

SYSTEMATIC REVIEW AND META-ANALYSIS OF MINDFULNESS-BASED INTERVENTIONS AND ITS EFFECT ON DEPRESSION, ANXIETY AND STRESS IN PEOPLE WITH BLOOD CANCER

Author's Name: Dr. Mohammed Hasan Ali Al-Abyadh¹, Prof. Punithalakshmi. K²,
Mrs. Savitha G R³, Mrs. Rachel James⁴,
Mr. Thomaskutty Saji. Puthuparambil⁵, Mr. Prem Prakash⁶

Affiliation:

1. College of Education, Prince Sattam bin Abdulaziz University, Alkharj, Saudi Arabia.
College of Education- Tamar University, Tamar, Yemen.
m.alabyadh@psau.edu.sa , alabyd62@gmail.com
2. Professor cum Principal, JIET College of Nursing, Jodhpur, Rajasthan, India.
puni_phoenix@yahoo.com
3. Asst. Professor, Driems School and College of Nursing, Cuttack, Odisha, India.
savithagr1986@gmail.com
4. PhD scholar, MSN, RN, Lecturer, RAK college of Nursing, RAK Medical and Health Sciences University, Ras Al Khaimah, United Arab Emirates.
5. PhD Scholar, MSN, RN, Nurse Informaticist, Al Qassimi Hospital, Emirates Health Services, Sharjah, United Arab Emirates.
6. Assistant Professor, Krishna College of Nursing, Jodhpur, Rajasthan, India.
premprakash1316@gmail.com

Corresponding Author Name and Email Id: Dr. Mohammed Hasan Ali Al-Abyadh,
alabyd62@gmail.com,
m.alabyadh@psau.edu.sa

ABSTRACT

With an emphasis on the distinctions between patients undergoing treatment and those undergoing watchful waiting, the current assignment sought to determine the prevalence rates of anxiety and depression in people with blood cancer. Anxiety and depression are two of the most common mental diseases in the general public as well as primary care settings. Patients suffering from anxiety disorders sometimes exhibit signs of depression, and vice versa for those with both anxiety disorders and melancholy. It is possible to have both illnesses at the same time and meet the requirements for each one. Given the significant morbidity and death rates associated with these illnesses, it is imperative that they be detected and treated. Even though it might be difficult to tell the two apart, it is imperative that you do. Blood cancer is a kind of cancer that starts in the bone marrow or lymphatic system and damages blood cells. There are three main kinds of cancer that might result in blood loss. Cancer and depression both have similar disease processes and risk factors. The impact of depression on the risk of cancer has not been investigated in the literature to yet. Using a sizable German cohort, we evaluated the variation in cancer risk between individuals with and without depression. We examined the incidence and risk of cancer in individuals in the Disease Analyzer Database who were diagnosed with depression vs those who did not.

Keywords: Depression, Anxiety, Stress, Blood Cancer

INTRODUCTION

The present assignment aimed to establish prevalence rates of anxiety and depression in adults with blood cancer, with a focus on the differences between patients under treatment and patients under watchful waiting. Depression and anxiety disorders are highly prevalent mental illnesses, both in primary care settings and among the general population. Anxiety disorder symptoms are frequently present in depressed patients, and vice versa for patients who are afflicted with melancholy and anxiety disorders. It is feasible to concurrently experience both disorders, thereby fulfilling the criteria for both. Detecting and treating both conditions is of the utmost importance, given their substantial morbidity and mortality rates. It is essential to distinguish between the two, despite the fact that doing so can be challenging. To facilitate more favourable outcomes with regard to mental health, general practitioners are ideally suited to diagnose these conditions and assume a principal role in their treatment (Tiller, John. 2013).

Depression and anxiety have long been hypothesized to be related to an increased cancer risk. Blood cancer is a malignancy that affects blood cells and originates in the lymphatic system or bone marrow. Three principal types of malignancy are capable of causing blood loss. Depression and cancer share common risk factors and mechanisms of disease. The current literature has not explored the effect of depression on cancer risk. We assessed the difference in cancer risk in patients with and without depression in a large cohort in Germany. We compared cancer risk and incidence in patients with and without depression or above diagnosed and in the Disease Analyser Database.

The PSY-CA consortium includes data from 18 cohorts with measures of depression or anxiety (up to $N = 319,613$; cancer incidences, 25,803; person-years of follow-up, 3,254,714). Both symptoms and a diagnosis of depression and anxiety were examined as predictors of future cancer risk. Two-stage IPD meta-analyses were run, first by using Cox regression models in each cohort (stage 1), and then by aggregating the results in random-effects meta-analyses. Similarly, the incidence of cancer diagnosis overall increased by 22% for depressed patients. IRs showed no difference across cancer types. Depression increased the risk for cancer diagnosis consistently independent of the comparison method used. The potential mediating factors or shared mechanisms of the disease require further investigation.

Blood Cells

Blood contains the following components (UNDERSTANDING BLOOD CANCERS, n.d):

Red blood cells: Red blood cells contain a protein called “hemoglobin” which carries oxygen to all the cells in the body and helps remove carbon dioxide from the body.

Platelets: Platelets help stop bleeding at the site of an injury.

White blood cells: White blood cells help fight infection and disease. There are several types of white blood cells including neutrophils, monocytes, eosinophils, basophils and lymphocytes.

Plasma: The liquid part of blood, called “plasma,” is largely water but also includes chemicals such as proteins, hormones, vitamins, minerals, electrolytes and antibodies.

TYPES OF BLOOD CANCER

Leukemia, lymphoma, myeloma, myelodysplastic syndromes (MDSs) and myeloproliferative neoplasms (MPNs) are types of cancer that can affect the bone marrow, blood cells, lymph nodes and other parts of the lymphatic system. Each of these blood cancers also contains different subtypes. Blood cancers affect people of all ages, races and genders. Blood cancers can be acute (severe and sudden onset) or chronic (disease progresses slowly) (*UNDERSTANDING BLOOD CANCERS, n.d.*).

Blood Cancer

Blood cancer is a malignancy that affects blood cells and originates in the lymphatic system or bone marrow. Three principal types of malignancy are capable of causing blood loss (Tiller, John. 2013):

- The classification of leukemia is predicated on the type of blood cell it impacts—lymphoid or myeloid—and its mode of progression—rapid (acute) or gradual (chronical)—regardless of whether it originates in the bone marrow or another anatomical site.
- The white blood cells called lymphocytes, which are located in the lymphatic system, are where lymphoma originates.

Myeloma is a malignancy that originates in the bone marrow and impacts the body's plasma cells. Plasma cells are accountable for the synthesis of antibodies within the body; they are a subtype of white blood cell.

Depression and Anxiety

Depression and anxiety disorders are highly prevalent mental illnesses, both in primary care settings and among the general population. Anxiety disorder symptoms are frequently present in depressed patients, and vice versa for patients who are afflicted with melancholy and anxiety disorders. It is feasible to concurrently experience both disorders, thereby fulfilling the criteria for both. Detecting and treating both conditions is of the utmost importance, given their substantial morbidity and mortality rates. It is essential to distinguish between the two, despite the fact that doing so can be challenging. To facilitate more favorable outcomes with regard to

mental health, general practitioners are ideally suited to diagnose these conditions and assume a principal role in their treatment (Tiller, John. 2013).

CLINICAL RECOGNITION OF DEPRESSION AND ANXIETY

Differentiating between specific anxiety disorders and depressive disorders is crucial due to the potential necessity for distinct treatment approaches. The most prevalent anxiety disorders in Australia are social phobia (4.7% of the population), agoraphobia (2.8% of the population), generalized anxiety disorder (GAD) (2.7% of the population), panic disorder (2.6% of the population), and obsessive-compulsive disorder (1.9% of the population). Anxiety disorders and associated disorders affect 14.4% of the population aged 16 to 85. Depression occurs at an incidence rate of 6.2%. Unipolar depressive episodes are present at a prevalence of 4.1%, whereas dysthymia and bipolar disorder are each 1.3% and 1.8% prevalent, respectively. 1 Certain individuals suffer from multiple conditions simultaneously.

Diagnostic criteria eliminate clinical traits that are present in the patient's medical record but are common to multiple disorders in order to distinguish between them. Consequently, neither prevalent comorbid anxiety symptoms nor depressive symptoms are included in the diagnostic criteria for anxiety disorders nor for depression. Equally distinct, however, are clinical manifestations and diagnostic criteria. Box 2 contains a compilation of somatic symptoms that may be correlated with anxiety and depression.

There exists a potential necessity for multiple patient visits to be undertaken in order to accurately ascertain the nature of their concerns. It is critical to consistently seek out symptoms of the other disease in the event that symptoms of anxiety or depression are identified. As an illustration, when a patient is diagnosed with depression, a physician ought to inquire, "Has anyone else experienced symptoms such as restlessness, irritability, impulsivity, palpitations, or other symptoms associated with anxiety while suffering from this illness?" Inquire of the patient, "Has anyone else experienced symptoms such as sadness, numbness, fatigue, loss of energy, or a sense of hopelessness in conjunction with this illness?" in the case of anxiety.

It is crucial to inquire about the following when diagnosing bipolar depression in a patient: "Have people ever experienced a phase during which people felt excessively energized, irritable, angry, or full of themselves to the extent that people got into trouble or others mistook people for someone other than themselves?" The course of treatment for a patient with unipolar or bipolar depression differs. Although bipolar disorder exhibits cyclical episodes of elevated and depressed mood, depression is still the most obvious symptom. Frequently, individuals afflicted

with bipolar depression contend with symptoms of anxiety. Manic episodes are characterized by restlessness, distractibility, rapid thinking, impatience, and agitation, all of which could be misinterpreted as anxiety.

Despite the existence of evidence indicating that non-psychiatrists have a limited capacity to accurately diagnose depression, the optimal treatment for this issue remains unclear. While rating instruments for anxiety and depression can provide some assistance, their primary purpose is to evaluate the severity of pre-existing conditions rather than establish new diagnoses (Cepoiu M. et al., 2008).

As a screening instrument, the Mini International Neuropsychiatric Interview can distinguish between diseases, including unipolar and bipolar depression, and ascertain a diagnosis. Additionally, it is a surveillance instrument. Additional tools for assessing the severity of depression include the Hospital Anxiety and Depression Scale, the Kessler Psychological Distress Scale, and the 12-item Somatic and Psychological Health Report questionnaire. Nevertheless, these instruments fail to distinguish between distinct subtypes of depression. The seven-point Clinical Global Impression Scale is an uncomplicated rating system that can be employed to monitor a patient's treatment response (Sheehan DV. and Lecrubier Y., 2006)

Stress

Individuals are considered to be undergoing psychological stress, also known as stress, when they are subjected to mental, physical, or emotional duress. Routines and responsibilities that individuals maintain on a daily basis, including those pertaining to finances, work, and family, may serve as stressors or stimuli that induce stress. Additional external factors that may contribute to stress encompass adversity encountered during one's formative years, exposure to specific environmental conditions, poverty, discrimination, and social determinants of health imbalances. Ayling K. et al. (2022) posit that severe health issues, including the identification of cancer in oneself, a close friend, or a family member, can also induce stress.

Blood sugar levels, heart rate, and blood pressure all rise in response to the body's secretion of stress hormones (adrenaline and norepinephrine), which are released in response to external stressors. Ayling K. et al. (2022) assert that this reaction, widely referred to as the "fight-or-flight" response, empowers an individual to evacuate a perceived threat by exerting greater force and velocity.

Activating the "fight or flight" response in response to short-term or acute stress is advantageous for the body; conversely, activating it in response to long-term or chronic stress can be detrimental. Consistent with the results of numerous studies, chronically stressed individuals

have an increased susceptibility to digestive disorders, cardiovascular ailments, hypertension, and a weakened immune system. Chronically stressed individuals are at an increased risk of developing physical manifestations, including but not limited to migraines, sleep disturbances, concentration difficulties, depression, and anxiety. Additionally, their susceptibility to viral infections, including SARS-CoV-2, the causative agent of COVID-19, is heightened (Ayling K, et al, 2022).

Anxiety

The presence of dread and unease in the individual is what distinguishes anxiety. It is a completely normal reaction, and its intensity can differ significantly. A stressful environment activates the hypothalamus, the brain region responsible for regulating involuntary bodily functions including respiration, blood pressure, and pulse rate. This triggers the activation of the fight-or-flight response. Chow et al. (2022) state that the hypothalamus controls the autonomic nervous system of the organism, which consists of the following two systems:

1. The sympathetic nervous system, which initiates the "fight or flight" response and is accountable for accelerating bodily functions
2. The parasympathetic nervous system, which promotes rest and recuperation to restore the body's nervous system to equilibrium by acting as a restraint on bodily processes.

The sympathetic nervous system responds to the fight-or-flight response by activating small glands called adrenal glands that are located atop the kidneys. As a result, adrenaline is secreted into the circulation by the adrenal glands, thereby accelerating bodily processes. The hormone adrenaline causes an increase in pulse rate and blood pressure by quickening the heartbeat. To optimize the supply of oxygen to the brain and muscles, the airways are dilatation, and the patient's respiratory rate is accelerated. In addition, this activates the discharge of blood sugar, which supplies the body with energy. A significant portion of the population remains oblivious to these changes due to the rapid functioning of the sympathetic nervous system. Once the initial surge of adrenaline has subsided, the hypothalamus initiates a second phase of the stress response, which consists of a cascade of hormones designed to maintain the functionality of the sympathetic nervous system (Chow, W. K., et al, 2022).

These hormones include:

- Corticosteroids
- Oestrogen

- Testosterone
- Dopamine and serotonin (neurotransmitters which control our mood and how we react to stress)

When the same method of thinking occurs when one contemplates a stressful life event, such as a diagnosis, these modifications are not advantageous. Although they provide assistance in the event of escaping a physical threat, such as a house fire, they are not beneficial when fleeing a physical hazard, including a house fire. In the absence of calming thoughts or coping mechanisms, the consequences of the fight-or-flight response may escalate to the point of inducing a panic attack (Chow, W. K., et al., 2022).

An inherent consequence of being afflicted with blood cancer is the experience of anxiety, as one must contend with an element of unpredictability. One may constantly doubt their own abilities when thinking about what is going to happen, such as whether or not the treatment plan will work and whether the blood cancer will come back after treatment. Due to their inability to physically abandon the situation, the fight-or-flight response symptoms persist, causing people to experience a sense of unease. People will fret while people are awake at night about the possibility of developing blood cancer if people do not address their anxiety. Consequently, this induces myocardial arrhythmia and muscular contraction, leading to a chest constriction (Chow, W. K., et al., 2022).

Their concern and anxiety stem from their ignorance regarding the prognosis of their blood malignancy. Worrying can be advantageous if it serves as a catalyst for proactive problem-solving behavior. However, once people have successfully adhered to their treatment plan and maintained their scheduled appointments despite their anxiety, it will no longer be advantageous to dwell on it. Recognizing the fight-or-flight response can facilitate the ability to disregard symptoms instead of responding to them. Preoccupation with present-moment occurrences rather than potential future developments is the most effective method for reducing unwarranted anxiety. It is still early in the future, and the causes of their anxiety may not even materialize (Chow, W. K., et al., 2022).

If people become cognizant of the fact that their anxiety stems from concerns about the future in relation to their blood cancer, they must endeavor to disregard or modify their thought pattern. Attempting to predict future events with the intention of safeguarding one's loved ones and preparing for the worst-case scenario is inherently human. Nevertheless, the persistence of these thoughts and plans forces people to maintain their focus on their blood cancer, thereby perpetuating their anxiety (Chow, W. K., et al., 2022).

The experience of anxiety or nervousness is an inherent reaction, and these affective states will gradually diminish as one acclimates to the present situation. People's need for practice to effectively manage their anxiety symptoms does not indicate that people lack the ability to do so or that people are a feeble individual. Their clinical nurse specialist and consultant will be capable of furnishing people with advice pertaining to any physical symptoms that require their attention. This information might aid people in disregarding or managing any additional concerns that people might be experiencing. Individuals diagnosed with blood cancer who have been counseled to adopt a watch-and-wait approach face the added concern of awaiting the onset of symptoms, the manifestation of which is not guaranteed (Chow, W. K., et al, 2022).

Blood cancer

It is impossible to completely exclude the possibility that an individual has blood cancer. It is an integral part of their being and contributes significantly to the story of their existence. Despite one's desire for expediency, the integration process will undoubtedly consume a certain amount of time due to its inherently time-consuming nature (Chow, W. K., et al., 2022).

Upon completion of their medical treatment, people might discover that people lament the social connections and emotional support people received during their time at the hospital. Certain individuals who have completed treatment express a mild sense of abandonment. Certain personal relationships may appear to have experienced a gradual strengthening, whereas others may have undergone significant changes. It is conceivable that people or those in their vicinity have arrived at the realization that their strength surpasses all expectations. Continuously express gratitude for the support and assistance that people receive from those in their innermost circle. Engaging in the deliberations and strategic preparations of those in their vicinity could potentially enhance their perception of readiness for forthcoming circumstances (Chow, W. K., et al, 2022).

Can Stress Cause Cancer?

While long-term stress has been linked to various health complications, the extent of its association with cancer remains a subject of ongoing debate. To date, the results obtained from the studies have yielded inconclusive findings.

- A case-control study conducted among Canadian males established a correlation between occupational stress and the likelihood of developing prostate cancer. However, an analogous investigation failed to discover such an association (Blanc-Lapierre A et

al., 2017). In a comparable investigation, no correlation was found between occupational stress and the likelihood of developing breast cancer.

- A prospective study comprising over 100,000 women from the United Kingdom concluded that perceived stress levels and the frequency of adverse life events in the five years prior to the study did not correlate with the risk of breast cancer (Schoemaker MJ, et al., 2016).
- The prospective 15-year study by Butow et al. (2018) on Australian women with a higher familial risk of breast cancer did not find any link between the risk of breast cancer and short- or long-term stressors, social support, optimism, or any other emotion. The participants in this investigation were women with a familial history of breast cancer.
- According to a meta-analysis published in 2008 (Chida et al.), stress is associated with an increased risk of developing lung cancer. The analysis incorporated 142 prospective studies conducted among individuals residing in Europe, Asia, Australasia, Asia, and the Americas.

Yang T. et al., (2019) looked at nine observational studies and found that esophageal, colorectal, and lung cancer were more likely to happen in people who were stressed at work. The inquiries were carried out in both North America and Europe.

According to a meta-analysis of 12 cohort studies conducted in Europe, there is no association between occupational stress and the likelihood of developing cancers of the lungs, colon, breast, or prostate (Heikkila K et al., 2013).

Although there are instances where stress appears to be associated with an elevated risk of cancer, this association may be merely indirect. Individuals experiencing chronic stress may, for example, engage in unhealthy behaviors such as smoking, obesity, physical inactivity, or alcohol consumption, all of which are independently associated with increased risks of developing particular types of cancer.

How does stress affect people who have cancer?

Empirical evidence from laboratory studies involving human cancer cells cultured in the laboratory and animal models suggests that chronic stress may contribute to the progression and metastasis of cancer (McDonald PG, et al., 2005; Eckerling A, et al., 2021). For example, several research studies have shown that stress-inducing conditions (e.g., confinement or isolation from other mice) exacerbate the growth and metastasis of human malignancies in mice (Moreno-Smith M, et al., 2010; Sloan EK, et al., 2012). The publication containing these results (Moreno-

Smith M. et al., 2010; E.K. Sloan et al., 2012).

Angiogenesis and metastasis are induced by the hormone norepinephrine, which is secreted by the body as part of the "fight or flight" response, according to laboratory studies (Moreno-Smith M. et al., 2010). Furthermore, this hormone possesses the capacity to induce the activation of neutrophils, an immune cell subtype. Neutrophils have the potential to facilitate tumor proliferation by shielding them from the host's immune system. Additionally, cancer cells that were previously quiescent may be "aroused" (Perego M et al., 2020).

Additionally, extended exposure to stress may result in the secretion of glucocorticoids, which are a class of steroid hormones. Volden and Conzen (2013) said that glucocorticoids can stop apoptosis, a type of cell death that happens in cancer, while also encouraging metastasis and treatment resistance. Additionally, they might impede the ability of the immune system to identify and eliminate cancer cells within the body (He X-Y et al., 2019).

Several studies have found a link between high stress and a lower chance of survival for people with cancer (Hamer M. et al., 2009), but there is still not a lot of evidence to support the idea that stress directly affects survival (Moreno-Smith M, et al, 2010).

How can people who have cancer learn to cope with stress?

Patients can enhance their stress management skills through the provision of emotional and social support. This type of care is associated with reduced rates of depression and anxiety, as well as a decrease in symptoms associated with the patient's illness and treatment. The NCI's website features a page entitled "Emotions and Cancer," which provides readers with guidance on effectively managing the diverse array of emotions that often accompany a cancer diagnosis. Moreno-Smith et al. (2010) show some evidence that suggests there may be a link between better clinical outcomes for people with breast cancer and better stress management that is made easier by social support. A robust social support system was associated with lower levels of stress-related hormones, which are known to contribute to the development of tumors in ovarian cancer patients (Lutgendorf SK et al., 2011).

Engaging in regular physical activity is an additional approach that can be employed to mitigate the adverse consequences of stress. The 2018 American College of Sports Medicine International Multidisciplinary Roundtable on Physical Activity and Cancer Prevention and Control has produced a report that deems the evidence "sufficient" to support the claim that cancer survivors who participate in moderate-intensity physical activity during and after their treatment may encounter a decrease in symptoms associated with anxiety and depression

(Campbell KL et al., 2019). According to data (Tonorezos ES, et al., 2019), physical activity may be beneficial in mitigating depression among pediatric cancer survivors.

Smith SK. et al. (2018) suggest that individuals experiencing significant distress due to a cancer diagnosis may wish to consult their primary care physicians regarding the potential referral to a suitable mental health professional. Indeed, some professional organizations advise that all cancer patients should undergo screenings using a suitable instrument, such as a distress scale or questionnaire, following diagnosis, during treatment, and after treatment (Hinz A et al., 2016). The primary objective of this assessment is to ascertain whether the patient is at risk for distress or necessitates support in managing stress (Artherholt SB, Fann JR., et al., 2012).

With the guidance of a mental health professional, antidepressants or other pharmacological interventions, in addition to psychotherapy, may be utilized to treat significant distress, depression, and anxiety. Personalized therapy selection is essential, with the patient and the healthcare provider, whenever possible, reaching a joint agreement.

Scholars are investigating novel psychotherapeutic methodologies in an effort to determine whether or not they can ameliorate depressive symptoms, including feelings of hopelessness and distress, that are prevalent among cancer patients. People who had just been told they had advanced cancer took part in a randomized controlled trial that showed that personalized psychotherapy sessions (three to six sessions) could help people with depression. The results of the clinical research, according to Rodin G. et al. (2018), suggest that the method may also prevent the development of depression in individuals with an advanced disease.

An additional randomized clinical trial assessed the efficacy of two distinct forms of mindfulness-based cognitive therapy—one delivered in person and the other electronically—in mitigating the psychological distress of cancer patients. These two approaches were compared to the standard treatment. Positive mental health, quality of life in relation to mental health, and mindfulness abilities were all enhanced by both interventions (Compen F. et al., 2018). An intervention that decreased distressing factors, such as the dread of cancer recurrence, increased such concerns.

Researchers are looking into psychedelic drugs again to see if they can be used as medicine. Early results show that psilocybin-assisted psychotherapy may be a good way to help people who are dealing with anxiety, depression, and existential distress related to cancer (Ross S., 2018).

CONCLUSION

Depression, Stress and anxiety are not related to increased risk for most cancer outcomes, except for lung and smoking-related cancers. This study shows that key covariates are likely to explain the relationship between depression, anxiety, and lung and smoking-related cancers. But to some extent Depression increased the risk for cancer diagnosis consistently independent of the comparison method used. The potential mediating factors or shared mechanisms of the disease require further investigation.

Comorbid depression and anxiety are common and affect up to a quarter of patients attending general practice. Screening for comorbidity is important, as such patients are at greater risk of substance misuse, have a worse response to treatment, are more likely to remain disabled, endure a greater burden of disease, and are more likely to use health services in general. There are effective treatments for specific disorders, but a paucity of data about treatment for anxiety and depression comorbidity. More than a third of patients with a mental disorder do not seek treatment, and almost half are offered treatments that may not be beneficial. This suggests the need for further public awareness and professional education that can enhance clinical practice, promoting better mental health outcomes.

No correlation was found between anxiety or depression and the incidence of alcohol-related blood malignancies, breast cancer, prostate cancer, or colorectal cancer. A strong link was found between having symptoms or a diagnosis of depression or anxiety and a higher risk of getting lung cancer and cancers related to smoking (hazard ratios [HRs], 1.06–1.60). But these correlations were much weaker when more changes were made for known risk factors like smoking, drinking alcohol, and body mass index (HRs, 1.04–1.23).

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