

# Lessons Learned from the MAPP Research Network

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# What is MAPP?

The **M**ultidisciplinary **A**pproach to the Study of Chronic **P**elvic **P**ain (MAPP)

Multi-institutional, collaborative network

NIH Funding

Dedicated to the study of ...  
IC/BPS and CP/CPPS ...

Urologic Chronic Pelvic Pain  
Syndrome (UCPPS)

# Why Do We Need MAPP?

- Lack of clinical advancement in the field of UCPPS
- Little Interdisciplinary work
- New literature (and clinical experience) suggesting that UCPPS likely represents a heterogeneous group of patients, many of whom suffer from pain that reaches far beyond the urogenital system.

**Better Phenotyping = Better Outcomes**



# MAPP Organization

## ◆ Recruitment Discovery Sites (Urologic and Non-Urologic Expertise)

- Northwestern University
- UCLA
- University of Iowa
- University of Michigan
- University of Washington
- Washington University in St. Louis

## ◆ Specialized Discovery Sites

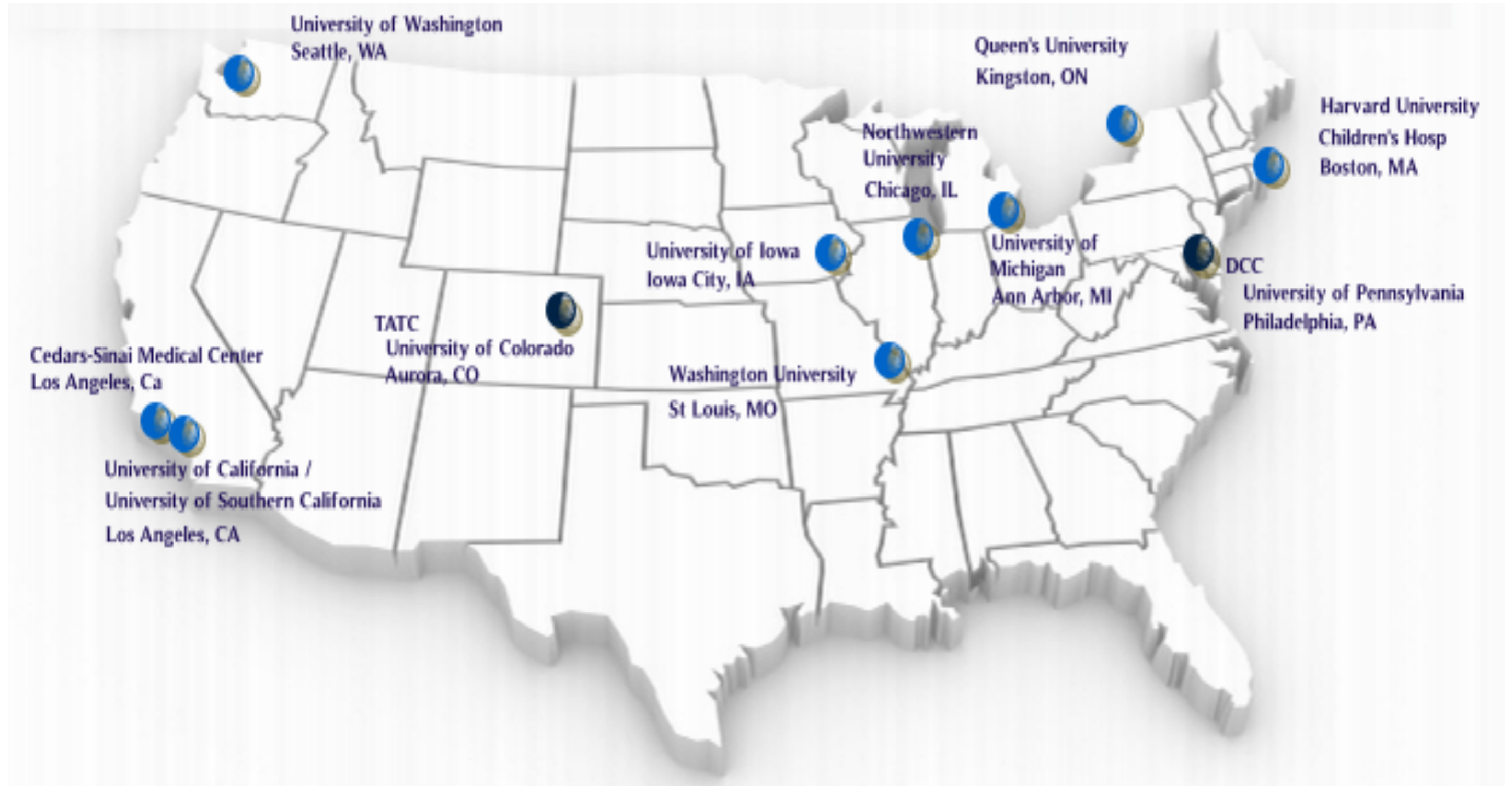
- Boston Children's, Queens University, Cedars Sinai

## ◆ Data Coordinating Center – University of Pennsylvania

## ◆ Tissue and Technology Core – University of Colorado

## ◆ NIDDK

# MAPP Research Network Sites



# Broad Goals of the MAPP Network

- To better understand the *treated natural history* of UCPPS.
- To identify clinical factors and research measurements that will define clinically relevant sub-groups of these patients for future clinical trials.
- Address underlying disease pathophysiology and natural history using patient cohorts, biospecimens and animal models

# MAPP Subject Recruitment

## ◆ Broad inclusion criteria

- Diagnosis of IC/BPS or CP/CPPS
- Age 18+
- Standard exclusions (pelvic malignancy, neurologic disorders, etc)
- Target was 50% with symptoms < 2 years

## ◆ Controls

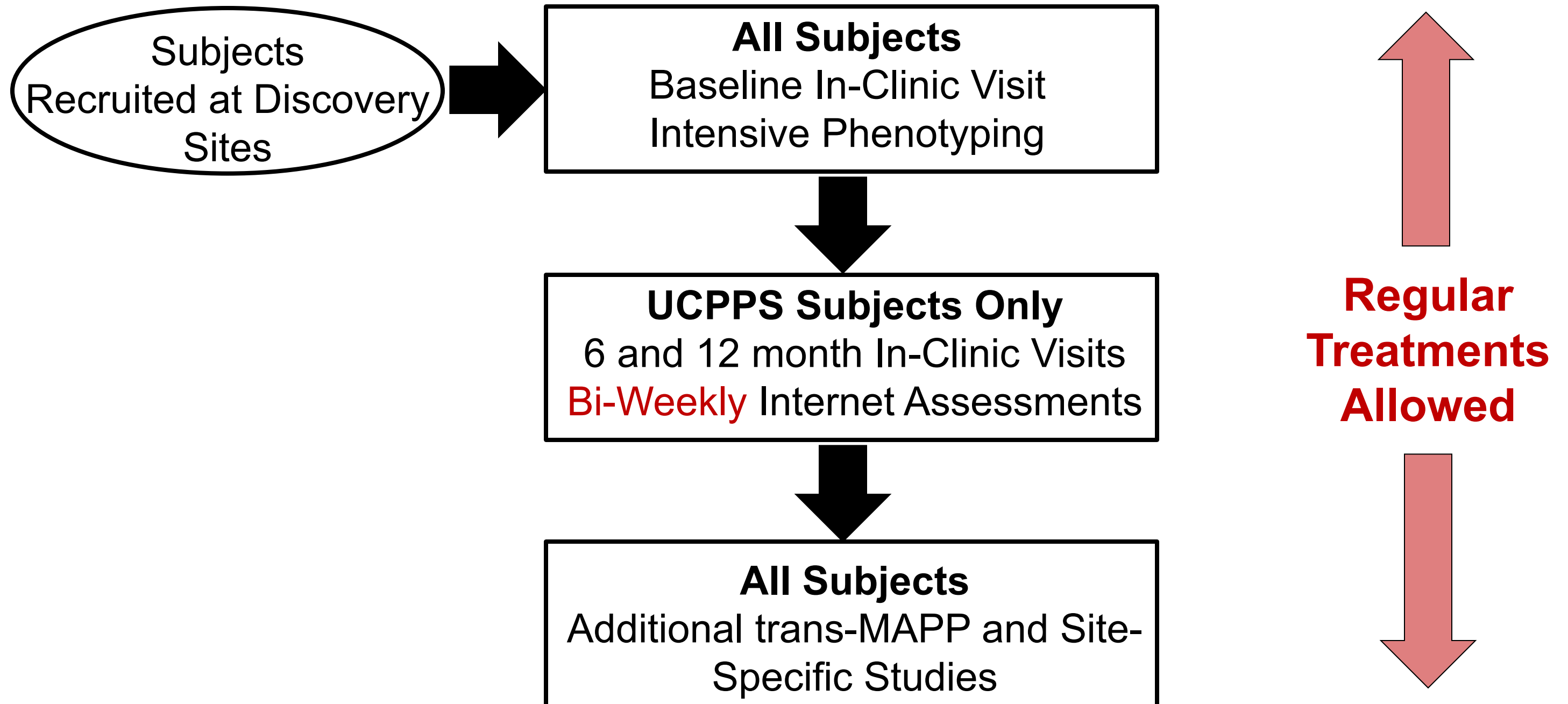
- Asymptomatic
- 'Positive' controls – with fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome

# Baseline Data

- ◆ **Demographics**
- ◆ **Medical History**
- ◆ **Urologic Symptoms**
- ◆ **Pain Symptoms**
- ◆ **Psychosocial Symptoms**
- ◆ **Physical Examination**
- ◆ **Biospecimens**
  - urine, blood, DNA
- ◆ **Neuroimaging**
- ◆ **Quantitative Sensory Testing**



# MAPP Study Flow



# MAPP Cohorts By Sex

Sex	UCPPS	Healthy Controls	Positive Controls	Total
Male	191	182	44	417
Female	233	233	156	622
Total	424	415	200	1,039

# MAPP Epidemiology - Phenotyping Study

## Study Subjects

- ◆ **Demographic and clinical characteristics are similar to other cohorts in the literature**
  - Men => mean age 46.8yrs, mean symptom duration 7.8 yrs, mean CPSI score 22.5
  - Women => mean age 40.5yrs, mean symptom duration 9.1 yrs, mean ICSI score 10.8

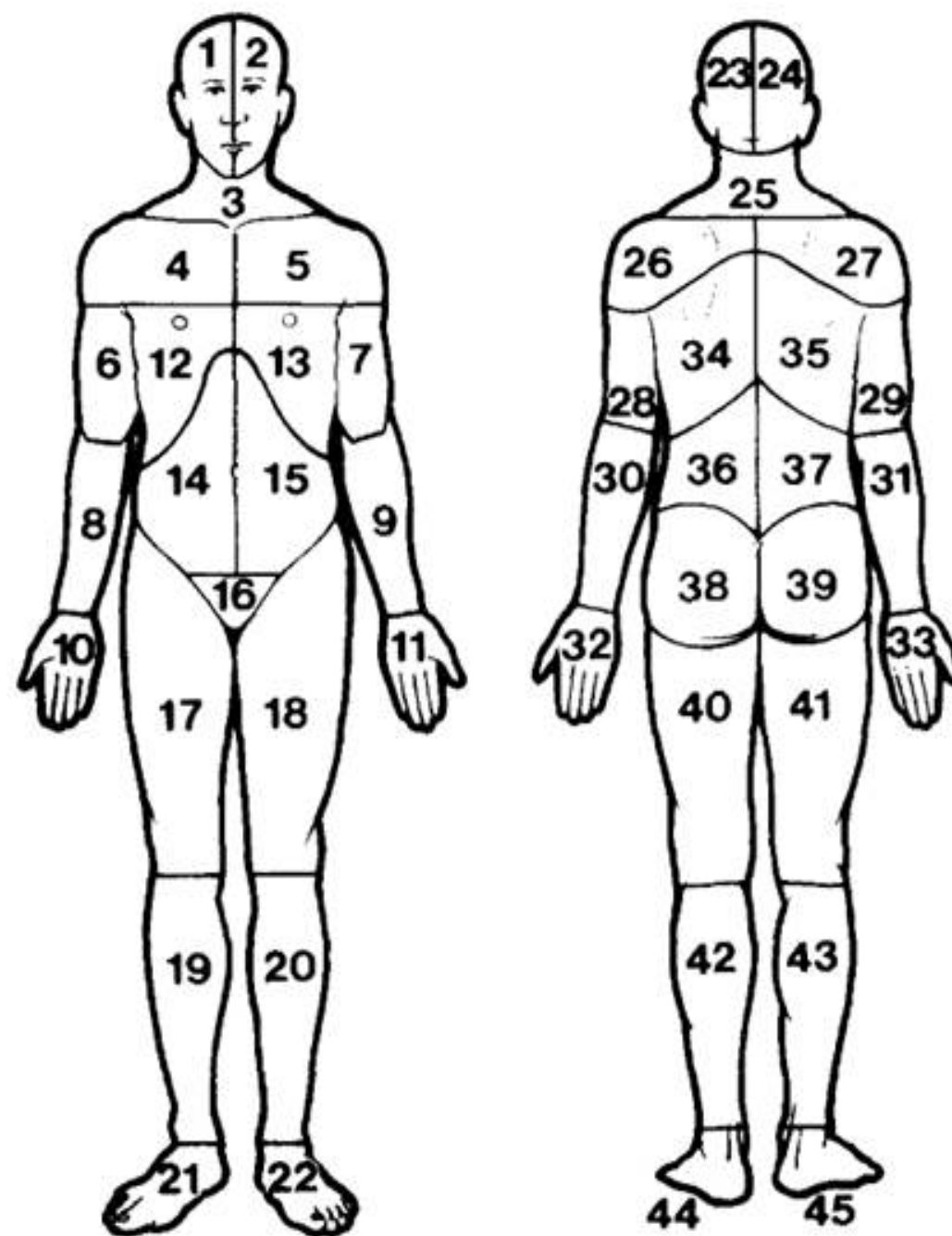
Clemens et al. J Urol 2015;193:1554.

- ◆ **Biweekly Internet-based assessments for 12 months**
  - 83% missed no more than 3 of the planned 26 contacts!

# MAPP Epidemiology-Phenotyping Study

## Location of Reported Pain from Body Map

- ◆ **Pelvic Pain Only**
  - Areas 14, 15 or 16
  - 26%
- ◆ **Pelvic Pain and Beyond**
  - 74%
  - “Centralized” phenotype
  - More severe UCPPS symptoms



# MAPP Epidemiology-Phenotyping Study Findings

## UCPPS and Other Pain Syndromes

- ◆ Psychosocial symptoms were similar in UCPPS subjects and “positive” controls with fibromyalgia, IBS, chronic fatigue syndrome
- ◆ Chronic overlapping pain conditions (fibromyalgia, IBS, chronic fatigue syndrome) in UCPPS patients
  - 43% females, 30% males
  - More severe UCPPS symptoms
  - Worse QOL
  - More psychosocial symptoms

Krieger et al. J Urol 2015;193:1254.

# MAPP Epidemiology-Phenotyping Study Findings

## Bladder-Sensitivity Phenotype

- ◆ **Urinary urgency due to pain/ pressure/discomfort**
- ◆ **Pain that worsens with bladder filling**
- ◆ **One or more positive response:**
  - 88% of women
  - 75% of men
  - Suggests overlap in symptoms between IC/BPS and CP/CPPS
  
- ◆ **Bladder hypersensitivity associated with:**
  - More severe UCPPS symptoms
  - More non-urologic pain
  - Worse QOL

Lai et al. J Urol, 2016

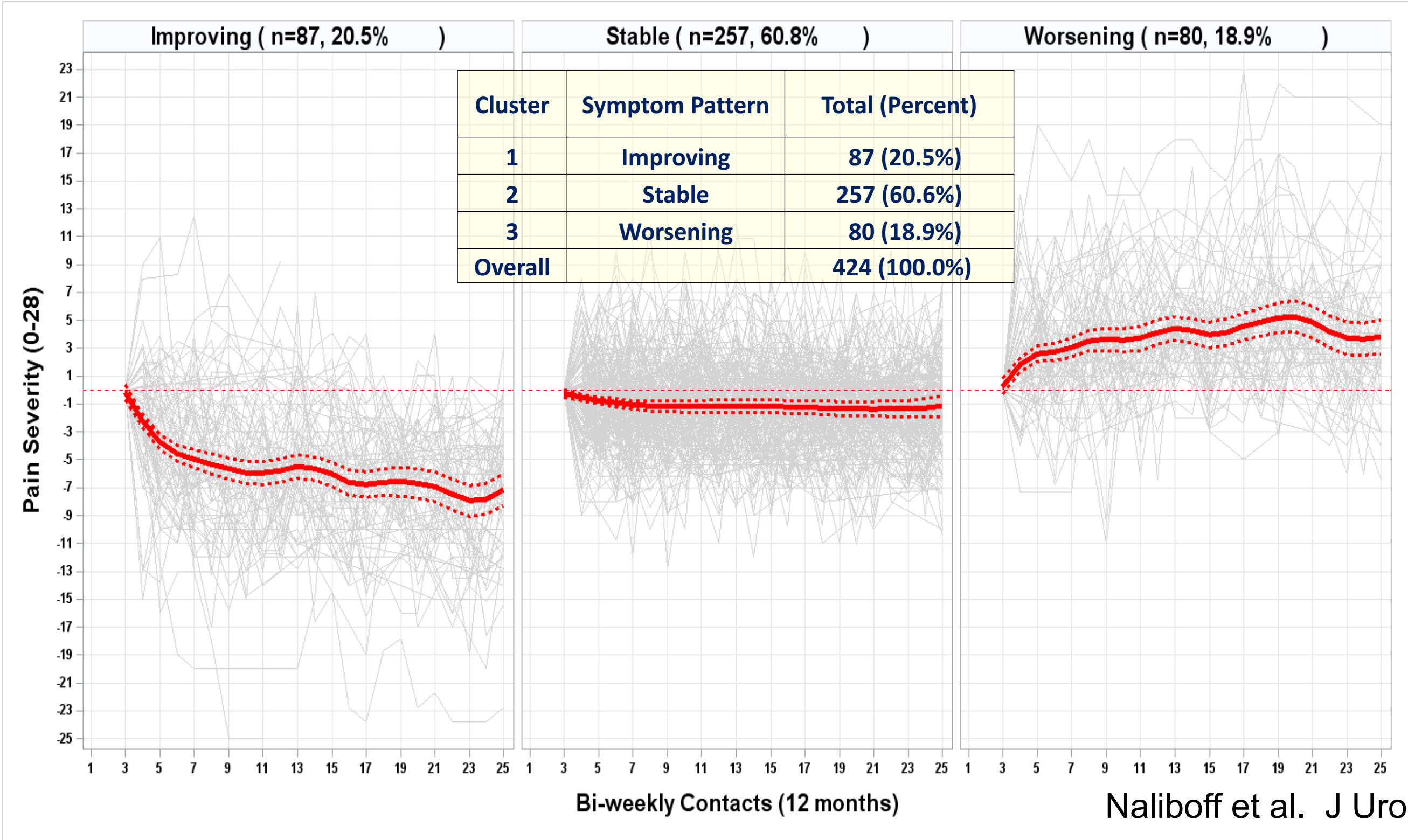
# MAPP Epidemiology-Phenotyping Study Findings

## Symptom Assessment

- ◆ **Baseline questionnaire responses - two factors provided the best psychometric description of items:**
  - Pain symptoms
  - Urinary symptoms
- ◆ **Equivalent results in men and women**
- ◆ **Longitudinal analysis – pain and urinary symptoms track differently**
- ◆ **These findings suggest that pain and urinary symptoms should be examined separately, rather than using a ‘composite’ symptom score.**

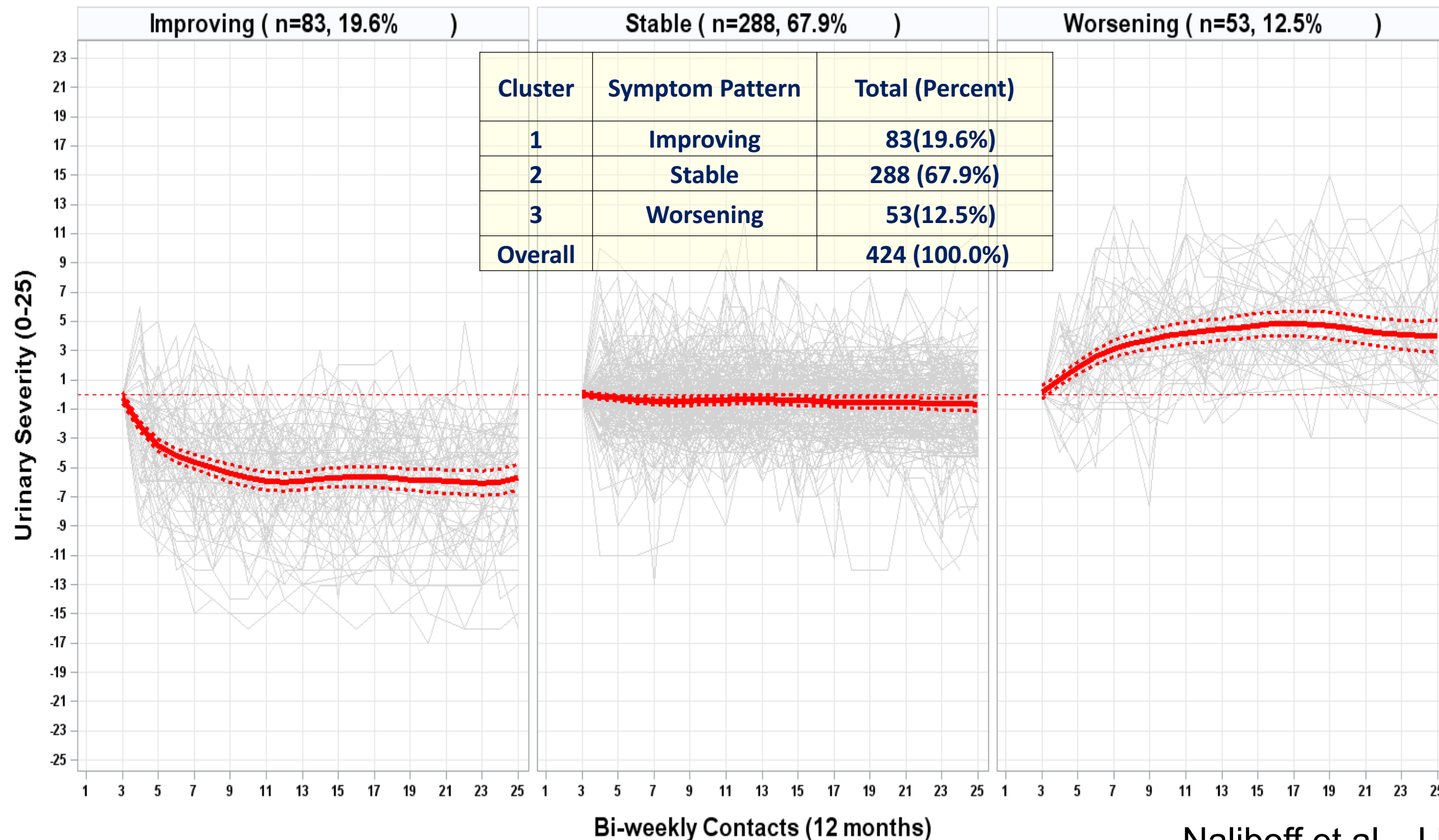
Griffith et al. J Urol, 2016

# Pain Severity Functional Clusters: Absolute Change





# Urinary Severity Functional Clusters: Absolute Change



Naliboff et al. J Urol, 2017

# Change in Symptoms Over 12 Months

**Significant predictors of better outcomes** included:

- Higher baseline symptom severity
- Less widespread pain and non-urologic symptoms
  - CMSI and body map
- Better overall physical health
  - SF-12 physical, PROMIS sleep, PROMIS fatigue
- Better overall mental health
  - SF-12 mental, pain catastrophizing, perceived stress

Naliboff et al. J Urol, 2017

# Change in Symptoms Over 12 Months

## No impact:

- Age, sex, symptom duration, anxiety, depression
  - CMSI and body map
  
- Better overall physical health
  - SF-12 physical, PROMIS sleep, PROMIS fatigue
  
- Better overall mental health
  - SF-12 mental, pain catastrophizing, perceived stress

Naliboff et al. J Urol, 2017

# MAPP Epidemiology-Phenotyping Study Findings

## Symptom Flares

- ◆ **Females reported 507 symptom flares, Males reported 297 flares**
- ◆ **95% reported at least one flare**
  - 1-4 flares => 26%
  - 5-9 flares => 28%
  - 10+ flares => 41%
- ◆ **More common with 'centralized' phenotype and with more severe bladder symptoms ('bladder' phenotype)**
- ◆ **Focus groups**
  - Flares vary in symptom type, severity and duration (minutes to days)
  - Unpredictable
  - Lead to social avoidance and isolation

Sutcliffe S et al. Int Urogynecol J 2015;26:1047

# Regression to the Mean

- ◆ Early symptom changes (regression to the mean) were common and impacted the assessment of symptom trajectory over time.

	Improved	No Change	Worse
Week 0-48 Data	25.2-37.7%	56.8-68.9%	5.4-5.9%
Week 4-48 Data	15.0-24.8%	65.8-78.5%	6.1-9.4%

Stephens-Shields et al. J Urol 2016

# MAPP Epidemiology-Phenotyping Study Findings

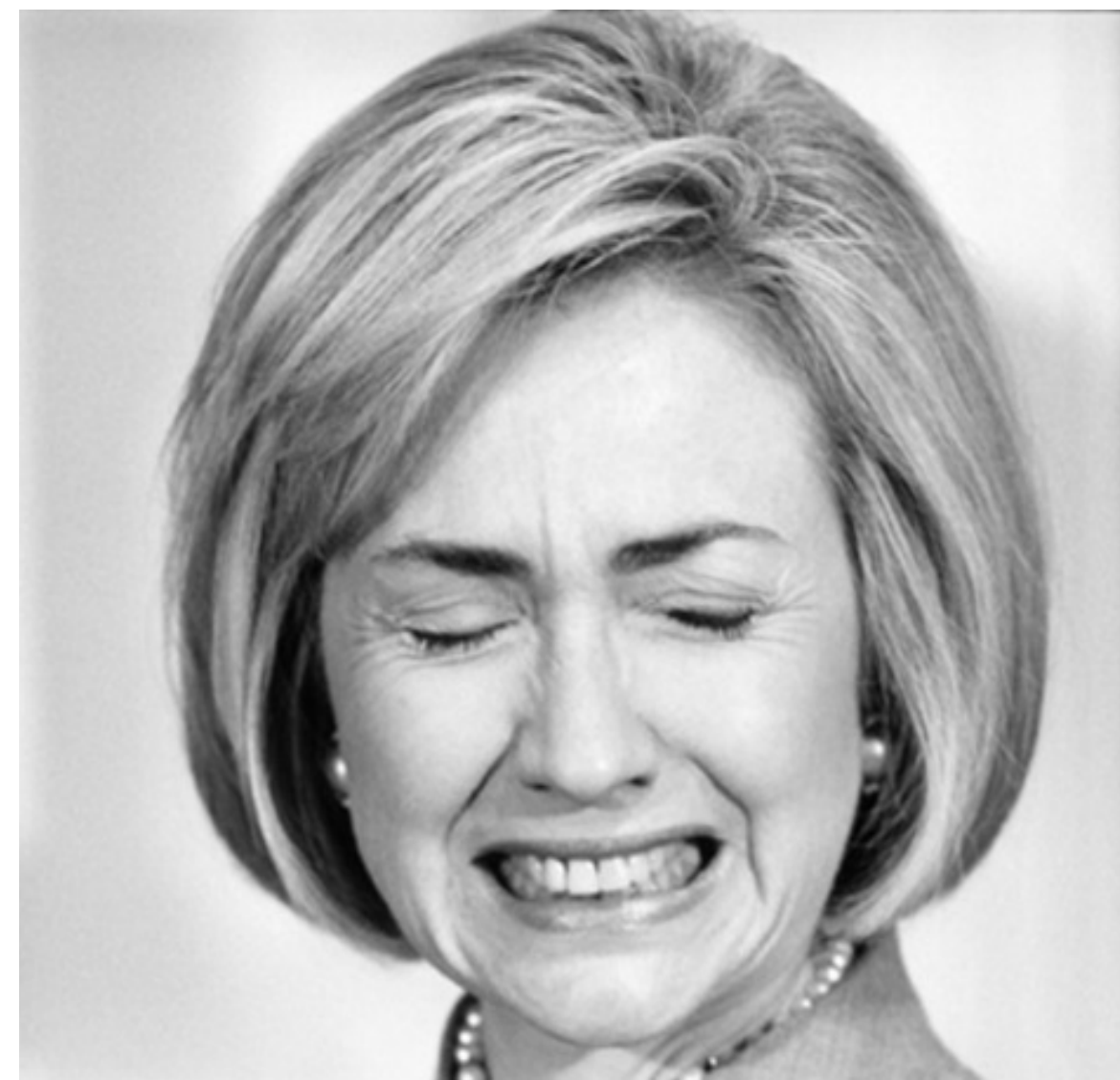
## Summary

- ◆ **Clinical phenotyping of UCPPS patients should focus on at least 3 important factors:**
  - Pain localization (presence of pain outside of the pelvis)
  - Presence of chronic overlapping pain conditions
  - Bladder hypersensitivity
- ◆ **We should consider abandoning ‘total symptom scores’ and instead utilize dual outcomes (pain symptoms, urinary symptoms)**

Griffith et al. J Urol, 2016

# MAPP Study Findings

## Pain Testing







# Pain Testing - Summary Findings

## Pain Sensitivity

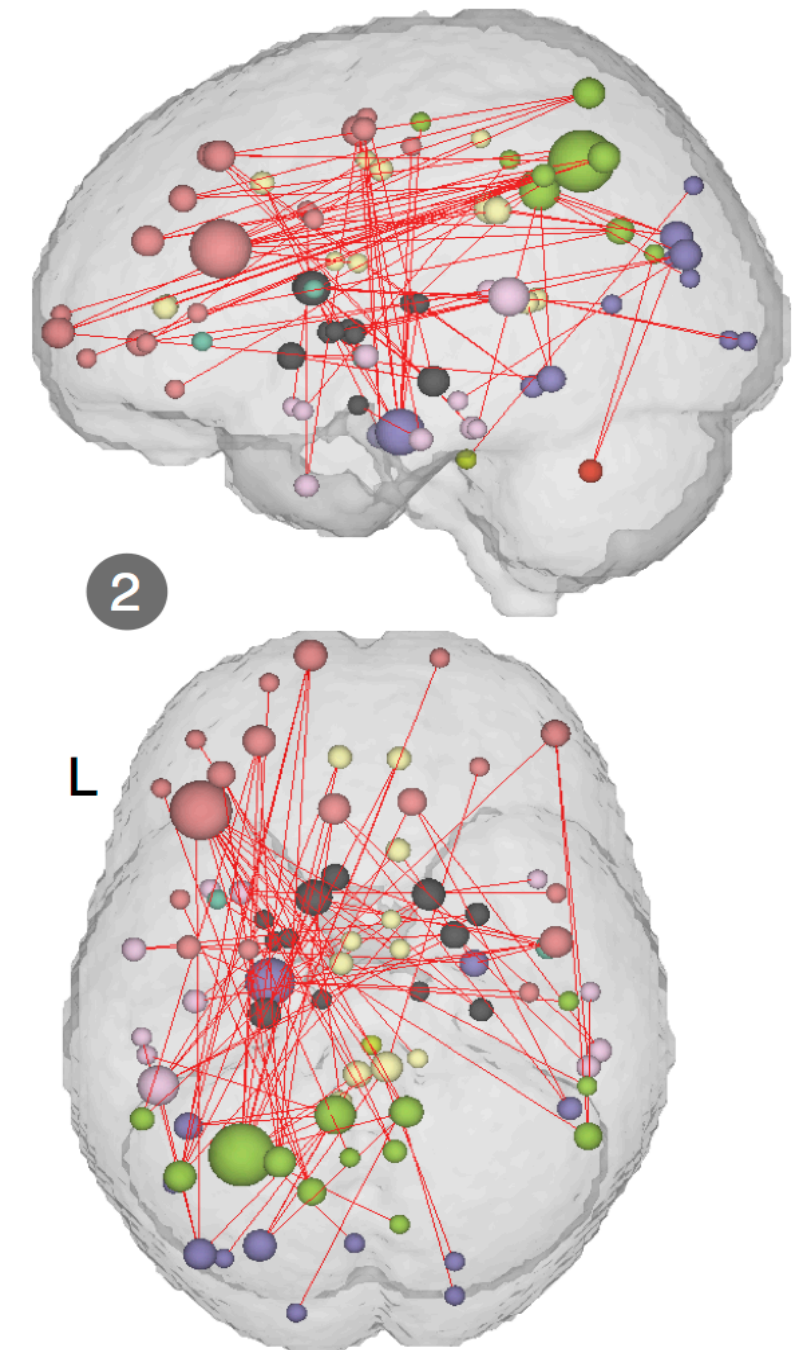
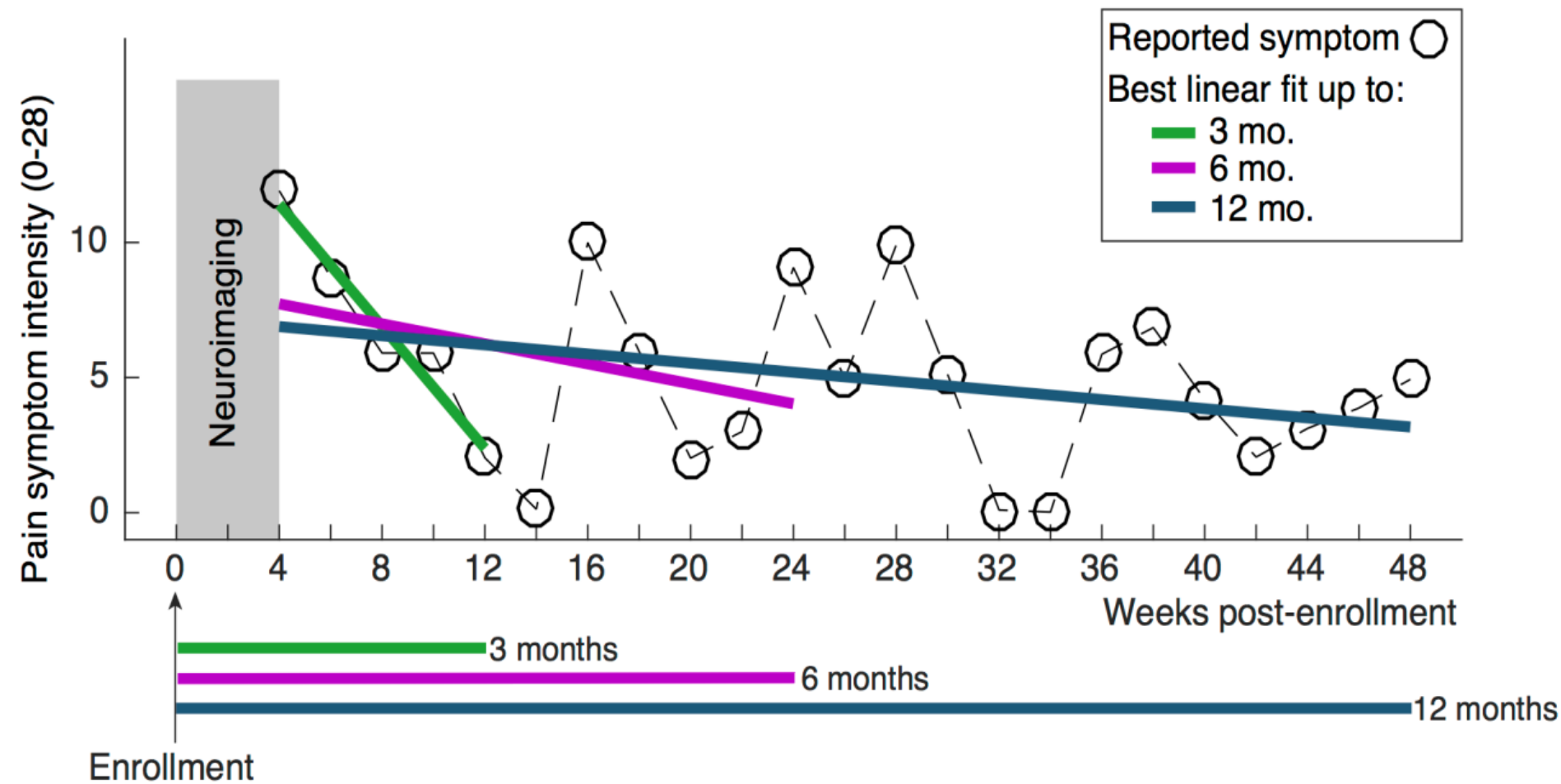
- Positive Controls > Healthy Controls
- UCPPS > Healthy Controls
- **Positive Controls = UCPPS**

## Increased pain sensitivity was associated with:

- Increased UCPPS symptom severity
- More Flares
- Less likelihood of symptom improvement

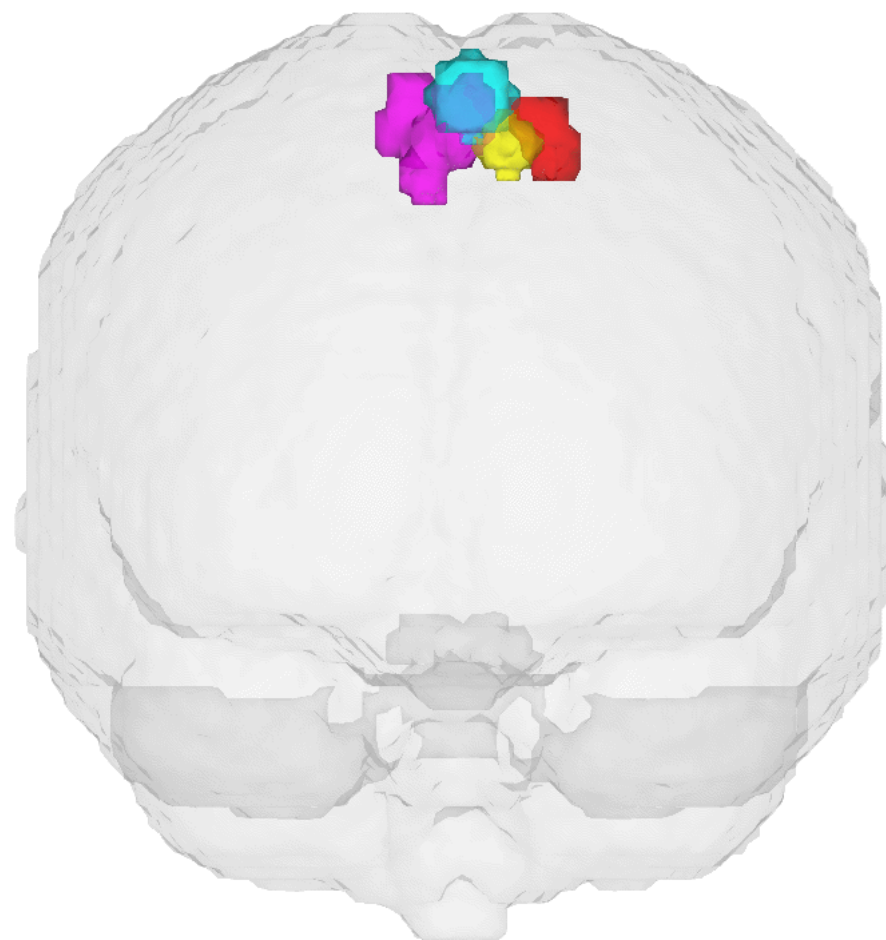
# MAPP Network Neuroimaging Highlights

- ◆ Resting State Functional Connectivity Predicts Longitudinal Symptom Change in UCPPS



# MAPP Network Neuroimaging Highlights

## ◆ Explain pathophysiology



### UCPPS/Control Differences:

RS-fMRI ● Kilpatrick et al., 2014  
Kutch et al., 2015

T1 ● Kairys et al., 2015

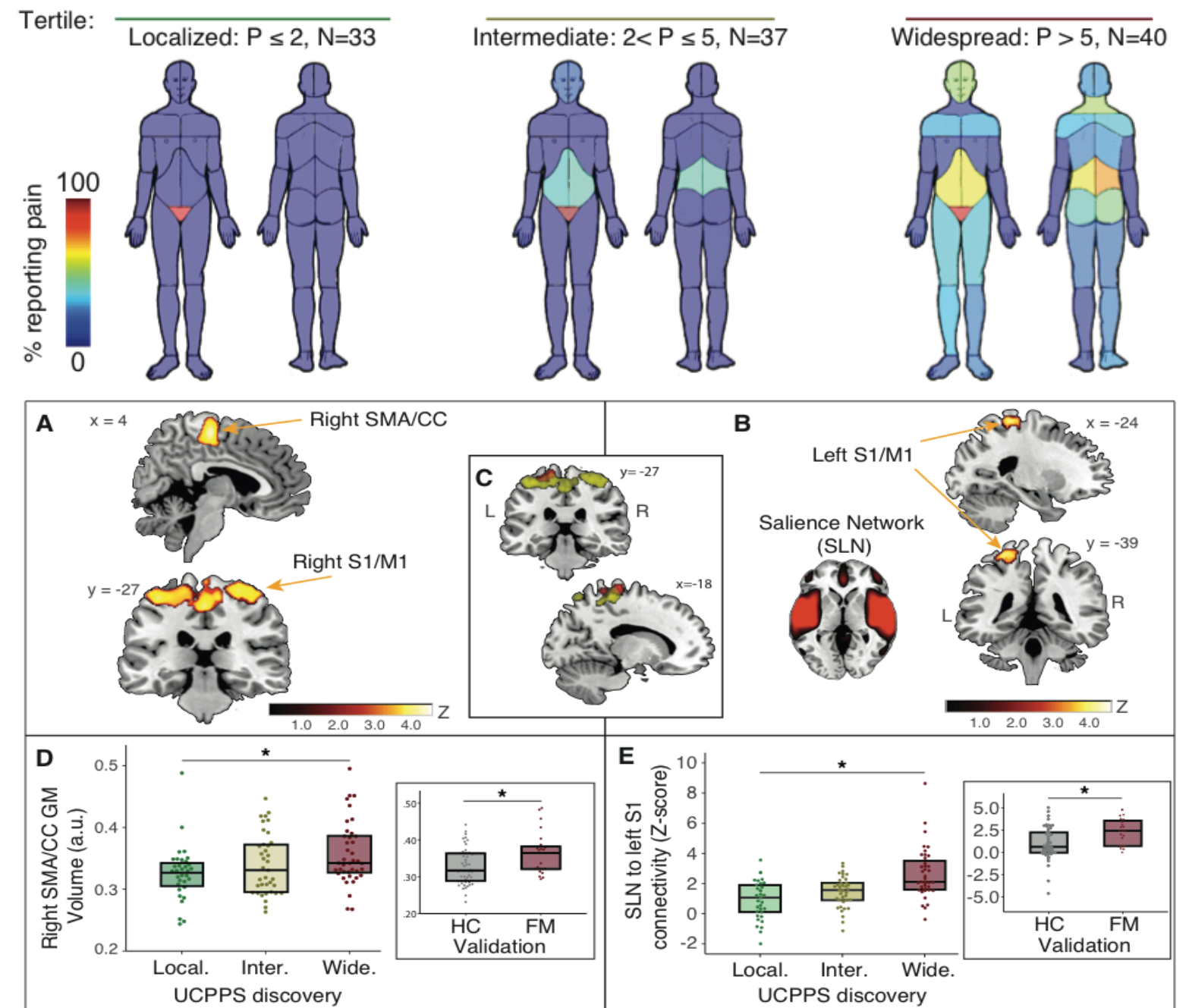
DTI ● Woodworth et al., 2015

### Region specific to pelvic floor

● Asavasopon et al., 2014  
Rana et al., 2015

# MAPP Network Neuroimaging Highlights

- ◆ Structural and functional differences exist in UCPPS patients with widespread pain.
- ◆ These findings match up with fibromyalgia patients.



# MAPP Study

## Future Directions

- ◆ **Second phase of the MAPP Research Network: 2015 to 2019**
- ◆ **Assessment of symptom patterns and corresponding biologic change through longer follow-up**
- ◆ **Evaluation of promising candidate biomarkers**
- ◆ **Longitudinal neuroimaging and quantitative pain testing**
- ◆ **In-depth assessment of treatment response**
- ◆ **Identification of clinically relevant UCPPS patient sub-groups**

## Multi-Disciplinary Approach to the Study of Chronic Pelvic Pain

A A A

[About MAPP](#)

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[Core Sites](#)

[Projects](#)

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### Welcome to the MAPP Research Network Home Page



MAPP News

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Urological Phenotyping

Non-Urological Phenotyping

Neuroimaging / Neurobiology

Biomarkers

Organ Cross-Talk / Pain Pathways

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Department of Health & Human Services (HHS)



### A New Look at Urological Chronic Pelvic Pain ...

To help better understand the underlying causes of the two most prominent chronic urological pain syndromes—interstitial cystitis/painful bladder syndrome (IC/PBS) and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS)—the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH), has launched a new and novel research study.

The NIDDK's Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network embraces a systemic—or whole-body—approach in the study of IC/PBS and CP/CPPS. In addition to moving beyond traditional bladder- and prostate-specific research directions, MAPP Network scientists

are investigating potential relationships between these two urological syndromes and other chronic conditions that are sometimes seen in IC/PBS and CP/CPPS patients, such as irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome.

The multidisciplinary (i.e., scientists employing a variety of research approaches) MAPP Network includes researchers with clinical, epidemiological, and basic research expertise, all working collaboratively: