

Danielle Perro¹, Lysia Demetriou¹, Lydia Coxon¹, Michal Krassowski¹, Pedro Abreu Mendes², Claire Lunde¹, Kurtis Garbutt¹, Allison Vitonis³, Lars Arendt-Nielsen^{4,5}, Qasim Aziz⁶, Judy Birch⁷, Andrew Horne⁸, Anja Hoffman⁹, Lone Hummelshoj¹⁰, Jane Meijlink¹¹, Esther Pogatzki-Zahn¹¹, Christine Sieberg¹³, Rolf-Detlef Treede¹⁴, Christian Becker¹, Francisco Cruz², Stacey Missmer¹⁵, Krina Zondervan¹, Jens Nagel¹⁶, Katy Vincent¹, on behalf of the TRiPP Consortium

¹University of Oxford, Oxford, UK, ²IBMC, Porto, Portugal, ³Brigham and Women's Hospital and Harvard Medical School, Boston, USA, ⁴Aalborg University, Aalborg, Denmark, ⁵Aalborg University Hospital, Aalborg, Denmark, ⁶Barts and The London School of Medicine and Dentistry, Queen Mary University of London UK, ⁷Pelvic Pain Support Network, Poole, UK, ⁸University of Edinburgh, Edinburgh, UK, ⁹Bayer AG, Berlin, Germany, ¹⁰Endometriosis.org, UK, ¹¹International Painful Bladder Foundation, Naarden, The Netherlands, ¹²University Hospital Muenster, Muenster, Germany, ¹³Boston Children's Hospital, Boston, USA, ¹⁴Heidelberg University, Mannheim, Germany, ¹⁵Brigham and Women's Hospital and Harvard Medical School, Boston, US, ¹⁶Pharmaceuticals Division, Bayer AG, Wuppertal, Germany. **For author conflict of interest statements, please refer to reference four.

Introduction

Widespread pain is highly burdensome amongst people suffering from chronic pain, and localised pain conditions (i.e. UCPPS¹, BPS², migraine³). However, little is known about the impact it may have on women living with different chronic pelvic pain (CPP) pathologies. The Translational Research in Pelvic Pain (TRiPP) project aims to better understand the pain mechanisms underlying CPP in women with a focus on endometriosis-associated pain (EAP) and bladder pain syndrome (BPS). Treatments for these conditions target the pelvis, however, for many these prove ineffective at managing their pain. Therefore, there is an urgent need to better phenotype such conditions, with a particular focus on the systemic impacts of disease. In line with previous literature, we hypothesised that widespread pain would be highly burdensome in the TRiPP cohort, and a widespread pain phenotype would be associated with poorer psychological health, fatigue, poor sleep, and an increased prevalence of comorbidities¹.

This study aims to:

1. Characterise extra-pelvic pain according to previously published protocols
2. Understand the relationship between factors impacting quality of life and widespread pain
3. Determine prevalence of comorbidities between widespread pain groups
4. Investigate psychophysical pain testing measures between widespread pain groups, to assess sensory perturbations

Methods

Participants: Women between ages 18-50 years old, from one of three TRiPP study sites (Oxford, UK; Porto, Portugal; Boston, USA, REC Reference: 19/TH/0030)

Widespread pain characterisation: Michigan Body Map was used to quantify extra-pelvic pain. The MaPP protocol¹ was followed to categorise chronic pelvic pain participants into the isolated (no additional regions), intermediate (1-2 additional regions) or widespread pain groups (3-7 additional regions)

Questionnaire measures: painDETECT, Hospital Anxiety and Depression Scale (HADS), Pain Catastrophizing Scale, PROMIS fatigue and sleep scales, self-reported comorbidities. Measures were scored according to published methods. PROMIS scales were scored using the HealthMeasures Scoring Service.

Psychophysical testing: The standard DFNS QST protocol was followed. Presented results are at the control site (dorsum foot). Scores were Z-transformed using age and sex matched reference data. The CPM paradigm was performed sequentially. Test stimulus= pressure algometer applied to dorsum foot three times (mean calculated), conditioning stimulus=pressure cuff on left arm maintained at maximum tolerance for 60 seconds. The test stimulus was immediately applied before and after the conditioning stimulus. Percent change was calculated as follows: $(PPT2_{average} - PPT1_{average}) / PPT1_{average} \times 100$.

Statistical analyses: Shapiro-Wilks was used to test the normality assumption. The non-parametric Jonckheere Terpstra test for trend or ANOVA and post-hoc linear test for trend, chi-square test, Pearson correlation were used. Analyses were performed using PRISM 9.

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Results

- N=108 women with chronic pelvic pain and n=50 control women were included
- 69.4% of women with chronic pelvic pain experienced pain in ≥ 1 extra-pelvic region

Characterising widespread pain in TRiPP

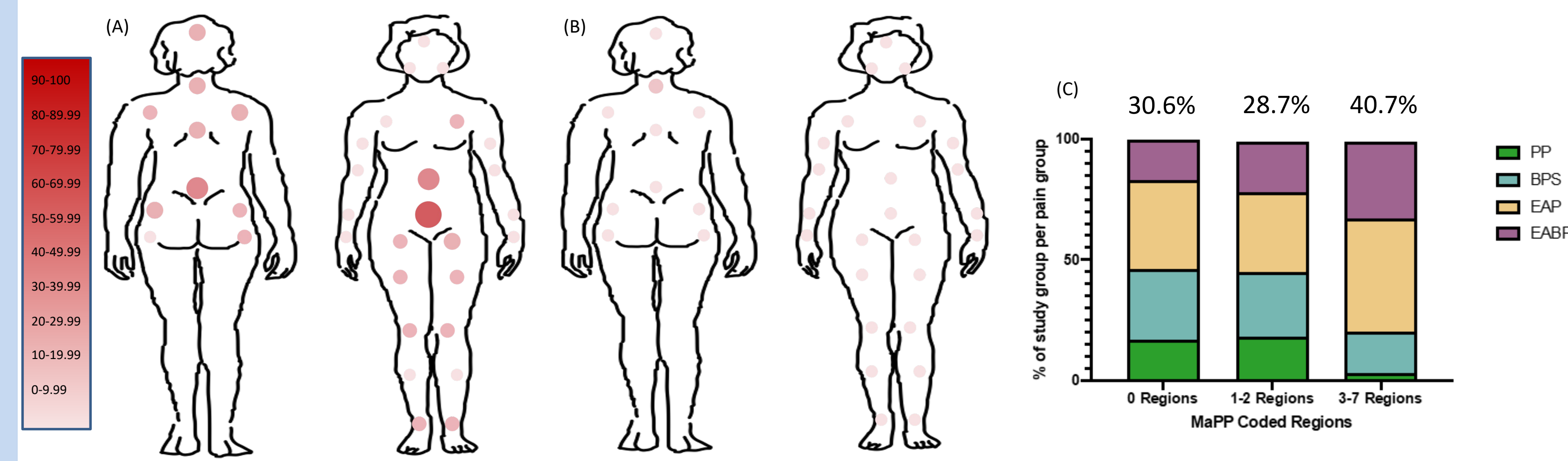


Figure 1. Pain spread and percentage of (A) CPP or (B) control participants experiencing pain in that region. (C) Percentage of each MaPP coded region comprised of each TRiPP study group.

Relationship between widespread pain & psychological health

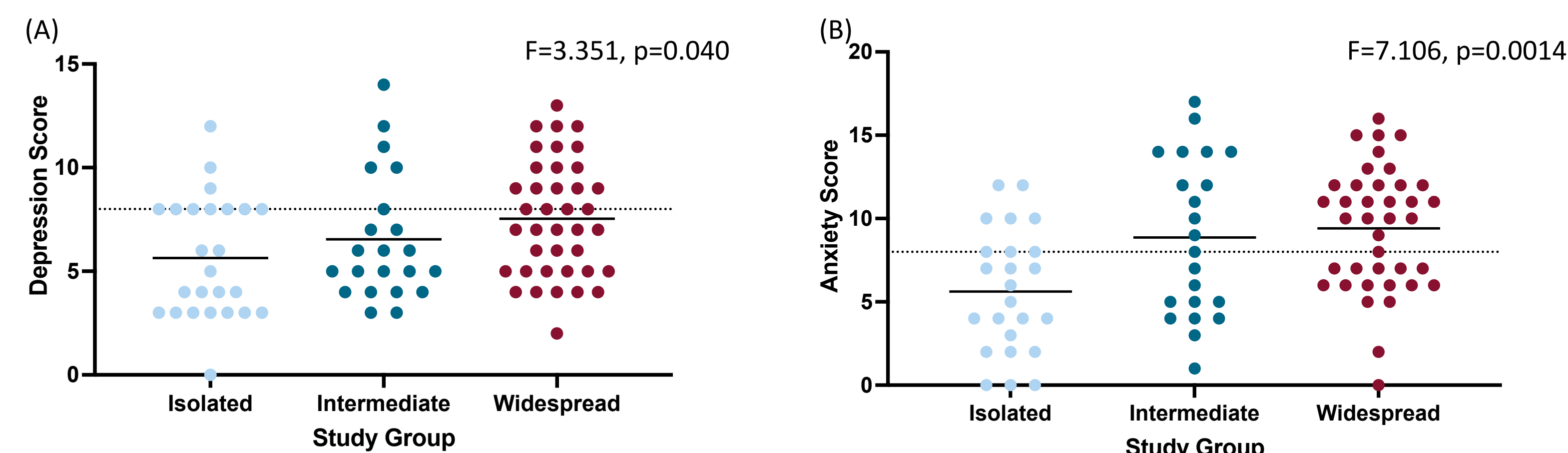


Figure 2. (A) HADS-D scores by widespread pain grouping, and (B) HADS-A scores by widespread pain grouping

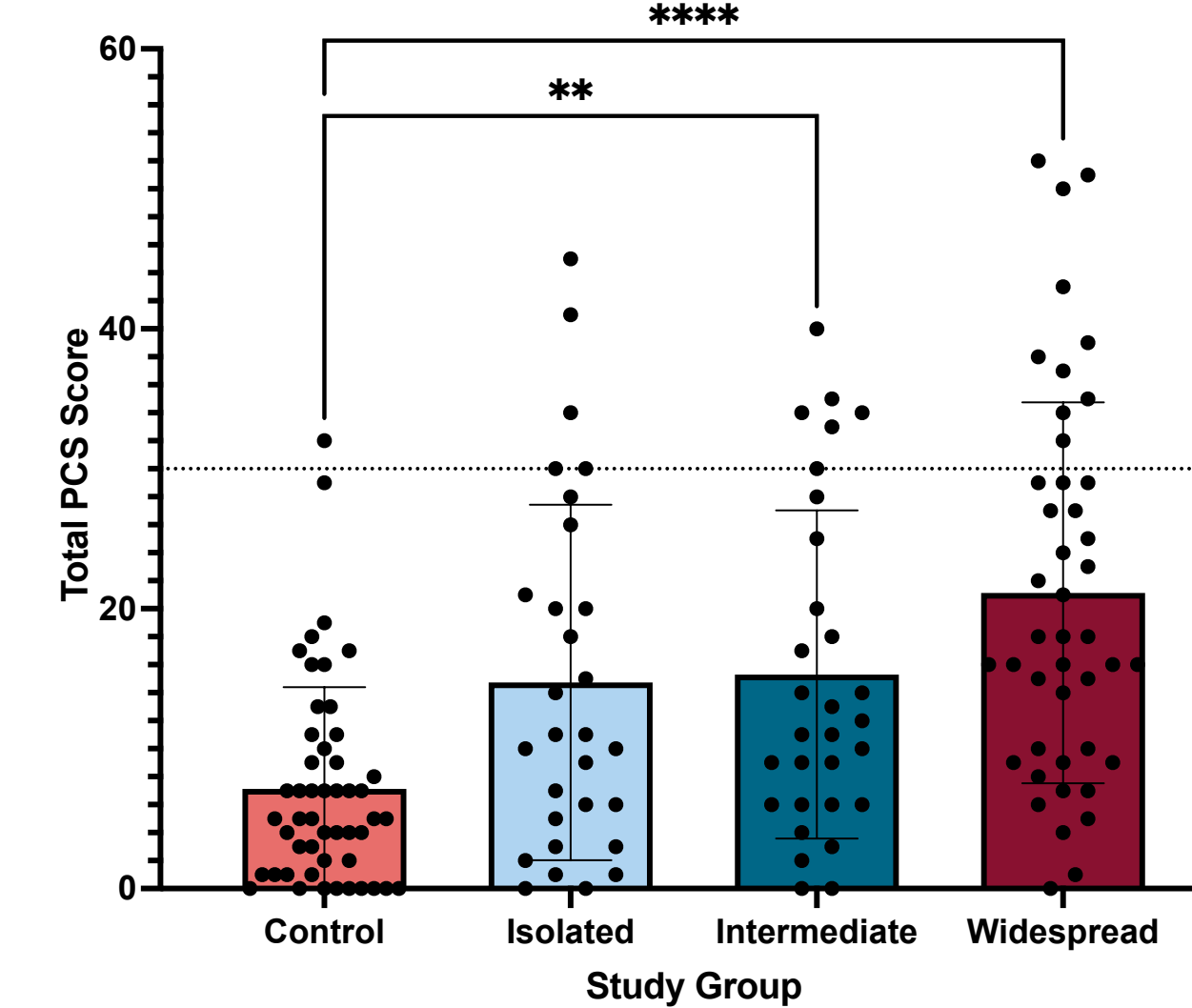


Figure 3. Total pain catastrophizing scale score by widespread pain grouping. $**=p<0.01, ****=p<0.0001$

References

1. Lai, H. H., et al. (2017). Characterization of Whole Body Pain in Urological Chronic Pelvic Pain Syndrome at Baseline: A MAPP Research Network Study. *Journal of Urology*, 198(3), 622–631.
2. Tripp, D. A., et al. (2012). Mapping of pain phenotypes in female patients with bladder pain syndrome/interstitial cystitis and controls. *European Urology*, 62(6), 1188–1194.
3. Barad, M. J., et al. (2021). Characterization of chronic overlapping pain conditions in patients with chronic migraine: A CHOIR study. *Headache*, 61(6), 872–881.
4. Demetriou, L., Coxon, L., Krassowski, M., Rahmioglu, N., Arendt-Nielsen, L., Aziz, Q., ... & Vincent, K. (2022). Deep phenotyping of women with endometriosis-associated pain and bladder pain syndrome: the TRiPP (Translational Research in Pelvic Pain) study protocol. *medRxiv*.

Conclusions

- ❖ Nearly 70% of participants with CPP experience extra-pelvic pain
- ❖ Widespread pain is highly burdensome, and associated with:
 - ❖ Higher depression and anxiety scores
 - ❖ Higher pain catastrophizing scores
 - ❖ More fatigue and worse sleep
- ❖ QST showed sensory perturbations in the intermediate and widespread pain group; CPM showed no between group differences
- ❖ Widespread pain should be considered in a clinical context; use of a body map could improve personalised approach to treatment

Contact: danielle.perro@wrh.ox.ac.uk
Twitter: @dperro_wrh

Comorbidities

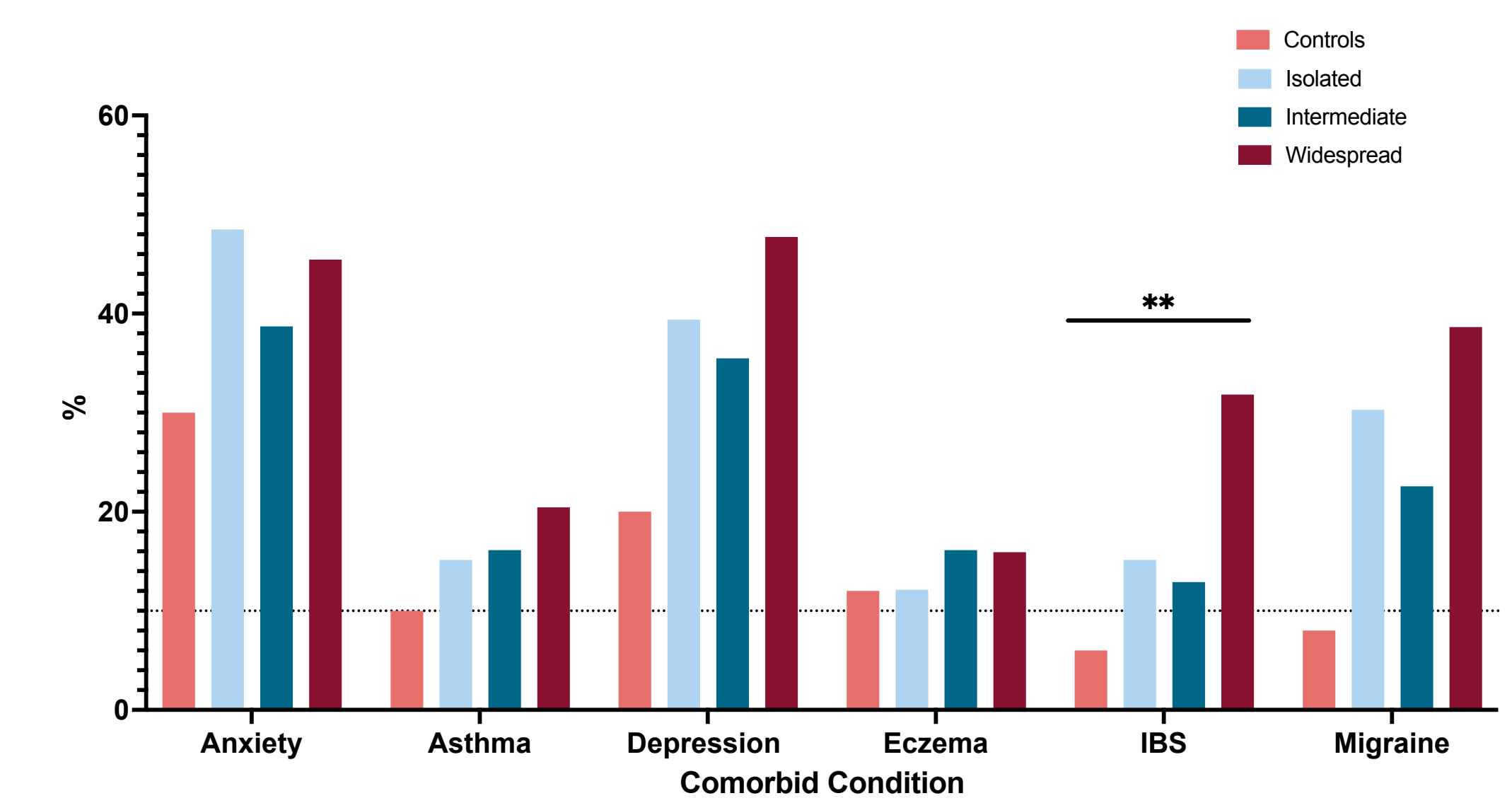


Figure 4. Common comorbidities by widespread pain group. IBS analysis; $p=0.0027$

Relationship between widespread pain & PROMIS fatigue & sleep

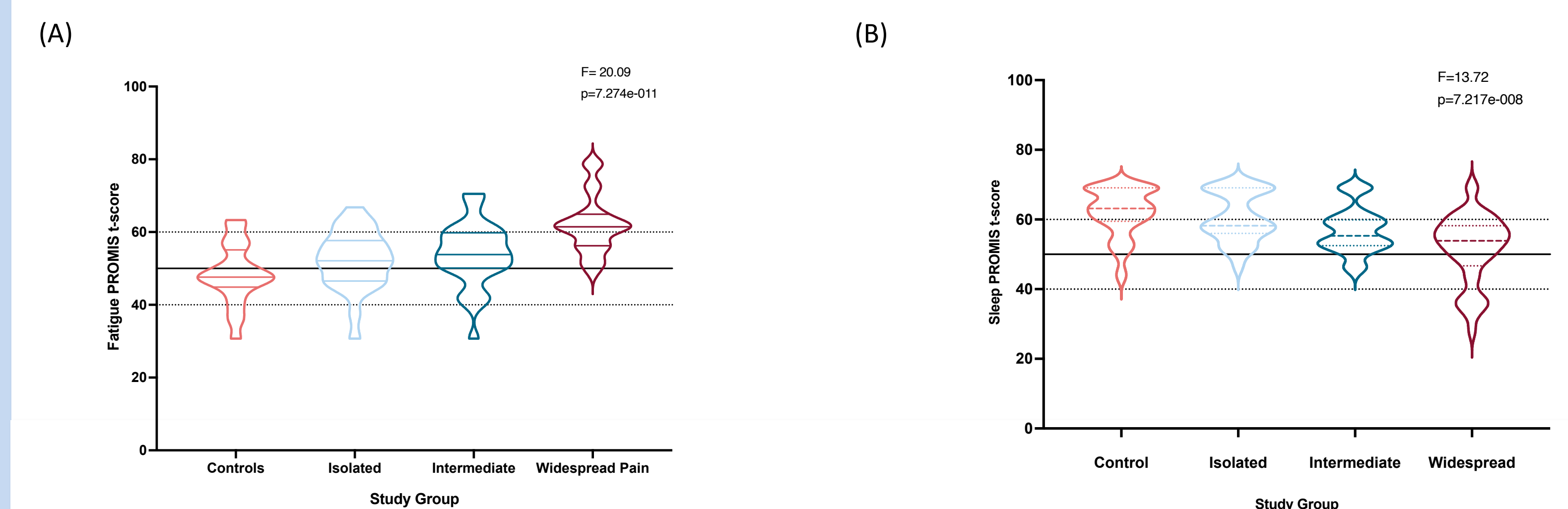


Figure 5. (A) Fatigue PROMIS t-scores by widespread pain grouping, and (B) Sleep PROMIS t-scores by widespread pain grouping

Psychophysical pain testing: QST and conditioned pain modulation

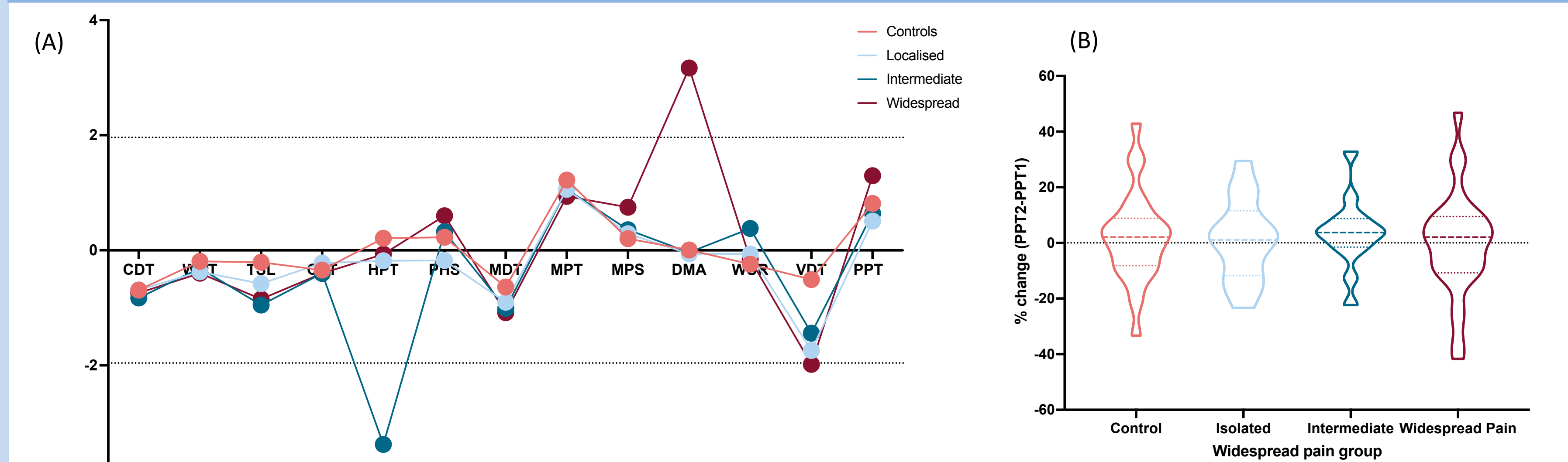


Figure 6. (A) DFNS QST Z-transformed scores at the dorsum of the foot, by widespread pain group (B) Conditioned pain modulation effect by widespread pain groups