Supplemental Information

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| Psychiatric Disorder | Relationship with Chronic Pain |
| Schizophrenia spectrum disorders | Rates of chronic pain in those with schizophrenia found to be higher in some studies (veteran cohort, (1)), or are similar or lower compared to populations without schizophrenia (2–4).  Some studies mention other schizophrenia spectrum disorders apart from schizophrenia (5). |
| Bipolar disorder | Having bipolar disorder often means also having conditions associated with chronic pain e.g. type 2 diabetes & (especially) migraine (6–9).  Those with bipolar disorder also tend to also have chronic pain in general, at higher rates than people without bipolar disorder (8,10,11).  It is not known if chronic pain-bipolar relationship is different in type 1 vs type 2 BPD, except some studies of migraine specifically where this is more prevalent with bipolar 2 vs in a mixed bipolar (1 and 2) sample (12). |
| Obsessive-compulsive and related disorders | Women with fibromyalgia are 4-5x more likely to have OCD than those without (13), and the most prevalent comorbid physical condition in cohort with OCD was chronic pain (14). In a cohort of older adults with OCD, higher pain intensity was reported but pain prevalence was similar to general population (~20%) (15).  Research on OCD-chronic pain overlap in general seems sparse (16).  With related disorders such as body dysmorphic disorder, excoriation disorder, hoarding disorder, trichotillomania, fewer studies on the overlap with pain exist. With trichotillomania and excoriation (skin-picking), there is some question as to whether pain perception varies compared to non-OCRD populations (but should be noted many studies are of induced, acute pain) (17). Those with hoarding disorder more likely to report chronic pain (18,19). |
| Neurodevelopmental disorders other than ADHD | Autism spectrum disorder: autistic people may have pain perception differences (again, this is not necessarily chronic pain). Some studies show a lot of chronic pain experienced by autistic people is GI related (20–23).  Hypermobility spectrum disorders (often associated with chronic pain) have a higher prevalence in autistic people (24,25).  Intellectual disability (ID) can often be a key symptom in mendelian pain/chronic pain disorders (e.g. Charcot-Marie Tooth disease (26)) but in terms of general complex-trait chronic pain those with ID might be at higher risk of developing painful conditions in some studies, but in other studies prevalence matches chronic pain prevalence in the general population (27–31).  There are few studies examining other neurodevelopmental disorders and chronic pain relationships, e.g., in childhood onset fluency disorder (stuttering), specific learning disorder(s), motor disorder, tic disorder, and stereotypic movement disorder. |
| Feeding and eating disorders | Disordered eating generally in adolescents common in chronic pain cohorts (32,33).  Case reports of patients with pica note chronic pain in stomach or mouth being directly linked to consumption of e.g. brick pieces, rather than general / unexplained chronic pain associated with having pica (34,35). In children with sickle cell, a condition involving significant and chronic pain, higher risk for pica is observed (36,37). Chronic pain can also result from rumination disorder in adolescents (38).  There is some evidence of differences in pain perception in people with anorexia nervosa, and of differences in general perception of sensation (39). Some studies show increased rates of AN in chronic pain cohorts (40), or strong relationships between chronic pain and developing AN (41).  Some studies find endometriosis to be associated with lower BMI (42–45) and therefore there may be relationship between AN and this chronic pain condition  Some studies show an elevated pain threshold - but this is acute pain (and in a cohort considered to be recovered from BN) (46). There is also evidence of acute pain processing disturbances (47). Abdominal pain is common in BN, but may not be strictly chronic (48). Other studies show increased BN in those with migraine, irritable bowel syndrome, and chronic facial pain (reviewed by (49)), and some studies show slight increase in BN in adolescents with chronic pain (33)– though this increase is much smaller compared to adolescents with AN.  Eating behaviour is “frequently disturbed” in adolescents with chronic pain - this could amount to ARFID (49), in addition some people with ARFID present with longstanding abdominal pain (50).  Binge-eating disorder has also been associated with chronic pain (51–53). |
| Anxiety disorders | Those with generalized anxiety disorder are twice as likely to have chronic pain (54) and those with chronic pain are more likely to have comorbid anxiety disorder of any kind (55–57).  Panic disorder and social anxiety disorder are also associated with chronic pain & chronic pain conditions/ conditions associated with chronic pain (such as cancer, arthritis and diabetes) in some studies (13). |
| Depressive disorders | The relationship between understudied depressive disorders e.g. premenstrual dysphoric disorder (PMDD) and chronic pain is unclear - pain variation in menstrual cycle has been previously documented (both in terms of acute/pain sensitivity and worsening symptoms in chronic pain conditions), but there are not many studies of PMDD-chronic pain relationship in particular, though pain is noted (back pain, breast pain, though not chronic) as part of PMDD symptoms, (58–60). |
| Substance-related/ addictive disorders | 8-12% of people with chronic pain and prescribed opioids go on to develop opioid use disorder (OUD) in the USA vs 0.6% in the general population (61,62).  Other studies find high rates (60%+) of OUD in chronic pain cohorts (63,64).  Large proportions of some cohorts with alcohol use disorder (AUD) are using alcohol to self-medicate chronic pain (65), and increased prevalence of AUD has been found in chronic pain cohorts (66). |

Supplementary Table 1: Relationships between chronic pain and DMS-5 psychiatric diagnoses: further detail.

References

1. Birgenheir DG, Ilgen MA, Bohnert ASB, Abraham KM, Bowersox NW, Austin K, et al. Pain conditions among veterans with schizophrenia or bipolar disorder. Gen Hosp Psychiatry. 2013 Sep 1;35(5):480–4.

2. Engels G, Francke AL, van Meijel B, Douma JG, de Kam H, Wesselink W, et al. Clinical Pain in Schizophrenia: A Systematic Review. J Pain. 2014 May;15(5):457–67.

3. Stubbs B, Mitchell AJ, De Hert M, Correll CU, Soundy A, Stroobants M, et al. The prevalence and moderators of clinical pain in people with schizophrenia: A systematic review and large scale meta-analysis. Schizophr Res. 2014 Dec;160(1–3):1–8.

4. Owen-Smith A, Stewart C, Sesay MM, Strasser SM, Yarborough BJ, Ahmedani B, et al. Chronic pain diagnoses and opioid dispensings among insured individuals with serious mental illness. BMC Psychiatry. 2020 Jan 31;20(1):40.

5. Almeida JG de, Braga PE, Lotufo Neto F, Pimenta CA de M. Chronic Pain and Quality of Life in Schizophrenic Patients. Rev Bras Psiquiatr. 2013 Feb;35(1):13–20.

6. DE HERT M, CORRELL CU, BOBES J, CETKOVICH-BAKMAS M, COHEN D, ASAI I, et al. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. World Psychiatry. 2011 Feb;10(1):52–77.

7. Carvalho AF, Firth J, Vieta E. Bipolar Disorder. N Engl J Med. 2020 Jul 2;383(1):58–66.

8. Failde I, Dueñas M, Agüera-Ortíz L, Cervilla JA, Gonzalez-Pinto A, Mico JA. Factors associated with chronic pain in patients with bipolar depression: a cross-sectional study. BMC Psychiatry. 2013 Apr 15;13:112.

9. Leo RJ, Singh J. Migraine headache and bipolar disorder comorbidity: A systematic review of the literature and clinical implications. Scand J Pain. 2016 Apr 1;11(1):136–45.

10. Nicholl BI, Mackay D, Cullen B, Martin DJ, Ul-Haq Z, Mair FS, et al. Chronic multisite pain in major depression and bipolar disorder: cross-sectional study of 149,611 participants in UK Biobank. BMC Psychiatry. 2014 Dec;14(1):350.

11. Stubbs B, Eggermont L, Mitchell AJ, De Hert M, Correll CU, Soundy A, et al. The prevalence of pain in bipolar disorder: a systematic review and large-scale meta-analysis. Acta Psychiatr Scand. 2015;131(2):75–88.

12. Low NCP, Du Fort GG, Cervantes P. Prevalence, Clinical Correlates, and Treatment of Migraine in Bipolar Disorder. Headache J Head Face Pain. 2003 Oct;43(9):940–9.

13. Asmundson GJG, Katz J. Understanding the co‐occurrence of anxiety disorders and chronic pain: state‐of‐the‐art. Depress Anxiety. 2009 Oct;26(10):888–901.

14. Subramaniam M, Abdin E, Vaingankar JA, Chong SA. Obsessive–compulsive disorder: prevalence, correlates, help-seeking and quality of life in a multiracial Asian population. Soc Psychiatry Psychiatr Epidemiol. 2012 Dec;47(12):2035–43.

15. Walid MS. Pain in Nursing Home Residents andCorrelation with Neuropsychiatric Disorders. Pain Physician. 2009 Sep 14;5;12(5;9):877–80.

16. Sloley C, Shipton EA, Bell C, Williman J. Protocol for a mixed-method cohort study investigating the prevalence and impact of obsessive–compulsive disorder (OCD) in chronic pain rehabilitation. BMJ Open. 2021 Aug;11(8):e052288.

17. Grant JE, Chamberlain SR. Exploring the neurobiology of OCD: clinical implications. Psychiatr Times. 2020 Mar 2;2020:exploring-neurobiology-ocd-clinical-implications.

18. Bates S, Chang WC, Hamilton CE, Chasson GS. Hoarding disorder and co-occurring medical conditions: A systematic review. J Obsessive-Compuls Relat Disord. 2021 Jul;30:100661.

19. Nutley SK, Camacho MR, Eichenbaum J, Nosheny RL, Weiner M, Delucchi KL, et al. Hoarding disorder is associated with self-reported cardiovascular / metabolic dysfunction, chronic pain, and sleep apnea. J Psychiatr Res. 2021 Feb;134:15–21.

20. Lanyi J, Flynn C, Mannion A, Maher L, Naughton K, Leader G. Abdominal Pain in Children and Adolescents with Autism Spectrum Disorder: a Systematic Review. Rev J Autism Dev Disord [Internet]. 2021 May 11 [cited 2022 Jan 10]; Available from: https://link.springer.com/10.1007/s40489-021-00257-8

21. McElhanon BO, McCracken C, Karpen S, Sharp WG. Gastrointestinal Symptoms in Autism Spectrum Disorder: A Meta-analysis. Pediatrics. 2014 May 1;133(5):872–83.

22. Wasilewska J, Klukowski M. Gastrointestinal symptoms and autism spectrum disorder: links and risks – a possible new overlap syndrome. Pediatr Health Med Ther. 2015 Sep 28;6:153–66.

23. Penzol MJ, Salazar de Pablo G, Llorente C, Moreno C, Hernández P, Dorado ML, et al. Functional Gastrointestinal Disease in Autism Spectrum Disorder: A Retrospective Descriptive Study in a Clinical Sample. Front Psychiatry. 2019 Apr 10;10:179.

24. Baeza-Velasco C, Cohen D, Hamonet C, Vlamynck E, Diaz L, Cravero C, et al. Autism, Joint Hypermobility-Related Disorders and Pain. Front Psychiatry. 2018;9:656.

25. Baeza-Velasco C, Sinibaldi L, Castori M. Attention-deficit/hyperactivity disorder, joint hypermobility-related disorders and pain: expanding body-mind connections to the developmental age. ADHD Atten Deficit Hyperact Disord. 2018 Sep;10(3):163–75.

26. Nagappa M, Sharma S, Taly AB. Charcot Marie Tooth [Internet]. StatPearls [Internet]. StatPearls Publishing; 2021 [cited 2022 Apr 26]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562163/

27. McGuire BE, Kennedy S. Pain in people with an intellectual disability. Curr Opin Psychiatry. 2013 May;26(3):270–5.

28. Doody O, Bailey ME. Interventions in pain management for persons with an intellectual disability. J Intellect Disabil. 2019 Mar 1;23(1):132–44.

29. Doody O, Bailey ME. Understanding pain physiology and its application to person with intellectual disability. J Intellect Disabil. 2019 Mar 1;23(1):5–18.

30. Doody O, E. Bailey M. Pain and pain assessment in people with intellectual disability: Issues and challenges in practice. Br J Learn Disabil. 2017;45(3):157–65.

31. Raiter A, Merbler A, Burkitt CC, Symons FJ, Oberlander TF. Pain in individuals with intellectual disabilities. In: Clinical Pain Management [Internet]. John Wiley & Sons, Ltd; 2022 [cited 2022 Apr 26]. p. 439–49. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/9781119701170.ch42

32. Pianucci L, Sonagra M, Greenberg BA, Priestley DR, Gmuca S. Disordered eating among adolescents with chronic pain: the experience of a pediatric rheumatology subspecialty pain clinic. Pediatr Rheumatol. 2021 Dec;19(1):16.

33. Sim LA, Lebow J, Weiss K, Harrison T, Bruce B. Eating Disorders in Adolescents With Chronic Pain. J Pediatr Health Care. 2017 Jan;31(1):67–74.

34. Advani S, Kochhar G, Chachra S, Dhawan P. Eating everything except food (PICA): A rare case report and review. J Int Soc Prev Community Dent. 2014;4(1):1–4.

35. Nayak SV, Kini R, Shetty U, Rao PK, Kashyap RR, Bhandarkar G. Pica - an eating disorder: A report and review. Arch Med Health Sci. 2017 Jan 1;5(1):82.

36. O’Callaghan ET, Gold JI. Pica in Children With Sickle Cell Disease: Two Case Reports. J Pediatr Nurs. 2012 Dec 1;27(6):e65–70.

37. Rodrigues N, Shih S, Cohen LL. Pica in Pediatric Sickle Cell Disease. J Clin Psychol Med Settings. 2021 Mar;28(1):6–15.

38. Khan S, Hyman PE, Cocjin J, Lorenzo CD. RRumination syndrome in adolescents. J Pediatr. 136(4):4.

39. Di Lernia D, Serino S, Cipresso P, Riva G. Ghosts in the Machine. Interoceptive Modeling for Chronic Pain Treatment. Front Neurosci [Internet]. 2016 [cited 2022 Jan 14];10. Available from: https://www.frontiersin.org/article/10.3389/fnins.2016.00314

40. Gerhardt A, Hartmann M, Schuller-Roma B, Blumenstiel K, Bieber C, Eich W, et al. The Prevalence and Type of Axis-I and Axis-II Mental Disorders in Subjects with Non-Specific Chronic Back Pain: Results from a Population-Based Study. Pain Med. 2011 Aug;12(8):1231–40.

41. Tegethoff M, Belardi A, Stalujanis E, Meinlschmidt G. Comorbidity of Mental Disorders and Chronic Pain: Chronology of Onset in Adolescents of a National Representative Cohort. J Pain. 2015 Oct;16(10):1054–64.

42. Holdsworth-Carson SJ, Dior UP, Colgrave EM, Healey M, Montgomery GW, Rogers PA, et al. The association of body mass index with endometriosis and disease severity in women with pain. J Endometr Pelvic Pain Disord. 2018 Jun 1;10(2):79–87.

43. Tang Y, Zhao M, Lin L, Gao Y, Chen GQ, Chen S, et al. Is body mass index associated with the incidence of endometriosis and the severity of dysmenorrhoea: a case–control study in China? BMJ Open. 2020 Sep 6;10(9):e037095.

44. Lafay Pillet MC, Schneider A, Borghese B, Santulli P, Souza C, Streuli I, et al. Deep infiltrating endometriosis is associated with markedly lower body mass index: a 476 case-control study. Hum Reprod. 2012 Jan 1;27(1):265–72.

45. Yong L, Weiyuan Z. Association between body mass index and endometriosis risk: a meta-analysis. Oncotarget. 2017 Jan 31;8(29):46928–36.

46. Stein D, Kaye WH, Matsunaga H, Myers D, Orbach I, Har-Even D, et al. Pain perception in recovered bulimia nervosa patients. Int J Eat Disord. 2003 Nov;34(3):331–6.

47. Klabunde M, Collado D, Bohon C. An interoceptive model of bulimia nervosa: A neurobiological systematic review. J Psychiatr Res. 2017 Nov;94:36–46.

48. Monteleone P, Brambilla F. Multiple Comorbidities in People with Eating Disorders. In: Sartorius N, Holt RIG, Maj M, editors. Key Issues in Mental Health [Internet]. Basel: S. KARGER AG; 2014 [cited 2022 Apr 26]. p. 66–80. Available from: https://www.karger.com/Article/FullText/365532

49. Sim L, Harbeck Weber C, Harrison T, Peterson C. Central Sensitization in Chronic Pain and Eating Disorders: A Potential Shared Pathogenesis. J Clin Psychol Med Settings. 2021 Mar;28(1):40–52.

50. Bourne L, Bryant-Waugh R, Cook J, Mandy W. Avoidant/restrictive food intake disorder: A systematic scoping review of the current literature. Psychiatry Res. 2020 Jun;288:112961.

51. Brownley KA, Berkman ND, Peat CM, Lohr KN, Cullen KE, Bann CM, et al. Binge-Eating Disorder in Adults. Ann Intern Med. 2016 Sep 20;165(6):409–20.

52. Olguin P, Fuentes M, Gabler G, Guerdjikova AI, Keck PE, McElroy SL. Medical comorbidity of binge eating disorder. Eat Weight Disord - Stud Anorex Bulim Obes. 2017 Mar;22(1):13–26.

53. Kessler RC, Berglund PA, Chiu WT, Deitz AC, Hudson JI, Shahly V, et al. The Prevalence and Correlates of Binge Eating Disorder in the World Health Organization World Mental Health Surveys. Biol Psychiatry. 2013 May;73(9):904–14.

54. Csupak B, Sommer JL, Jacobsohn E, El-Gabalawy R. A population-based examination of the co-occurrence and functional correlates of chronic pain and generalized anxiety disorder. J Anxiety Disord. 2018 May;56:74–80.

55. Gureje O, Von Korff M, Kola L, Demyttenaere K, He Y, Posada-Villa J, et al. The relation between multiple pains and mental disorders: Results from the World Mental Health Surveys. Pain. 2008 Mar;135(1):82–91.

56. Kroenke K, Outcalt S, Krebs E, Bair MJ, Wu J, Chumbler N, et al. Association between anxiety, health-related quality of life and functional impairment in primary care patients with chronic pain. Gen Hosp Psychiatry. 2013 Jul 1;35(4):359–65.

57. Carleton RN, Afifi TO, Taillieu T, Turner S, El-Gabalawy R, Sareen J, et al. Anxiety-related psychopathology and chronic pain comorbidity among public safety personnel. J Anxiety Disord. 2018 Apr;55:48–55.

58. Terzi R, Terzi H, Kale A. Evaluating the relation of premenstrual syndrome and primary dysmenorrhea in women diagnosed with fibromyalgia. Rev Bras Reumatol Engl Ed. 2015 Jul;55(4):334–9.

59. Maharaj S, Trevino K. A Comprehensive Review of Treatment Options for Premenstrual Syndrome and Premenstrual Dysphoric Disorder. J Psychiatr Pract. 2015 Sep;21(5):334–50.

60. Palit S, Bartley EJ, Kuhn BL, Kerr KL, DelVentura JL, Terry EL, et al. Endogenous inhibition of pain and spinal nociception in women with premenstrual dysphoric disorder. J Pain Res. 2016 Feb 11;9:57–66.

61. Speed TJ, Parekh V, Coe W, Antoine D. Comorbid chronic pain and opioid use disorder: literature review and potential treatment innovations. Int Rev Psychiatry. 2018 Sep 3;30(5):136–46.

62. Lipari RN. Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health. 2018;82.

63. Hser YI, Mooney LJ, Saxon AJ, Miotto K, Bell DS, Huang D. Chronic pain among patients with opioid use disorder: Results from electronic health records data. J Subst Abuse Treat. 2017 Jun;77:26–30.

64. Orhurhu V, Olusunmade M, Urits I, Viswanath O, Peck J, Orhurhu MS, et al. Trends of Opioid Use Disorder Among Hospitalized Patients With Chronic Pain. Pain Pract. 2019;19(6):656–63.

65. Vadivelu N, Kai AM, Kodumudi G, Haddad D, Kodumudi V, Kuruvilla N, et al. Recommendations for Substance Abuse and Pain Control in Patients with Chronic Pain. Curr Pain Headache Rep. 2018 Apr;22(4):25.

66. Maleki N, Tahaney K, Thompson BL, Oscar-Berman M. At the intersection of alcohol use disorder and chronic pain. Neuropsychology. 2019;33(6):795–807.