

## DIFFERENTIAL IMPACT OF IPSS STORAGE AND VOIDING SYMPTOM SUB-SCORES IN PATIENTS TAKING TADALAFIL 5MG ONCE-DAILY FOR LUTS ASSOCIATED WITH BPH

### Hypothesis / aims of study

Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) are a mixture of voiding and storage complaints. While changes in total International Prostate Symptom Score (IPSS) measure overall treatment response, the relative contributions of IPSS storage and voiding sub-scores remain unclear [1]. We hypothesize that reduction in storage symptoms predominantly improves patient bother and quality-of-life (QoL) following tadalafil therapy for LUTS/BPH. Using a new mathematical model, we investigated whether improvement in storage symptoms following tadalafil differentially drives patient satisfaction.

### Study design, materials and methods

A systematic analysis of pooled data from four randomized, placebo-controlled, double-blind, clinical trials in 1462 men (736 tadalafil, 726 placebo) with LUTS/BPH was undertaken. The intent of this analysis was to confirm IPSS and Benign Prostatic Hyperplasia Impact Index (BII) measurement models and to build a structural equation model (SEM) by combining them. The model was constructed using a bottom-up process that involved four incremental steps: 1) BII factor model, 2) IPSS storage and voiding factor model (assuming bi-directional effect between storage and voiding), 3) IPSS storage and voiding factor model (assuming unidirectional effect between storage and voiding), and 4) Primary model. The primary (final) model included IPSS and BII together with the IPSS-QoL question at endpoint (12 weeks of treatment), as well as variables for treatment (tadalafil, placebo) and age. Initially each measurement model was tested to sufficiently fit the data, then latent variables were set in a causal relationship to build a SEM. Each sequential model was created only if data were fit sufficiently (Probability for Test of Close Fit [PTCF] <0.05). Conclusions were only drawn from the primary model after satisfactory completion of the bottom-up procedure that ensured sufficient validation of the model at each step. Analyses were implemented using the PROC CALIS procedure (SAS version 9.2).

### Results

All measurement models in the bottom-up procedure achieved sufficient fits, including the primary model that demonstrated sufficient fit to model interdependence of storage, voiding, bother, and QoL (PTCF <0.0001; Figure 1). The primary model confirmed previous findings from clinical trials that treatment with either tadalafil or placebo improves storage and voiding symptoms as evidenced by reductions in IPSS questions 1-7 and BII questions 1-4 (Figure 1). Each IPSS storage question (frequency, urgency, nocturia) and voiding question (incomplete emptying, intermittency, weak stream, straining to void) appeared to nearly equally reflect the respective sub-score. Storage had a two-fold greater effect on voiding (0.61;  $P<0.0001$ ) vs. voiding on storage (0.28;  $P<0.0001$ ). Likewise, the direct effect of storage on bother was two-fold greater than voiding (0.64 storage, 0.29 voiding; each  $P<0.0001$ ). The bother factor directly impacted QoL by the largest magnitude (-0.83), albeit largely driven by the storage component ( $P<0.0001$ ).

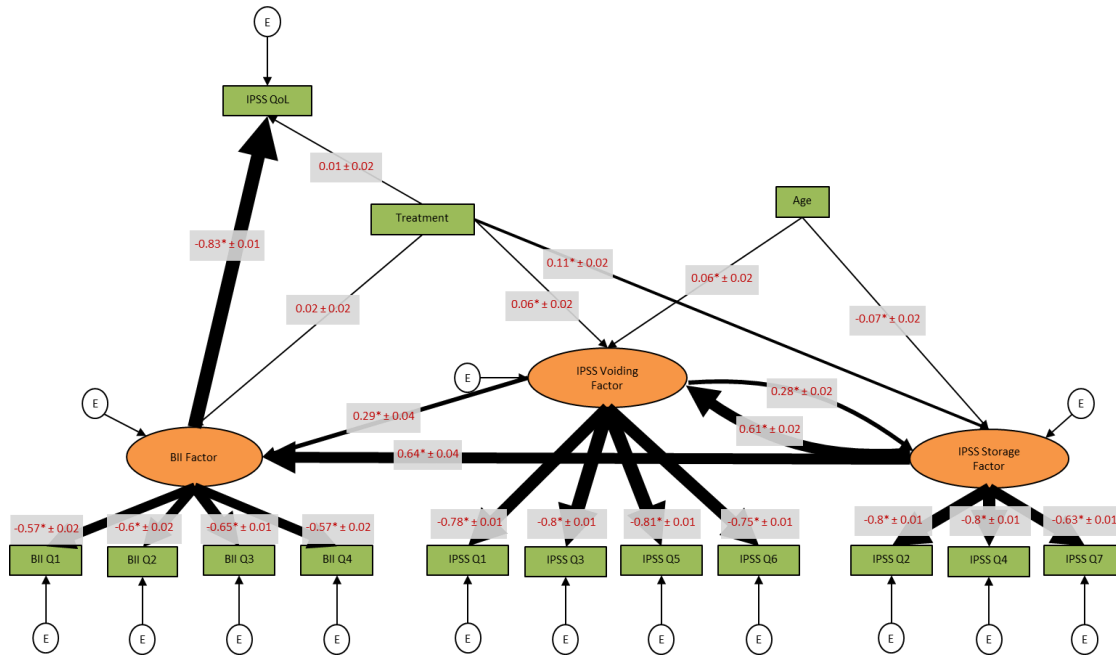
### Interpretation of results

The model demonstrates the separate influence of the IPSS storage and voiding sub-scores on patient bother and QoL in response to therapy in men with BPH/LUTS. Bladder storage was shown to mainly drive the bother factor and thereby QoL improvements significantly more than voiding.

### Concluding message

This model suggests that improvement in storage symptoms has a greater overall impact on the bother factor and QoL than reduction in voiding symptoms. Thus, clinicians should recognize the relatively larger bother of storage symptoms and therapy should be predominately directed at alleviating storage symptoms.

Figure 1  
Primary model derived by structural equation modelling



BII = BPH Impact Index, E = error; IPSS = International Prostate Symptom Score; Q = question; QoL = quality-of-life

References

1. Chapple CR, Roehrborn CG, McVary K, Ilo D, Hennes C, Viktrup L. Effect of tadalafil on male lower urinary tract symptoms: an integrated analysis of storage and voiding international prostate symptom subscores from four randomised controlled trials. Eur Urol 2015;67:114-22.

References

1. Chapple CR, Roehrborn CG, McVary K, Ilo D, Hennes C, Viktrup L. Effect of tadalafil on male lower urinary tract symptoms: an integrated analysis of storage and voiding international prostate symptom subscores from four randomised controlled trials. Eur Urol 2015;67:114-22.

Disclosures

**Funding:** Eli Lilly and Company **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Helsinki Helsinki: Yes **Informed Consent:** Yes