Multidisciplinary Approach to the Study of Chronic Pelvic Pain
An NIH sponsored study

MAPP research network Newsletter

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Words from our Chair

Dear MAPP Participants,

As some of you may be aware, enrollment has begun in our second phase of the MAPP study. In this next phase, our research will be focusing on symptom pattern changes as well as which may predict whether a patient will respond to a certain therapy. Additionally in this next phase, our research team will be utilizing some of the most promising research methods in the pain field in order to better characterize urologic chronic pelvic pain symptoms (UCPPS) patients.

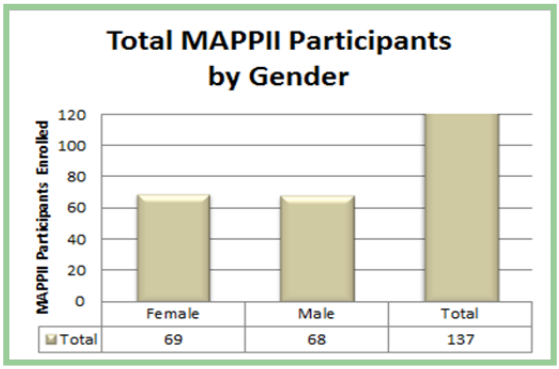
In this edition of the MAPP newsletter, we are very excited to share some information about our new phase, also known as MAPP SPS (Symptom Patterns Study). Additionally, we wanted to share some preliminary information that we learned from the original MAPP study, in which you were a valued and dedicated participant.

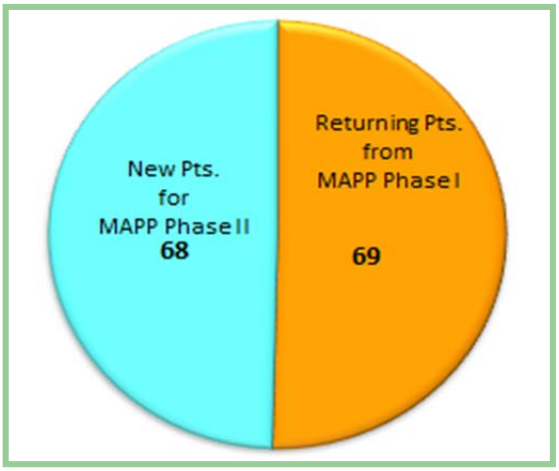
Thank you again for your participation and stay tuned as we continue working towards finding a cause, as well as a cure, for these syndromes.

Sincerely,
J. Quentin Clemens, MAPP Research Network Chair

Update on MAPP 2 Enrollment

The MAPPII Symptoms Patterns Study is open for recruitment and is actively seeking new female and male participants. So far, 137 participants have been enrolled. 69 females and 68 males are now participating in MAPPII SPS. The aims and hypotheses for the study will be supported by a balanced recruitment of female and male participants so that it will be possible to assess patterns of symptoms over time by gender. To date, the recruiting centers for the MAPPII SPS have maintained a close balance of female and male participants to achieve the goals of the study.





MAPPII SPS is recruiting new participants and also is welcoming back participants who were enrolled in the MAPP Phase I Epidemiology and Phenotyping Study (EPS). 68 new participants are enrolled in MAPPII SPS. 69 returning participants from MAPPI EPS are enrolled in MAPPII SPS.

New participants are being recruited at current MAPP network clinics as well as new partner clinics.

Returning MAPP Phase I participants will not only contribute to MAPPII SPS efforts but also provide insight into long-term data collection and symptom assessment since at the end of MAPPII SPS they will have provided data, in some cases for a number of years beyond that of the Symptoms Patterns Study.

MEET THE TATC

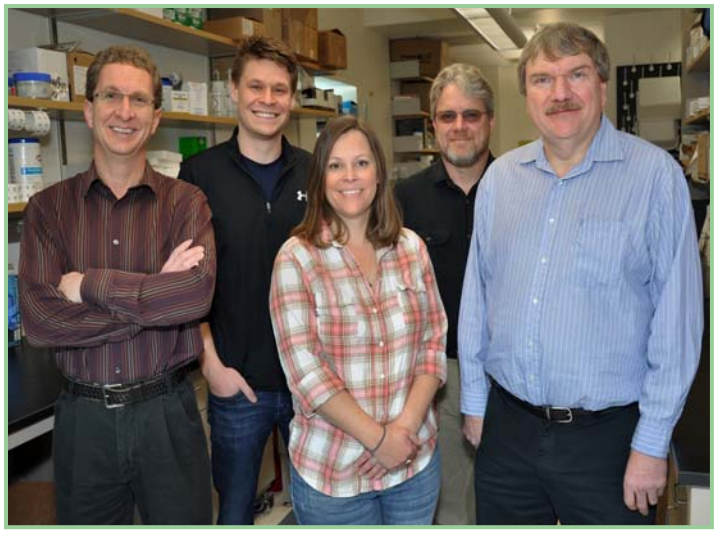
Located on the University of Colorado Denver Anschutz Medical Campus in Aurora Colorado, the Tissue and Technology Core (TATC) is the central repository responsible for biological specimen processing, storage, and distribution for the MAPP Research Network.

TATC staff develops and assemble all kits used to collect biological specimens (such as blood, urine, and saliva samples) at the MAPP participant recruitment sites. This ensures standardization of specimen collections among the six sites. The kits are requested by your local research coordinator and then distributed to the site.

After the specimens are collected, the information is entered into a database. The specimens are associated to the visit and to the de-identified data collected in the participant surveys. The de-identified specimens are then shipped from the site to the TATC by your research coordinator.

Once received by the TATC the collection data is entered into a TATC database. Swab and salivette specimens are stored in the barcoded collection tube at -80^{0}C. Blood and urine specimens are centrifuged and divided into smaller volumes in several smaller tubes.

When a MAPP Network member wants to analyze the samples, the request is submitted to the TATC. The selected specimens are taken from the freezer, put into a box, and shipped to the requesting network member, who then performs the sample analysis. The results are then combined with the data collected in the surveys, the MRI data, as well as the pain testing data. The information is then analyzed and published in scientific journals where it can be used to promote understanding of pelvic pain conditions and shed light on symptom patterns and potential treatments for patients.



From left to right:
M. Scott Lucia, MD, TATC Director;
Zachary Grasmick, Research Coordinator;
Andrea Osypuk, Research Coordinator;
Bob Dayton, Data Manager;
Adrie van Bokhoven, Ph.D., TATC Co-Director;
Not pictured- Storey Wilson, Data Manager

(M)APP Technology and Clinical Research Merge

In the second phase of the MAPP study, mobile technology will be used as a way to collect patient pelvic pain data throughout the day. We call this study the (M)APP, which combines MAPP with apps. This mobile app is being created to help collect real-time data in people who suffer from chronic pelvic pain symptoms.

MAPP researchers hope that collecting patient information via a smartphone app will produce an accurate picture of how pelvic pain changes throughout the day. The (M)APP app will ask patients questions about their pain, mood, and stress levels four times a day. Additionally, push notification technology will be used as a way to remind patients when it is time for an assessment.

The (M)APP study was created as collaboration between researchers at the University of Iowa and Northwestern University. Enrollment in the alpha-testing phase has already begun at Iowa and Northwestern (ten patients per site). Feedback from these initial participants will direct any necessary changes before this technology is implemented across all 6 discovery sites.

MAPP 1 Facts – What did we learn?

Clinical Observations

Those presenting with other non-urological pain syndromes have more severe UCPPS symptoms than patients with UCPPS only.

Participants with additional syndromes (such as Irritable Bowel syndrome, fibromyalgia, and chronic fatigue syndrome) reported more severe urological symptoms.

Those with 'bladder sensitivity phenotypes' report more severe symptoms than UCPPS participants who do not report bladder hypersensitivity.

Additionally, men and women with bladder hypersensitivity phenotypes characterized by painful filling and/or painful urgency had more severe UCPPS symptoms, more generalized non- urologic symptoms/syndromes, and poorer quality of life.

In order to better characterize the patients' clinical experience, 'urological pain' and 'urinary symptoms' should be assessed separately.

Pain, and not urinary symptoms, was associated with symptoms of depression, suggesting that different symptoms of UCPPS vary in their impact on patients.

Psychological and Social Factors

Psychological and social factors are recognized to have a major influence on quality of life and other outcomes related to chronic pain. The MAPP study is the first to compare a large sample size of men and women with UCPPS on a broad range of emotional and social variables.

Results found that:

- Men and women with UCPPS showed similar levels of stress related to emotional and social issues.
- UCPPS patients experienced more psychological and social issues than age- and sex- matched controls without pain
- Greatest psychological and social struggles involved quality of life, mood, stress levels, and presence of non- urological symptoms
- Level of psychological and social stress was not solely attributed to level of UCPPS symptom severity
- Presence of non- urological pain syndrome (such as fibromyalgia, IBS, and chronic fatigue syndrome) was associated with more severe UCPPS symptoms, as well as higher rates of depression and anxiety.

Next Newsletter:

Neuroimaging results will be reviewed so stay tuned!

Terminology used in the MAPP Research Network

Bladder Sensitivity Phenotype – A distinct subgroup of UCPPS patients who report more severe symptoms than patients with UCPPS only.

Control – Something that is not treated or exposed to testing in an experiment in order to serve as a comparison to others that have undergone treatment or exposure. For example, in MAPP II SPS, we are recruiting participants who do not experience pelvic pain as controls.

Focus group – A small group of people whose opinions about something are studied to learn the opinions that can be expected from a larger group.

Flare triggers – An environmental factor which can increase the chance of a worsening of bladder pain symptoms. Some common IC triggers include diet, medicines, exercise, sexual intercourse, hormone fluctuations, stress, certain modes of transportation or long trips, and even tight clothing.

Quantitative Sensory Testing – Refers to a battery of testing methods which assess how sensitive people are to pain and how their pain changes over time.

Toll-like receptors – Refers to a class of proteins that play a key role in the immune system.

Cortisol –A steroid hormone which is released in response to stress.

Chronic Pelvic Pain and IC Flares

Flares, which are acute worsening of symptoms, are often reported by patients with UCPPS. Additionally, no previous studies have been done to systematically examine the characteristics of a flare in UCPPS patients or the impact of flares on the patient. Therefore, in MAPP 1, a major focus was to better understand symptom flares experienced by UCPPS patients. An important focus of MAPP I studies was to prospectively assess the incidence of UCPPS symptom flares over a 12-month follow-up period.

Results from frequent symptom assessments found that nearly 80% of all MAPP participants reported at least one UCPPS flare, more frequently in women than in men. Among the 233 female UCPPS patients, 507 flares were reported, whereas among the 191 male UCPPS patients, 297 flares were reported.

During the MAPP 1 study, a "Flare Risk Questionnaire" was administered to participants during a UCPPS symptoms flare, as well as when they were not having an active flare. By doing this, each participant served as his or her own control for the study. Questions asked in the "Flare Risk Questionnaire" were about factors which could potentially incite flares (also known as "flare triggers").

Another tool that was utilized to collect data on flares in MAPP 1 was UCPPS patient focus group studies. UCPPS patients who participated in these focus groups indicated that there are many different types of UCPPS flares which vary in symptom presentation, severity, and duration. However, increased flare frequency is a significant component of overall symptom severity and morbidity.

Focus group participants also indicated that the unpredictability of flares is another important factor that impacts UCPPS patient's daily lives. Patients reported that when flares occur without any sense of why or when, this leads to increased distress and negative impact on daily function. Additionally, focus group participants reported that frequent flares can significantly impact social avoidance and isolation.

More research is needed in this field in order to figure out what causes flares. In the second phase of MAPP, mobile technology capabilities will be utilized to examine short term flare patterns and risk factors.

Publication Spotlight:

Inflammation and Symptom Change in Interstitial Cystitis/Bladder Pain Syndrome: a Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network. Schrepf A., O'Donnell MA, Luo Y, Bradley CS, Kreder KJ, Lutgendorf SK. *Urology. 2016 Jan 5 [Epub ahead of print].* ScienceDirect

In this manuscript (published in the Urology Journal on January 5, 2016), MAPP investigators explored the association of inflammation elicited by Toll-like receptor (TLR) stimulation in one type of cell found in the blood. Additionally, cortisol regulation levels (which were measured from saliva) were examined and compared with reported changes in urinary symptoms and symptom flares over a 48 week period.

Participants who took part in this study were 24 women who met the criteria for IC/BPS. These participants supplied blood, as well as three days' worth of cortisol samples collected from saliva. Participants also completed questionnaires two times a month which asked about their urinary pain symptoms and reported flares. Results showed that inflammation of the Toll-Like Receptors from the collected blood cells, as well as certain cortisol regulation patterns were associated with less improvement in genitourinary pain over time. Additionally, results showed that a high level of TLR inflammation was associated with less improvement in urinary symptoms.

This study concluded that using TLR inflammation information and studying cortisol regulation levels may be used as markers of symptom changes in IC/BPS patients. However, future research needs to be done in order to determine that these inflammatory factors could help in identifying patients who will struggle to improve with treatment. Future MAPP studies, including the MAPP SPS study, have been designed to determine whether or not centrally acting treatments reduce markers of inflammation while improving pain and urinary symptoms.

Read more about this study, as well as other MAPP publications on our MAPP Research Network Website!
Go to **http://www.mappnetwork.org/** and click on **"MAPP Publications"** in the navigation panel on the left hand side

Want to get involved?

Sites are currently enrolling in the **MAPP 2 Study**!
If you are interested in getting involved, please contact your MAPP 1 site investigators' office. Please see below for contact information:

http://www.mappnetwork.org/
Click *Recruiting Sites* on the top navigation

Send Us Your Feedback!

This newsletter is for you! Please tell us what you want to know about MAPP 2. We will try to answer your questions in future newsletters. Please send your questions, comments, and suggestions to:

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