis. This variability renders it a problematic endpoint to validate across different study populations. Moreover, focusing on BPH excludes other potential causes of urinary symptoms in older men.

LUTS represent a cluster of chronic urinary disorders that occurs among 15–60% of men over the age of 40 years [2–7]. LUTS describe a phenotype for a group of disorders affecting the lower urinary tract that share a common clinical manifestation. The term LUTS allows for a broad, uniform, and consistent description of urinary symptoms at a population level without identification of organ-specific or disease-specific causes.

## 2 Benign prostatic hyperplasia

**Table 1 Lifestyle factors for benign prostatic hyperplasia and lower urinary tract**

Increased risk	Decreased risk	Unclear risk
Obesity	Exercise	Lipids
Diabetes	Moderate alcohol	Smoking
Meat and fat	Vegetables	

For this reason, LUTS – as measured by the American Urological Association Symptom Index (AUA-SI) or International Prostate Symptom Score (I-PSS) – has become the preferred term for studying urinary symptoms in populations in recent epidemiological studies [4,5,7,8]. Still, as most men with LUTS have BPH and most men with BPH have LUTS, the two terms remain intertwined in the contemporary treatment and study of urinary disorders in older men. This review, therefore, includes studies that used either of the endpoints.

### **Lifestyle factors associated with increased risks of benign prostatic hyperplasia and lower urinary tract symptoms**

The following factors are associated with increased risks of BPH and LUTS.

#### **Obesity**

Increased adiposity has been consistently associated with increased ultrasound and MRI-determined prostate volume, the greater the amount of adiposity, the greater the prostate volume. Increased body weight, BMI, and waist circumference [9] have been associated with increased prostate volume. In the Baltimore Longitudinal Study of Aging (BLSA), each 1 kg/m<sup>2</sup> increase in BMI corresponded to a 0.41 ml [95% confidence interval (CI) –0.15 to 0.84] increase in prostate volume (*P* trend = 0.06) [9]. Obesity has also been associated with prostate enlargement: in the BLSA, obese (BMI ≥ 35 kg/m<sup>2</sup>) participants had a 3.5-fold increased risk of prostate enlargement compared to nonobese (BMI < 25 kg/m<sup>2</sup>) participants [9]. A recent analysis of more than 16 000 radical prostatectomy specimens validated these findings, observing that each 1 kg/m<sup>2</sup> increase in preoperative BMI was associated with a 0.45 g (95% CI 0.35–0.55 g) increase in total prostate weight (*P* trend < 0.001) and a 70% increased risk of prostate enlargement comparing obese to nonobese men [odds ratio (OR) 1.70, 95% CI 1.32–2.20] (J.K. Parsons and M. Han, unpublished data).

A majority of studies, involving tens of thousands of men, have noted that obesity is associated with increased risks of both BPH and LUTS [10<sup>\*</sup>]. Recent studies include a 7-year prospective analysis of 5700 men participating in the Prostate Cancer Prevention Trial (PCPT) [11], an investigation of 21 700 Norwegian men in the second

Nord-Trøndelag Health Study (HUNT-2) [12], and a cohort study of 2800 men in the National Health and Nutrition Examination Survey (NHANES III) [13].

#### **Diabetes**

Disruptions in glucose homeostasis have been strongly and robustly associated with a higher likelihood of prostate enlargement, BPH, and LUTS. Higher serum concentrations of IGF-1 and IGFBP-3 have been associated with increased risk of clinical BPH and BPH surgery. Physician-diagnosed diabetes, increased serum insulin, and elevated fasting plasma glucose have been associated with increased prostate volume and increased risks of BPH and LUTS in multiple different cohorts cumulatively incorporating tens of thousands of men [9,14–22].

#### **Diet: meat, fat, and dairy**

Although results from dietary studies previously were inconsistent, emerging data now indicate that both macronutrients and micronutrients may substantially influence lower urinary tract health. Red meat and fat products have been associated with increased risks of BPH and LUTS [23].

### **Lifestyle factors associated with decreased risk of benign prostatic hyperplasia and lower urinary tract symptoms**

The following factors are associated with decreased risks of BPH and LUTS.

#### **Physical activity and exercise**

Increased physical activity and exercise have been robustly and consistently linked with decreased risks of BPH and LUTS [1]. A meta-analysis of 11 published studies (*n* = 43 083 men) indicated that moderate to vigorous physical activity was associated with up to a 25% decreased risk of BPH or LUTS relative to a sedentary lifestyle, with the magnitude of the protective effect increasing with higher levels of activity [24].

#### **Alcohol**

Like exercise, moderate alcohol intake also appears to be protective against BPH [1,23]. However, unlike exercise, the same protective effect does not appear to apply to LUTS. A meta-analysis of 19 published studies, incorporating 120 091 men, observed up to a 35% decreased likelihood of BPH among men who drank daily, but an increased risk of LUTS [25].

#### **Diet: vegetables**

Vegetables are associated with decreased risks of BPH and LUTS [23]. Similarly, higher blood levels of lycopene and carotene, which occur in high concentrations in vegetables, have been inversely associated with LUTS [26,27].

## Lifestyle factors for which associations with benign prostatic hyperplasia and lower urinary tract symptoms are unclear

Associations of BPH and LUTS with the following factors remain unclear:

### Lipids and lipoproteins

Abnormal serum concentrations of lipids and lipoproteins are well-described risk factors for cardiovascular disease and include elevated serum LDL cholesterol, decreased serum HDL cholesterol, and increased serum triglycerides. There are relatively little data on potential associations of these factors with BPH and LUTS. No clear patterns have emerged. There have been at least six studies, three showing positive and three showing null associations [1,14,15,21,28,29].

### Smoking

Data regarding associations of smoking, BPH, and LUTS are conflicting. Although several studies support the existence of an inverse, protective effect of smoking on the risks of BPH and LUTS, several others have reported either no or increased risk. Thus, no definitive conclusions may be drawn at this time [1].

## Potential lifestyle interventions for benign prostatic hyperplasia and lower urinary tract symptoms

Despite this robust body of observational data linking lifestyle to BPH and LUTS, there remains a paucity of clinical trials exploring whether modifications in lifestyle may alter the natural history of these conditions. Potential lifestyle-based interventions include weight loss, exercise, and dietary modification (i.e., reducing fat intake and increasing vegetable intake). There have as yet been no randomized clinical trials of these interventions for BPH or LUTS.

However, at least two medical therapies based on modulation of metabolic pathways related to lifestyle have been the focus of clinical trials: intensive glycemic control and statin use. Both trials produced null results.

### Glycemic control

The urological assessment component of the Epidemiology of Diabetes Interventions and Complications (Uro-EDIC) follow-up study of the Diabetes Control and Complications Trial (DCCT) was a post hoc analysis of a randomized clinical trial comparing intensive to conventional glycemic control in type 1 diabetics [20]. The aim was to substantiate whether intensive glycemic control can reduce the risk of LUTS in men with type 1 diabetes. Intensive treatment consisted of insulin

administered three or more times daily by injection or infusion pump coupled with rigorous monitoring of blood glucose levels.

The study included 591 men. No associations were observed between LUTS, as measured by the AUA-SI, and intensive glycemic control, indicating that intensive glycemic control did not result in decreased LUTS severity in men with type 1 diabetes. Still, since these men were younger (mean  $\pm$  SD,  $44.6 \pm 6.6$  years) and had type 1 rather than type 2 diabetes, the results of this trial may not apply to the broader population of older diabetic men, who are typically at risk for LUTS. Further studies of glycemic control are needed.

### Statins

A putative association of higher serum statin concentrations with BPH and LUTS would suggest the potential for preventing or improving urinary symptoms by lowering serum cholesterol. A randomized clinical trial of 319 patients, however, showed no differences in I-PSS, prostate volume, urinary flow rate, PSA, or quality of life among BPH patients treated for 6 months with atorvastatin compared to controls [30].

## Conclusion

In summary, modifiable lifestyle factors, including obesity, diabetes, exercise, alcohol, and diet, contribute substantially to the development of BPH and LUTS. These lifestyle variables offer feasible therapeutic targets to delay disease onset, prevent progression, or attenuate symptoms. Although these data are observational and should thus serve primarily as a guide for informing the design of future clinical trials, there is little, if any, downside to promotion of healthy lifestyle interventions – weight loss, exercise, decreasing meat and fat intakes, and increasing vegetable intake – among BPH and LUTS patients, particularly since these interventions possess proven benefits to overall and cardiovascular health.

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## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 84).

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