# The pursuit of euthymia

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*Psychiatrists often consider the positive characteristics displayed by a patient in their clinical judgment, yet current assessment and treatment strategies are shifted on the side of psychological dysfunction. Euthymia is a transdiagnostic construct referring to the presence of positive affects and psychological well-being, i.e., balance and integration of psychic forces (flexibility), a unifying outlook on life which guides actions and feelings for shaping future accordingly (consistency), and resistance to stress (resilience and tolerance to anxiety or frustration). There is increasing evidence that the evaluation of euthymia and its components has major clinical implications. Specific instruments (clinical interviews and questionnaires) may be included in a clinimetric assessment strategy encompassing macro-analysis and staging. The pursuit of euthymia cannot be conceived as a therapeutic intervention for specific mental disorders, but as a transdiagnostic strategy to be incorporated in an individualized therapeutic plan. A number of psychotherapeutic techniques aiming to enhance positive affects and psychological well-being (such as well-being therapy, mindfulness-based cognitive therapy, and acceptance and commitment therapy) have been developed and validated in randomized controlled clinical trials. The findings indicate that flourishing and resilience can be promoted by specific interventions leading to a positive evaluation of one's self, a sense of continuing growth and development, the belief that life is purposeful and meaningful, satisfaction with one's relations with others, the capacity to manage effectively one's life, and a sense of self-determination.*

**Key words:** Euthymia, psychological well-being, resilience, mental health, clinimetrics, positive psychology, well-being therapy, mindfulness-based cognitive therapy, acceptance and commitment therapy

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About sixty years ago, M. Jahoda published an extraordinary book on positive mental health[1]. She denied that "the concept of mental health can be usefully defined by identifying it with the absence of a disease. It would seem, consequently, to be more fruitful to tackle the concept of mental health in its more positive connotation, noting, however, that the absence of disease may constitute a necessary, but not sufficient, criterion for mental health."[1]

She outlined criteria for positive mental health: autonomy (regulation of behavior from within), environmental mastery, satisfactory interactions with other people and the milieu, the individual's style and degree of growth, development or self-actualization, and the attitudes of an individual toward his/her own self (self-perception/acceptance). The book indicated that mental health research was dramatically weighted on the side of psychological dysfunction[1].

It took a long time before such imbalance started being corrected, as a result of several converging developments that occurred in the late 1990s.

First, C. Ryff[2] introduced a method for the assessment of Jahoda's psychological dimensions based on the self-rating Psychological Well-Being (PWB) scales. This questionnaire disclosed that ill-being (e.g., major depressive disorder) and well-being were independent although interrelated dimensions[3,4]. This means that some individuals might have high levels of both ill-being and well-being, while others might have major mental disorders and poor psychological well-being, and further individuals might have no major mental disorders and high levels of psychological well-being.

Further, the naive conceptualization of well-being and distress as mutually exclusive (i.e., well-being is lack of distress and should result from removal of distress) was challenged by clinical research. Patients with a variety of mental disorders who were judged to have remitted on symptomatic grounds still presented with impairment in psychological well-being compared to healthy control subjects[5,6].

Second, impairments in psychological well-being were found to be a substantial risk factor for the onset and recurrence of mental disorders, such as depression[7,8]. Psychological well-being thus needs to be incorporated in the definition of recovery[9]. There has been growing recognition that interventions that bring the person out of negative functioning may not involve a full recovery, but the achievement of a neutral position[9]. Jahoda[1] had postulated that a full recovery can be reached only through interventions which facilitate progress toward restoration or enhancement of psychological well-being.

A third converging development occurred as the concept of positive mental health became the target of an increasing amount of research[10]. Its domains were very broad, such as the presence of multiple human strengths (rather than the absence of weaknesses), including maturity, dominance of positive emotions, subjective well-being, and resilience[10].

Yet, probably the strongest input to the consideration of psychological well-being came from the positive psychology movement initiated by the American Psychological Association in the year 2000[11], which had a huge impact on psychology and the society in general in a very short time. The movement can be credited with delivering the message that psychology needs to consider the positive as well as the negative, an issue that was much later extended to psychiatry[12]. Yet, this movement attracted considerable criticism[13,14]. Positive psychology developed outside the clinical field and, not surprisingly, its oversimplified approach (happiness and optimism, the more the better) was likely to clash with the complexities of clinical reality[13,14].

Despite these developments, consideration of psychological well-being has had a limited impact so far on general practice. The aim of this review is to illustrate that clinical attention to psychological well-being requires an integrative framework, which may be subsumed under the concept of euthymia[15], as well as specific assessment and treatment strategies. Such an approach may unravel innovative and promising prospects both in clinical and preventive settings.

## EUTHYMIA AS AN INTEGRATIVE FRAMEWORK

In 1991, Garamoni et al[16] suggested that healthy functioning is characterized by an optimal balance of positive and negative cognitions and affects, and that psychopathology is marked by deviations from this balance. Treatment of psychiatric symptoms may induce improvement of well-being, and, indeed, scales describing well-being were found to be more sensitive to medication effects than those describing symptoms[17]. In turn, changes in well-being may affect the intensity of symptomatology[18,19].

Excessively elevated levels of positive emotions can also become detrimental[13], and are more connected with mental disorders and impaired functioning than with psychological well-being.

Optimal balanced well-being can be different from person to person, according to factors such as personality traits, social roles, cultural and social context. Table 1 outlines the bipolar nature of Jahoda-Ryff's dimensions[20]. Appraisal of positive cognitions and affects thus needs to occur in the setting of an integrative framework, which may be provided by the concept of euthymia.

This term has a Greek origin and results from the combination of *eu*, well, and *thymos*, soul. The latter element, however, encompasses four different meanings: life energy; feelings and passions; will, desire and inclination; thought and intelligence. Interestingly, the corresponding verb (*euthymeo*) means both "I am happy, in good spirits" and "I make other people happy", "I reassure and encourage".

The definition of euthymia is generally ascribed to Democritus: one is satisfied with what is present and available, taking little heed of people who are envied and admired and observing the lives of those who suffer and yet endure[21]. It is a state of quiet satisfaction, a balance of emotions that defeats fears.

The Latin philosopher Seneca translated the Greek term euthymia by *tranquillitas animi* (a state of internal calm and contentment) and linked it to psychological well-being as a learning process. Happiness is not everything, and what is required is *felicitatis intellectus*, the awareness of well-being. Plutarch, who attempted a synthesis of Greek and Latin

**Table 1** The spectrum of dimensions of psychological well-being

| IMPAIRED LEVEL | BALANCED LEVEL | EXCESSIVE LEVEL |
|---|---|---|
| **Environmental mastery** | | |
| The person feels difficulties in managing everyday affairs; he/she feels unable to improve things around; he/she is unaware of opportunities. | The person has a sense of competence in managing the environment; he/she makes good use of surrounding opportunities; he/she is able to choose what is more suitable to personal needs. | The person is looking for difficult situations to be handled; he/she is unable to savoring positive emotions and leisure time; he/she is too engaged in work or family activities. |
| **Personal growth** | | |
| The person has a sense of being stuck; he/she lacks sense of improvement over time; he/she feels bored and uninterested in life. | The person has a sense of continued development; he/she sees one's self as growing and improving; he/she is open to new experiences. | The person is unable to elaborate past negative experiences; he/she cultivates illusions that clash with reality; he/she sets unrealistic standards and goals. |
| **Purpose in life** | | |
| The person lacks a sense of meaning in life; he/she has few goals or aims and lacks sense of direction. | The person has goals in life and feels there is meaning to present and past life. | The person has unrealistic expectations and hopes; he/she is constantly dissatisfied with performance and is unable to recognize failures. |
| **Autonomy** | | |
| The person is over-concerned with the expectations and evaluations of others; he/she relies on judgment of others to make important decisions. | The person is independent; he/she is able to resist to social pressures; he/she regulates behavior and self by personal standards. | The person is unable to get along with other people, to work in team, to learn from others; he/she is unable to ask for advice or help. |
| **Self-acceptance** | | |
| The person feels dissatisfied with one's self; he/she is disappointed with what has occurred in past life; he/she wishes to be different. | The person accepts his/her good and bad qualities and feels positive about past life. | The person has difficulties in admitting his/her own mistakes; he/she attributes all problems to others' faults. |
| **Positive relations with others** | | |
| The person has few close, trusting relationships with others; he/she finds difficult to be open. | The person has trusting relationships with others; he/she is concerned about welfare of others; he/she understands give and take of human relationships. | The person sacrifices his/her needs and well-being for those of others; low self-esteem and sense of worthlessness induce excessive readiness to forgive. |

cultures, criticized the concept of euthymia involving detachment from current events, as portrayed by Epicurus, and underscored the learning potential of mood alterations and adverse life situations.

In the psychiatric literature, the term euthymia essentially connotes the lack of significant distress. When a patient, in the longitudinal course of mood disturbances, no longer meets the threshold for a disorder such as depression or mania, as assessed by diagnostic criteria or by cut-off points on rating scales, he/she is often labelled as euthymic. Patients with bipolar disorder spend about half of their time in depression, mania or mixed states[22]. The remaining periods are defined as euthymic[23-27]. However, considerable fluctuations in psychological distress were recorded in studies with longitudinal designs, suggesting that the illness is still active in those latter periods, even though its intensity may vary[28]. It is thus questionable whether subthreshold symptomatic periods truly represent euthymia[28].

Similar considerations apply to the use of the term euthymia in unipolar depression and dysthymia. Again, euthymia is often defined essentially in negative terms[29], as a lack of a certain intensity of mood symptoms, and not as the presence of specific positive features that characterize recovery[9].

Jahoda[1] outlined a characteristic that is very much related to the concept of euthymia. She defined it as integration: the individual's balance of psychic forces (flexibility), a unifying outlook on life which guides actions and feelings for shaping future accordingly (consistency), and resistance to stress (resilience and tolerance to anxiety or frustration). It is not simply a generic (and clinically useless) effort of avoiding excesses and extremes. It is how the individual adjusts the psychological dimensions of well-being to changing needs.

In the past decades, there has been an increasing interest in the concepts of flexibility and resilience portrayed by Jahoda[1]. Psychological flexibility has been viewed[30] as the ability to: recognize and adapt to various situational demands; change one's paradigms when these strategies compromise personal or social functioning; maintain balance among important life domains; display consistency in one's behavior and deeply held values. The absence of flexibility is linked to depression, anxiety and the general tendency to experience negative emotions more frequently, intensely and readily, for longer periods of time, in what has been subsumed under the rubric of neuroticism[30].

Resilience has been defined as the capacity to maintain or recover high well-being in the face of life adversity[31]. Looking for the presence of wellness following adversity involves a more demanding and rigorous conception of resilience than the absence of illness or negative behavioral outcomes, the usual gold standards. Examples are provided by life histories of persons regaining high well-being following depression, or the ability to sustain psychological well-being during serious or chronic illness. Resilience is thus conceptualized as a longitudinal and dynamic process, which is related to the concept of flourishing. Issues such as leading a meaningful and purposeful life as well as having quality ties to others affect the physiological substrates of health[32]. The concept of subjective incompetence (a feeling of being trapped or blocked because of a sense of inability to plan or start actions toward goals) stands as opposite to that of resilience[33]. Individuals who perceive themselves as incompetent are uncertain and indecisive as to their directions and aims.

Fava and Bech[15] defined a state of euthymia as characterized by the following features (Figure 1):

- Lack of mood disturbances that can be subsumed under diagnostic rubrics. If the subject has a prior history of mood disorder, he/she should be in full remission. If sadness, anxiety or irritable mood are experienced, they tend to be short-lived, related to specific situations, and do not significantly affect everyday life.
- The subject has positive affects, i.e., feels cheerful, calm, active, interested

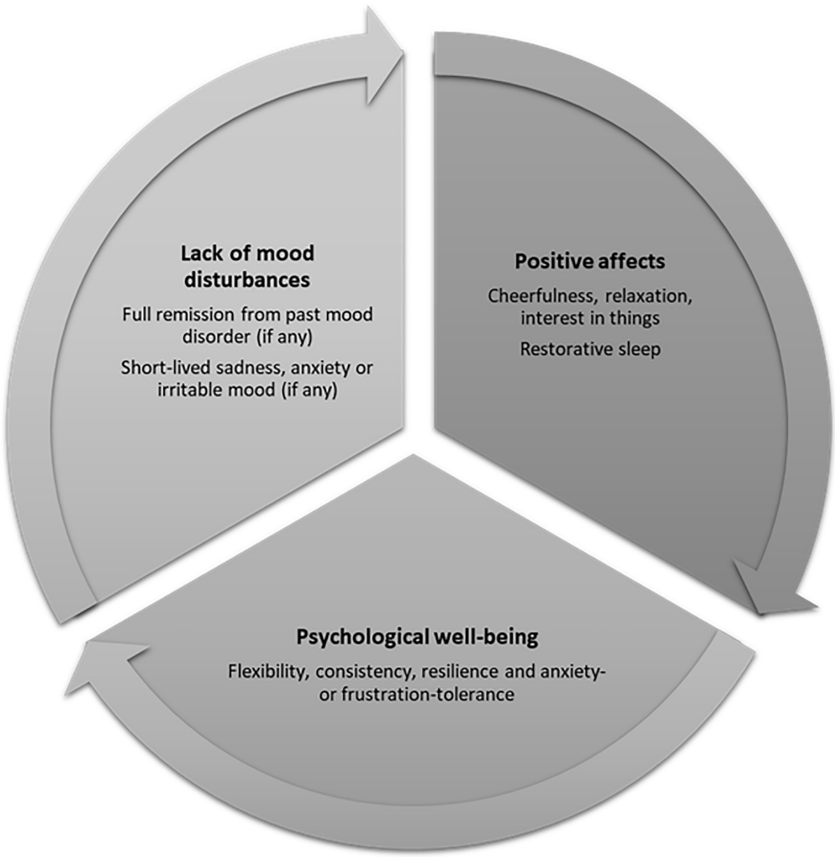


**Figure 1** The concept of euthymia

in things, and sleep is refreshing or restorative.
- The subject manifests psychological well-being, i.e., displays balance and integration of psychic forces (flexibility), a unifying outlook on life which guides actions and feelings for shaping future accordingly (consistency), and resistance to stress (resilience and tolerance to anxiety or frustration).

This definition of euthymia, because of its intertwining with mood stability, is substantially different from the concept of eudaimonic well-being, that has become increasingly popular in positive psychology[34]. Indeed, research on psychological well-being can be summarized[35] as falling in two general groups: the hedonic viewpoint focuses on subjective well-being, happiness, pain avoidance and life satisfaction, whereas the eudaimonic viewpoint, as portrayed by Aristotle, focuses on meaning and self-realization and defines well-being in terms of degree to which a person is fully functioning or as a set of wellness variables such as self-actualization and vitality. However, the two viewpoints are inextricably linked in clinical situations, where they also interact with mood fluctuations[14]. The eudaimonic perspective ignores the complex balance of positive and negative affects in psychological disturbances[13,16].

Whether an individual meets the criteria of euthymia or not, it is important to evaluate its components in clinical practice and to incorporate them in the psychiatric examination. There is, in fact, extensive evidence that positive affects and well-being represent protective factors for health and increase resistance to stressful life situations[6,32,36-38].

## CLINICAL ASSESSMENT OF POSITIVE AFFECTS AND PSYCHOLOGICAL WELL-BEING

Clinical assessment is aimed to exploring the presence of positive affects and psychological well-being, as well as their interactions with the course and characteristics of symptomatology. In order to analyze these characteristics in an integrative way, we need a clinimetric perspective[39-41]. The term "clinimetrics" indicates a domain concerned with the measurement of clinical issues that do not find room in customary clinical taxonomy. Such issues include the types, severity and sequence of symptoms; rate of progression in illness (staging); severity of comorbidity; problems in functional capacity; reasons for medical decisions (e.g., treatment choices), and many other aspects of daily life, such as well-being and distress[39-43].

### Positive affects

While there have been considerable efforts to quantify and qualify psychological distress[44], much less has been done about assessing positive affects such as feeling cheerful, calm, active, interested in things, friendly[45,46].

Self-rating scales and questionnaires have been the preferred method of evaluation, and there are several instruments available[45,46]. Two instruments stand out for their clinimetric properties: the World Health Organization-5 Well-Being Index (WHO-5)[47] and the Symptom Questionnaire (SQ)[17].

The WHO-5 scale consists of five items that cover a basic life perception of a dynamic state of well-being. Such items have been incorporated in the Euthymia Scale[15], that has been found to entail clinimetric validity and reliability[48]. The Symptom Questionnaire is a self-rating scale with 24 items referring to relaxation, contentment, physical well-being and friendliness, and 68 items referring to anxiety, depression, somatization and hostility-irritability[17]. Extensive clinical research has documented its sensitivity to change and ability to discriminate between different populations[45].

In their clinical practice, psychiatrists weigh positive affects to evaluate the overall severity and the characteristics of a disorder. For instance, in order to discriminate depression from sadness, psychiatrists look for instances of emotional well-being that interrupt depressed mood and for reactivity to environmental factors. Indeed, the DSM-5 requires the presence of depressed mood most of the day, nearly every day, for the diagnosis of major depression. Psychiatrists also weigh the intensity of positive emotions and their borders with elation and behavioral activation to determine the bipolar characteristics of a mood disorder. However, current formal assessment strategies fail to capture most of this information[49]. Table 2 outlines the Clinical Interview for Euthymia (CIE), that covers such missing areas. The first five items explore the contents of positive affects, as depicted by the WHO-5[47].

### Psychological well-being

There are several instruments to assess psychological well-being states and dimensions[45,46].

The PWB scales have been used extensively in clinical settings[6]. They encompass 84 items and six dimensions (environmental mastery, personal growth, purpose in life, autonomy, self-acceptance, and positive relations with others)[2]. The questionnaire, because of its length, may be problematic to use in a busy clinical setting. A shorter version, the 6-item part of the PsychoSocial Index[50,51], has been developed and submitted to clinimetric validation: it was found to be a sensitive measure of well-being, yet it does not allow differentiation of the various dimensions. A structured interview based on the PWB scales[2] has also been devised[14].

A 10-item self-rating scale, the Acceptance and Action Questionnaire (AAQ-II), is available to measure psychological flexibility[52,53]. Yet, flexibility is only one component of euthymia.

Further, both the PWB scales and derived indices and the AAQ-II provide assessment of the impaired and optimal levels, but do not yield information about excessive levels. Such information is included in the CIE (Table 2). Items 6 to 17 of the interview assess both polarities of psychological well-being dimensions developed by Jahoda[1] and measured by the PWB scales[2]. The interview also allows to collect information about flexibility, resilience and consistency (items 18 to 22).

**Table 2** The Clinical Interview for Euthymia (CIE)

**POSITIVE AFFECTS**

1. Do you generally feel cheerful and in good spirits? YES NO
2. Do you generally feel calm and relaxed? YES NO
3. Do you generally feel active and vigorous? YES NO
4. Is your daily life filled with things that interest you? YES NO
5. Do you wake up feeling fresh and rested? YES NO

**DIMENSIONS OF PSYCHOLOGICAL WELL-BEING**

***Environmental mastery***

6. In general, do you feel that you are in charge of the situation in which you live? YES NO
7. Are you always looking for difficult situations and challenges? YES NO

***Personal growth***

8. Do you have the sense that you have developed and matured a lot as a person over the years? YES NO
9. Do you often fail to understand how things go wrong and/or set standards that you are unable to reach? YES NO

***Purpose in life***

10. Do you enjoy making plans for the future and working to make them a reality? In doing this, do you get a sense of direction in your life? YES NO
11. Are you constantly dissatisfied with your performance? YES NO

***Autonomy***

12. Is it more important for you to stand alone on your own principles than to fit in with others? YES NO
13. Are you able to ask for advice or help if needed? YES NO

***Self-acceptance***

14. In general, do you feel confident and positive about yourself? YES NO
15. Do you have difficulties in admitting your own mistakes, and/or attribute all problems to other people? YES NO

***Positive relations with others***

16. Do you have many people who want to listen when you need to talk and share your concerns, that is, do you feel that you get a lot out of your friendships? YES NO
17. Do you tend to sacrifice your needs and well-being to those of others? YES NO

**FLEXIBILITY AND CONSISTENCY**

18. If you become sad, anxious or angry, is it for a short time? YES NO
19. Do you keep on thinking of negative experiences? YES NO
20. Are you able to adapt to changing situations? YES NO
21. Do you try to be consistent in your attitudes and behaviors? YES NO
22. Are you able to handle stress most of the times? YES NO

## Integration with psychiatric symptomatology

In most instances of diagnostic reasoning in psychiatry, the process ends with the identification of a disorder, according to a diagnostic system. Such a diagnosis (e.g., major depressive disorder), however, encompasses a wide range of manifestations, comorbidity, severity, prognosis and responses to treatment[54]. The exclusive reliance on diagnostic criteria does not reflect the complex situations that are encountered in clinical practice[54]. It needs to be integrated with positive affects and psychological well-being, as well as with a broad range of further elements, including stress, lifestyle, subclinical symptoms, illness behavior and social support, in a longitudinal perspective[54].

This approach is in line with the traditional psychopathological assessment, as outlined by M. Roth[55]: "looking before and after" into the lives of patients, considering the "stressful life circumstances that have surrounded the onset of illness, the premorbid personality and its Achilles heels, the historical record of the patient's development, adjustment in childhood, the relationship with parents, sexual life within and out of marriage, his achievements and ambitions, his interpersonal relationships, his adaptation in various roles and the strength or brittleness of his self-esteem"[55].

Two technical steps may facilitate the integration of the assessments of psychological well-being and distress.

The first technical step involves the clinimetric use of macro-analysis[42,54,56]. This method starts from the assumption that in most cases of mental disorders there are functional relationships with other more or less clearly defined problem areas, and that the targets of treatment may vary during the course of disturbances. For instance, let us consider the case of a woman with a recurrent major depressive disorder whose current episode has only partially remitted (see Figure 2). Clinical interviewing focused on symptoms may disclose the presence of residual symptoms (e.g., sadness, diminished interest in things, guilt, irritability), problems in the family (e.g., interpersonal frictions with her mother, recurrent thoughts regarding the loss of her father two years before) and unsatisfactory interpersonal relationships (e.g., repeated failures in romantic relationships). Clinical interviewing focused on euthymia may disclose low levels of autonomy (e.g., lack of assertiveness in many situations) and personal growth (e.g., strong feelings of dissatisfaction with her life and a sense of stagnation), and low self-acceptance (e.g., dissatisfaction with herself). As depicted in Figure 2, macro-analysis helps to identify the main problem areas in this specific situation.

Macro-analysis can be supplemented by micro-analysis, which may consist of dimensional measurements, such as observer- or self-rating scales to assess positive affects and psychological well-being[42,54,56]. The choice of these instruments is dictated by the clinimetric concept of incremental validity[54]: each aspect of psychological measurement should deliver a unique increase in information in order to qualify for inclusion.

The second technical step requires reference to the staging method, whereby a disorder is characterized according to severity, extension and longitudinal development[57,58]. The clinical meaning linked to the presence of dimensions of psychological well-being varies according to the stage of development of a disorder, whether prodromal, acute, residual or chronic[54]. Further, certain psychotherapeutic strategies can be deferred to a residual stage of psychiatric illness, when state-dependent learning has been improved by the use of medications[59]. The planning of treatment thus requires determination of the symptomatic target of the first line approach (e.g., pharmacotherapy), and tentative identification of other areas of concern to be addressed by subsequent treatment (e.g., psychotherapy)[59].

## PSYCHOTHERAPEUTIC TECHNIQUES

Every successful psychotherapy, regardless of its target, is likely to improve subjective well-being and to reduce symptomatic distress[60]. Many psychotherapeutic techniques aimed to increase psychological well-being have been developed, although only a few have been tested in clinical settings[61-63].

A specific psychotherapeutic strategy has been developed according to Jahoda's concept of euthymia[1]. Well-being therapy (WBT) is a manualized, short-term psychotherapeutic strategy that emphasizes self-observation, with the use of a structured diary, homework and interaction between patient and therapist[14,20,64]. It can be differentiated from positive psychology

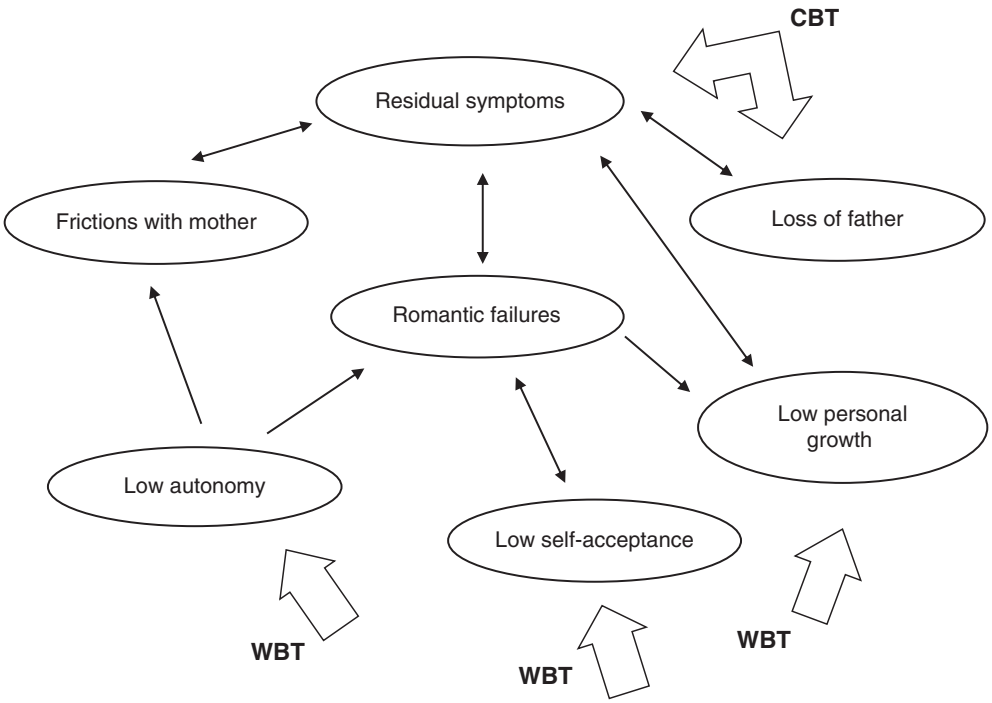


**Figure 2** Macro-analysis of a partially remitted patient with recurrent major depressive disorder with therapeutic targets. CBT – cognitive behavior therapy, WBT – well-being therapy

interventions[62] on the basis of the following features: a) patients are encouraged to identify episodes of well-being and to set them into a situational context; b) once the instances of well-being are properly recognized, the patient is encouraged to identify thoughts and beliefs leading to premature interruption of well-being (automatic thoughts), as is performed in cognitive behavior therapy (CBT) but focusing on well-being rather than distress; c) the therapist may also reinforce and encourage activities that are likely to elicit well-being; d) the monitoring of the course of episodes of well-being allows the therapist to identify specific impairments or excessive levels in well-being dimensions according to Jahoda's conceptual framework[1]; e) patients are not simply encouraged to pursue the highest possible levels of psychological well-being in all dimensions, as is the case in most positive psychology interventions, but also to achieve a balanced functioning[15].

Another psychotherapeutic strategy intended to increase psychological well-being is mindfulness-based cognitive therapy (MBCT)[65], which is built on the Buddhist philosophy of a good life. Its main aim is to reduce the impact of potentially distressing thoughts and feelings, but it also introduces techniques such as mindful, non-judgmental attention and mastery, and pleasure tasks that may be geared to a good life[66]. However, the good life that is strived for is a state involving detachment, as portrayed by Epicurus, and not necessarily euthymia, as depicted by Plutarch.

Acceptance and commitment therapy (ACT)[67] is aimed to increase psychological flexibility[53]. It consists of an integration of behavioral theories of change with mindfulness and acceptance strategies. Unlike WBT, ACT argues that attempts at changing thoughts can be counterproductive, and encourages instead awareness and acceptance through mindfulness practice.

There are also further psychotherapeutic approaches, such as Padesky and Mooney's strengths-based CBT[68] and forgiveness therapy[69], that have been suggested to increase well-being, but await adequate clinical validation[66].

## APPLICATIONS

The pursuit of euthymia in a clinical setting cannot be conceived as a therapy for specific mental disorders, but as a trans-diagnostic strategy to be incorporated in a therapeutic plan. Psychotherapeutic interventions aimed at psychological well-being are not suitable for application as a first line treatment of an acute psychiatric disorder[20,64]. However, most patients seen in clinical practice have complex and chronic disorders[54]. It is simply wishful thinking to believe that one course of treatment will be sufficient for yielding lasting and satisfactory remission. The use of psychotherapeutic strategies aimed at euthymia should thus follow clinical reasoning and case formulation facilitated by the use of macro-analysis and staging.

The treatment plan should be filtered by clinical judgment taking into consideration a number of clinical variables, such as the characteristics and severity of the psychiatric episode, co-occurring symptomatology and problems (not necessarily syndromes), medical comorbidities, patient's history, and levels of psychological well-being[54]. Such information should be placed among other therapeutic ingredients, and will need to be integrated with patient's preferences[70].

In the following sections, we illustrate a number of applications of strategies for enhancing and/or modulating psychological well-being. All these indications should be seen as tentative since, even when efficacy is supported by randomized controlled trials, the specific role of strategies modulating well-being in determining the outcome cannot be elucidated with certainty, because they are incorporated within more traditional approaches and a dismantling analysis is rarely implemented.

### Relapse prevention

In 1994, a randomized controlled trial introduced the sequential design in depression[71]. Depressed patients who had responded to pharmacotherapy were randomly assigned to CBT or to clinical management, while antidepressant medications were tapered and discontinued. This design was subsequently used in a number of randomized controlled trials and was found to entail significant benefits in a meta-analysis[72].

The sequential model is an intensive, two-stage approach, where one type of treatment (psychotherapy) is applied to improve symptoms which another type of treatment (pharmacotherapy) was unable to affect. The rationale for this approach is to use psychotherapeutic strategies when they are most likely to make a unique and separate contribution to patient's well-being and to achieve a more pervasive recovery by addressing residual symptomatology. The sequential design is different from maintenance strategies for prolonging clinical responses obtained by therapies in the acute episodes, as well as from augmentation or switching strategies addressing lack of response to the first line of treatment[71,72].

Three independent randomized controlled trials using the sequential combination of cognitive therapy and WBT were performed in Italy[73,74], Germany[75] and the US[76]. In other trials that took place in Canada[77] and the Netherlands[78], some principles of WBT were used in addition to standard cognitive therapy. Further, there have been several investigations[79-87] in which MCBT was applied to the residual stage of depression after pharmacotherapy.

From the available studies, we are unable to detect whether the pursuit of psychological well-being was a specific effective ingredient and what was the mechanism decreasing the likelihood of relapse. Nonetheless, the clinical results that have been obtained are impressive, and the sequential model seems to be a strategy that has enduring effects in the prevention of the vexing problem of relapse in depression. It is conceivable, and yet to be tested, that similar strategies may involve significant advantages in terms of relapse rates also in other psychiatric disorders.

### Increasing the level of recovery

The studies that used a sequential design clearly indicated that the level of remission obtained by successful pharmacotherapy

could be increased by a subsequent psychotherapeutic treatment[72]. Clinicians and researchers in clinical psychiatry often confound response to treatment with full recovery[9]. A full recovery can be reached only through interventions which facilitate progress toward restoration or enhancement of psychological well-being[1].

In a randomized controlled trial, patients with mood or anxiety disorders who had been successfully treated by behavioral (anxiety disorders) or pharmacological (mood disorders) methods were assigned to either WBT or CBT for residual symptoms[18]. Both WBT and CBT were associated with a significant reduction of those symptoms, but a significant advantage of WBT over CBT was detected by observer-rated methods. WBT was associated also with a significant increase in PWB scores, particularly in the personal growth scale[18].

A dismantling study in generalized anxiety disorder[19] suggested that an increased level of recovery could indeed be obtained with the addition of WBT to CBT. Patients were randomly assigned to eight sessions of CBT, or to CBT followed by four sessions of WBT. Both treatments were associated with a significant reduction of anxiety. However, significant advantages of the CBT/WBT sequential combination over CBT were observed, both in terms of symptom reduction and psychological well-being improvement[19].

While the clinical benefits of WBT in increasing the level of recovery have been documented in depression[64] and generalized anxiety disorder[19], this appears to be a possible target for a number of other mental health problems. Indeed, the issue of personal growth is attracting increasing interest in psychoses[88], and a role for WBT in improving functional outcomes as an additional ingredient to CBT in psychotic disorders has been postulated[89].

## Modulating mood

WBT has been applied in cyclothymic disorder[90], a condition that involves mild or moderate fluctuations of mood, thoughts and behavior without meeting formal diagnostic criteria for either major depressive disorder or mania.

Patients with cyclothymic disorder were randomly assigned to the sequential combination of CBT and WBT or clinical management. At post-treatment, significant differences were found in outcome measures, with greater improvements in the CBT/WBT group. Therapeutic gains were maintained at 1- and 2- year follow-up.

The results thus indicated that WBT may address both polarities of mood swings and is geared to a state of euthymia[15]. Can the target of euthymia decrease vulnerability to relapse in bipolar spectrum disorders[91]? This is an important area that deserves specific studies.

## Treatment resistance

A considerable number of patients fail to respond to appropriate pharmacotherapy and/or psychotherapy[54]. In a randomized controlled trial, MBCT was compared to treatment-as-usual (TAU) in treatment-resistant depression[92]. MBCT was significantly more efficacious than TAU in reducing depression severity, but not the number of cases who remitted.

A subsequent study[93] investigated the effectiveness of MBCT + TAU versus TAU only for chronic, treatment-resistant depressed patients who had not improved during not only previous pharmacotherapy but also psychological treatment (i.e., CBT or interpersonal psychotherapy). At post-treatment, MBCT + TAU had significant beneficial effects in terms of remission rates, quality of life, mindfulness skills, and self-compassion, even though the intent to treat (ITT) analysis did not reveal a significant reduction in depressive symptoms.

A number of case reports have suggested that WBT may provide a viable alternative when standard cognitive techniques based on monitoring distress do not yield any improvement or even cause symptomatic worsening in depression, panic disorder, or anorexia nervosa[64]. These data are insufficient to postulate a role for psychotherapies enhancing or modulating psychological well-being in these patient populations, yet this approach may yield new insights into this area.

## Suicidal behavior

The relationship between future-directed thinking (prospection) and suicidality has been recently analyzed[94], and a potential innovative role for well-being enhancing psychotherapies has been postulated. Working on dimensions such as purpose in life may counteract suicidal behavior. Indeed, positive mental health was found to moderate the association between suicidal ideation and suicide attempts[95].

An issue that is not sufficiently appreciated is also the experience of mental pain that many suicidal patients may present. ACT was found to significantly reduce suicidal ideation as well as mental pain compared to relaxation in adult suicidal patients[96].

## Discontinuing psychotropic drugs

Psychotropic drug treatment, particularly when it is protracted in time, may cause various forms of dependence[97]. Withdrawal symptoms do not necessarily wane after drug discontinuation and may build into persistent post-withdrawal disorders[98]. These symptoms may constitute a iatrogenic comorbidity that affects the course of illness and the response to subsequent treatments[97].

Discontinuation of antidepressant medications such as selective serotonin reuptake inhibitors, duloxetine and venlafaxine represents a major clinical challenge[99,100]. A protocol based on the sequential combination of CBT and WBT in post-withdrawal disorders has been devised[101] and tested in case reports[102].

## Post-traumatic stress disorder

There has been growing awareness of the fact that traumatic experiences can also give rise to positive developments, subsumed under the rubric of post-traumatic growth[103]. Positive changes can be observed in self-concept (e.g., new evaluation of one's strength and resilience), appreciation of life opportunities, social relations, hierarchy of values and priorities, spiritual growth.

Well-being enhancing strategies may be uniquely suited for facilitating the process of post-traumatic growth. Two cases have been reported on the use of WBT, alone or in sequential combination with exposure, for overcoming post-traumatic stress disorder, with the central trauma being discussed only in the initial history-taking session[104].

### Improving medical outcomes

The need to include consideration of psychosocial factors (functioning in daily life, quality of life, illness behavior) has emerged as a crucial component of patient care in chronic medical diseases[37]. These aspects also extend to family caregivers of chronically ill patients and health providers[36]. There has also been recent interest in the relationship between psychological flexibility and chronic pain[105]. It is thus possible to postulate a role for psychotherapeutic interventions modulating psychological well-being in the setting of medical diseases, to counteract the limitations and challenges induced by illness experience. The process of rehabilitation, in fact, requires the promotion of well-being and changes in lifestyle as primary targets of intervention[106].

In recent years, there has been increasing evidence suggesting that stressful conditions may elicit a pattern of conserved transcriptional response to adversity (CTRA), in which there is an increased expression of pro-inflammatory genes and a concurrent decreased expression of type 1 interferon innate antiviral response and IgG antibody synthesis[107]. Such patterns have been implicated in the pathophysiology of cancer[108] and cardiovascular diseases[109]. Frederickson et al[110] reported that individuals with high psychological well-being presented reduced CTRA gene expression, which introduces a potential protective role for psychological well-being in a number of medical disorders.

### Improving health attitudes and behavior

Unhealthy lifestyle (e.g., smoking, physical inactivity, excessive eating) is a major risk factor for many of the most prevalent medical and psychiatric diseases[36,111]. Lifestyle modification focused on weight reduction, increased physical activity, and dietary change is recommended as first line therapy in a number of disorders, yet psychological distress and low levels of well-being are commonly observed among patients with chronic conditions and represent important obstacles to behavioral change[36].

It has been argued that enduring lifestyle changes can only be achieved with a personalized approach that targets psychological well-being[112]. As a result, strategies pointing to euthymia need to be tested in lifestyle interventions and in the prevention of mental and physical disorders.

## CONCLUSIONS

Customary clinical taxonomy and evaluation do not include psychological well-being, which may demarcate major prognostic and therapeutic differences among patients who otherwise seem to be deceptively similar since they share the same diagnosis. A number of psychotherapeutic strategies aimed to increase positive affects and psychological well-being have been developed. WBT, MBCT and ACT have been found effective in randomized controlled clinical trials.

An important characteristic of WBT is having euthymia as a specific target. This perspective is different from interventions that are labelled as positive but are actually distress oriented. An additional novel area in psychotherapy research can ensue from exploring euthymia as a characteristic of successful psychotherapists, as the Greek verb equivalent implies.

The evidence supporting the clinical value of the pursuit of euthymia is still limited. However, the insights gained may unravel innovative approaches to the assessment and treatment of mental disorders, with particular reference to decreasing vulnerability to relapse, increasing the level of recovery, and modulating mood.

These fascinating developments should be welcome by all those who are disillusioned with the current long-term outcomes of mental disorders. These outcomes may be unsatisfactory not because technical interventions are missing, but because our conceptual models, shifted on the side of psychological dysfunction, are inadequate.

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