

Pain management in people with severe mental illness: an agenda for progress

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Prevalence and impact of pain in people with severe mental illness (SMI)

There is growing recognition that people with SMI have substantially poorer physical health and die 15-20 years prematurely, largely due to poor physical health.³⁰ SMI often refers to schizophrenia-spectrum (psychosis), bipolar, and major depressive disorders, following WHO and World Psychiatric Association terminology.^{21,39} The global prevalence of schizophrenia is 0.28% (95% uncertainty interval: 0.24-0.31)¹⁶, of bipolar disorder is 0.7% (0.6-0.8)²⁸, and of major depression is 4.4% (4.1-4.7).²⁷ SMI is associated with increased likelihood of physical health problems (e.g., diabetes, HIV)³⁰ with a high burden of pain.^{1,49}

Although the pain-depression relationship has been studied extensively, innovations are still needed to optimize pain management in people with comorbid major depression.^{6,48} Pain management in people with bipolar and psychotic disorders is under-researched.^{106,109} This review will highlight diagnostically specific challenges for pain management across major depression, bipolar disorder, and psychosis, and discuss methodological approaches that may prove useful for improving pain management across them. This review does not capture other mental disorders that are often comorbid with and complicate pain management. These include anxiety³, post-traumatic stress³², substance use⁷³, and personality disorders,^{23,51} which are sometimes categorised with SMI when they cause severe functional impairment.⁸⁸ Given the brevity of this review, we have chosen the narrower SMI definition to begin to advance this discussion.

Depression and pain commonly co-occur, although estimates of pain prevalence in people with depression vary widely (15-100%; mean 65%).⁶ Pain prevalence is also high in people with bipolar disorder: one meta-analysis ($k=22$)

found that 29% of people with bipolar disorder ($n=171,352$) reported pain, over double the risk of healthy controls ($n=12,342,577$).¹⁰⁶ Some doubt arises from unvalidated pain assessments used by many studies in the review.¹⁰⁶

The pain-psychosis association is complex. Meta-analyses of experimental studies show that adults with schizophrenia have elevated pain thresholds and tolerance, independent of antipsychotic medication.¹¹⁰ However, a meta-analysis ($k=14$) found that 35% of people with schizophrenia ($n=242,703$) reported clinical pain, similar to age- and sex-matched controls without mental illness ($n=4,259,221$).¹⁰⁹ Given heightened cardiometabolic burden in psychosis³⁵ and the association between pain and cardiometabolic risk factors, such as obesity³⁷ and diabetes, this raises the possibility that pain may be underrecognized or underreported in this group.¹⁰⁹ Adding to this complexity, in one study of people with psychosis ($n=438$), comorbid depressive symptoms were associated with clinically-relevant pain.¹⁰⁷ Therefore, pain reporting may be diagnostically specific, with psychosis associated with under-reporting and (comorbid) depression with increased reporting.

As in the general population, pain is associated with increased disability and poorer quality of life in people with SMI.^{70,107} Importantly, both SMI and pain are associated with increased suicide risk.^{34,89} However, pain is not routinely assessed and managed in this population¹⁰⁷ and pain communication and assessment might be obscured by the nature of the SMI. Among people with psychosis, reduced self- and clinician-identification of pain may partially explain under or late recognition of conditions that commonly present with pain, such as appendicitis and cardiovascular disease; this may also partially explain the higher rates of late, inadequate or absent treatment, adding to excess morbidity and mortality.^{19,30,103,109} Routine assessment

and management of pain and its causes needs to improve in this population. There is also urgency to find ways to identify acute time-sensitive conditions earlier if pain is not serving as an indicator.

Understanding pain and its treatment in people with SMI: Where is the evidence?

Understanding of biopsychosocial^{26,67,117} influences on pain and related disability in people with SMI, particularly those with psychosis and bipolar disorder, is scarce and may be diagnostically-specific. Research is needed to reconcile comparable rates of reported clinical pain in people with psychosis and healthy controls with mechanisms underpinning reduced experimental pain sensitivity.^{109,110} Increased striatal dopamine⁴⁶ may contribute to pain under-reporting in this population, given converse evidence of a negative association between striatal dopamine and pain in Parkinson's.⁹² In contrast, serotonin and norepinephrine depletion may account for the depression-pain link.³⁶ Of course, mechanisms explaining differences in pain reporting in SMI are likely multifactorial. Presently, research is lacking to understand whether and how positive symptoms (e.g., delusions and hallucinations), negative symptoms (e.g., poverty of speech), and thought disorder influence the meaning attributed to pain and related behavioral responses. One qualitative study of veterans with bipolar disorder and persistent pain described their sense of disconnecting from pain, and overactivity during manic episodes, which increases pain.¹¹⁴ However, investigation of variations in the experience, impact, and communication of pain associated with different SMI

features (e.g., negative symptoms or depressive co-morbidities in schizophrenia and mania in bipolar disorder) is in its infancy.^{107,110,114}

Understanding of pain treatments in people with SMI is also limited. Recommendations for managing persistent pain include exercise, psychological therapy, and analgesic optimisation (where indicated).^{77,78} However, to increase sample homogeneity, people with SMI are often excluded from randomized-controlled trials (RCTs) of pain treatments. Evidence is thus needed to understand the applicability of existing pain treatments to this population.

Psychological and exercise-based treatments are often combined to reduce pain-related distress and disability. Meta-analyses of RCTs show that cognitive-behavioral therapy (CBT) for pain produces small to medium-sized improvements in disability and mood compared to treatment as usual.¹¹⁸ However, little is known about the efficacy of psychologically-informed interdisciplinary pain management for people with SMI as they are often excluded from trials. Of 75 trials in the 2020 Cochrane review of psychological therapies for pain,¹¹⁸ 60% explicitly excluded people with SMI (Table 1). Psychosis/schizophrenia was the most common exclusion (35% of studies), followed by any serious psychiatric disorder (23%). Of the remaining trials, only one reported the sample proportion with comorbid SMI, so we know very little about the efficacy of psychological treatments for pain in this population. This is echoed in clinical practice. For example, an audit from a large pain clinic in England indicated complex mental health needs (e.g., severe depression) as one of the most common exclusion reasons from interdisciplinary treatment or short-term individual psychological therapy for pain.⁵⁸

Pharmacological management of pain in SMI is complicated by the potential for harmful side effects and interactions with psychotropic medications and the

underlying mental health condition.^{50,65,85} Antidepressants, including serotonin-noradrenaline reuptake inhibitors, are effective for pain management in the absence of depression¹¹³ and of course may improve co-morbid depression⁶⁴; however, unopposed anti-depressants may destabilise mood in bipolar disorder. Collaborative pharmacological and psychological care for comorbid pain and major depression is promising, but scarce.²

The potential benefits and harms of other analgesics need careful consideration for people with SMI, as in the general population. In particular, people with major depression and bipolar disorder (but not schizophrenia⁸⁴) are more likely than age- and sex-matched controls without mental illness to receive long-term opioids and experience adverse effects. Research is needed to determine if these findings persist following reduced opioid prescribing in many countries. Cannabis and cannabinoids are increasingly discussed for pain despite evidence that cannabis use is associated with increased risk of psychosis and increased risk of relapse and rehospitalization among people with psychosis.^{43,72,99} Guidelines advise against antipsychotics, gabapentinoids, benzodiazepines, and ketamine for chronic primary pain⁷⁸, but where used for psychiatric comorbidities^{8,98,100} they may help comorbid pain. Recent advances in drugs targeting sleep disturbance^{53,56} and transcranial magnetic stimulation⁶² may prove fruitful for comorbid pain and SMI. There is a particular evidence gap for analgesics in people with bipolar disorder and psychosis and research is thus needed. Medication optimisation for pain and SMI must occur alongside an interdisciplinary approach.⁷⁸

Psychological and exercise-based interventions for SMI in the wider context: synergies with pain management

For decades, pharmacological interventions were the main treatment offered for SMI. However, evidence for psychological treatments in psychosis, bipolar disorder, and severe depression has increased significantly. There has also been a growing focus on exercise-based interventions in this population.

Cognitive-behavioral treatments

CBT for psychosis, bipolar disorder, and depression employs cognitive and behavioral strategies to reduce distress and illness-related disabilities, facilitate adaptive coping, and support recovery goals. Individualised formulations of problem development, maintenance, and exacerbation is a central feature. CBT has efficacy for improving symptoms of psychosis, bipolar disorder, and severe depression.^{20,83,101,115} There is clear overlap in the use of CBT for these disorders and evidence-based cognitive-behavioral methods for pain, including facilitating use of adaptive strategies to manage distressing thoughts and feelings and engage in personally-meaningful activities in the presence of difficulties.^{47,118} This overlap can facilitate integration of cognitive-behavioral treatments for pain and SMI.

Family and carer interventions

Many people with SMI are closely supported by 'informal' carers, primarily close relatives, whose support is key in determining outcomes.⁷⁹ For those with family contact, family interventions are associated with reduced relapse and hospitalisation in people with psychosis and bipolar disorder.^{12,18,87,90} Family

members often identify physical health problems and facilitate timely receipt of assessments and interventions.⁸² Therefore, family members are key in advocating for and supporting people with SMI to manage pain and its causes. It is also important to consider how certain caregiver behaviours and communication patterns, such as invalidating or overly solicitous responses toward pain expression may impact distress and disability in people with SMI and pain.¹⁴

Importantly, caregiving can adversely affect carer well-being. Carers of people with psychosis are less likely to continue caregiving when in poor health, hence the importance of identifying factors that adversely impact their health.⁸² Common mental disorders, sleep difficulties, and isolation are common in SMI carers.^{60,102} Additionally, reports of pain may be elevated in carers of people with psychosis compared to non-carer peers, although the mechanisms underpinning this are unclear.⁴⁰ Understanding how pain is experienced, communicated, and managed in SMI carers is important to develop tailored interventions. For example, delivering cognitive-behavioural approaches for pain jointly for people with SMI and their carers may enable both individuals to develop more adaptive responses to pain and create a healthier caregiving relationship. The need for a joint cognitive-behavioural approach has been discussed for couples affected by pain, but there is limited evidence to date.¹³

Exercise-based treatments

Persistent pain and SMI are, individually, associated with low physical activity.^{105,112} As it does in the general population, persistent pain also influences the ability of people with SMI to be active.^{108,111} Thus, despite the plethora of benefits of

physical activity for physical health, pain, and mental health seen in meta-analyses of RCTs in persistent pain³³ and SMI populations¹¹², both disorders are associated with underactivity.

Little is known about specific levels and benefits of physical activity for individuals with persistent pain and SMI. Exercise-based treatments hold great promise to improve health, wellbeing, and social connections in this group, as in the general population.⁸⁶ Specifically, recent European¹¹² and World Psychiatric Association guidelines identify that physical activity (including aerobic and resistance training) can reduce risk for SMI onset and improve mental health symptoms, cognition, quality of life, and cardiorespiratory fitness in people with SMI.³¹ However, data on the impact of physical activity for pain in SMI is unclear, despite the positive effects noted in persistent pain generally.^{33,97}

People with persistent pain and SMI experience a range of barriers to physical activity, including low mood and motivation, fatigue, isolation, lack of support, stigma, financial constraints, and service fragmentation.^{29,71} The multitude of barriers to and any facilitators of physical activity in people with SMI and persistent pain need to be better understood. This could help to develop or repurpose models of increased movement in this population. Historically, access to physical activity has been low, but the recent focus on improving the physical health, particularly metabolic health, of those with SMI has seen an increase,^{59,71,93} although effects are not well evaluated particularly in the context of pain in this population.

Opportunities to improve integration of care for pain and SMI

There is recognition of the need to better integrate physical and mental health services, with notable innovations to this end.^{5,55,76} At present, however, treatments for pain and SMI often occur in isolation within separate services and serially, despite clear synergies. Research is needed to understand how to optimise treatment integration and how to best adapt existing pain management pathways so that they are used by and work well for people with SMI. Opportunities to improve integration of care are briefly outlined.

Improving pain recognition and assessment

Identifying people with SMI who have or are at risk of experiencing pain is essential.¹⁰⁹ Research should explore differences in pain communication between people with psychosis, bipolar disorder, and severe depression and healthcare professionals' sensitivity to that communication and how this might vary depending on patient racial and ethnic minority status. The latter point is particularly important as people from racial and ethnic minority groups are disproportionately diagnosed with SMI (e.g., schizophrenia)⁸⁰ and conditions where pain constitutes a primary component (e.g., sickle cell), and experience higher healthcare inequalities.^{45,80} Pain assessment exclusively based on self-report may be challenging for people with psychosis who are less likely to self-identify pain and, depending on service setting, might be more inclined to underplay difficulties due to concerns of receiving additional services/treatments. Therefore, nonverbal assessment of pain behaviour is important.^{41,42} Additionally, families or close friends can provide vital information given their critical caregiving role and should thus be included in the pain

assessment process where possible. Nonverbal assessments of pain behaviours, such as facial expressions (e.g. grimacing), body movements (e.g. guarding), and interpersonal changes (e.g. not wanting to be touched), are well-validated in other populations where self-report is problematic, such as dementia.⁴² Research is needed to determine the utility of these tools in people with psychosis.

Reports of severe pain in people with SMI may contribute to inappropriate medical management of pain, such as long-term opioid prescribing.⁸⁴ Severe pain may prompt use of invasive treatments, which must be carefully considered as, for example, people with psychosis and bipolar disorder have increased risk of infection and re-admission following surgery for painful conditions compared to those without mental illness.⁵² Aggressive pain treatment may lead to under recognition and treatment of SMI. Therefore, early detection of SMI in people with severe pain is also imperative to enable provision of appropriate treatment and reduce the risk of iatrogenic harm.

Despite increasing awareness and willingness to discuss mental health, SMI continues to be highly stigmatised,⁷⁴ which may further impede pain recognition. Healthcare professionals underestimate pain in the presence of perceived 'psychosocial' problems,²² making discounting of pain in people with SMI particularly likely. Indeed, there is evidence that they experience diagnostic overshadowing for physical healthcare.³⁰ In addition to limiting treatment access, pain-related invalidation, stigma, and discrimination exacerbate distress.^{94,95,96} Investigation is needed to understand the impact of intersecting experiences of stigma and discrimination in people with SMI and pain, and how to address these. At the structural level¹⁰⁴, for example, service planning and funding that enable integration of treatments for pain and SMI may reduce stigma and discrimination experienced

when fragmented services exclude people.⁷¹ At the interpersonal level, role plays developed with people with lived experience may be useful for training to improve clinicians' communication with people with pain and SMI so interactions are empathic and respectful.^{25,104} At the individual level, psychological interventions may help people respond effectively to the personal impacts of stigma and discrimination, although effects may be modest in the absence of intervention at the other levels.^{96,104}

Stakeholder involvement

Meaningful involvement of people with lived experience of SMI and pain will be crucial.^{7,11,81,91} to improve existing pain management pathways and develop integrated treatments. Involvement of a range of stakeholders is also needed, including carers, mental health, and pain management clinicians from primary to tertiary care, healthcare commissioners, policymakers, and third sector organisations. Stakeholder involvement can include, for example, Priority Setting Partnerships, which can be modelled after exemplary work in paediatric pain.⁹ Stakeholders can provide crucial input to shape pain assessment and intervention tailoring, identify meaningful treatment targets, optimize pathways into treatment, and clinician training. Drawing again from work in paediatric pain,¹⁵ stakeholders can shape dissemination and implementation of knowledge about research and best practice.

Treating and evaluating the individual

To rapidly advance understanding of pain management in people with SMI, innovations in treatment evaluation are needed. RCTs are the gold standard for evaluating interventions, but require highly selected samples, protocol-adherent treatment delivery, and group-based analysis.⁷⁶ This limits their potential to inform flexible treatment delivery that addresses the context and complexity of individuals in practice.¹¹⁶

Single-case experimental designs (SCEDs) are well suited to advance development of integrated treatments in a manner that appreciates the heterogeneity of diagnostically specific challenges relating to pain and SMI. SCEDs are a rigorous alternative to RCTs that can enable personalized care.^{17,61,63,68,116} In SCEDs, the individual is their own control via intensive, repeated measurement during baseline and treatment phases.^{68,75} Multiple SCEDs can be undertaken informing multiple treatment approaches with heterogeneous participants using fewer resources than would a single RCT with a homogenous sample.^{68,75} The frequency of assessments in SCEDs provides greater opportunity than RCTs to evaluate treatment mechanisms, necessary to improve effectiveness.¹⁰

SCEDs are not without limitations. The baseline phase can be demanding, and is not feasible when urgent treatment is needed, such as for active suicidality.⁵⁴ The generalizability of SCEDs has been questioned, but replication across patients and settings allows generalizability to be tested.⁵⁴ While RCTs offer many advantages, SCEDs are highlighted here as a lesser used methodology with underexplored possibilities for developing and evaluating treatments in people with pain and SMI.

Implementation science

Implementation science holds promise to ensure that research into new models of care has real-world impact. Implementation science is “the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and hence, to improve the quality and effectiveness of health services and care”²⁴(p. 1). Implementation frameworks draw on behavioral and social science and identify individual (e.g. clinician knowledge, motivation, professional role/identity) and structural-level (e.g. resources, organizational culture, policy) factors that influence intervention uptake.^{4,15,44,57,66} The number and complexity of available theories can present a challenge for implementation research, particularly where empirical findings are underused in refining theory.⁵⁸

Nonetheless, implementation theories may help identify barriers to and facilitators of integrating existing and novel treatments for pain and SMI in practice. For example, quantitative and qualitative methods can investigate knowledge, skill, and perceptions about professional roles for pain/SMI treatment among clinicians in pain and mental health services. This could inform novel training and supervision models, which could be developed using implementation principles to ensure uptake, scalability, and sustainability.³⁸ Additionally, linking existing datasets of, for example, referral patterns and treatment outcomes from primary to tertiary care can provide insight into opportunities for integration across the system. There are emerging local examples of how rapid communication between mental and physical health services can improve outcomes for people with SMI.⁶⁹

As an example of bringing different methods together, dataset linkages may identify repeat referrals of patients between pain and mental health services.

Interviews with mental health clinicians may reveal a need for training in pain management, while interviews with pain clinicians may reveal perceptions that the format (e.g., group-based) or duration (e.g., number of sessions) of commissioned treatment is unsuitable for people with pain and SMI. Together, these data could argue for more collaboration and mutual training between pain and mental health clinicians, and co-production with service users, to better deliver holistic pain management within their services. Surveys of service funders could identify key targets (e.g., reduced referrals, improved patient satisfaction) that would allow this model to be sustainably funded.

To conclude, there is an urgent need to advance research and practice to improve pain management in people with SMI. This work should draw on synergies in the existing evidence for managing pain and SMI. Meaningful involvement of people with lived experience is essential to advance this agenda.

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Table 1. SMI exclusion criteria listed in RCTs included in the most recent Cochrane review of psychological therapies for chronic pain

SMI exclusion criteria	Frequency (%) of trials reporting the exclusion†
Psychosis/schizophrenia*	26 (34.7%)
'Any serious psychiatric or psychological disorder'*	17 (22.7%)
Suicide risk	10 (13.3%)
Bipolar disorder*	7 (9.3%)
Severe/'significant' depression	6 (8.0%)
'Any serious Diagnostic and Statistical Manual axis II disorder'	5 (6.7%)
Any mental disorder (nature/severity not specified)	4 (5.3%)
'Any serious Diagnostic and Statistical Manual axis I disorder'	3 (4.0%)

Note: 45/75 (60%) of trials in the 2020 Cochrane review of psychological treatments for chronic pain¹¹⁸ explicitly excluded people for at least one of the reasons listed above. Exclusion criteria of the primary studies were reviewed by the authors of the current topical review.

†% was computed from the total number of trials (n=75). The mental health exclusion criteria are not mutually exclusive and studies often reported multiple mental health exclusions, including for other mental health problems not classed as SMI.

*Some studies described the presence of these disorders without further qualification, while others qualified exclusion if the disorder was 'poorly controlled or untreated'.

References

- [1] Abbott CA, Malik RA, van Ross ER, Kulkarni J, Boulton AJ. Prevalence and characteristics of painful diabetic neuropathy in a large community-based diabetic population in the UK. *Diabetes Care* 2011;34:2220-2224.
- [2] Aragonès E, Rambla C, López-Cortacans G, Tomé-Pires C, Sánchez-Rodríguez E, Caballero A, Miró J. Effectiveness of a collaborative care intervention for managing major depression and chronic musculoskeletal pain in primary care: A cluster-randomised controlled trial. *J Affect Disorders* 2019;252:221-229.
- [3] Asmundson GJ, Katz J. Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. *Depress Anxiety* 2009;26:888-901.
- [4] Atkins L, Francis J, Islam R, O'Connor D, Patey A, Ivers N, Foy R, Duncan EM, Colquhoun H, Grimshaw JM, Lawton R, Michie S. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. *Implement Sci* 2017;12:1-18.
- [5] Attoe C, Lillywhite K, Hinchliffe E, Bazley A, Cross S. Integrating mental and physical health care: the mind and body approach. *Lancet Psychiat* 2018;5:387-389.
- [6] Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity - a literature review. *Arch Intern Med* 2003;163:2433-2445.
- [7] Belton J, Smith B. The IASP Global Alliance of Partners for Pain Advocacy (GAPPA): Incorporating the lived experience of pain into the study of pain. 2020. <https://relief.news/2020/03/18/the-iasp-global-alliance-of-pain-patient-advocates-gappa-incorporating-the-lived-experience-of-pain-into-the-study-of-pain/> (Accessed July 10, 2021).
- [8] Berlin RK, Butler PM, Perloff MD. Gabapentin therapy in psychiatric disorders: a systematic review. *Prim Care Companion CNS Disord* 2015;17.

- [9] Birnie KA, Dib K, Ouellette C, Dib MA, Nelson K, Pahtayken D, Baerg K, Chorney J, Forgeron P, Lamontagne C, Noel M, Poulin P, Stinson J. Partnering for pain: a priority setting partnership to identify patient-oriented research priorities for pediatric chronic pain in Canada. *CMAJ Open* 2019;7:E654–E664.
- [10] Burns JW. Mechanisms, mechanisms, mechanisms: it really does all boil down to mechanisms. *Pain* 2016;157:2393-2394.
- [11] Callard F, Rose D. The mental health strategy for Europe: why service user leadership in research is indispensable. *J of Ment Health* 2012;21:219-226.
- [12] Camacho-Gomez M, Castellvi P. Effectiveness of family intervention for preventing relapse in first-episode psychosis until 24 months of follow-up: a systematic review with meta-analysis of randomized controlled trials. *Schizophr Bull* 2020;46:98-109.
- [13] Cano A, Corley AM, Clark SM, Martinez SC. A couple-based psychological treatment for chronic pain and relationship distress. *Cog Behav Practice* 2018;25:119-134.
- [14] Cano A, Williams ACdC. Social interaction in pain: Reinforcing pain behaviors or building intimacy? *Pain* 2010;149:9-11.
- [15] Chambers CT. From evidence to influence: dissemination and implementation of scientific knowledge for improved pain research and management. *Pain* 2018;159:S56-S64.
- [16] Charlson FJ, Ferrari AJ, Santomauro DF, Diminic S, Stockings E, Scott JG, McGrath JJ, Whiteford HA. Global epidemiology and burden of schizophrenia: findings from the global burden of disease study 2016. *Schizophr Bull* 2018;44:1195-1203.
- [17] Chisari C, McCracken LM, Cruciani F, Moss-Morris R, Scott W. Acceptance and

Commitment Therapy for women living with Vulvodynia: A single-case experimental design study of a treatment delivered online. *J Context Behav Sci* 2021; 23:15-30.

[18] Claxton M, Onwumere J, Fornells-Ambrojo M. Do family interventions improve outcomes in early psychosis? A systematic review and meta-analysis. *Front Psychol* 2017;8:371.

[19] Cooke BK, Magas LT, Virgo KS, Feinberg B, Adityanjee A, Johnson FE. Appendectomy for appendicitis in patients with schizophrenia. *Am J Surg* 2007;193:41-48.

[20] Cuijpers P, Clignet F, van Meijel B, van Straten A, Li J, Andersson G. Psychological treatment of depression in inpatients: a systematic review and meta-analysis. *Clin Psychol Rev* 2011;31:353-360.

[21] De Hert M, Correll CU, Bobes J, Cetkovich-Bakmas M, Cohen D, Asai I, Detraux J, Gautam S, Möller H-J, Ndetei DM, Newcomer JW, Uwakwe R, Leucht S. Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry* 2011;10:52-77.

[22] De Ruddere L, Goubert L, Stevens MAL, Deveugele M, Craig KD, Crombez G. Health care professionals' reactions to patient pain: impact of knowledge about medical evidence and psychosocial influences. *J Pain* 2014;15:262-270.

[23] Dixon-Gordon KL, Conkey LC, Whalen DJ. Recent advances in understanding physical health problems in personality disorders. *Curr Opin Psychol* 2018;21:1-5.

[24] Eccles MP, Mittman BS. Welcome to *Implementation Science*. *Implement Sci* 2006;1:1-3.

[25] Edmond SN, Keefe FJ. Validating pain communication: current state of the science. *Pain* 2015;156:215-219.

[26] Edwards RR, Dworkin RH, Sullivan MD, Turk DC, Wasan AD. The role of

psychosocial processes in the development and maintenance of chronic pain. *J Pain* 2016;17:T70-T92.

[27] Ferrari AJ, Charlson FJ, Norman RE, Flaxman AD, Patten SB, Vos T, Whiteford HA. The epidemiological modelling of major depressive disorder: application for the Global Burden of Disease Study 2010. *PLoS One* 2013;8:e69637.

[28] Ferrari AJ, Stockings E, Khoo JP, Erskine HE, Degenhardt L, Vos T, Whiteford HA. The prevalence and burden of bipolar disorder: findings from the Global Burden of Disease Study 2013. *Bipolar Disorders* 2016;18:440-450.

[29] Firth J, Rosenbaum S, Stubbs B, Gorczynski P, Yung AR, Vancampfort D. Motivating factors and barriers towards exercise in severe mental illness: a systematic review and meta-analysis. *Psychol Med* 2016;46:2869-2881.

[30] Firth J, Siddiqi N, Koyanagi A, Siskind D, Rosenbaum S, Galletly C, Allan S, Caneo C, Carney R, Carvalho AF, Chatterton ML, Correll CU, Curtis J, Gaughran F, Heald A, Hoare E, Jackson SE, Kisely S, Lovell K, Maj M, McGorry PD, Mihalopoulos C, Myles H, O'Donoghue B, Pillinger T, Sarris J, Schuch FB, Shiers D, Smith L, Solmi M, Suetani S, Taylor J, Teasdale SB, Thornicroft G, Torous J, Usherwood T, Vancampfort D, Veronese N, Ward PB, R YA, Killackey E, Stubbs B. The Lancet Psychiatry Commission: a blueprint for protecting physical health in people with mental illness. *Lancet Psychiat* 2019;6:675-712.

[31] Firth J, Solmi M, Wootton RE, Vancampfort D, Schuch FB, Hoare E, Gilbody S, Torous J, Teasdale SB, Jackson SE, Smith L, Eaton M, Jacka FN, Veronese N, Marx W, Ashdown-Franks G, Siskind D, Sarris J, Rosenbaum S, Carvalho AF, Stubbs B. A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. *World Psychiatry* 2020;19:360-380.

- [32] Fishbain DA, Pulikal A, Lewis JE, Gao J. Chronic pain types differ in their reported prevalence of post-traumatic stress disorder (PTSD) and there is consistent evidence that chronic pain is associated with PTSD: an evidence-based structured systematic review. *Pain Med* 2017;18:711-735.
- [33] Foster NE, Anema JR, Cherkin D, Chou R, Cohen SP, Gross DP, Ferreira PH, Fritz JM, Koes BW, Peul W, Turner JA, Maher CG. Prevention and treatment of low back pain: evidence, challenges, and promising directions. *Lancet* 2018;391:2368-2383.
- [34] Fu X-L, Qian Y, Jin X-H, Yu H-R, Wu H, Du L, Chen H-L, Shi Y-Q. Suicide rates among people with serious mental illness: a systematic review and meta-analysis. *Psychol Med* 2021:1-11.
- [35] Gaughran F, Stahl D, Stringer D, Hopkins D, Atakan Z, Greenwood K, Patel A, Smith S, Gardner-Sood P, Lally J, Heslin M, Stubbs B, Bonaccorso S, Kolliakou A, Howes O, Taylor D, Di Forti M, David AS, Murray RM, Ismail K. Effect of lifestyle, medication and ethnicity on cardiometabolic risk in the year following the first episode of psychosis: prospective cohort study. *Br J Psychiatry* 2019;215:712-719.
- [36] Goesling J, Clauw DJ, Hassett AL. Pain and depression: an integrative review of neurobiological and psychological factors. *Curr Psychiatry Rep* 2013;15:421-428.
- [37] Goodson NJ, Smith BH, Hocking LJ, McGilchrist MM, Dominiczak AF, Morris A, Porteous DJ, Goebel A. Cardiovascular risk factors associated with the metabolic syndrome are more prevalent in people reporting chronic pain: results from a cross-sectional general population study. *Pain* 2013;154:1595-1602.
- [38] Greenhalgh T, Papoutsi C. Spreading and scaling up innovation and improvement. *BMJ* 2019;365-372.

- [39] Gronholm PC, Chowdhary N, Barbui C, Das-Munshi J, Kolappa K, Thornicroft G, Semrau M, Dua T. Prevention and management of physical health conditions in adults with severe mental disorders: WHO recommendations. *Int J Ment Health Sy* 2021;15:1-10.
- [40] Gupta S, Isherwood G, Jones K, Van Impe K. Assessing health status in informal schizophrenia caregivers compared with health status in non-caregivers and caregivers of other conditions. *BMC Psychiatry* 2015;15:162.
- [41] Hadjistavropoulos T, Craig KD, Duck S, Cano A, Goubert L, Jackson PL, Mogil JS, Rainville P, Sullivan MJ, Williams ACdC, Vervoort T, Fitzgerald T. A biopsychosocial formulation of pain communication. *Psychol Bull* 2011;137:910-939.
- [42] Hadjistavropoulos T, Herr K, Prkachin KM, Craig KD, Gibson SJ, Lukas A, Smith JH. Pain assessment in elderly adults with dementia. *Lancet Neurol* 2014;13:1216-1227.
- [43] Haroutounian S, Arendt-Nielsen L, Belton J, Blyth FM, Degenhardt L, Di Forti M, Eccleston C, Finn DP, Finnerup NB, Fisher E, Fogarty AE, Gilron I, Hohmann AG, Kalso E, Krane E, Mohiuddin M, Moore RA, Rowbotham M, Soliman N, Wallace M, Zinboonyahoon N, Rice AS. International Association for the Study of Pain Presidential Task Force on Cannabis and Cannabinoid Analgesia: research agenda on the use of cannabinoids, cannabis, and cannabis-based medicines for pain management. *Pain* 2021;162:S117-S124.
- [44] Harvey G, Kitson A. PARIHS revisited: from heuristic to integrated framework for the successful implementation of knowledge into practice. *Implement Sci* 2015;11:1-13.
- [45] Haywood Jr C, Tanabe P, Naik R, Beach MC, Lanzkron S. The impact of race and disease on sickle cell patient wait times in the emergency department. *Am J*

Emerg Med 2013;31:651-656.

[46] Howes OD, McCutcheon R, Owen MJ, Murray RM. The role of genes, stress, and dopamine in the development of schizophrenia. *Biol Psychiatry* 2017;81:9-20.

[47] Hughes LS, Clark J, Colclough JA, Dale E, McMillan D. Acceptance and commitment therapy (ACT) for chronic pain. *Clin J Pain* 2017;33:552-568.

[48] IsHak WW, Wen RY, Naghdechi L, Vanle B, Dang J, Knosp M, Dascal J, Marcia L, Gohar Y, Eskander L, Yadegar J, Hanna S, Sadek A, Aguilar-Hernandez L, Danovitch I, Louy C . Pain and depression: a systematic review. *Harvard Rev Psychiat* 2018;26:352-363.

[49] Jiao JM, So E, Jebakumar J, George MC, Simpson DM, Robinson-Papp J. Chronic pain disorders in HIV primary care: clinical characteristics and association with healthcare utilization. *Pain* 2016;157:931-937.

[50] Johnson AG, Seideman P, Day RO. Adverse drug interactions with nonsteroidal anti-inflammatory drugs (NSAIDs). *Drug Safety* 1993;8:99-127.

[51] Kalira V, Treisman GJ, Clark MR. Borderline personality disorder and chronic pain: a practical approach to evaluation and treatment. *Curr Pain Headache Rep* 2013;17:350.

[52] Kamalopathy P, Kurker KP, Althoff AD, Browne JA, Werner BC. The impact of mental illness on postoperative adverse outcomes after outpatient joint surgery. *J Arthroplasty* 2021;36:2734-2741.

[53] Kasper S, Hajak G, Wulff K, Hoogendijk WJ, Montejo AL, Smeraldi E, Rybakowski JK, Quera-Salva M-A, Wirz-Justice AM, Picarel-Blanchot F, Baylé FJ. Efficacy of the novel antidepressant agomelatine on the circadian rest-activity cycle and depressive and anxiety symptoms in patients with major depressive disorder: a randomized, double-blind comparison with sertraline. *J Clin Psychiat* 2010;71.

- [54] Kazdin AE. Single-case experimental designs. Evaluating interventions in research and clinical practice. *Behav Res Ther* 2019;117:3-17.
- [55] King's Health Partners. Mind and body: joining up mental and physical healthcare. 2021. <https://www.kingshealthpartners.org/our-work/mind-and-body> (Accessed August 5, 2021).
- [56] Kishi T, Matsunaga S, Iwata N. Suvorexant for primary insomnia: a systematic review and meta-analysis of randomized placebo-controlled trials. *PloS One* 2015;10:e0136910.
- [57] Kislov R, Pope C, Martin GP, Wilson PM. Harnessing the power of theorising in implementation science. *Implement Sci* 2019;14:1-8.
- [58] Knight L, Guildford B, Daly-Eichenhardt A, McCracken L. Assessment and patient selection process for a pain management programme: a case study in specialty care. *Br J Pain* 2018:74-81.
- [59] Konkoly Thege B, Emmanuel T, Hill S, Wells L. Effectiveness of a complex psychosocial intervention to reduce metabolic syndrome in psychiatric outpatients with severe/persistent mental illness. *Current Psychol* 2021: <https://doi.org/10.1007/s12144-021-02269-3>
- [60] Kuipers E, Onwumere J, Bebbington P. Cognitive model of caregiving in psychosis. *Br J Psychiatry* 2010;196:259-265.
- [61] Lavefjord A, Sundström FT, Buhrman M, McCracken LM. Assessment methods in single case design studies of psychological treatments for chronic pain: A scoping review. *J Context Behav Sci* 2021;21:121-135.
- [62] Leung A, Shirvalkar P, Chen R, Kuluva J, Vaninetti M, Bermudes R, Poree L, Wassermann EM, Kopell B, Levy R. Transcranial magnetic stimulation for pain, headache, and comorbid depression: INS-NANS Expert Consensus Panel review

and recommendation. *Neuromodulation* 2020;23:267-290.

[63] Linton SJ, Nicholas M, Shaw W. Why wait to address high-risk cases of acute low back pain? A comparison of stepped, stratified, and matched care. *Pain* 2018;159:2437-2441.

[64] Marangell LB, Clauw DJ, Choy E, Wang F, Shoemaker S, Bradley L, Mease P, Wohlreich MM. Comparative pain and mood effects in patients with comorbid fibromyalgia and major depressive disorder: secondary analyses of four pooled randomized controlled trials of duloxetine. *Pain* 2011;152:31-37.

[65] Martins SS, Keyes KM, Storr CL, Zhu H, Chilcoat HD. Pathways between nonmedical opioid use/dependence and psychiatric disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug Alcohol Depend* 2009;103:16-24.

[66] May C, Finch T. Implementing, embedding, and integrating practices: an outline of normalization process theory. *Sociology* 2009;43:535-554.

[67] McCracken LM, Morley S. The psychological flexibility model: A basis for integration and progress in psychological approaches to chronic pain management. *J Pain* 2014;15:221-234.

[68] McDonald S, Quinn F, Vieira R, O'Brien N, White M, Johnston DW, Sniehotta FF. The state of the art and future opportunities for using longitudinal n-of-1 methods in health behaviour research: a systematic literature overview. *Health Psychol Rev* 2017;11:307-323.

[69] McGrath R. Consultant Connect one year on - aiming big and improving communication. 2021. https://www.kingshealthpartners.org/latest/3334-consultant-connect-one-year-on-aiming-big-and-improving-communication?utm_medium=email&utm_campaign=Kings%20Health%20Partners

%20News%20%2017%20June&utm_content=Kings%20Health%20Partners%20News%20%2017%20June+CID_e0e01994d68d42dd08dcd92f2deaf217&utm_source=Email%20marketing%20software&utm_term=Consultant%20Connect%20one%20year%20on (Accessed August 5, 2021)

[70] McIntyre RS, Konarski JZ, Wilkins K, Bouffard B, Soczynska JK, Kennedy SH.

The prevalence and impact of migraine headache in bipolar disorder: results from the Canadian Community Health Survey: CME. *Headache* 2006;46:973-982.

[71] Melamed OC, Fernando I, Soklaridis S, Hahn MK, LeMessurier KW, Taylor VH.

Understanding engagement with a physical health service: a qualitative study of patients with severe mental illness. *Can J Psychiat* 2019;64:872-880.

[72] Mohiuddin M, Blyth FM, Degenhardt L, Di Forti M, Eccleston C, Haroutounian S,

Moore A, Rice AS, Wallace M, Park R, Gilron I. General risks of harm with cannabinoids, cannabis, and cannabis-based medicine possibly relevant to patients receiving these for pain management: an overview of systematic reviews. *Pain* 2021;162:S80-S96.

[73] Morasco BJ, Gritzner S, Lewis L, Oldham R, Turk DC, Dobscha SK. Systematic

review of prevalence, correlates, and treatment outcomes for chronic non-cancer pain in patients with comorbid substance use disorder. *Pain* 2011;152:488-497.

[74] Morgan AJ, Reavley NJ, Ross A, San Too L, Jorm AF. Interventions to reduce

stigma towards people with severe mental illness: Systematic review and meta-analysis. *J Psychiatric Res* 2018;103:120-133.

[75] Morley S. *Single Case Methods in Clinical Psychology: A Practical Guide*. New York, NY: Routledge, 2017.

[76] Naylor C, Parsonage M, McDaid D, Knapp M, Fossey M, Galea A. Long-term

conditions and mental health: the cost of co-morbidities. *The King's Fund* 2012.

<http://eprints.lse.ac.uk/id/eprint/41873> (Accessed August 5, 2021).

[77] NICE. Neuropathic pain in adults: pharmacological management in non-specialist settings. 2013. <https://www.nice.org.uk/guidance/cg173> (Accessed July 15, 2021).

[78] NICE. Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. 2021.

<https://www.nice.org.uk/guidance/ng193> (Accessed July 15, 2021)

[79] Norman RM, Malla AK, Manchanda R, Harricharan R, Takhar J, Northcott S. Social support and three-year symptom and admission outcomes for first episode psychosis. *Schizophr Res* 2005;80:227-234.

[80] Olbert CM, Nagendra A, Buck B. Meta-analysis of Black vs. White racial disparity in schizophrenia diagnosis in the United States: Do structured assessments attenuate racial disparities? *J Abnorm Psychol* 2018;127:104-115.

[81] Omeni E, Barnes M, MacDonald D, Crawford M, Rose D. Service user involvement: impact and participation: a survey of service user and staff perspectives. *BMC Health Services Research* 2014;14:1-13.

[82] Onwumere J, Howes S, Shiers D, Gaughran F. Physical health problems in people with psychosis: the issue for informal carers. *Int J Soc Psychiate* 2018;64:381-388.

[83] Oud M, Mayo-Wilson E, Braidwood R, Schulte P, Jones SH, Morriss R, Kupka R, Cuijpers P, Kendall T. Psychological interventions for adults with bipolar disorder: systematic review and meta-analysis. *Br J Psychiatry* 2016;208:213-222.

[84] Owen-Smith A, Stewart C, Sesay MM, Strasser SM, Yarborough BJ, Ahmedani B, Miller-Matero LR, Waring SC, Haller IV, Waitzfelder BE, Sterling SA, Campbell CI, Hechter RC, Zeber JE, Copeland LA, Sherrer JF, Rossom R, Simon G. Chronic pain

diagnoses and opioid dispensings among insured individuals with serious mental illness. *BMC Psychiatry* 2020;20:1-10.

[85] Pacchiarotti I, Bond DJ, Baldessarini RJ, Nolen WA, Grunze H, Licht RW, Post RM, Berk M, Goodwin GM, Sachs GS, Tondo L, Findling RL, Youngstrom EA, Tohen M, Undurraga J, González-Pinto A, Goldberg JF, Yildiz A, Altshuler LL, Calabrese JR, Mitchell PB, Thase ME, Koukopoulos A, Colom F, Frye MA, Malhi GS, Fountoulakis KN, Vázquez G, Perlis RH, Ketter TA, Cassidy F, Akiskal H, Azorin JM, Valentí M, Mazzei DH, Lafer B, Kato T, Mazzarini L, Martínez-Aran A, Parker G, Souery D, Ozerdem A, McElroy SL, Girardi P, Bauer M, Yatham LN, Zarate CA, Nierenberg AA, Birmaher B, Kanba S, El-Mallakh RS, Serretti A, Rihmer Z, Young AH, Kotzalidis GD, MacQueen GM, Bowden CL, Ghaemi SN, Lopez-Jaramillo C, Rybakowski J, Ha K, Perugi G, Kasper S, Amsterdam JD, Hirschfeld RM, Kapczinski F, Vieta E. The International Society for Bipolar Disorders (ISBD) task force report on antidepressant use in bipolar disorders. *Am J Psychiatry* 2013;170:1249-1262.

[86] Penedo FJ, Dahn JR. Exercise and well-being: a review of mental and physical health benefits associated with physical activity. *Curr Opin Psychiatry* 2005;18:189-193.

[87] Pharoah F, Mari JJ, Rathbone J, Wong W. Family intervention for schizophrenia. *Cochrane Database Syst Rev* 2010;12.

[88] Public Health England. Severe mental illness (SMI) and physical health inequalities: briefing. 2018. <https://www.gov.uk/government/publications/severe-mental-illness-smi-physical-health-inequalities/severe-mental-illness-and-physical-health-inequalities-briefing> (Accessed December 6, 2021).

[89] Racine M. Chronic pain and suicide risk: a comprehensive review. *Prog Neuropsychopharmacol Biol Psychiatry* 2018;87:269-280.

- [90] Reinares M, Bonnín C, Hidalgo-Mazzei D, Sánchez-Moreno J, Colom F, Vieta E. The role of family interventions in bipolar disorder: a systematic review. *Clin Psychol Rev* 2016;43:47-57.
- [91] Rose D. Service user/survivor-led research in mental health: epistemological possibilities. *Disabil Soc* 2017;32:773-789.
- [92] Rukavina K, Leta V, Sportelli C, Buhidma Y, Duty S, Malcangio M, Chaudhuri KR. Pain in Parkinson's disease: new concepts in pathogenesis and treatment. *Curr Opin Neurol* 2019;32:579-588.
- [93] Schmitt A, Maurus I, Rossner MJ, Röh A, Lembeck M, von Wilmsdorff M, Takahashi S, Rauchmann B, Keeser D, Hasan A, Malchow B, Falkai P. Effects of aerobic exercise on metabolic syndrome, cardiorespiratory fitness, and symptoms in schizophrenia include decreased mortality. *Front Psychiat* 2018;9:690.
- [94] Scott W, Garcia Calderon Mendoza del Solar M, Kemp H, McCracken LM, de C Williams AC, Rice ASC. A qualitative study of the experience and impact of neuropathic pain in people living with HIV. *Pain* 2020;161:970-978.
- [95] Scott W, Jackson SE, Hackett RA. Perceived discrimination, health, and wellbeing among adults with and without pain: a prospective study. *Pain* 2021. doi: 10.1097/j.pain.0000000000002368
- [96] Scott W, Yu L, Patel S, McCracken LM. Measuring stigma in chronic pain: preliminary investigation of instrument psychometrics, correlates, and magnitude of change in a prospective cohort attending interdisciplinary treatment. *J Pain* 2019;20:1164-1175.
- [97] Searle A, Spink M, Ho A, Chuter V. Exercise interventions for the treatment of chronic low back pain: a systematic review and meta-analysis of randomised controlled trials. *Clin Rehab* 2015;29:1155-1167.

- [98] Short B, Fong J, Galvez V, Shelker W, Loo CK. Side-effects associated with ketamine use in depression: a systematic review. *Lancet Psychiat* 2018;5:65-78.
- [99] Sideli L, Trotta G, Spinazzola E, La Cascia C, Di Forti M. Adverse effects of heavy cannabis use: even plants can harm the brain. *Pain* 2021;162:S97-S104.
- [100] Sim F, Sweetman I, Kapur S, Patel MX. Re-examining the role of benzodiazepines in the treatment of schizophrenia: a systematic review. *J Psychopharmacol* 2015;29:212-223.
- [101] Sitko K, Bewick BM, Owens D, Masterson C. Meta-analysis and meta-regression of Cognitive Behavioral Therapy for Psychosis (CBTp) across time: the effectiveness of CBTp has improved for delusions. *Schizophr Bulln Open* 2020;1:sgaa023.
- [102] Smith LM, Onwumere J, Craig T, Kuipers E. Role of poor sleep in determining distress in caregivers of individuals with early psychosis. *Early Interv Psychiatry* 2019;13:613-618.
- [103] Solmi M, Fiedorowicz J, Poddighe L, Delogu M, Miola A, Høye A, Heiberg IH, Stubbs B, Smith L, Larsson H, Attar R, Nielsen RE, Cortese S, Shin JI, Fusar-Poli P, Firth J, Yatham LN, Carvalho AF, Castle DJ, Seeman MV, Correll CU. Disparities in screening and treatment of cardiovascular diseases in patients with mental disorders across the world: systematic review and meta-analysis of 47 observational studies. *Am J Psychiatry* 2021:appiajp202121010031.
- [104] Stangl AL, Earnshaw VA, Logie CH, van Brakel W, Simbayi LC, Barré I, Dovidio JF. The Health Stigma and Discrimination Framework: a global, crosscutting framework to inform research, intervention development, and policy on health-related stigmas. *BMC Med* 2019;17:31.
- [105] Stubbs B, Binnekade TT, Soundy A, Schofield P, Huijnen IP, Eggermont LH.

Are older adults with chronic musculoskeletal pain less active than older adults without pain? A systematic review and meta-analysis. *Pain Med* 2013;14:1316-1331.

[106] Stubbs B, Eggermont L, Mitchell A, De Hert M, Correll C, Soundy A, Rosenbaum S, Vancampfort D. The prevalence of pain in bipolar disorder: a systematic review and large-scale meta-analysis. *Acta Psychiatr Scand* 2015;131:75-88.

[107] Stubbs B, Gardner-Sood P, Smith S, Ismail K, Greenwood K, Patel A, Farmer R, Gaughran F. Pain is independently associated with reduced health related quality of life in people with psychosis. *Psychiatry Res* 2015;230:585-591.

[108] Stubbs B, Koyanagi A, Schuch F, Firth J, Rosenbaum S, Gaughran F, Mugisha J, Vancampfort D. Physical activity levels and psychosis: a mediation analysis of factors influencing physical activity target achievement among 204 186 people across 46 low-and middle-income countries. *Schizophr Bull* 2017;43:536-545.

[109] Stubbs B, Mitchell AJ, De Hert M, Correll CU, Soundy A, Stroobants M, Vancampfort D. The prevalence and moderators of clinical pain in people with schizophrenia: a systematic review and large scale meta-analysis. *Schizophr Res* 2014;160:1-8.

[110] Stubbs B, Thompson T, Acaster S, Vancampfort D, Gaughran F, Correll CU. Decreased pain sensitivity among people with schizophrenia: a meta-analysis of experimental pain induction studies. *Pain* 2015;156:2121-2131.

[111] Stubbs B, Vancampfort D, Firth J, Hallgren M, Schuch F, Veronese N, Solmi M, Gaughran F, Kahl KG, Rosenbaum S, Ward PB, Carvalho AF, Koyanagi A. Physical activity correlates among people with psychosis: data from 47 low-and middle-income countries. *Schizophr Res* 2018;193:412-417.

[112] Stubbs B, Vancampfort D, Hallgren M, Firth J, Veronese N, Solmi M, Brand S,

Cordes J, Malchow B, Gerber M, Schmitt A, Correll CU, De Hert M, Gaughran F, Schneider F, Kinnafick F, Falkai P, Möller HJ, Kahl KG. EPA guidance on physical activity as a treatment for severe mental illness: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH). *Eur Psychiatry* 2018;54:124-144.

[113] Sultan A, Gaskell H, Derry S, Moore RA. Duloxetine for painful diabetic neuropathy and fibromyalgia pain: systematic review of randomised trials. *BMC Neurol* 2008;8:1-9.

[114] Travaglini LE, Kuykendall L, Bennett ME, Abel EA, Lucksted A. Relationships between chronic pain and mood symptoms among veterans with bipolar disorder. *J Affect Disord* 2020;277:765-771.

[115] Turner DT, Reijnders M, van der Gaag M, Karyotaki E, Valmaggia LR, Moritz S, Lecomte T, Turkington D, Penadés R, Elkis H, Cather C, Shawyer F, O'Connor K, Li ZJ, de Paiva Barretto EM, Cuijpers P. Efficacy and moderators of cognitive behavioural therapy for psychosis versus other psychological interventions: An individual-participant data meta-analysis. *Front Psychiatry* 2020;11:402.

[116] Vohra S. N-of-1 trials to enhance patient outcomes: identifying effective therapies and reducing harms, one patient at a time. *J Clin Epidemiol* 2016;76:6-8.

[117] Williams ACdC, Craig KD. Updating the definition of pain. *Pain* 2016;157:2420-2423.

[118] Williams ACdC, Fisher E, Hearn L, Eccleston C. Psychological therapies for the management of chronic pain (excluding headache) in adults. *Cochrane Database Syst Rev* 2020;8:CD007407.