# Progression and Remission of Urologic Symptoms in the Community: Results of a Longitudinal Cluster Analysis Approach

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**OBJECTIVE** To investigate the natural history of urologic symptom progression and remission by means of cluster analysis in a large, well-characterized cohort of men and women.

**METHODS** Cluster analysis was used to assign men and women to symptom clusters on the basis of the prevalence of 14 self-reported urologic symptoms. Data were analyzed from the Boston Area Community Health study at baseline (T1) and 5-year follow-up (T2). Cluster progression was defined as any change from a less symptomatic to a more symptomatic cluster; conversely, cluster remission was defined as movement from more symptomatic to less symptomatic clusters. Logistic regression models examined the association of sociodemographic, psychosocial, and health outcome measures with cluster progression and remission.

**RESULTS** Follow-up data were available from 4145 participants (1610 men; 2535 women). More than two thirds of men (69.2%) and women (68.2%) had stable symptom cluster assignments. Cluster progression occurred in 280 of 1610 (15.2%) men and 390 of 2535 (14.6%) women; cluster remission in 280 of 1610 (15.6%) men and 409 of 2535 (17.4%) women. In multivariate analyses, cluster progression was twice as common in men with incident depression (odds ratio = 2.43, 95% confidence interval 1.26-4.67) and 3 times more likely in men with ≥3 comorbidities at baseline. Urologic surgeries were uncommon in men and women and were not consistently related to cluster progression or remission.

**CONCLUSION** Urologic symptom clusters were relatively stable over a 5-year follow-up period for more than two thirds of men and women in our sample. Specific risk factors for progression were identified in men and women. UROLOGY 83: 1041–1050, 2014. © 2014 Elsevier Inc.

Urologic symptoms in the general population are described as the "tip of an iceberg,"[1] with most symptoms unreported and unacknowledged in medical practice.[2-7] Moreover, leading experts in the field have called for a less narrow or organ-centered focus and have advocated instead for "beyond the bladder" conceptualizations of urologic symptoms in relation to patient's overall health and function.[8,9] Responding to these challenges, new approaches have been proposed for classifying urologic symptoms in men and women, including the use of multimethod, multisymptom approaches such as cluster analysis.[10-15]

Cluster analysis is a validated method for classifying groups of individuals with potentially similar characteristics or properties.[16-18] The method has been used to classify individuals with medical or psychiatric disorders with some success.[19-22] More recently, we have reported the correlates and predictors of urologic symptom clusters in men and women and their associations with age, comorbidities, quality of life, and treatment seeking, among other health-related variables,[10,11] and our results have been confirmed by other investigators using similar methods.[13,15] Using the cluster analysis method, we identified 4 primary urologic symptom clusters among women and 5 clusters in men, which were strongly associated with adverse quality of life outcomes and increased health care use.[10,11,23]

The present study aimed to extend our earlier cross-sectional findings by examining movement within and across symptom clusters over time and rates of progression and remission defined as movement from less to more symptomatic clusters. The present study is the first to examine change or stability in urologic symptom clusters over time and to assess long-term predictors of cluster progression and remission.

**Financial Disclosures:** *The authors declare that they have no relevant financial interests.*
**Funding Support:** *This project was supported by the National Institute of Diabetes and Digestive and Kidney Diseases, Grant Nos. R21DK081844 and U01DK56842. The content of this work is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Diabetes and Digestive and Kidney Diseases or the National Institutes of Health.*

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*Submitted: August 2, 2013, accepted (with revisions): December 24, 2013*




http://dx.doi.org/10.1016/j.urology.2013.12.051

## MATERIALS AND METHODS

### Study Population

The Boston Area Community Health (BACH) Survey is an observational prospective cohort study of men and women designed to assess the epidemiology of urologic symptoms in a racially and/or ethnically diverse population-based sample.[1,2] BACH recruited a random sample of 5502 residents (2301 men and 3201 women) aged 30-79 years from 3 racial and/or ethnic groups in Boston, MA. Participants completed an in-person interview at baseline (occurring between 2002 and 2005, hereinafter T1) and approximately 5 years later (2006-2010, hereinafter T2). Further details of the study population and enrollment are available elsewhere.[1,2] All participants provided written informed consent. The study was approved by the New England Research Institutes' Institutional Review Board. T2 follow-up interviews were obtained for 4145 individuals (1610 men and 2535 women) from the 5152 eligible individuals, resulting in a conditional response rate of 80.5%. Participants ineligible for follow-up included those deceased, incarcerated, on active military duty, or too ill to participate. Loss to follow-up among nonrespondents was mostly because of inability to contact and was more common for Hispanics, those aged 70-79 years at baseline, and men, but there were no significant differences in lower urinary tract symptoms (LUTS) at baseline.

### Urinary Symptom Data and Cluster Assignment

Full details on the cluster analysis methods, response scales, and symptom thresholds are given elsewhere.[10,11] Briefly, urologic symptoms were assessed at T1 and T2 using standard, validated instruments. LUTS was assessed with the International Prostate Symptom Score (IPSS),[24] incontinence symptoms by the Sandvik Incontinence Scale (urgency incontinence, stress incontinence, terminal dribble, and postvoid dribble).[25] Symptoms of overactive bladder were assessed by a combination of questions assessing frequency and perceived frequency of urination, voiding urgency, and urgency incontinence. Nocturia was assessed with 2 questions on the number of voids nightly after falling asleep. Severity of symptoms was measured by frequency of symptom occurrence in the past month or 7 days. Each item was also scored on a 6-point ordinal scale (range, 1-6), and scores were then range standardized (range, 0-1) before analysis. The 14 items are shown in Table 1.

### Analysis Sample and Cluster Analysis Methods

Participants were included in the cluster analysis if they reported at least 1 of 14 symptoms more often than "rarely" on the 6-point ordinal scales, and if data were not missing for any of the 14 symptoms. To identify the number of clusters in the data, a hierarchical clustering approach was used, in which each subject begins as his or her own cluster and subjects are grouped into clusters by their common symptoms. For the present study, we used discriminant analyses to reclassify symptomatic subjects (at least 1 of the 14 symptoms endorsed) into known groups based on the previous cluster analyses. Consistency in the definitions of cluster assignment from T1 to T2 was maintained to permit formal progression and remission analyses, as planned. Cluster analyses were performed separately on male and female individuals.

As described in our previous publications,[10-12] we identified 5 distinct symptom clusters among men and 4 among women. Among symptomatic men, about half were assigned to cluster 1, which was characterized by a low overall prevalence of voiding symptoms (mean = 1.4). Clusters 2, 3, and 4 had intermediate levels, whereas cluster 5 was characterized by a high prevalence and frequency of nearly all 14 urologic symptoms, with a mean of 9.9 symptoms. Among women, 54% of symptomatic women were assigned to cluster 1, which was characterized by storage symptoms, including nocturia and frequency, with a mean of 1.4 symptoms. Cluster 2 was characterized by a higher prevalence of frequency symptoms and nocturia, with a mean of 3.9 symptoms. Clusters 3 and 4 were characterized by the presence of incontinence with mean symptoms of 3.3 and 7.6, respectively, whereas cluster 4 in women had a high prevalence of nearly all urologic symptoms.

### Longitudinal Change Measure

Our primary outcome measure, cluster progression, was defined as a change in cluster membership for an individual over time from the asymptomatic or movement from a less to more symptomatic cluster. In men, symptom clusters were classified as asymptomatic or minimally symptomatic (clusters 0, 1), moderately symptomatic (clusters 2, 3, 4), or highly symptomatic (cluster 5). Men who progressed from any of the lower categories to a higher category met the definition of progression. In women, progression was similarly defined as change from clusters (0, 1) to (2, 3, 4), or progression from an intermediate cluster (2, 3) to cluster 4. In both genders, cluster progression was evaluated specifically among those participants who were able to progress, that is, not already in the most severe category at T1. The analytical sample size for progression is 1546 in men and 2379 in women.

The secondary outcome, cluster remission, was defined similarly as changing classification from a higher to a lower cluster. Thus, cluster remission was defined in men who changed from cluster 5 to a lower cluster or from an intermediate cluster (ie, 2, 3, 4) to the asymptomatic group or cluster 1 (minimally symptomatic). In women, remission was defined as change from cluster 4 to a lower cluster (ie, 0, 1, 2, 3) or from an intermediate cluster (2, 3) to a lower one (ie, 0, 1). As with progression, cluster remission was not assessed in participants who were asymptomatic at T1 and thus ineligible to remit. The analytical sample size for remission is 1124 in men and 1920 in women.

Independent predictors include selected sociodemographics and health-related measures. Sociodemographics include age, race and/or ethnicity (black, Hispanic, and white), and socioeconomic status (SES) at T2. Health measures include smoking status, number of comorbidities, physical activity, waist circumference (WC) and body mass index (BMI), IPSS, and C-reactive protein levels (CRP). IPSS[24] and CRP levels[26] were included as covariates in the present study because of our previous cross-sectional findings showing significant associations with these measures.[26]

Urologic medication use was evaluated at T1 and T2, and included benign prostatic hyperplasia (BPH) medications (alpha-blockers, 5-alpha reductase inhibitors), and medications used for overactive bladder and/or urinary incontinence (eg, oxybutynin chloride [Ditropan], transdermal oxybutynin chloride [Ditropan Transdermal], tolterodine tartrate [Detrol], darifenacin hydrobromide [Enablex], solifenacin succinate [Vesicare], tropsium chloride [Sanctura], fesoterodine fumarate [Toviaz], propantheline bromide [Pro-Banthine], and hyoscyamine [Levsin]). On the basis of bivariate analyses, change measures of incident obesity (change from BMI <30 at T1 to BMI ≥30 at T2), incident depression (change from nondepressed at T1 to depressed at T2) and incident weight gain (BMI change >2.5 in women; >3.0 in men) were also examined.