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## Associations between Modest Weight Changes and Onset and Progression of Lower Urinary Tract Symptoms in Two Population-Based Cohorts

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### Abstract

**OBJECTIVE**—Obesity has been associated with lower urinary tract symptoms (LUTS) in aging men. We conducted a study to determine if weight changes were associated with risk of developing LUTS.

**METHODS**—The study population consisted of men participating in *The Olmsted County Study of Urinary Symptoms and Health Status among Men (OCS)* and the *Flint Men's Health Study (FMHS)*. Weight loss and weight gain were defined as a change of at least 5% of baseline weight. LUTS progression was measured by calculating AUASI score slopes over four years of follow-up in both cohorts. Additional Cox proportional hazard models were constructed to determine if weight changes were associated with later development of moderate-to-severe symptoms or with a 4-point increase in AUASI score (OCS cohort only).

**RESULTS**—Weight changes were not associated with LUTS progression (all  $p > 0.05$ ). Additionally, the rate at which AUASI scores changed did not vary by weight change. Finally, in the OCS cohort, weight changes were not associated with risk of developing a moderate-to-severe AUASI score or having a 4-point or greater increase in AUASI score.

**CONCLUSIONS**—Modest weight loss may not prevent the onset or progression of LUTS. However, modest weight gain may not contribute to changes in LUTS.

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## Keywords

weight loss; weight gain; lower urinary tract symptoms; benign prostatic hyperplasia; BPH; LUTS

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## INTRODUCTION

Lower urinary tract symptoms (LUTS) affect a substantial proportion of aging men, ranging from 10% among men in their forties to more than 70% among men 80 years of age and older.<sup>1–4</sup> Moderate-to-severe LUTS are associated with a substantially decreased quality of life.<sup>5–7</sup> Moreover, the annual healthcare costs associated with treatment of LUTS (and associated benign prostatic hyperplasia; BPH) are substantial, with estimates ranging from 2 to 4 billion dollars per year.<sup>8,9</sup> Therefore, behavioral interventions that safely and reliably reduce a man's need for medical therapy and/or surgery are likely to promote health, improve the quality of care, and have significant economic implications.

With some studies suggesting that heavier men, or those with larger waist circumferences, are more likely to have LUTS,<sup>10–13</sup> weight loss may be one such intervention. However, prior studies reported cross-sectional associations, and it remains unknown how weight may affect the development of LUTS over time. More importantly, it remains unclear whether changes in weight, either weight loss or weight gain, might be associated with the likelihood of developing LUTS or the likelihood of LUTS progression. For example, if weight loss is associated with a decreased risk of later developing LUTS, or if weight loss slows the progression of LUTS, high-risk groups could be targeted with weight loss treatment plans to reduce the incidence of this common condition.

To address these questions, we took advantage of the longitudinal data available from two cohort studies of community-dwelling men: *The Olmsted County Study of Urinary Symptoms and Health Status among Men (OCS)* and the *Flint Men's Health Study (FMHS)*. The OCS and FMHS have very similar designs, but the OCS includes only white men, while the FMHS includes only black men. Combining data from these two population-based cohorts provided the ideal opportunity to determine whether changes in weight were associated with the onset and progression of LUTS in two racially diverse populations.

## MATERIALS AND METHODS

### Study Populations

**The Olmsted County Study (OCS)**—The initial study cohort was constructed through creation of an age-stratified sampling frame that identified approximately 95% of the men 40–79 years of age predicted to be residing in Olmsted County, Minnesota by the 1990 US Census.<sup>3,14</sup> The community medical records of a random sample of potential participants were screened for indications of prostate surgery, denervated or surgically treated bladder, urethral stricture, or debilitating central nervous system disease. Following exclusion of individuals with these characteristics, 3,874 were invited to participate, and 2,115 (55%) were enrolled in the cohort. All study participants were visited in their homes by study coordinators. At that time, participants completed questionnaires that included questions similar to the American Urological Association Symptom Index (AUASI).

All of the men in the cohort have been followed biennially since 1990. At each round of follow-up, all men completed similar questionnaires, including the AUASI. Men who died or were lost to follow-up during the course of the study were replaced during rounds 2 and 3, resulting in a total of 2,447 study participants. The 9<sup>th</sup> round of follow-up (16 years) was completed in August 2007, and the median length of follow-up for the men in this cohort is

13.8 years (25<sup>th</sup>, 75<sup>th</sup> percentile: 9.2, 15.7 years). The analyses in this study included men who participated in rounds 1 and 3 and had weight measures available at both points in time (n=1,674).

**The Flint Men's Health Study (FMHS)**—The FMHS cohort was designed to be a parallel cohort for the OCS. In the FMHS, a probability sample of black men was selected from households located in Genesee County, Michigan in 1996.<sup>15</sup> Eligible men were stratified into ten-year age groups: 40–49, 50–59, 60–69, and 70–79. Men in the older age groups, 60–79 years, were over-sampled. A subject was ineligible if he reported a history of prostate cancer or a prior operation on the prostate gland. A trained interviewer from the University of Michigan Institute for Social Research contacted each sample household, identified 732 eligible subjects, and performed a detailed in-home interview. This interview included completion of the AUASI as well as demographic and other lifestyle information.

Four years after baseline (2000), 432 of the men who participated in the baseline clinical exam were eligible and invited to complete the same study protocol described above. Of the 432 men, 186 (43%) were available and agreed to participate. Men with a positive biopsy, missing round 1 data or missing weight data were removed from the analyses (n=18), leaving 168 men who participated in both the baseline and follow-up rounds.

### Measurement of weight change

Weight was measured on all study participants by a study assistant at baseline and at approximately 4 years of follow-up for all men in both the OCS and FMHS using a standard protocol and a beam balance scale.<sup>16</sup> For this study, weight loss and weight gain were defined as weight lost or gained between baseline and 4 years after initial enrollment. Given data suggesting that even modest weight loss may have clinical benefit, weight loss was classified as any weight loss, and as loss of at least 5% of baseline body weight.<sup>17</sup> Weight gain was also defined as gain of at least 5% of baseline body weight. All analyses were performed using both definitions; however, results were similar regardless of definition, so only results for change of at least 5% of baseline body weight are presented.

### Measuring changes in LUTS

At least 4 years of follow-up were available for both the OCS and FMHS cohorts. For the initial analyses, changes in LUTS were measured by calculating annual change in AUASI score from baseline to 4 years of follow-up. Development of moderate-to-severe LUTS (AUASI score >7) or having at least a 4-point increase in AUASI score were also examined as secondary endpoints in the OCS cohort.

### Analyses

Characteristics of the combined study populations at baseline and 4 years of follow-up are presented. Measurements across weight change categories were assessed and tested for trends. Analyses were adjusted for age and race. The empirical distribution of annual change (points/year) in AUASI score was calculated by dividing the difference between the baseline and 4-year follow-up AUASI score measures by the number of years between the measurements. Additionally in OCS men, Cox proportional hazards models were used to estimate the associations between changes in weight and future development of adverse urologic outcomes. Follow-up was from the definition of weight change (4-year follow-up) until the first occurrence of the outcome being analyzed or date of last follow-up. Separate analyses were conducted for each outcome and men with the outcome before the 4-year follow-up (prevalent cases) were removed. Multivariable models were used to adjust for potential confounders including baseline age, weight, diabetes, hypertension, and regular physical activity.

## RESULTS

The study population consisted of 168 black men and 1,674 white men. Characteristics of the combined study population are shown in Table 1. At 4 years of follow-up, 8% of the population had lost  $\geq 5\%$  of their baseline weight, while 40% of the population had gained  $\geq 5\%$  of their baseline weight.

Age was strongly associated with changes in urinary symptoms over the 4 year period, as older men were more likely to experience an increase in AUASI score in that time frame (Table 2). However, weight loss and weight gain were not significantly associated with changes in AUASI score (Table 2). Additionally, the rate at which AUASI scores changed did not vary by weight change (Table 3). The men who lost  $\geq 5\%$  of their baseline weight had a median annual increase of 0.3 points in their AUASI score per year, compared to a median change of 0.0 points per year among those who did not lose any weight. Similarly, men who gained  $\geq 5\%$  of their baseline weight had the same median change in AUASI score as those who did not gain any weight (0 points per year in both groups; Table 3).

Finally, we examined the risk of developing moderate-to-severe symptoms (AUASI score  $>7$ ) or having a 4-point increase in AUASI score after 4 years of follow-up in the OCS cohort. Neither weight loss nor weight gain were associated with risk of developing a moderate-to-severe AUASI score, or having at least a 4-point increase in AUASI score (Table 4).

## DISCUSSION

In this study, we found that modest weight changes over a 4-year period were not associated with risk of developing moderate-to-severe LUTS. Additionally, weight changes were not associated with the rate at which LUTS progressed. While modest weight loss may have other health benefits, these data suggest that neither weight loss or weight gain play a substantial role in LUTS progression.

Several studies have linked being overweight, or having a larger waist circumference, to an increased prevalence of LUTS.<sup>10,12,13</sup> These previous studies were cross-sectional, and therefore it was not possible to determine whether changes in weight might influence the development of the onset of LUTS. Kristal and colleagues conducted a longitudinal study among men participating in the Prostate Cancer Prevention Trial and found that men with a higher body mass index (BMI) or a larger waist-hip ratio were more likely to develop severe LUTS compared to men with lower BMIs or smaller waist-hip ratios.<sup>11</sup> In this study, LUTS were defined as International Prostate Symptom Scores of at least 15, corresponding to “severe” LUTS as measured by the AUASI. It may be that higher BMI or waist-hip ratios are risk factors for later developing severe LUTS, but not more moderate LUTS. In our study, modest weight loss was not associated with risk of developing either moderate or severe LUTS, suggesting that while higher BMIs may be risk factors for developing severe LUTS, modest weight loss may not influence the development of either moderate or severe LUTS (data not shown). It is not clear, however, why modest weight gain was not associated with LUTS development or progression in this study. A relatively small proportion of our population was in obese BMI range, and a small proportion had severe LUTS, compared to the Kristal study. If obese men are the most likely to develop severe LUTS, we may not have had the power to detect such an association in our study. Instead, our results suggest that men in the normal to overweight BMI categories may not be at high risk of moderate-to-severe LUTS if their weight increases by 5% or more.

As our study was not a clinical trial, it is possible that uncontrolled confounders may have been responsible for the lack of association we observed between modest weight changes

and development of LUTS. For example, it was not possible for us to determine the reasons for weight changes in our study population. Men who lost  $\geq 5\%$  of their baseline weight were older compared to those who lost less weight, and it is possible that these men developed age-related conditions that resulted in weight loss, but also increased their risk for LUTS. We conducted a secondary analysis stratifying our results by baseline age, but still did not observe a protective effect of weight loss in the younger age group (data not shown).

It is also possible that our lack of association between weight loss and LUTS could be because more significant weight changes are necessary to see positive associations. A weight change of 5% or more corresponded to a loss or gain of approximately 9 pounds in the OCS cohort and 9.7 pounds in the FMHS cohort. A more significant change in weight (such as  $\geq 10\%$  of baseline weight) could potentially have been significantly associated with these outcomes. Very few men in our study had a weight loss of this magnitude (35 (2.1%) men in the OCS, 10 (6.0%) men in the FMHS). However, 211 (12.6%) men in the OCS and 15 (8.9%) men in the FMHS had a weight gain of 10% or greater. We conducted secondary analyses examining the associations between these larger changes and the outcomes of interest, and still did not observe significant associations between these levels of weight change and LUTS onset or progression (data not shown). Finally, a significant proportion of both study populations became lost to follow-up during study follow-up. However, the characteristics of those who were lost to follow-up did not differ substantially from those who remained in the study, suggesting that participation bias is unlikely to account for our findings.<sup>18,19</sup>

## CONCLUSIONS

We found that a weight loss or a weight gain of  $\geq 5\%$  of baseline body weight were not associated with onset or progression of LUTS in two populations of aging men. These results suggest that modest weight loss may have limited utility in preventing LUTS onset or progression. Conversely, modest weight gain may not promote onset or progression of LUTS.

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## DISCLOSURES

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**Table 1**

## Characteristics of the study population

Characteristic	N=1,842
Baseline	Median (Q1, Q3)
Age (years)	54.0 (47.2, 63.1)
Weight (kg)	84.8 (77.1, 94.4)
BMI (kg/m <sup>2</sup> )	26.9 (24.5, 29.4)
AUASI score	5 (2, 9)
At 4 years of follow-up	Median (Q1, Q3)
Weight (kg)	87.9 (79.0, 98.0)
Change in weight (kg)	3.1 (-0.2, 6.2)
BMI (kg/m <sup>2</sup> )	28.3 (25.8, 31.1)
Change in BMI (kg/m <sup>2</sup> )	1.4 (0.3, 2.5)
AUASI score	6 (2, 10)
From baseline to 4-year follow-up	N (%)
No weight loss	1,367 (74.2)
Lost <5% of baseline weight	328 (17.8)
Lost ≥5% of baseline weight	147 (8.0)
From baseline to 4-year follow-up	N (%)
No weight gain	483 (26.2)
Gained <5% of baseline weight	621 (33.7)
Gained ≥5% of baseline weight	738 (40.1)

**Table 2**Associations between changes in weight and changes in urologic outcomes over 4 years of follow-up<sup>†</sup>

Characteristic	Decrease in AUASI score (N=702)	No change in AUASI score (N=232)	Increase in AUASI score (N=904)	P value *
	Median (Q1, Q3)	Median (Q1, Q3)	Median (Q1, Q3)	
Baseline age (years)	52.4 (46.5, 62.2)	51.6 (45.5, 59.0)	55.3 (48.6, 64.2)	<0.0001
Baseline weight (kg)	86.2 (77.1, 95.3)	85.5 (78.4, 94.3)	83.9 (75.8, 93.8)	0.51
Baseline body mass index (kg/m <sup>2</sup> )	27.0 (24.5, 29.5)	27.2 (25.0, 29.4)	26.6 (24.4, 29.3)	0.49
	N (%)	N (%)	N (%)	
No weight loss	515 (73.4)	179 (77.1)	672 (74.3)	0.68
Lost <5% of baseline weight	135 (19.2)	41 (17.7)	149 (16.5)	
Lost ≥5% of baseline weight	52 (7.4)	12 (5.2)	83 (9.2)	
	N (%)	N (%)	N (%)	
No weight gain	191 (27.2)	53 (22.8)	236 (26.1)	0.47
Gained <5% of baseline weight	226 (32.2)	91 (39.2)	303 (33.5)	
Gained ≥5% of baseline weight	285 (40.6)	88 (37.9)	365 (40.4)	

<sup>†</sup>Four men did not have a symptom score assessment at baseline so change in symptom score cannot be calculated and therefore they are excluded from this table

\* Test for trend P value adjusted for age and race



**Table 3**Rate of change in AUASI score (points/year) by weight loss categories<sup>†</sup>

	N	Median (Q1, Q3)	P value*
No weight loss	1366	0.0 (-0.5, 0.9)	0.32
Lost <5% of baseline weight	325	0.0 (-0.6, 0.9)	
Lost ≥5% of baseline weight	147	0.3 (-0.4, 1.1)	
No weight gain	480	0.0 (-0.6, 0.9)	0.79
Gained <5% of baseline weight	620	0.0 (-0.5, 0.9)	
Gained ≥5% of baseline weight	738	0.0 (-0.5, 0.9)	

<sup>†</sup> Four men did not have a symptom score assessment at baseline so change in symptom score cannot be calculated and therefore they are excluded from this table

\* Adjusted for baseline age and race

**Table 4**

Risk of developing an elevated AUASI score by weight loss category (OCS cohort only)

	AUASI score >7		4-point increase in AUASI score	
	Unadjusted* HR (95% CI)	Adjusted+ HR (95% CI)	Unadjusted* HR (95% CI)	Adjusted+ HR (95% CI)
No weight loss	Reference	Reference	Reference	Reference
Lost <5% of baseline weight	1.03 (0.77, 1.37)	0.95 (0.71, 1.28)	1.05 (0.85, 1.29)	1.00 (0.81, 1.25)
Lost ≥5% of baseline weight	1.21 (0.81, 1.80)	1.06 (0.71, 1.59)	1.04 (0.77, 1.42)	0.96 (0.70, 1.32)
No weight gain	Reference	Reference	Reference	Reference
Gained <5% of baseline weight	0.93 (0.70, 1.23)	0.99 (0.75, 1.31)	0.96 (0.78, 1.17)	0.99 (0.80, 1.22)
Gained ≥5% of baseline weight	0.95 (0.73, 1.24)	1.05 (0.80, 1.38)	0.95 (0.77, 1.15)	1.01 (0.83, 1.24)

\* Prevalent cases (859 of the 1,674 men for AUASI score>7 and 483 of the 1,674 men for a 4-point increase in AUASI score) of each outcome removed.

+ Analyses adjusted for baseline age, weight, diabetes, hypertension, and regular physical activity.