Pain Collaborative Network Conference 2021 Report

On **26 November 2021**, Crohn's & Colitis UK hosted its second Pain Collaborative Network conference. The event was a great success with over 50 chronic pain experts, clinicians, and patients in attendance from across the UK and Europe.

Our panel of experts included **Professor Christine Norton, Dr David Bulmer, Dr Amanda C de C Williams, Emma Cox, Anwen Thomas, Professor Qasim Aziz, Lucy Youdale and Professor Geoff Woods.**

We ran three workshops on visceral pain (pain in or around internal organs) with themes including: mechanisms of visceral pain and novel targets for treatment; clinical assessment of pain; and psychological treatments for pain.

This report provides the key themes and priority areas highlighted by experts in attendance.

This report is intended to inform pain researchers and clinicians, as well as people affected by chronic pain. The views below were captured from clinicians/researchers in attendance at the conference and are their own and do not necessarily reflect the views of their institution or of Crohn's & Colitis UK.

Patient perspective

The conference kicked off with a powerful opening speech from Crohn's & Colitis UK's Research Champion Anwen Thomas. Anwen has lived with Ulcerative Colitis and chronic pain for over 15 years. Anwen talked about her experience:

> **"Pain is a constant unwanted companion in my life that does not journey alone. It's accompanied by chronic fatigue, general malaise and at times has a psychological impact on daily living and the need for me to change aspects of my life to accommodate its constant demands. It's a very discontented companion vying for pole position with my Ulcerative Colitis. I find the relationship a complex and exhausting one at times."**

Anwen Thomas
Research Champion

She went onto to describe the psychological impact of pain on her life. She described her experience of catastrophising about her pain and worrying if it means something more sinister.

Anwen has never been formally treated for pain, neither via medication nor psychological interventions and has self-managed by using stress relieving techniques.

Emma Cox, CEO of Endometriosis UK provided her perspective on the experience of people living with endometriosis and chronic pain. After listening to Anwen, Emma said there are definite commonalities in pain experience between IBD and endometriosis. Endometriosis is a hidden disease and people are often told the pain is in their head. Emma described being shocked at the number of young women in their early teens with severe period pain being medicated with the contraceptive pill, without identifying the real cause. Pain for people with endometriosis can be constant, while for others it can be cyclical in nature. There is research now to show it may be linked to the hormonal cycle. Like Anwen, for many women it can be a relief or even a pleasure to get a formal diagnosis, as it can mean that someone finally believes you. Research shows over 90% of those with endometriosis believe the pain has impacted negatively or very negatively on their mental health.

30 – 50% of people who have surgery have recurrent pain within a few years, because endometriosis can grow back. Patients are rarely referred for pain management and generally, other than being offered strong opioids, no other pain management strategies are looked at.

Psychological interventions for chronic visceral pain

To watch the full workshop, please click here

Dr Amanda Williams, clinical psychologist from University College London opened the discussion on treating pain via psychological interventions and the current resistance to using this approach.

The clinical dilemma in treating pain is finding a balance between attending to pain and attending to the disease. The current balance tends to go towards focusing on the disease and the pain is assumed to follow in the wake of it. However, it is now known that pain and active disease don't always co-exist simultaneously. There is a need to look beyond pain as a diagnostic indicator of disease and consider pain itself.

To date, the focus on the pain psychology field has been on musculoskeletal pain. There is a need for more fundamental exploratory work in visceral disease about the meaning of pain and its emotional aspects. There is now an increased interest in the psychology of visceral pain as a direct consequence of patients being encouraged to

voice their thoughts on their experiences which will hopefully lead to a more integrated understanding of chronic pain.

There has been a problem of "selling" the psychological aspect of the treatment of pain to both clinicians and to patients who have struggled for years to be believed. The availability of services to support patients psychologically with pain does seem to come from a top-down level often depending on the consultant's interest in the area. Psychologists in IBD services are currently not focussed on areas such as pain. Understanding how psychological interventions can provide benefits and reduce costs of care will make it easier to leverage more funding into psychological interventions and psychologists in IBD services.

Priority research questions identified from psychological interventions workshop

- Create an accessible explanation of pain in IBD for patients to support self-management and make psychological therapies more acceptable
- Mapping inequalities in what is offered to patients to help with pain, clinicians' beliefs, and access to psychological referral for treatment
- Pain assessment that samples qualities of pain, with hope of contributing to phenotyping. Scales for impact of pain that adequately sample problems associated with visceral pain
- Options for targeting pain vs coping with pain as an outcome
- Qualitative explorations around patients' own experience of pain associated with IBD.

Visceral pain assessment

To watch the full workshop, please click here.

Professor Qasim Aziz, a Neurogastroenterologist from Queen Mary University led the discussion on chronic visceral pain assessment and management. Chronic pain management in IBD is immensely challenging for clinicians. Clinicians are trained to treat the disease they specialise in but are not always trained to treat chronic pain associated with many conditions. Clinicians are trained around the broad principles of pain management but if someone doesn't fall neatly within a certain category, this can cause them difficulties and care can become fragmented for patients experiencing pain.

There is currently a lack of funding for integrated care models for the treatment of pain. One of the key questions to tackle is how to facilitate chronic pain management and create integrated teams to help manage this.

In terms of research, there is recognition that there is a need to collect data which will be meaningful to researchers who want to look at different aspects of pain. Examples of IBD data resources include the Swiss IBD Cohort and the IBD BioResource. There is an opportunity to use these data repositories to answer bigger questions and there is a need for researchers to work collaboratively in this effort.

Currently there is no suitable outcome measure that is routinely used to accurately capture pain in IBD and health related quality of life associated with it. There is a need for the right clinical assessment tool to measure pain experience which can also become research relevant.

Priority research questions identified from visceral pain assessment workshop

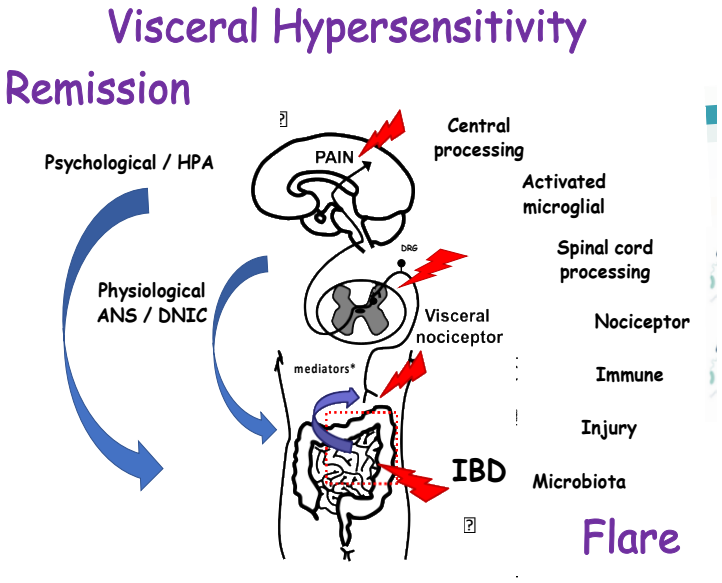
- Qualitative and quantitative research to look at developing a Patient Reported Outcome Measure (PROM) specific to IBD pain which captures multiple dimensions of pain experience including psychological aspects over a period of time, correlating with physiological measures. Assessment of how relevant this tool would be for researchers. Could it help with phenotyping patients? Once developed, how do we get researchers/clinicians/pharma to use the condition specific tool?
- Consider other ways of assessing pain rather than asking for multiple pages of questions. Research into using heat maps? To demonstrate deep visceral pain, 3D techniques will also need to be investigated
- Other factors also have an impact; sleep, smoking, drinking etc. How do we make the connection between them and pain and develop an overall assessment tool?
- Wearables development – could enhance the information we're getting from a questionnaire by taking measurements at the same time as completion e.g. heart rate variability. Will provide a better idea of what day-to-day life is like for a patient
- There are many factors that influence pain that are modifiable. Capturing these over time is very important. Both patients & healthcare professionals should recognise these factors and start having conversations about what could be changed.

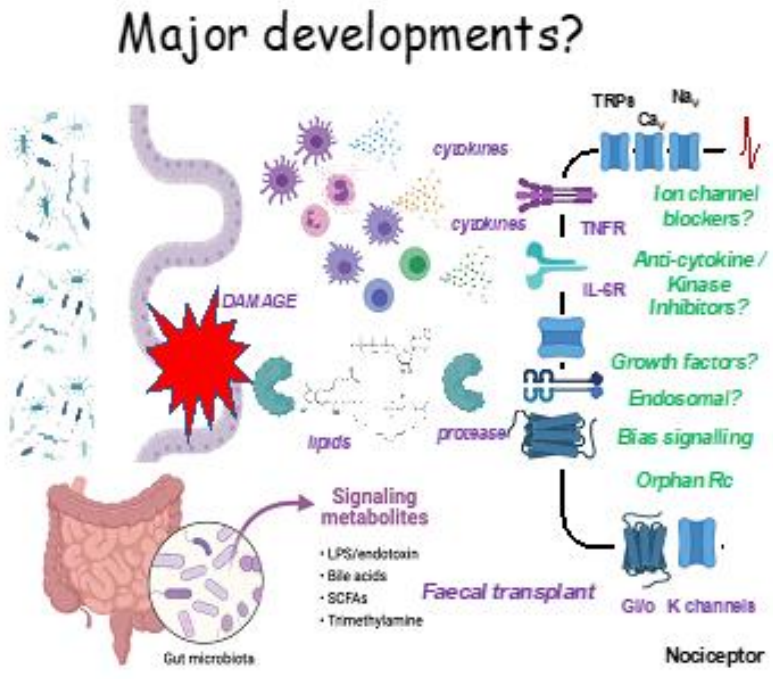
Mechanisms underpinning chronic visceral pain

To watch the full workshop, please click here.

Dr David Bulmer, Assistant Professor at the University of Cambridge led discussions on the mechanisms underpinning chronic visceral pain. In recent years our understanding of the factors that interact with visceral pain receptors in the gut

has advanced considerably. Past research has largely focused on mediators released by tissue injury and how these "Damage Associated Mediators" stimulate pain sensing nerves (nociceptors), however we now know that the microbiota and immune cells within the gut also make important contributions to pain signalling. Important discoveries have been made on spinal cord processing of pain; work led in the UK by Prof Andrew Todd/Dr David Hughes at the University of Glasgow. However, these findings have yet to be investigated for visceral pain and consequently our understanding of visceral pain processing within the spinal cord is very limited. There is some very interesting work on activated microglia (P2X4) driving central sensitisation which is worthy of further investigation for visceral pain. This is a relatively new target area with most microglial data coming from animal models. It might therefore be more sensible with regard to short term therapeutic development to focus on areas with established translation of findings to humans.





An added complication of pain in IBD is the difference between the mechanisms of pain between flare and remission. As such it is not clear whether treating pain in flare or remission is the best way to prevent chronic pain as the mechanisms involved are not identical. In remission, peripheral drivers may be reduced, consistent with the resolution of injury and immune response although the microbiota / resident immune cells may still be altered. Instead, visceral nociceptors may be sensitised by prior inflammation, such that previously innocuous bowel movements now cause pain. A lot of drug discovery has been targeted towards the treatment of peripheral hypersensitivity.

There has also been research into finding an objective biomarker in central processing. Work looking at certain brain areas activated by fMRI seems to have finally found a measurable pain matrix through an imaging approach which potentially produces an objective biomarker for pain which is usually such a subjective experience. This could potentially allow a more reliable measurement of the pain experience.

There has also been work on beta adrenoreceptor antagonists which have shown they may dampen down memories of traumatic events, creating an opportunity to reprogramme adverse painful experiences, and reduce the impact of past painful experiences in the present.

Physiological pathways of descending projections through the autonomic nervous system are very amenable to device therapies. Early data on vagal nerve stimulation suggests this may have a major impact on the field with initial studies suggesting efficacy for the treatment of pain. Combining devices with small molecule therapies may also increase efficacy, which alongside the typically low side effect profile of devices is extremely desirable.

Priority research questions identified from visceral pain mechanism workshop

- Understanding mechanisms of pain in remission
- What is the role of the microbiota in chronic visceral pain?
- Develop a PhD cohort (x5), across different labs to help develop the critical mass and future experts required to tackle visceral pain