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## Lifestyle and LUTS: what is the correlation in men?

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### Abstract

**Purpose of review**—the primary purpose of this review is to provide an overview of the current evidence linking lifestyle factors and lower urinary tract symptoms (LUTS), and their relevance in men. An extensive literature search from January 2013 to August 2014 was conducted, reviewed and summarized in conjunction with key prior evidence.

**Recent findings**—The main findings from this review include: 1) Epidemiological data repeatedly show a favorable relationship between a healthy eating habits and regular physical activity level and a lower risk for LUTS or progression of LUTS, 2) certain specific nutrients or dietary factors may contribute to the link between diet and LUTS due to their anti-inflammatory potential, and 3) very little research has been conducted to test the epidemiological findings in randomized controlled trials.

**Summary**—Rigorously designed clinical trials are needed to confirm the association between lifestyle factors and LUTS and the effect of lifestyle modification on the development or progression of LUTS. Nevertheless, a healthy lifestyle is known to closely relate with chronic diseases like cardiovascular disease and diabetes. Thus, promoting a healthy lifestyle with good quality diet and regular physical activity is beneficial not only for potentially improving or reducing LUTS but also for cardiovascular and overall health. Clinicians are encouraged to include healthy lifestyle counseling in their routine care for patients with LUTS.

### Keywords

LUTS; lifestyle; prostate; diet

### Introduction

Lower urinary tract symptoms (LUTS) refers to a group of medical symptoms that involve dysfunctional urinary voiding.[1] LUTS can be broken into irritative symptoms (urinary frequency, urgency, dysuria (i.e. painful voiding), and nocturia) and obstructive symptoms (hesitancy, poor stream, post-void dribbling, overflow incontinence). LUTS is commonly

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measured and quantified using the International Prostate Symptom Score (IPSS) (or the American Urological Association Symptom Score), which is a validated instrument that contains 7 questions relating to irritative and obstructive voiding.[2] While present in both males and females, we will focus this review on males since LUTS has been closely related to benign prostate hyperplasia (BPH) and much of the extant literature focuses on BPH not just LUTS. In addition, LUTS has also been associated with many systemic factors such as metabolic syndrome, diabetes, and cardiovascular disease, unrelated to the prostate but all of which are in and of themselves related to various lifestyle factors. Thus, this review examines the current evidence on the association between lifestyle factors and LUTS in men.

Importantly, there is a large body of evidence linking lifestyle factors and LUTS (see review by Patel et al. and Raheem et al.).[3,4] The goal of the current study was not to perform a complete or systematic review of the topic. Rather, we sought to provide a general overview relying on previously published review articles [3] augmented by a literature search focusing on articles published in the last 18 months.

## Methods

A detailed PubMed literature search was conducted using key word combinations of LUTS and diet, lifestyle, or nutrient. Articles published in English and between January 1, 2013 and August 25, 2014 were included in the review.

## Prevalence and public health burden

Symptomatic LUTS represents the most common urologic disease among older males, affecting nearly 40% of men 40 years and older, and increases substantially with age, impacting more than half of the men 60 years and above. [5] On a population level, LUTS is a major health burden, and has significant impact on health care cost and productivity in the US. [6] On the individual level, LUTS results in increased risks of mortality, depression, falls and diminished health-related quality-of-life. [7–9]

## Pathophysiology

LUTS can result from many conditions. As noted, one of the most common causes of LUTS is BPH. BPH is defined as pathological enlargement of the prostate, typically in the central zone, which is the zone of the prostate surrounding the urethra. This enlargement in turns puts pressure on urethra, increasing outlet resistance leading to LUTS. However, there are other causes of LUTS in men including prostatic inflammation, bladder dysfunction, urinary tract infections, and prostate cancer/bladder cancer being some of the more common causes. The importance of inflammation as a contributor to LUTS is particularly relevant as inflammation can be modifiable by lifestyle changes (see below).

## Risk factors

Standard risk factors for LUTS include non-modifiable factors such as age, geography, and genetics.[10] More recently, there has been a growing interest in modifiable risk factors for LUTS including obesity, diet, and physical activity.[11] Below we review the state-of-the-

art thinking including our opinions regarding the links between obesity, diet, physical activity and LUTS.

## Obesity

As noted, a chief cause of LUTS is BPH (i.e. prostatic enlargement). As such, it is noteworthy that multiple studies have consistently shown that obesity is associated with larger prostate size.[12] More recently, we found that obesity also predicted future prostate volume growth.[13] Not only is obesity related to prostate size, but it is directly related to LUTS as well as complications from LUTS such as the need for BPH surgery and initiation of BPH medical therapy.[12,14,15] In a prospective study of 6461 men, obesity and weight gain during adulthood were associated with an increased risk of either LUTS development or worsening.[16] In addition, being overweight was associated with a significantly higher risk for symptomatic progression based on the IPSS in a prospective study of 1740 elderly men 65 years old.[17] A separate study found that a greater abdominal fat mass predicted the progression of LUTS symptoms in a population based cohort of 780 men.[11] Finally, obesity also predicts a poorer response to standard therapies for LUTS. Specifically, two prospective randomized controlled trials testing 5 alpha-reductase inhibitors for prostate cancer prevention found that finasteride and dutasteride were less effective in preventing clinical LUTS progression and reducing prostate size, respectively, in obese men.[12,13]

Given the clear link between obesity and LUTS, a key unanswered question is whether reversing obesity (i.e. weight loss) can improve LUTS among men with symptomatic LUTS. While some studies have shown that comprehensive lifestyle changes that included weight loss but not as the sole intervention improved LUTS symptoms, none studied weight loss alone and none included a group of men who specifically had symptomatic LUTS.[18–20] While in general the studies showed that dietary interventions that induce weight loss may improve LUTS with greater weight loss correlating with greater improvements, these studies suffer from multiple limitations. First, none of the studies specifically targeted men with symptomatic LUTS. Rather the studies focused on obese men often with diabetes. Thus, the clinical relevance of reducing an IPSS in an asymptomatic man is unknown. Second, all of these studies were either single-arm [21] or included two active intervention arms [19,20]. Importantly in the randomized trials, no differences were seen between the two intervention arms. However, given the lack of a control arm, whether the “significant” improvements in LUTS were due to the intervention or the well-known waxing and waning symptoms of LUTS is unknown. Finally, none of the studies clearly delineated a primary outcome. Rather the studies were undertaken to assess the general impact of the intervention of urological health with many outcomes being examined. Thus, whether the “significant” improvements in LUTS reflect a type I error due to multiple testing is unknown.[20] Collectively, while these studies generally support the hypothesis that weight loss may improve LUTS, well-designed prospective randomized controlled trials are urgently needed to determine if weight loss is effective at either improving LUTS symptoms or reducing the risk of LUTS progression.

## Diet

Beyond obesity, certain dietary factors have been associated with LUTS. Not surprising given the link between obesity and LUTS, increased total energy intake has been associated with LUTS.[22] In addition, energy-adjusted red meat, fat, cereals, bread, poultry and starch have been associated with increased risks of symptomatic LUTS whereas total protein, dairy, vegetables, fruits, polyunsaturated fatty acids, linoleic acid, carotenoids, vitamins A, C and D have been associated with decreased risks.[23,24] In addition, lower vitamin D status and caffeine intake were associated with a greater risk for LUTS or symptoms of LUTS.[3,24–28] For micronutrients, higher serum levels of vitamin E, lycopene, selenium and carotene have been associated with reduced risk of LUTS.[3,26,29]

The studies on the association of singular nutrient or food factor with LUTS are consistent with studies that examined the whole dietary pattern. Poor overall dietary quality, as indicated by the Healthy Eating Index, and reflected by a lower intake of fruits and vegetables and a higher intake of red meats and fat, was associated with a greater self-reported LUTS among 1385 men aged 40 years in the 2000–2001 NHANES survey.[30]

In summary, it appears that fruits and vegetables as well as anti-oxidant and anti-inflammatory micronutrients such as carotenoids and vitamins A and C are associated with lower risk of LUTS. However, to date no clinical trial has specifically tested this idea. As many factors that are associated with lower LUTS risk all have anti-inflammatory properties, these observations are consistent with a growing hypothesis that inflammation may play a role in the pathophysiology of LUTS.[31] For example, serum c-reactive protein, a marker of inflammation, was borderline associated with symptoms of LUTS among 2337 older men 60 years and over in the NHANES III survey.[32] Thus, while no definitive conclusions can be drawn as of today, understanding the potential role of inflammation in the etiology of LUTS is a ripe area of research particularly as inflammation can be modified by lifestyle changes. Furthermore, clinical trials examining dietary interventions to modulate LUTS symptoms or prevent progression are desperately needed.

## Physical activity

Physical activity is another lifestyle factor that has been linked with LUTS. Specifically, increased physical activity has been linked with decreased risk of LUTS across multiple studies.[3,12,15,33] Men who are physically active are at lower risk of nocturia, the most common and bothersome of LUTS.[34] Indeed, a meta-analysis of 11 published studies with over 43,000 men found that moderate to vigorous physical activity reduced the risk of LUTS by as much as 25% compared to a sedentary lifestyle, with stronger effects seen with higher levels of activity.[35] In addition, a greater physical activity at baseline predicted improvement in LUTS symptoms in a 5 year prospective study of 780 men, aged 35 to 80 at baseline.[11] However, despite the consistent evidence that physical activity is linked with LUTS, randomized clinical trials are lacking. In a small study, Khoo et al randomized 90 obese sedentary men to moderate-intensity (<150 min/wk) or high-intensity exercise (200–300 min/wk) for 24 wks.[36] While both groups had improvements in LUTS as measured by the IPSS, the differences between arms were not significant. Moreover, neither group was selected for LUTS, but rather due to their obesity status. Thus, while the extant literature

supports the hypothesis that physical activity may improve LUTS, prospective randomized trials are lacking.

### **LUTS: current treatments are less than ideal**

For subjects who remain bothered by their symptoms despite simple lifestyle alterations (altering fluid intake to drink the majority of liquids during the day and to avoid drinking after dinner; reducing or eliminating caffeine intake), medications are the first line of therapy. There are 4 classes of medications recommended to treat LUTS: alpha-blockers, 5-alpha reductase inhibitors (5ARi), anticholinergics, and more recently phosphodiesterase type 5 inhibitors (PDE5i).[1] While all agents are effective to some degree in some subjects, there are many limitations to the current treatments for LUTS. First, they have side effects including orthostatic hypotension (alpha-blockers), sexual side effects and possibly increased risk of high-grade prostate cancer (5ARi), dry mouth and constipation (anticholinergics), dizziness and stuffy nose and visual disturbances (PDE5i). Second, none of the treatments treat the underlying pathophysiology of LUTS but rather treat the symptoms. Third, many men with LUTS have no other medical problems. Thus, they are often reluctant to take medications as they are otherwise “healthy”. Fourth, for men who are willing to take medications it is often because they are taking many other medications and thus don’t see one additional medication as a burden. However, as the number of medications taken increases, the risk for drug-drug interactions also increases. Fifth, none of the medications improves overall health. An ideal treatment for symptomatic LUTS would be one that was efficacious with minimal toxicity, minimal costs, and improved overall health. To date, no such therapy exists.

### **LUTS: lifestyle interventions as the ideal treatment?**

Given the strong epidemiological evidence to support a role of obesity, lack of physical activity, and a diet low in anti-oxidants and overall dietary quality as predisposing or exaggerating factors to LUTS, it stands to reason that a lifestyle intervention that modifies these risk factors may reduce bothersome LUTS. However, as detailed above in the individual sections, few if any randomized trials have examined the comprehensive lifestyle interventions for LUTS management or prevention of progression.

We firmly believe that the time has come to perform well designed clinical trials evaluating lifestyle interventions for men with or at risk of developing LUTS. While the outcomes of those trials are obviously unknown, the worst case is that men lose weight, become more physically active, and improve their overall health with no benefit of their LUTS. If that is the worst case scenario, what are we waiting for?

## **Conclusion**

LUTS is a major source of morbidity for men with a high cost associated with treatment. Despite strong epidemiological data to support a role for lifestyle factors (obesity, diet, and lack of physical activity) in LUTS etiology and progression (see Summary table below), only limited human trial data exists to support this, all of which has major limitations. The updated guidelines for BPH published by the American Urological Association in 2011

listed “obesity and lifestyle interventions” as number one on their list of high priority research areas.[1] Despite this, a rigorously designed RCT of lifestyle interventions for men with LUTS with adequate sample size has never been completed. Regardless, lifestyle factors including weight loss, regular physical activity and a healthy diet have been associated with a lower risk for or improvement of LUTS. As such, clinicians are encouraged to promote these factors for overall health management and potentially for management of LUTS.

## Abbreviations

<b>LUTS</b>	lower urinary tract symptoms
<b>BPH</b>	Benign Prostate Hyperplasia

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- of special interest
  - of outstanding interest
  - an interesting insight into...
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**Key points**

(3–5 key points/sentences that summarize your article)

- Consistent epidemiological evidence supports a link between lifestyle factors including dietary intake, physical activity and obesity, and LUTS.
- Randomized controlled trials are lacking to test the effectiveness of lifestyle intervention on the incidence or progression of LUTS.
- Promoting a healthy lifestyle with a healthy weight, good quality diet, and regular physical activity benefits overall health and may benefit LUTS.

**Table**

Summary:

<b>Lifestyle factors</b>	<b>May be beneficial</b>	<b>May contribute to risk</b>
Dietary intakes	Good quality diet including fruits, vegetables, protein, vitamins A, C, D and polyunsaturated fatty acids.	Diets with increased red meats, fat, and lower levels of vitamin D, selenium, carotene, and lycopene.
Physical activity	Regular physical activity	Sedentary lifestyle
Body weight	A healthy weight	Overweight and obesity

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