

REVIEW ARTICLE

THE BONE-BRAIN AXIS? BIOPSYCHOSOCIAL ASPECTS OF ORTHOPEDICS AND A MENTAL WELLBEING ACTION PLAN IN MUSCULOSKELETAL CARE

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ABSTRACT

The aim: To review the biopsychosocial aspects of psychiatric comorbidity in patients with musculoskeletal conditions and recommend a relevant mental health action plan.

Materials and methods: Keywords (orthopedics, psychiatry, mental health) were used to list down and analyze the literature in PubMed and Google Scholar. All types of articles, including original research, systematic reviews, and meta-analyses, along with gray literature dating back to 2000. We excluded studies reporting a significant conflict of interest and findings dispersed through popular media instead of peer-reviewed journals.

Conclusions: The biopsychosocial aspects of the “bone – brain axis” need to be better addressed by means of a pragmatic approach involving all concerned parties and acknowledging the challenges and limitations along the way.

KEY WORDS: orthopedics, psychiatry, biopsychosocial model, mental health, bone – brain axis

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INTRODUCTION

The connection between musculoskeletal and mental health has been hypothesized since the antiquity, being summarized in the *mens sana in corpore sano* (a healthy mind resides within a healthy body) grecoroman concept and the humoral theory of diseases[1]. The definition of health as a state of physical, mental and social wellbeing rather than the absence of a disease in 1948 has helped to shed light to the mental manifestations of corporeal diseases[2].

Musculoskeletal conditions include acute and chronic locomotor disorders, with a detrimental impact on individuals' functionality and quality of life. Pain and disability are the most common manifestations, resulting in mental health decline, elevated risk of developing other chronic diseases and increased all-cause morbidity and mortality[3]. According to the WHO, the Disability-adjusted life years (DALYs) associated with musculoskeletal conditions have increased to up to 6.6% of the global disease burden[4]. Musculoskeletal conditions affect 1.7 billion people worldwide and constitute a major contributor to disability, with low back pain being the single leading cause of disability in 160 countries[5].

Evidence suggests that up to 40% of patients in orthopedic wards suffer from mental health conditions [5]. The interplay between musculoskeletal and psychiatric conditions, described as the bone – brain axis, has been recognized by studies investigating the increased prevalence of fractures in elderly with dementia, osteoporosis and hypertension associated with calcium metabolism[6]. Simultaneously, practitioners of specialties different from psychiatry desire further training in mental health due to a potential lack of skills related to the prevention, early detection and management of mental health conditions. Particularly, orthopedics are less likely to refer their patients to psychiatrists, despite being able to notice signs of psychological disorders[6]. This stated, it is crucial to investigate the biopsychosocial aspects of the bone – brain axis, raise awareness among healthcare workers and create more space for mental health screening and interventions in orthopedic wards.

THE AIM

To summarize the existing knowledge about the etiological connection between mental and musculoskeletal conditions, to assess the relevant disease burden and propose a mental wellbeing action plan in musculoskeletal care.

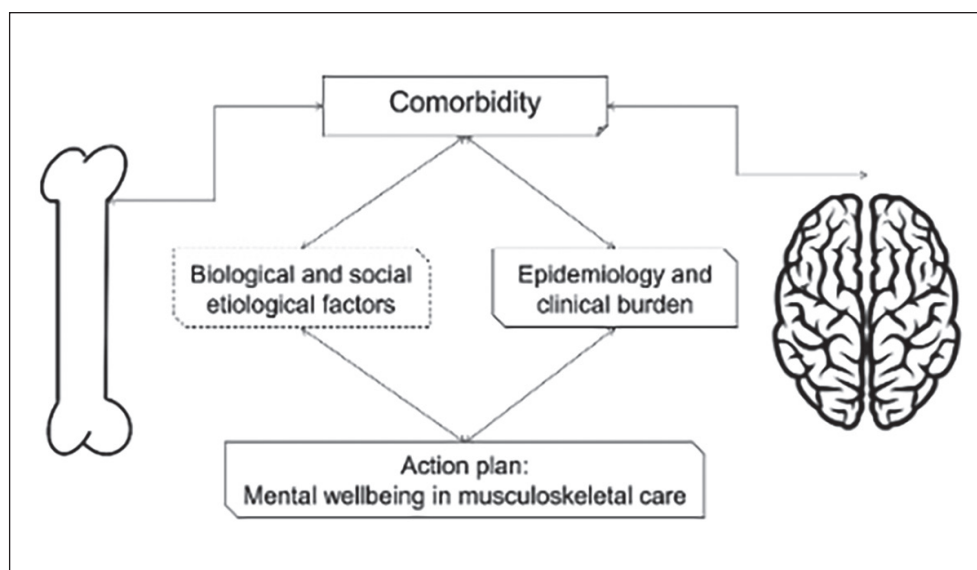


Fig 1. The biopsychosocial concept of the bone-brain axis on the basis of etiological and epidemiological evidence

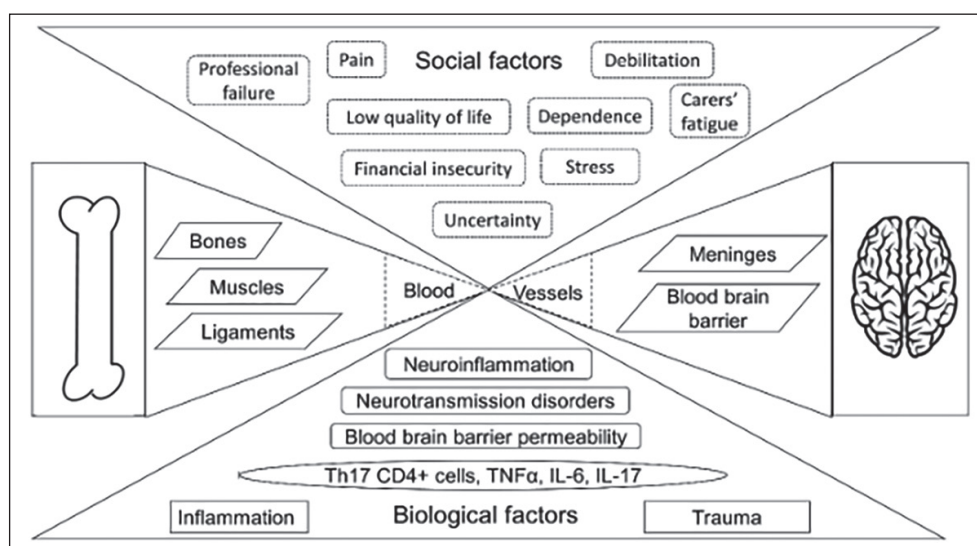


Fig. 2. The socio-biological background of the bone – brain axis

MATERIALS AND METHODS

Keywords (orthopedics, psychiatry, mental health) were used to list down and analyze the literature in PubMed and Google Scholar. All types of articles, including original research, systematic reviews, and meta-analyses, along with gray literature dating back to 2000. We excluded studies reporting a significant conflict of interest and findings dispersed through popular media instead of peer-reviewed journals.

REVIEW AND DISCUSSION

ETIOLOGICAL CONNECTION BETWEEN MENTAL AND MUSCULOSKELETAL CONDITIONS

Biological and social factors contribute to the interplay of musculoskeletal and mental conditions. In arthritis, pro-inflammatory factors, such as Th17 CD4+ cells, TNFα,

IL-6, IL-17 decrease the expression of tight junctions (TJ) of the blood–brain barrier (BBB) increasing its permeability. Oxidative molecules penetrate the central nervous system (CNS) promoting neuroinflammation and synaptic dysfunction[6]. Negative modulation of serotonergic neurotransmission due to degradation of tryptophan and hyperactivity of the hypothalamus–pituitary–adrenal (HPA) axis may lead to the manifestation of depressive symptoms [7,8].

Patients with autoimmune musculoskeletal conditions experience cognitive impairment due to chronic inflammation (brain fog). Mechanisms involved in this condition include: cytokines interfering with neurotransmitter release, proinflammatory cytokine- mediated increase in the uptake and breakdown of monoaminic neurotransmitters (serotonin, noradrenaline and dopamine), oxidative stress induced by the oxidation of tetrahydrobiopterin, indoleamine-2-, and 3-dioxygenase-mediated removal of

tryptophan from the serotonin pathway and astrocyte-mediated inhibition of dopamine release [9].

Polytrauma patients may develop psychiatric symptoms related to traumatic brain injury. Concussions, penetrating injuries, closed head injuries, skull fractures, hematomas, lacerations and contusions lead to brain hypoxia and diffuse axonal injuries. Such lesions have been associated with a decrease in dopamine, serotonin and acetylcholine levels, an event implicated in the pathophysiology of various neuropsychiatric disorders from dementia to depression [10]. Peripheral nerve damage also affects neuronal plasticity and somatosensory cortical representation at the CNS resulting in chronic pain and depression as described in the context of phantom limb pain [11].

Beyond biology, several social factors seem to contribute to the development of psychiatric symptoms among these patients. Pain, fatigue, disability, low quality of life, increased costs, dispute with insurance agencies and withdrawal from professional activity constitute potential risk factors for the mental wellbeing of patients with traumatic injuries, congenital deformities, mechanical and autoimmune musculoskeletal conditions, as well as of their carers. Prolonged symptoms and suffering in combination with uncertainty for the prognosis of the disease and the financial security of their dependents also lead to stress, depression and sleep disorders [12].

The coexistence of biological and social factors (Figure 2) is in line with the social determinants of health and the socio-biological translation theory [13].

PSYCHIATRIC COMORBIDITY IN ORTHOPEDIC WARDS

Research focusing on orthopedic inpatients has reported psychiatric comorbidities with prevalence ranging from 19% to 86%, due to the lack of homogeneous diagnostic criteria [14].

Several studies have assessed psychiatric comorbidities among inpatients in orthopedic and musculoskeletal wards. Vijay et al. (1988) screened 302 orthopedic outpatients with the General Health Questionnaire (GHQ-5) and reported potential psychiatric comorbidity in 41% of them, particularly in those with chronic inflammatory and degenerative musculoskeletal conditions [15]. Lange et al. (2001) referred 39 in-patients of an orthopedic department for mental health assessment. Following a consultation with mental health professionals, psychiatric comorbidity (ICD-10 Chapter F (V)) was diagnosed in 95% of the patients. 30% of these patients were incapable of managing their musculoskeletal condition as outpatients because of their mental health status. In 40% of them, psychiatric comorbidity was associated with (i) inadequate psychosocial adaptation to chronic symptoms and disability, and (ii) long term orthopedic complications [16]. It is noteworthy that although orthopedic wards' personnel was able to notice psychiatric comorbidity, they would request psychiatric consultation mostly for "difficult" patients [14]. Schwartz et al (2010) investigated patient records from the mus-

culoskeletal departments of 507 hospitals in California, USA between 2001 and 2009. Their findings suggest that psychiatric conditions were the commonest comorbidity (24.7%) in admitted patients with musculoskeletal injury. Among them, the most common diagnoses were dementia (14.3%) and depression (6.9%). In comparison to patients with no psychiatric history, patients with psychiatric comorbidities had a higher likelihood of prolonged hospitalisation (7 or more days), surgical complications, and even in-hospital death [17]. Buller et al. (2016) assessed a cohort representative of 526,185 inpatients with humeral fractures from the USA National Hospital Discharge Survey between 1990 and 2007. The study reported an independent association between depression, anxiety, and dementia with increased likelihood of in-hospital adverse events. Depression was linked to higher rates of inpatient blood transfusion, while depression, schizophrenia, and dementia increased the possibility of non-routine discharge or transfer to a different inpatient facility. Moreover, a diagnosis of schizophrenia was associated with a mean of 12 more days of inpatient care [18].

Degen et al. (2016) studied the presence of upper extremity musculoskeletal complaints among workers with symptoms of depression, anxiety and post-traumatic stress disorder (PTSD) by means of the Patient Health Questionnaire (PHQ). The analysis of the responses of 418 individuals suggested that workers suffering from neck pain had significantly higher screening rates of depressive symptoms (62.5% versus a mean of 20.1%) and anxiety/panic disorder (37.5% versus a mean of 12.9%) in comparison to other complaints (shoulder, hand pain etc). Similarly, patients with chronic pain had higher rates of depression (54.5% versus a mean of 20.1%) and anxiety – panic disorder (63.6% versus a mean of 12%) [19].

McCrabb et al. (2019) conducted a cross – sectional study about the prevalence of smoking, alcohol consumption and addiction among orthopedic inpatients in two major hospitals in Australia. They reported higher prevalence of smoking among inpatients (21.8%) in comparison to the general population of Australia (13.8%). More than half of the patients (51.8%) reported alcohol consumption at hazardous levels during the last year, and about 9.7% reported use of cannabis during the last month [20]. Furthermore, Yang et al. (2020) investigated retrospectively the prevalence of emotional distress among 1994 orthopedic inpatients in China by means of the "Huaxi Emotional-Distress Index" (HEI). Emotional disorders were traced in 8.1% of the sample, while 1% had severe emotional distress according to the HEI index. The latter was positively associated with injury severity, high visual analogue score (VAS) and lengthy and/or arduous surgery [21]. Ohliger et al. (2020) evaluated 553 orthopaedic patients divided in two cohorts, before and during the COVID-19 pandemic. Patients in the during-the-pandemic cohort had a higher prevalence of psychiatric diagnoses and a more frequent history of interpersonal violence (43% vs 26%) compared with the before-the-pandemic cohort [22].

A number of studies have also investigated the association of psychiatric comorbidities with orthopedic proce-

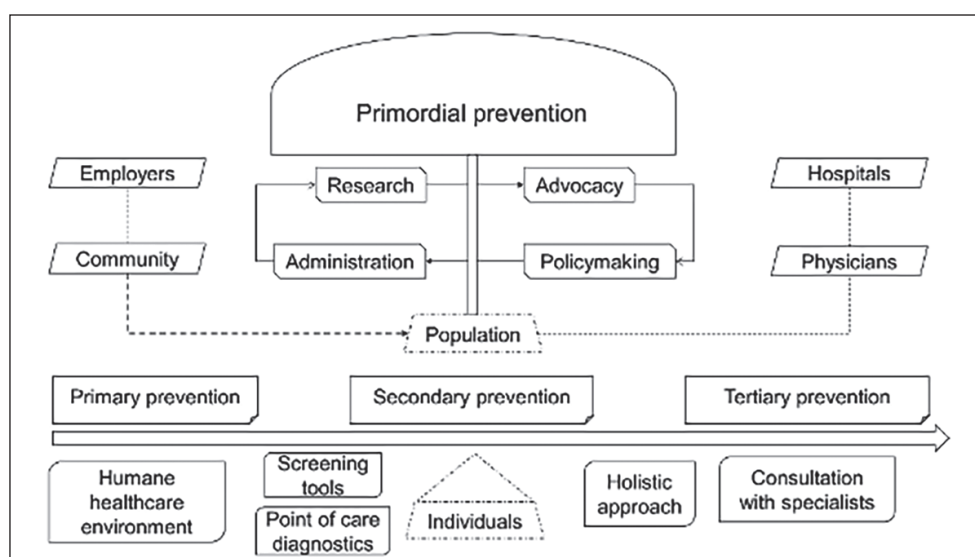


Fig. 3. A mental wellbeing action plan in musculoskeletal care

dures and their outcomes. Buller et al. (2014) assessed the association between a history of dementia, depression or schizophrenia and the outcomes and morbidity following total hip or total knee replacement, two of the most common orthopedic procedures. In a cohort representative of 8,379,490 patients, depression, dementia and schizophrenia were associated with higher likelihood of adverse events, with schizophrenia and depression linked to higher odds of perioperative blood transfusion. All these comorbidities appeared to increase the odds of non-routine discharge, while dementia was associated with higher in-patient mortality [23]. Bot et al. (2014) retrieved data from the National Hospital Discharge Survey (NHDS) database, to assess psychiatric comorbidity among 348,824 patients having undergone partial or total shoulder arthroplasty between 1990 and 2007. The most prevalent conditions in this sample were depression (4.4%), anxiety disorder (1.6%), dementia (1.5%) and schizophrenia (0.6%). All the disorders were associated with a higher likelihood of non – routine discharge. Psychiatric history, with the exception of schizophrenia, was linked to higher rates of adverse events, while depression and schizophrenia were associated with increased odds of perioperative blood transfusion [24]. Frank et al. (2020) investigated a cohort of 378 patients from a Veterans Healthcare Center in the USA and reported that patients with major depression or depressive disorder had 1.78 times higher rates of opioid use prior to spine surgery in comparison with patients with other or no comorbidities [25].

Baron et al. (2021) screened patient records (57.7% male) in the Humana claims database in the USA. This study assessed 226,402 patients between 2007 and the first quarter of 2017. Psychiatric comorbidities were twice as common in patients undergoing common sports medicine/orthopedic procedures (21.21%) in comparison with the entire database. These patients most frequently underwent repair of the rotator cuff (28%), hip labral repair (26.3%) and meniscectomy (25%). On top of this, psychiatric comorbidity

was associated with a 50% increase in healthcare costs for orthopedic procedures[26]. Broggi et al. (2021) conducted a retrospective analysis of complications among elderly (>65) patients after undergoing open reduction internal fixation (ORIF) and intramedullary nailing (IMN) due to traumatic injury between 2009 and 2019 according to the Truven Marketscan claims database in the USA. In 78,435 patients, preoperative depression was associated with up to 1.3 times higher odds for surgical site infections, wound complications and non-union following ORIF. The same was associated with up to 1.44 higher odds of surgical site infections, wound complications, visit for pain and pneumonia following IMN [27].

The available evidence highlights the increased prevalence of dementia, depression, and anxiety – panic disorder among patients with orthopedic conditions. It also seems that psychiatric comorbidity has a negative effect on elective surgery. Depression, anxiety disorder, dementia and, at a smaller scale, schizophrenia increase perioperative morbidity, hospitalization, short and mid-term postoperative complications and mortality. Mental disorders come with a higher cost of care and burden for carers, leading to biopsychosocial stalemate. Nevertheless, the existing research is heterogeneous. Despite the existence of large-scale studies, the criteria and methods used for the diagnosis and classification of mental health conditions differ rendering the comparison between studies difficult. The majority of the studies has been conducted in countries with large databases such as USA, Australia and China in a retrospective manner. Access to healthcare and insurance system databases is necessary for similar studies in other countries. In countries and territories with a shortage of data databases – registries and prospective studies can be organized simultaneously. In the coming years, more evidence will support less invasive procedures and conservative management, and it will be also noteworthy to assess the impact of unnecessary surgical operations on existing psychiatric comorbidities [28].

A PROPOSED MENTAL WELLBEING ACTION PLAN IN MUSCULOSKELETAL CARE

During the last decade, there is interest in mental wellbeing action plans. The WHO has released an action plan for mental health applicable between 2013 and 2020 [29]. The Department of Health of the United Kingdom has also laid down its mental health strategy in the form of an action plan effective between 2020 and 2030 [30]. The aforementioned action plans can be implemented across a number of fields (healthcare facilities, workplaces, community) and concern the population at country or global level. They are supported by potent health bodies, contain detailed consideration of resources involved. At this point, the authors are not capable of presenting such a comprehensive strategy for mental health care in musculoskeletal wards. This section rather outlines recommendations aiming to preventing, early diagnosing or sufficiently addressing psychiatric comorbidities in patients with orthopedic conditions.

The authors' approach follows the four levels of prevention (primordial, primary, secondary, tertiary). As established, primordial prevention targets underlying conditions leading to harmful exposures and causations of disease and entails interventions for the population or specific high – risk groups. Primary, secondary and tertiary prevention target specific causal factor, early – stage disease and established disease respectively. Related interventions target individuals at risk and patients (Figure 3).

At a primordial prevention level, governments, health bodies, patients and workers associations related to musculoskeletal health need to collaborate with mental health professionals. This collaboration should first investigate conditions with a potential to act as mental health risk factors in orthopedic care. Research identifying the most common comorbidities at regional level should be translated to administrative – and if necessary legislative – action at regional, national and local levels. Cost – effectiveness analyses related to the implementation of the necessary interventions ought to be conducted. Interventions should be designed aiming to mitigate mental health stressors such as negligent pain management, long waiting lists, unpleasant hospital environment, lack of etiquette in the interaction between patients, healthcare workers or the administrative personnel of the concerned facilities and uncertainty related to controversial insurance policies. The latter has been repeatedly highlighted by the American Psychological Association's annual "Stress in America" reports. Relevant action includes:

- Financial coverage of acute orthopedic trauma for uninsured patients and simplified or accelerated refund processes related to emergencies.
- Paid leaves from work for patients with orthopedic trauma, chronic or recurrent pain and disability. Family members – carers also need paid leaves. The state and insurance companies need to support employers afford the financial burden. Similarly, it is essential to include mental health-related expenses to the remuneration of occupational musculoskeletal injuries.
- Regular and confidential mental health assessments for individuals with musculoskeletal conditions at the

workplace, in the community or in specialized health-care facilities.

- Measures against the stigmatization of individuals whose musculoskeletal conditions affect their mental wellbeing (informative campaigns in workplaces, educational institutions and the community, sanctions for employers discriminating them).
- Digital tools (medical wearables monitoring behavior and behavior associated alterations of vital signs, smartphones with a history of activity and internet search) have major potential in identifying individuals with undiagnosed mental health disorders [31]. This technology can be used to assess the mental wellbeing of orthopedic inpatients and outpatients based on 1) sufficient research and 2) relevant medico-legal framework with respect to privacy.
- Reintroducing psychoorthopedics. This concept has been first introduced in the 1950s' with research assessing the effect of mental health disorders on posture [31]. Currently, integrating the epidemiology of psychiatric comorbidity in orthopedic wards with related clinical, public health, biological and social research can help reform clinical practice, workplaces and the community.

At a primary, secondary and tertiary prevention level, mental health risk factors, conditions and related symptoms need to be identified in both inpatients and outpatients:

- Healthcare facilities need to take action against conditions that may aggravate patients' and carers' mental wellbeing. These include long waiting lists, lack of attention to pain management and patients' comfort, unnecessary bureaucratic procedures and uncertainty.
- Discussing with the patients and their carers. Physicians, nurses and other healthcare professionals involved in everyday care can spot stressors aggravating the mental wellbeing of patients with or without psychiatric comorbidities. Special attention should be paid to noise, light and sleeping routine [32].
- Point of care mental health tools and screening tests for prevalent or life-threatening mental health conditions need to be incorporated in musculoskeletal history taking. In case of long – term hospitalization this can be repeated in due intervals.
- Consultation with mental health professionals needs to be enhanced in orthopedic care. Trainees should be instructed to collaborate with mental health professionals. To sustain such a culture a psychiatrist or a psychologist can regularly attend the rounds of orthopedic departments.
- Patients with psychiatric comorbidities need to receive their regular treatment. Hospitalization can have a negative effect on these patients leading physicians of non – psychiatric specialties including orthopedics to increase their sedatives' or antipsychotics dosage. It seems preferable to modify the treatment scheme in consultation with mental health professionals and reassess the patients during their hospitalization and outpatient monitoring time.

REAL WORLD LIMITATIONS AND CONSIDERATIONS

This strategy combines an umbrella leg targeting the population as a whole and a personalized leg focusing on individuals with or without psychiatric comorbidities. It is limited by scarce resources, workforce and decision-making. It is also important to secure the mental wellbeing of physicians and other professionals working there. Hospital administrations and healthcare professionals' associations should liaise musculoskeletal department and practices with psychologists and psychiatrists. Healthcare workers need to be encouraged to seek mental health professionals' attention, while confidentiality needs to be upheld and stigmatization – including the possibility or the fear of professional discrimination and sanctions – needs to be waived. This is a major concern, given that the prevalence of burnout is 50–60% higher among orthopedics in comparison to other surgical specialties [33, 34]. It is also noteworthy, that non-psychiatric comorbidities can decrease functionality in patients treated for musculoskeletal conditions [35].

COVID-19 is an additional factor perplexing the equation, because COVID-19 positive patients hospitalized for traumatic injury or other orthopedic conditions can face psychological burden and stigmatization. The need for a holistic approach to these individuals should not be shadowed by the restrictions of the pandemic [36]. When physical consultation and monitoring of such patients by mental health professionals is not possible, digital tools can be used. The same applies to orthopedic outpatients residing in remote areas or inpatients and outpatients in orthopedic departments without psychiatric coverage.

CONCLUSIONS

Psychiatric comorbidity constitutes a major concern in musculoskeletal care. The presence of biological and social factors leads to the development or the aggravation of neuropsychiatric disorders in individuals with musculoskeletal conditions. Mounting evidence highlights the prevalence and the detrimental impact of psychiatric comorbidity in patients undergoing conservative or surgical orthopedic treatment. Authorities, health bodies and hospital administrations need to take action to prevent, early detect and treat psychiatric comorbidities at population and individual level. The biopsychosocial aspects of the “bone – brain axis” need to be better mapped and addressed to a pragmatic approach involving all concerned parties and acknowledging the challenges and limitations along the way.

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Conflict of interest:

The Authors declare no conflict of interest.

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