Review

Is psyche-soma dichotomy still clinically appropriate?

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ABSTRACT

This article proposes a historical re-contextualisation of the mind-body relationship and offers some evidence-based reflections on the current clinical appropriateness of psyche-soma dichotomy and psychosomatics.

The debate concerning the mind-body relationship has a long medical, philosophical, and religious history, with psyche-soma dichotomy and psychosomatics alternating as the dominant clinical approach, depending on the prevalence of cultural orientations at different times. However, both models simultaneously benefit and limit the clinical practice.

The neurosciences have reduced the gap between psyche and soma diseases, which can now be seen as overlapping and sharing a common pathogenesis. Diseases should also be considered as illnesses by considering all of their bio-psychosocial aspects to avoid therapeutic failures due to only partially effective or ineffective interventions. Patient-centred care integrated with guideline recommendations may be the best means of uniting the psyche and the soma.

Introduction

The debate concerning the relationship between the mind and the body has a long medical, philosophical and religious history, with psyche-soma dichotomy and psychosomatics alternating as the dominant clinical approach depending on the prevalence of cultural orientations at different times. The view of the unity or division of the psyche and soma has varied from the holistic medico-philosophical approach of ancient Greece to the "biologisation" of the psychic aspects of scientific medicine.

This article proposes a historical re-contextualisation of the mind-body relationship and offers some evidence-based reflections on the clinical appropriateness of the different views.

Historical background

When proposing his humoral theory in ancient Greece, Hippocrates (IV century BC) tried to provide a unitary conception of human beings in which the body, mind and the environment were strictly interconnected. Centuries later, in 1662, Descartes replaced this perspective with his reflections on *res extensa* (the domain of science) and *res cogitans* (the domain of philosophy and theology) as a means of freeing science from religious influences (1). However, this was certainly not a real dichotomy as he wrote "*Inputs are passed on by the sensory organs to the epiphysis in the brain, and from there to the immaterial spirit"* (1). Unfortunately, posterity misunderstood the difference between *res extensa* and *res cogitans*, thus leading to the cultural and medical exclusion of *res cogitans* that has persisted ever since.

The biomedical model, that developed during the XIV century on the basis of the principles of reductionism and mind-body dualism, is still accepted today. It relates symptoms to pathophysiological mechanisms, which therefore become treatment targets, and attributes less importance to the subjective experiences of the individual. Treatments are not tailored to the patient, and patients are simply required to adhere as closely as possible to what is prescribed. Furthermore, the biomedical model also relates psychiatric symptoms to organic factors, as can be seen in Wilhelm Griesinger's 1868 assertion that "*Mental disease is brain disease*" (2).

The biomedical model favoured the study of human anatomy and has led to fundamental medical developments, but it runs the risk of ignoring symptoms that cannot be explained by physiological mechanisms and the scientific method, such as some psychological or psychiatric symptoms, or psychosocial factors influencing medical conditions.

This changed with the introduction of psychosomatics (3). The word "*psychosomatic*" first appeared in the medical literature in an article published in 1818 by Johann Christian August Heinroth (1773-1843) (4), the first professor of Psychology at the University of Leipzig, Germany. He was the leader of the "Psychiker" school, which suggested that the consideration of the mind was essential when treating illness, unlike the "Somatiker" school, which maintained that mental disorder was caused by bodily disease (5).

At the beginning of the XX century, there was a *rapprochement* between the philosophies of phenomenology (Edmund Husserl) and hermeneutics (Martin Heidegger) and the psychology of Wilhelm Wundt (1896), and psychiatrists such as Karl Jaspers and internists such as Viktor von Weizsäcker, also greatly influenced the development of psychosomatic medicine.

It was in this cultural context that Sigmund Freud (1856-1939) pronounced his famous statement: "*The ego is first and foremost a bodily ego. It is not merely a surface entity but is itself the projection of a surface. If we wish to find an anatomical analogy for it, we can best identify it with the 'cortical homunculus' of the anatomists, which stands on its head in the cortex…"*. These words marked the beginning of the recognition of many clinical and theoretical examples of mind-body interactions and psychoanalysts proposed that people who had difficulty in expressing rage can release their tensions at somatic level: *i.e.* unconscious factors may be relevant to the genesis of disease states.

Subsequently, disciples of Freud such as Franz Alexander (1891-1964) contributed to the study of somatic diseases that could be related to emotional factors, such as inflammatory bowel disease, peptic ulcer, hypertension, asthma, rheumatoid arthritis, eczema, etc., thus promoting an interdisciplinary scientific approach to the study of the human being (3) and leading to the foundation of scientific journals such as *Psychosomatics* (Journal of the Academy of Psychosomatic Medicine) in 1939 or *Psychosomatics and Medical Psychology* in 1948.

Finally, Roy Grinker coined the term *biopsychosocial* in 1954, and used it in his article entitled *"A struggle for eclectism"* to urge psychiatrists to incorporate advances in biology in their models rather than relying purely on psychoanalytic dogma (6). Some years later in 1977, based on the 1907 statement of Ludolf Von Krehl that "*We do not treat diseases, but sick people",* George Engel advocated the adoption of a new medical model that had a more comprehensive approach to patients: the *biopsychosocial model (BPSM)*. In his opinion, "*it is essential to know who the patient is, as well as what disease he has*" if we want to avoid treating a disease without considering the peculiarities of the person involved. In this sense, he began to emphasise the psychosocial aspects of illness, which must be seen as a result of interacting mechanisms at cellular, tissue, organic, interpersonal, and environmental levels (7).

The BPSM opened the transition from a disease framework that reflects the biomedical perspective of analysing symptoms and signs in order to formulate a diagnosis and prescribe specific treatments, to an illness framework based on the patient's perspective of his disease, which has the purpose of investigating the subjective experience of illness, and which is characterised by beliefs, emotions, perceptions, feelings, expectations, and adaptations. The BPSM integrates the biological and psychosocial aspects of the process of care. Grinker applied it to psychiatry to emphasise *"bio"* against psychoanalytic orthodoxy; Engel applied it to medicine to emphasise *"psychosocial"* against the biomedical approach.

The BPSM was partially ostracised by the medical journals that were more susceptible to the biomedical reductionism that simplifies treatments and neglects individual responses, something that was already going against clinical experience (8-10).

Today's clinical practice: the biomedical or biopsychosocial model?

It is now well established that illness is a complex experience that is not always exclusively somatic or exclusively psychic, but can only be understood by considering multiple perspectives. Among the many examples of the psyche-soma overlap, peptic ulcer disease has long been considered a classic psychosomatic illness, but it is often sustained by *Helicobacter pylori* and can only be cured by a therapeutic approach that addresses both its biological and psychological causes.

The bio-medical model may be limited in its approach to patients as can be seen in the case of medical guidelines, which are essential for ensuring that clinicians correctly use medical treatments, but cannot be applied in a differentiated manner, without considering the possible need for adaptations to individual cases. A drug can induce different genetic, metabolic, behavioural, or social responses that need customised adjustments in terms of choice, dose, titration, and so on. Even if a treatment is correctly proposed on the basis of guidelines, it must be tailored to psychological and environmental parameters: for example, fear of the drug, due a previous negative experience, may give rise to a nocebo effect that partially, or completely, compromises treatment adherence and therapeutic alliance (11, 12). However, this can be avoided by integrating the guidelines with psychosocial consensus statements, in order to ensure more personalised treatment.

On the other hand, the BPSM also has some limitations in clinical practice: developing an in-depth relationship with a patient often requires more time and resources than are available, and physicians may prefer to rely on a biomedical model that is more in line with their academic culture and training. Although they may theoretically agree with the BPSM. they are not always prepared to put it into practice.

The BPSM also has a number of other limitations (13):

- holism is not always an advantage because some diseases have a specific pathogenesis and are sufficiently explained by a restricted causal model, and some medical treatments can offer sufficient, even if partial, solutions, such as antibiotics, antipyretics, and various surgical interventions;
- the BPSM may be difficult for clinicians, patients, and caregivers to ap-

ply in all of its biological, psychological and social aspects because of time and resource constraints, or a tendency to give more weight one aspect, rather than another, on the basis of personal preferences, qualifications or expectations;
- integrated treatments are always more effective than individual treatments alone, but sometimes one method may be more viable.

In his paper, Nassir Ghaemi said that the BPSM was initially valuable as a reaction to biomedical reductionism but has played out its historical role (8); or it may be more advantageous to apply one model or the other depending on the conditions. As Osler said in 1932, "*Medicine is an art based on science, not simply a science, but also not merely an art*" (14), and other authors agree (15).

The current concept of disease

Combining the biomedical model and BPSM offers an opportunity for dialogue between the psyche-soma dichotomy and psychosomatics. Biopsychosocial factors may facilitate, sustain, or modify the course of a disease, and their relative weights may vary from disease to disease, from one person to another and, sometimes, from one time to another in the same person (8). Furthermore, no single disease, patient or condition can be simply reduced to one characterising aspect, as all the determinants are always equally relevant in all cases. At the same time, at any given moment, the reference culture and the limitations and possibilities of circumstances may give more weight to one of the bio, psycho or social elements, thus leading to a preference for the disease over the illness framework or *vice versa*; and, in some optimal cases, they may be integrated with one another in order to promote a shared understanding and complementary decision making.

Nevertheless, some open questions remain: is it still appropriate to acknowledge the psyche-soma dichotomy? And can we still consider psycho-social aspects as not biological? The neurosciences have recently reduced the gap between psyche and soma, as a result of the development of epigenetics, psycho-neuro-endocrine immunology, neuroimaging, and other approaches, and this raises the question as to whether we are approaching the Rosetta Stone of psychosomatics.

The psyche-soma relationship is being replaced by the co-pathogenetic hypothesis

Over the last few years, our view of the relationship between the psyche and the soma has developed from traditional concepts of inter-connection, influence (indirect activity and co-morbidity to the newer concepts of overlapping, causality (direct activity) and co-pathogenesis. Nowadays it is known that various psychic and somatic alterations share the same biological mechanisms, and have common physiological patterns and pathogeneses: for example, it is widely acknowledged that mood alterations are very frequently associated with pain (16), but this relationship cannot be fully explained by simple co-morbidity, as depression and pain share important pathogenic mechanisms (17-20) involving a series of factors:

- *Neurotransmitters*. A reduction in the levels of serotonin (5HT) and norepinephrine (NE) in limbic areas not only induces a depressed mood, but simultaneously also reduces the descendent inhibitory system and thus promotes an increase in pain; furthermore, dual anti-depressants (*e.g.* duloxetine, milnacipran, venlafaxine) effectively act on both depression and pain.

- *Hypotalamus-pituitary-adrenocortical (HPA) axis hyperactivity.* Depression can manifest itself under conditions of chronic stress, characterised by HPA axis hyperactivity. The functioning of the HPA axis is influenced by a subject's cognitive evaluation of, and emotional response to the stressor, which is why cognitive behavioural therapy (CBT) can reduce chronic stress. Nevertheless, the cascade of stress hormones, released upon HPA activation, increases the production of pro-inflammatory cytokines, and leads to the exacerbation of pain and a depressed mood.

- *Cytokines* play a dual role in the physical and emotional aspects of pain and mood: the increase in pro-inflammatory cytokines associated with diseases, such as cancer, causes pain and psycho-behavioural symptoms such as fatigue, depressed mood, and cognitive impairment (21-23). These symptoms are related to each other by neurotoxicity: the central nervous system (CNS) reacts to a stressor by activating microglia, which increases the production of inflammatory mediators (cytokines), and astrocytes, which increases the glutamate release causing neurotoxicity. The confirmation of the complex relationship between the psychological (mood) and somatic property (pain) of cytokines is provided by the immunological hypothesis of suicide during the use of interferon to treat multiple sclerosis (24-26), and the cytokine storm associated with COVID-19 (27); furthermore, the involvement of inflammation in the aetiopathogenesis of depression is suggested by the fact that patients with major depressive disorder and increased levels of pro-inflammatory cytokines (mainly IL-6, TNF-α and IL-1β) may benefit from anti-inflammatory treatment (28).

- *Excitotoxicity.* The persistent excitotoxicity associated with chronic stress leads to neuronal sufferance and death with parenchymal hypotrophy, as confirmed by the neuroimaging of hippocampal shrinkage (29), the biological substrate of depression and pain. Anti-depressants can counteract this process by favouring the production of neurotrophic factors.

- *Allopregnanolone* is a neuro-hormone that inhibits glutamatergic neurotransmission by negatively modulating N-methyl-D-aspartate receptors (NMDAR) function and potentiates GABAergic activity, thus acting on both depression and pain. Anti-depressants also act on mood and pain by favouring the synthesis of allopregnanolone (30, 31).

- *The microbiota* involved in the pathophysiology of many intestinal and extra-intestinal diseases provides a

further example of co-pathogenesis, as recent research has demonstrated that it regulates many of the physical and emotional aspects (mood, anxiety, stress) (32-34).

- *Oxytocin* is a paradigmatic example of dual (psychic and somatic) activity. It has long been known that its somatic activity strengthens uterine contractions and favours post-partum milk excretion, but more recent findings show that it also induces maternal behaviours, such as empathy, and potentiates social behaviours and bonding by increasing trust (35, 36).

The biological effects of psychological interventions

It is well known that biological drugs such as anti-depressants, steroids, and immuno-modulators can induce emotional changes, but it is possibly less widely known that psychological interventions can induce a biological response, as several studies have shown that psychotherapy enhances cancer survival and improves emotional disorders such as depression, anxiety, and stress (37, 38).

The effect of psychological interventions on the biological mechanisms of disease seems to be due to their capacity to induce neurobiological changes, such as increasing the immune activity of natural killer cells (39, 40). Studies have found that psychotherapy mediates the immune changes involved in survival (41) by down-regulating the expression of pro-inflammatory genes and up-regulated type I interferon response genes in circulating leukocytes (40, 41). Shields *et al*. have also recently shown that psychosocial interventions (especially CBT) are associated with positive changes in immunity over time, including an increase in beneficial and decrease in harmful immune functions (42, 43).

The biological activity of psychotherapies is also reflected in the brain changes induced by anti-pain treatments. A number of recent neuro-imaging studies have shown that psychological interventions such as CBT, meditation, mindfulness, and hypnosis can induce significant modifications in the brain areas and functions involved in modulating pain: for example, CBT favours a cortical control mechanism in patients with chronic pain by increasing the activation of the pre-frontal cortex (PFC), which is associated with executive cognitive control of pain. Moreover, the pain regulation induced by cognitive and meditative therapies can have a positive impact on nociceptive and non-nociceptive brain regions as it increases pre-frontal, orbito-frontal, somatosensory, anterior cingulate, and insula cortical activity, and decreases thalamus activation (44). The effects of hypnosis on pain are mediated by the activity of the anterior cingulate cortex (ACC), the area involved in the "suffering" component of pain and unpleasant affective reactions (45-47). Similarly, other studies have shown that inhibition of afferent nociceptive transmission can be explained by a dramatically decreased activity of the thalamus observed under hypnotic induction, and the hypnotic mediation of executive, salience, and default networks (48, 49). Mindfulness can also provide pain relief by favouring orbito-frontal and rostral anterior cingulate cortical regulation of the thalamus and primary somatosensory cortex, and de-activating the posterior cingulate cortex. Prolonged mindfulness training is also associated with pre-frontal de-activation and greater activation of the somatosensory cortex, thus moderating the perception of painful sensations (50-54).

The psyche-soma overlap requires an integrated approach

Given all the evidence mentioned above, psycho-social, and somatic factors should both be considered in order to obtain a complete clinical response in a number of diseases, and these interventions should be implemented by a patient-centred, interdisciplinary therapeutic approach in order to ensure the greatest improvement in a patient's condition.

For example, the treatment of chronic pain should move away from analgesic therapy alone and towards multi-dimensional interventions, that include the use of different drugs and emotional, behavioural, and cognitive treatments. Treating chronic pain with analgesics alone is considered satisfactory by only about 40% of patients, because the psychosocial components of pain are under-evaluated and under-treated (18).

Another example is the co-morbidity of depression and a somatic pathology such as the menopause, rheumatological disease, diabetes, or thyroid disorders, to which a complete response can be obtained using drugs that are active on both, such as hormones and anti-inflammatory treatments, including monoclonal antibodies (55, 56).

The impact of social factors on the soma

The socio-economic and relational components of the BPSM are integral parts of diagnosis and treatment. More than ten years ago, inspired by Kroenke *et al*. (57), Chida *et al*. (58), Pinquart *et al*. (59), Lutgendorf and Sood (60) pointed out that social adversities, such as isolation, considerably affect not only a patient's quality of life, but also disease progression, by modifying the cellular immune response, angiogenesis, invasion, anoikis, and inflammation (60).

Environmental factors, such as negative life events, socio-economic burdens, relationship difficulties, social isolation, and dysfunctional individual attitudes and coping strategies, stimulate the activation of the neuroendocrine response of the HPA axis, autonomic nervous system, catecholamines, glucocorticoids and other stress hormones and neuropeptides, and neuroendocrine stress hormones have a systemic effect on disease progression (60-67).

It is also known that emotional responses to psychosocial problems may be related to an increased chronic release of norepinephrine, as demonstrated by autonomic alterations under stress conditions.

Poor social support and distress can impair the immune activity of T cells, NK cells and neutrophils (64) and induce the up-regulation of 67 mesenchymal-characteristic gene transcripts and the downregulation of 63 epithelial-characteristic transcripts (65). On the other hand, social support favours resilience against stress, has positive

physiological and immune effects (66), and is related to less leukocyte pro-inflammatory and pro-metastatic gene expression (67).

The psyche and the soma in fibromyalgia

One clinical context that widely expresses the unity of the pathogenetic, clinical and therapeutic aspects of psychosomatics is the fibromyalgia syndrome (FM), about which there is still debate as to whether it should be defined as an illness or a disease. FM is characterised by the simultaneous presence of physical symptoms (pain, irritable bowel syndrome, headache, etc.), psychological disorders (depressed mood, anxiety, insomnia, alexithymia, etc.), and psychophysical symptoms (fatigue, cognitive disorders, etc.) (68), which may not only vary from patient to patient, but also within the same patient during its course. This greatly increases diagnostic difficulties because, on the basis of the concepts discussed above, these symptom clusters cannot just be considered co-morbidities, but need to be interpreted in terms of their co-pathogenesis (69-70). FM has been called a *chronic central sensitisation syndrome*, a condition that leads to alterations in a person's sensitivity to pain. It is clinically characterised by allodynia (pain in the absence of painful stimulation) and hyperalgesia (increased pain upon painful stimulation); it is neuro-physiologically characterised by reduced pain thresholds and prolonged electrophysiological responses; and it is psychologically characterised by the unpleasant quality of the perceived pain, a broadening of the pain attentive field, and catastrophism (71).

Early studies of FM focused on its *stress-related origin* (72-73) but, although the idea of stress and trauma is still very important (74), it is now clear that its pathogenesis is due to many different biopsychosocial factors such as genetic neuroendocrine, socio-cultural and, perhaps, even bio-humoral factors (75-76). This is confirmed by the fact that the symptoms of FM can be alleviated by treatments that modulate inflammation (77), and that anti-depressants are useful in decreasing the perception of pain even in non-depressed patients (78).

The origin of chronic widespread pain is very complex, and FM is a condition that allows us to reflect on some very important concepts, above all whether the location of the pain is in the brain (psyche) or the body (soma) (Fig. 1). In most patients, neuro-psycho-pharmacological treatments alone are unsatisfactory in controlling pain, and only an approach that covers all the pathogenic components of the syndrome leads a substantial improvement in symptoms. This underlines the centrality of the psychic dimension in the pathogenesis and treatment of FM pain and confirms the pathogenic unity of the psyche and the soma.

From this point of view, within the last few years, patient self-management has been emphasised as essential in the treatment for FM: the unsatisfactory result of a single therapeutic intervention advises the integration of multiple types of care (analgesics, psychoactive drugs, psychotherapies, physical exercise, relaxation techniques, physical care, etc.).

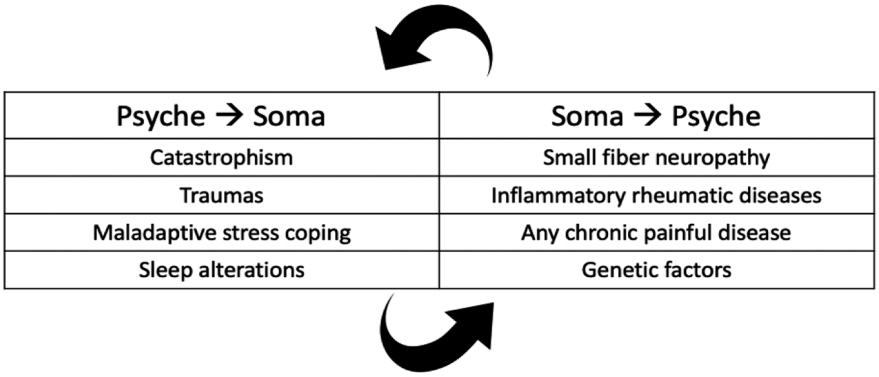

Fig. 1. The aetiopathogenetic conundrum of fibromyalgia syndrome: reciprocal influences and common psyche-soma pathways.

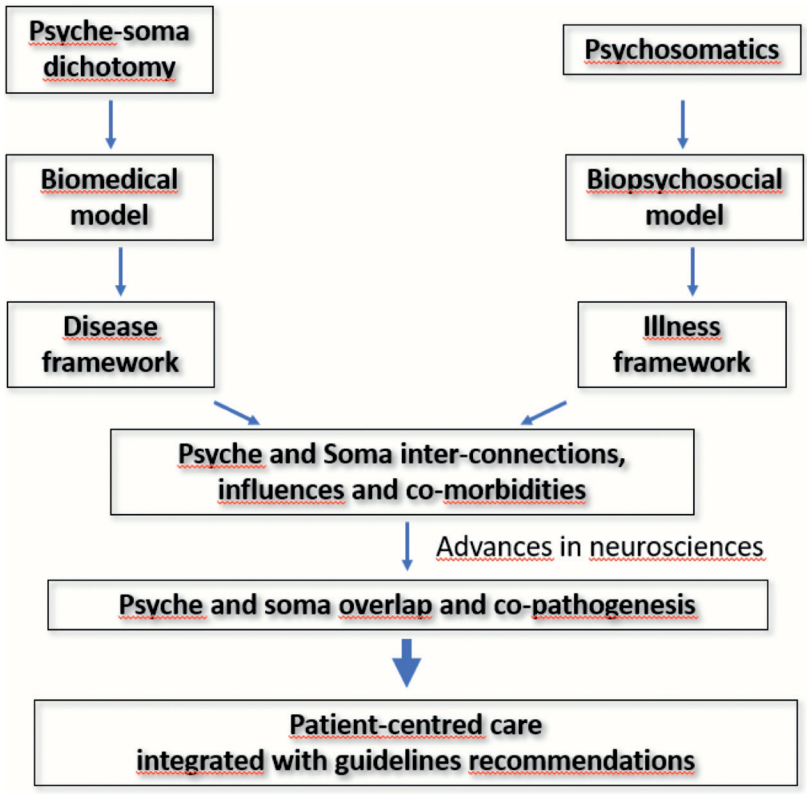

Fig. 2. Psyche-soma dichotomy or psychosomatics: which is more clinically appropriate?

Within this context, patient pro-activity, achieved through a psycho-educational approach and a close monitoring of his/her adherence to treatments, is of paramount relevance (79).

Conclusions and improvement proposals

Further evidence supporting the theoretical and neuroscientific basis of psychosomatics will improve our understanding of the way in which the mind and body share the same pathological pathways and curative strategies. It is also important to give more consideration to the interconnectedness and overlapping of the psyche and the soma in clinical practice: psychosomatics may be an old concept, but its clinical application is still hampered by cultural and economic resistances. The psychosomatic spectrum of therapeutic strategies needs to be broadened: diseases should also be confronted as illnesses requiring consideration of all their biopsychosocial features in a patient-centred manner in order to avoid therapeutic failures due to partially effective or ineffective interventions (Fig. 2).

Nonetheless, there is still a gap between theory and practice. This could depend both on the choices of healthcare institutions and on the individual healthcare professional's sensitivity, attention, awareness, and training on these aspects. In fact, individual attitudes can play a role in favouring or hindering integrated care. Training and education in psychosomatics should be improved: in an academic context, more interaction between different university departments, more interdisciplinary training, and more reciprocal influence among teaching subjects could be useful. For instance, it could be possible to deliver courses of psychology to medical students, courses of medicine to psychology students, or to delve into a subject which can be of common interest to several teachers of different professional backgrounds. In the workplace, interdisciplinary refresher courses or greater national and international information exchange among teams and healthcare centres could provide suggestions for new ways of applying the care models. Finally, we ought to remember the importance of healthcare professionals' personal characteristics: their personal difficulties, poor attitude to adequate communication, psychological concerns, personological traits, or work-related distress could negatively impact on their attitude towards the patient, creating distance from the ideal care. Hence, promoting and guaranteeing interventions and spaces for healthcare providers' self-care is a preventive and protective action that could contribute in overcoming the application limits of the BPSM.

To conclude, to apply this perspective to clinical practice, more economical, human, spatial and temporal resources should be invested to create education, new services and care pathways, also for the self-care of professionals. A holistic approach is necessary to effectively achieve interdisciplinarity, with various healthcare professionals working in an integrated and aligned way with the same patient. The BPSM should become an integral part of clinical practice whenever a psycho-social component can be assumed. The Hippocratic aim "*to cure sometimes, to heal often, to console always*" has all of the strengths and none of the weaknesses of the BPSM. The time and resources required may well increase but, in the long run, the clinical and human advantages gained will certainly justify the initial investment in terms of the quality and costs of care.

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