Review

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Prolonged Psychological Conflicts and Their Contribution to Cancer Onset and Treatment Responsiveness: An Integrative Narrative Review

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Highlights

- This review investigates how prolonged psychological conflicts may increase oncological vulnerability through psychoneuroimmunological pathways
- Chronic emotional trauma, unresolved grief, and adverse childhood experiences are identified as key psychosocial co-factors in cancer onset and immune dysregulation
- Posttraumatic stress symptoms and emotional repression may impair treatment responsiveness and elevate the risk of recurrence
- An integrative psycho-oncological model is proposed, emphasizing trauma-informed care and early psychological screening in oncology settings.

Abstract

Psychological trauma and chronic stress are increasingly acknowledged as relevant contributors to the onset and progression of somatic illness, including cancer. This integrative narrative review examines the potential role of prolonged and unresolved psychological conflicts, such as early-life adversity, toxic relational dynamics, chronic grief, and emotional invalidation, in modulating oncological vulnerability. Drawing from the fields of psycho-oncology, psychoneuroimmunology, and developmental psychopathology, we outline the psychobiological mechanisms through which chronic stress may impair immune surveillance, dysregulate the hypothalamic–pituitary–adrenal (HPA) axis, and promote low-grade systemic inflammation. These alterations can increase susceptibility to oncogenic infections (e.g., persistent Human Papillomavirus (HPV), reduce the body's capacity to repair cellular damage, and contribute to tumorigenesis. We further discuss how trauma-related disorders, including posttraumatic stress disorder (PTSD), may negatively affect treatment adherence, reduce responsiveness to chemotherapy and immunotherapy, and increase cancer recurrence risk. Moreover, we introduce the model of trauma–cancer–retraumatization, highlighting how a cancer diagnosis can both reactivate unresolved psychological trauma and amplify emotional distress. Empirical studies suggest that trauma-informed psychotherapeutic interventions targeting emotional processing, attachment security, and perceived agency may improve both psychological well-being and clinical outcomes in oncology patients. Based on this

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evidence, we recommend integrating systematic screening for adverse childhood experiences (ACEs) and trauma history into cancer care pathways. Recognizing and addressing the hidden burden of psychological conflict in oncology may support a more holistic approach to cancer prevention, treatment, and survivorship.

Keywords: psycho-oncology; psychological trauma; chronic stress; PTSD; cancer vulnerability

Introduction

Cancer remains one of the leading causes of mortality worldwide, with its incidence steadily increasing over recent decades. According to data from the Global Cancer Observatory [1], more than 19 million new cases and nearly 10 million cancer-related deaths were reported in 2020, with this trend projected to continue. While advances in molecular biology and genetic oncology have elucidated many mechanisms underlying carcinogenesis, they do not fully account for the variability in disease onset, progression, and treatment responsiveness. This gap has spurred growing interest in psychosocial factors that may contribute to oncological vulnerability [2–4].

In this context, chronic stress, psychological trauma, unresolved relational conflicts, and maladaptive coping mechanisms have emerged as potential co-factors in both cancer etiology and patient treatment response. Integrating the psychological dimension into modern oncology addresses a pressing need: to understand the cancer patient holistically, encompassing biological, emotional, and relational experiences.

Carcinogenesis is a multifactorial biological process. Although genetic and cellular mechanisms are well-studied, the influence of chronic psychological distress remains insufficiently explored. Recent research increasingly highlights the role of prolonged psychological trauma in compromising immune surveillance and promoting tumor development—particularly via psychoneuroimmunological (PNI) pathways. PNI provides a scientific framework for examining the interplay between the nervous, endocrine, and immune systems under chronic stress. Bio-psycho-social models offer new paradigms for understanding cancer etiology [5].

Over the 20th century, medical perspectives on cancer evolved from a reductionist view—centered exclusively on biological dysfunctions—to integrative approaches that acknowledge the psychological and relational dimensions of illness. A historical study by Hitzer and León-Sanz [6] shows that, between 1920 and 1960 in Germany, cancer was increasingly interpreted not only as a somatic event but also as a reflection of the patient's emotional history. This conceptual shift was influenced by the rise of psychoanalysis, which introduced the notion that physical symptoms may serve as symbolic expressions of unconscious conflict [7].

Groddeck, one of the founders of psychosomatic medicine, famously described disease as a "letter from the unconscious," suggesting that the body expresses what the psyche refuses to recognize [8]. Later, Franz Alexander, through Chicago School, formulated the theory of specific conflict, positing that distinct emotional conflicts are linked to particular somatic responses. He categorized cancer among psychosomatic diseases when it occurred in patients with unresolved emotional trauma or rigid affective suppression [9].

In 1977, George L. Engel advanced this integrative trajectory by proposing the bio-psycho-social model, which emphasized that health and illness cannot be fully understood without reference to an individual's psychological and social context [10]. This model marked a paradigm shift in medical thinking, emphasizing complex interdependencies among biological, emotional, and social factors.

While these contributions emphasized clinical or symbolic interpretations of mind–body interactions, the historical-cultural perspective offered by Hitzer and León-Sanz [6] demonstrates how broader intellectual movements, expressionism, medical humanism, and shifting philosophical worldviews, shaped the reimagining of cancer as a reflection of psychological suffering.

Taken together, these conceptual developments support the current effort to explore links between chronic psychological conflict and oncogenesis. They provide a solid foundation for the

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hypothesis that prolonged trauma, unconscious stress, and unresolved intrapsychic conflict may influence not only cancer onset but also treatment responsiveness.

Justification of the Review Topic

Exploring the relationship between psychological conflicts and cancer is relevant from several perspectives: it provides an explanatory framework for the evolution of certain forms of cancer, opens up the possibility of personalized psychological interventions, supports the integration of mind-body therapies into medical practice and, last but not least, contributes to reducing the stigmatization of the disease and increasing the patient's quality of life. In recent decades, progress in understanding the etiology of cancer has led to the identification of genetic, epigenetic, immunological and environmental factors involved in the onset and evolution of the disease. However, there are still numerous cases in which the etiology remains incompletely explained by strictly biological models. In this context, more and more research highlights the fact that psychological variables – unresolved trauma, chronic stress or lingering emotional conflicts – can influence biological processes involved in carcinogenesis, such as inflammation, immunosuppression or dysregulation of the neuro-endocrine axis [11,12].

In this sense, there are more and more theories that discuss the impact of emotional stress, which engages a series of mechanisms with hormonal, immunological and possibly genetic influences at the level of the organism. Thus emerged Psychoneuroimmunology (PNI), a scientific field of study introduced in 1975 by Dr. Robert Ader, professor of behavioral and psychosocial medicine at the University of Rochester in New York. He researched and demonstrated that the way we think influences our state of health. PNI investigates the interactions between the nervous system, the endocrine system and the immune system and the way in which these systems influence each other, as well as developing an understanding of how the immune system is influenced by both socio-behavioral and physiological factors [13].

The concept of illness encompasses organic or psychological disorders that affect a person's sense of well-being, disrupting their existence. Disturbing factors of a biological, physical or chemical nature, and last but not least, psychological ones, create pressure on the organism and generate counter-reactions by triggering more or less efficient adaptive reactions-mechanisms, which constitute buffers of balance. It should be emphasized that the balance between the physical and emotional spheres of the individual in a state of health is deeply disturbed with the onset of illness.

The World Health Organization defines mental health as "a state of well-being in which an individual realizes his or her own potential, can cope with the negative stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" [14]. The emergence of psychological imbalances, with elements of negative psychological health such as emotional disorders of anxiety and depression, affective and behavioral disorders, anger, pessimism, and dissatisfaction with one's current life, are the consequence of an individual's ineffective adaptation to life's problems and can cause chronic stress.

Franz Alexander, a pioneer in the field of psychoanalysis and psychosomatic medicine, describes the fundamental concepts on which the psychosomatic approach is based and presents the results of his study on the influence of emotions on bodily processes in health and disease. Dr. Alexander paints a clear picture of the psychological factors involved in a bodily process and shows that these factors should receive the same detailed analysis as physiological processes, developing the theory of specific conflict, which is based on the idea that the energy of a repressed emotion, varicosed on a certain organ, can constitute the trigger for dysfunction [9]. In short, it can be stated that there is an interdependence between emotions and somatics, and any excessive emotion, when there is no emotional buffer to buffer conflicts or trauma, can generate organic dysfunctions, mediated by neuro-viscero-vegetative pathways.

Later, the theory of bio-psycho-social models emerged, interdisciplinary models that analyze the interaction between biology, psychology and social factors with implications for psychiatry, health and human development, the vision opener being George L. Engel [10]. The fundamental precept

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consists in the postulation of the fact that "disease and health are the result of an interaction between biological, psychological and social factors", and mental suffering can become a trigger for a disease, for a genetically vulnerable person, when stressful life events occur, as a vulnerability-stress pattern. In the context of the multifactorial causality of diseases, it must be accepted that the somatic cannot be dissociated from the psychic, the "mind-body" binomial functioning interconnectedly.

The universe of each individual, from birth, is progressively "invaded" by interpersonal relationships, with a formative, modulating effect and we can say that in a way we carry the imprint of the quality of the relationships we have throughout our lives. Alfred Adler considered that human well-being and health are the consequence of the capacity to love, to work, as well as the capacity to establish friendships [15]. Humans are innately social, the world around us and the social interactions we experience continuously shape the formation of our identity and our developing understanding of the world itself. In our early childhood, our social interactions are extremely formative, because it is a time when we begin to form attachments that can have a huge influence on our well-being as we grow up.

In a review study conducted by Levine et al. in 2021, which constitutes a Scientific Statement From the American Heart Association, starting from the reality that "they are good as clinicians in treating diseases, but not as good in treating the patient" [16]. , which is actually a reinterpretation of the old dictum "there are no diseases, only patients", the correlation between psychological health and cardiovascular health is emphasized, psychological factors can generate processes and behaviors that determine cardiovascular diseases, and improving psychological health can have a beneficial impact on cardiovascular diseases.

The association of psychological stress caused by trauma, depression, anger with somatic diseases such as autoimmune diseases, cardiovascular diseases and respiratory diseases. is quite frequent, with possible physio-pathological alterations at the level of the nervous, neuro-endocrine and immune systems [17–19].

Continuing the theory of G. Engel's models, Daniel J. Siegel, professor of psychiatry at the University of California, Los Angeles (UCLA), developed in the 1990s IPNB or relational neurobiology, an interdisciplinary framework that brings together scientific disciplines to demonstrate how the mind, brain, and interpersonal relationships integrate, forming part of a single reality [20]. IPNB sees the mind as a process that regulates the flow of energy and information through its neurocircuitry, which is then shared and regulated between people through involvement, connection, and communication, processes within interpersonal relationships that can shape the maturation of the nervous system.

In addition to modern evidence from psychoneuroimmunology, some of the most influential theoretical models for understanding the connections between the psyche and disease come from psychoanalysis and classical physiology. The unconscious conflict model, formulated by Sigmund Freud and expanded by Georg Groddeck, postulates that somatic symptoms can represent a symbolic expression of a deep, unconsciously repressed psychic conflict. Thus, illness is not only an organic disorder but can also be a form of indirect communication of psychic suffering. On the other hand, the chronic stress theory, developed by Hans Selye, demonstrates that prolonged exposure to stress profoundly affects the functioning of the endocrine, nervous and immune systems, leading to adaptive wear and tear of the organism ("distress") and, possibly, to the emergence of chronic diseases, including cancer. The integration of these models into current research provides a complex framework for understanding the relationship between psychological conflict, chronic stress, and cancer vulnerability.

Complementing these classical models, the theory of allostasis [21] offers a contemporary view of how the body responds to stress. Allostasis describes the process by which the body maintains its internal balance by making adaptive physiological changes in response to environmental demands. However, under conditions of chronic psychological stress, this system becomes overtaxed, generating what the authors call "allostatic load" — a progressive biological wear and tear on the nervous, endocrine, and immune systems. This wear and tear can promote the emergence of

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persistent systemic imbalances, increasing the risk of chronic diseases, including metabolic, cardiovascular, and, according to recent research, oncological disorders. Therefore, integrating the allostatic model of stress into research on the relationship between the psyche and cancer allows for a deeper understanding of how emotional trauma and prolonged psychological conflict can influence biological vulnerability to disease.

In parallel, stress epigenetics provides a molecular framework through which psychological experiences can influence the expression of genes involved in immunity, inflammation, and cellular repair [22,23]. Studies have shown that severe or prolonged stress can induce stable epigenetic changes (e.g., DNA methylation, histone modifications), which affect the expression of key genes in tumor control processes.

Thus, these contemporary models significantly complement and extend the understanding of the relationship between psychological conflict, chronic stress, and oncological pathology. In epigenetics, psychological development can occur through the interaction between heredity and environment, with culture and the environment influencing personality development [24]. IPNB augments epigenesis, arguing that variable experiences/relationships can modify the regulatory molecules that control gene expression, thereby shaping the activity and structure of neuronal circuits. Similarly, there may be interference with onco-genetic processes, which may affect the development of cancer.

Starting from all these premises, we conducted this literature review on the possible involvement and contribution of psychological stress in the onset of cancer, in the responsiveness to treatment and the risk of relapse, a subject located at the border between psychology and medicine, with strong interferences.

Exploring the relationship between psychological conflict and cancer is necessary from at least three perspectives: etiological – to understand to what extent certain chronic psychological disorders can contribute to individual biological vulnerability, therapeutic – to substantiate psycho-oncological interventions as an integral part of multidisciplinary treatment in oncology and preventive / prognostic – to identify psychological risk factors and incorporate timely interventions that can reduce the risk of occurrence or recurrence.

In addition, the literature highlights that cancer patients with high levels of emotional distress have significantly lower quality of life, reduced adherence to treatment, and a worse prognosis [25]. Thus, understanding how chronic psychological conflicts contribute to the onset and progression of the disease may have a major impact on the way in which holistic care of the cancer patient is conceived. Therefore, the theme of the present article focuses precisely on this insufficiently explored and often ignored area in oncology research: the deep but subtle relationship between psychological suffering and somatic illness, with the aim of highlighting the importance of an interdisciplinary approach in oncology and medical psychology.

Defining the Concept of Prolonged Psychological Conflict

Prolonged psychological conflict refers to a deep-seated, long-lasting, and often unconscious emotional tension that remains unresolved over time, progressively depleting an individual's psychological and physiological resources. These conflicts may stem from early-life trauma (e.g., abuse, neglect, abandonment), persistent intrapsychic tensions (such as the struggle between autonomy and affiliation), toxic familial or relational dynamics, or unprocessed emotional losses, including grief, divorce, or rejection [26,27].

The "chronic" nature of such conflicts implies a continuous, though frequently latent, presence of psychological pressure that is not always conscious but exerts sustained stress on the individual's internal systems. In the absence of adequate emotional regulation and adaptive coping mechanisms, these unresolved tensions may accumulate into physiological stress, dysregulating the neuroendocrine–immune axis. Consequently, they function as latent vulnerability factors, potentially contributing to the onset or progression of various chronic diseases, including cancer [28,29].

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From a psychosomatic perspective, emotional energy that is repressed or not symbolically processed often seeks expression through somatic pathways. Unresolved psychological conflicts thus transcend being mere intrapsychic events; they represent systemic threats to the organism's equilibrium, fueling chronic inflammatory responses, immune dysfunctions, and possibly epigenetic alterations.

Psychological vulnerability can be both a constitutional trait and a consequence of environmental exposures. This vulnerability manifests as a heightened sensitivity to psychological stressors, ranging from isolated incidents to complex, enduring life adversities. As early as 1914, W.B. Cannon demonstrated that intense emotions such as fear and anger activate the sympatho-adreno-medullary axis, triggering adrenaline secretion, hyperglycemia, and autonomic responses — thereby highlighting the measurable biological imprints of emotional states [30,31].

Emotions, therefore, are not only subjective experiences but also psychobiological energies involving the central and peripheral nervous systems, the endocrine system, and the immune system. When sustained or intense — as in chronic shame, fear, helplessness, or despair — they may lead to maladaptive physiological patterns, including sleep disturbances, anxiety, depression, and inflammatory responses [32,33]. Engel's seminal 1977 bio-psycho-social model proposed that emotions should be considered vital signs, on par with pulse, temperature, and blood pressure, in the assessment of health [25].

Franz Alexander's classical "specific conflict" theory, which suggested that repressed emotional conflict manifests through somatic symptoms via the autonomic nervous system, continues to resonate in contemporary psychosomatic medicine. However, symbolic interpretations are now complemented by objective biological data — including inflammatory markers, neuroendocrine profiles, and stress-related biomarkers [34].

A systematic review by Guidi et al. [35] advances the concept of allostatic load, referring to the cumulative burden imposed by chronic stress exposure. This framework helps explain how prolonged negative psychological experiences and adverse life events are biologically embedded and may contribute to disease. Further studies, such as those by Volarić et al. [36], highlight how allostatic load varies based on sex, age, and type of stress exposure, refining earlier models by incorporating individual variability and biological evidence.

In this light, unresolved psychological conflict may indirectly create an internal environment conducive to carcinogenesis by disrupting immune surveillance, hormonal regulation, and cellular homeostasis. These effects are particularly relevant in individuals with pre-existing vulnerabilities.

In consequence, prolonged psychological conflict should no longer be viewed solely as a mental health issue. Rather, it constitutes a systemic risk factor with tangible biological consequences, including contributions to inflammation, immune dysregulation, and tumor-promoting physiological shifts. This supports the need for integrating psychological screening and trauma-informed care into oncological settings.

Materials and Methods

This study employed a narrative integrative review methodology, aiming to explore the potential links between prolonged psychological conflicts, trauma-related stress, and oncological vulnerability. The review was conducted between March and December 2025 and followed a conceptual and empirical framework, combining findings from psycho-oncology, psychoneuroimmunology, psychosomatic medicine, and developmental psychopathology.

A literature search was performed using the electronic databases PubMed, Scopus, Web of Science, and PsycINFO, covering publications from 2000 to The following keywords and Boolean combinations were used: "psychological trauma" AND "cancer","chronic stress" AND "immune dysregulation", "psychoneuroimmunology" AND "oncology", "childhood adversity" AND "cancer risk", "PTSD" AND "tumor progression", "trauma-informed care" AND "oncological outcomes".

Inclusion criteria comprised peer-reviewed articles, systematic reviews, meta-analyses, and empirical studies in English, with clear relevance to the psychobiological mechanisms linking

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psychological stress or trauma with cancer onset, progression, or treatment responsiveness. Exclusion criteria included non-peer-reviewed articles, commentaries without scientific backing, case reports lacking generalizability, and studies focused solely on genetic or molecular oncology without reference to psychological variables.

In total, over 198 sources were screened, of which approximately 110 met the inclusion criteria and were integrated into this review. The selection process prioritized methodological quality, conceptual relevance, and interdisciplinary integration. Both historical psychosomatic theories and recent empirical findings were included to provide a comprehensive and nuanced understanding of the subject.

Given the complexity and multidimensionality of the topic, this narrative review does not aim to provide statistical conclusions, but rather to synthesize current knowledge and identify patterns, gaps, and clinical implications regarding the role of psychological conflict and chronic stress in oncological processes.

Unresolved Trauma and Its Involvement in Chronic Diseases

Unresolved psychological trauma refers to an overwhelming emotional experience that has not been consciously processed or integrated and that, through defense mechanisms such as repression, dissociation, or avoidance, continues to exert a latent yet persistent influence on both psychological and somatic functioning. This lingering influence maintains a chronic state of psychophysiological stress and perpetuates unresolved emotional conflict.

Recent studies indicate that exposure to emotional trauma, especially during early developmental periods, is associated with long-term neurobiological and epigenetic alterations. Experiences such as emotional neglect, abuse, or abandonment have been shown to disrupt the HPA axis, increase stress reactivity, and induce structural and functional changes in brain regions responsible for emotional regulation, including the amygdala, insula, and medial prefrontal cortex [37]. These neurobiological disruptions may result in maladaptive stress response patterns and impair immune regulation and tissue repair mechanisms, contributing to systemic vulnerability.

Bessel van der Kolk [27] conceptualizes trauma as a rupture in the individual's capacity to integrate adverse experiences into a coherent life narrative. This rupture gives rise to psychological "knots" of unresolved tension, which may resurface somatically or behaviorally. Similarly, Gabor Maté [26] posits that the denial of emotional suffering results in a profound act of "self-betrayal," whereby unacknowledged emotional needs chronically disrupt the mind–body equilibrium and, in the presence of genetic predisposition, may contribute to the development of chronic illness, including cancer [38].

Therefore, in exploring the relationship between prolonged psychological conflict and oncological vulnerability, identifying and addressing unresolved trauma becomes essential. It represents a key element in understanding the pathways through which psychological suffering may affect physiological processes and offers critical guidance for the design of integrative psycho-oncological interventions.

Psychological Trauma Generated by Ongoing Conflicts

Ongoing psychological conflict does not merely reflect emotional tension but may itself constitute a significant traumatogenic factor, particularly when it exceeds the individual's psychological coping capacity. Trauma arising from persistent relational discord, such as chronic emotional invalidation, subtle psychological abuse, or the conflicting demands of dysfunctional family dynamics, belongs to the category of cumulative adverse experiences. These experiences have a profound impact on identity development, emotional regulation, and long-term physical health.

Unlike acute trauma, which stems from discrete events, chronic conflict-related trauma has an insidious and enduring nature. It gradually establishes itself as a persistent state of psychophysiological stress, either within dysfunctional interpersonal contexts or through enduring intrapsychic tensions between incompatible values, roles, and desires.

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Unresolved interpersonal conflicts may distort the individual's self-concept and relational schemas, perpetuating cycles of anxiety, guilt, emotional suppression, and repressed anger. In biologically vulnerable individuals, these affective patterns may facilitate the onset of chronic low-grade inflammation, disrupt cellular repair mechanisms, and induce epigenetic changes, mechanisms increasingly implicated in the pathogenesis and progression of oncological disease [11].

Moreover, intrapsychic conflicts, such as those arising from discrepancies between ideal self-images and external constraints, can give rise to a latent psychological strain that, while difficult to detect clinically, exerts a cumulative erosive effect on emotional and physiological resilience. Affected individuals often live in a state of heightened emotional vigilance, characterized by unsustainable internal energy expenditure over time.

Frequent sources of conflict-related trauma include toxic parental bonds, unresolved grief, internal loyalty dilemmas between familial obligations and personal autonomy, and misalignments between intrinsic values and societal expectations. Chronic exposure to these patterns may degrade emotional regulation, increase susceptibility to anxiety and depressive disorders, and raise the risk for severe somatic illnesses, including cardiovascular, autoimmune, and oncological conditions [16,38].

In conclusion, chronic conflict-related trauma, whether interpersonal or intrapsychic, should be recognized as a distinct and impactful form of pathogenic stress. Its persistent nature and cumulative burden necessitate clinical models and oncological risk assessments that are attuned to the psychological underpinnings of disease vulnerability.

Intrapsychic Conflicts, Depression and Cancer Vulnerability: Clinical and Empirical Convergences

Intrapsychic conflicts are internal psychological tensions, often unconscious, that arise from the contradiction between incompatible personal desires, values, needs, or ideals. These unresolved tensions may lead to chronic psychological distress when not integrated through conscious processing or symbolic elaboration, with potential psychosomatic consequences and negative effects on physical health.

The origin of this concept lies in Freudian psychoanalysis, which described the conflictual dynamics between psychic instances (id, ego, superego) and their manifestation in neurotic or psychosomatic symptoms. Modern psychodynamic frameworks, such as Operationalized Psychodynamic Diagnosis, have refined this theory, identifying several clinically relevant conflict patterns, including: autonomy vs. affiliation, self-expression vs. conformity, control vs. abandonment, personal worth vs. shame, and others [39–41]. When unresolved, such conflicts may result in latent emotional disequilibrium marked by cognitive rumination, emotional inhibition, diffuse anxiety, and a sense of helplessness.

These intrapsychic conflicts are often processed through defense mechanisms such as repression or projection, and if they remain unconscious and unresolved, they may contribute to physiological dysregulation. The sustained psychic strain caused by such inner tensions has been linked to chronic stress activation, inflammation, and immune dysfunction—mechanisms increasingly implicated in carcinogenesis.

Psychodynamic and cognitive models alike suggest that depression may develop as a downstream effect of unresolved conflicts [42,43]. Individuals experiencing chronic intrapsychic dissonance frequently report symptoms such as guilt, worthlessness, loss of meaning, and somatization (e.g., fatigue, gastrointestinal distress, chronic pain). In this view, depression is not merely an affective disorder, but also a psychosomatic indicator of unprocessed psychic suffering—one that may impair immune surveillance, disrupt neuroendocrine regulation (e.g., via HPA axis dysfunction), and increase oncological vulnerability.

Empirical evidence supports this conceptual framework. In a study by Vierl et al. [44], psychodynamic variables such as conflict resolution style and personality structural integration were significantly associated with depressive and somatic symptoms. Passive conflict management styles—such as withdrawal, guilt, or self-blame—were more strongly correlated with

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psychopathology than active coping styles. The authors emphasize that personality functioning serves as a mediator between latent conflicts and manifest symptomatology, with implications for clinical intervention.

In another important study, Vespa et al. [45] used cluster analysis to assess intrapsychic profiles in 236 women with breast cancer. Two distinct profiles emerged: "Love/Autonomy" and "Control/Hate". The latter group, characterized by self-criticism, emotional suppression, and neglect of internal needs, showed significantly higher levels of depression. These findings suggest that internal personality traits may moderate the psychological response to somatic illness and that not all cancer patients share the same psychodynamic vulnerability. Such intrapsychic factors may constitute a "psychological bridge" linking unresolved emotional suffering to increased cancer risk.

Furthermore, large-scale studies have explored the link between depression and cancer incidence. Mössinger and Kostev [46], in a retrospective analysis of over 235,000 patients, reported a 10–39% increased cancer risk in individuals with clinical depression, particularly for lung, gastrointestinal, breast, and urinary cancers. Another prospective cohort study from Baltimore indicated a significant correlation between depressive history and hormone-sensitive cancers, especially breast cancer [47]. More recent meta-analyses have confirmed that post-diagnosis depression is associated with increased cancer-specific mortality—by 23–83%, depending on tumor type [48].

However, the evidence is not uniform. Several studies, such as that by Lemogne et al. [49] based on the GAZEL cohort, have reported no clear association between depression and cancer incidence. Similarly, a meta-analysis by van Tuijl et al. [50] concluded that depression and anxiety were not significantly related to overall cancer risk, except in cases involving behavioral mediators (e.g., smoking). Methodological concerns, including publication bias and confounding variables, are frequently cited as limiting factors in interpreting these data [47,51].

Therefore, while the causal link between depression and cancer remains debated, there is compelling evidence that chronic depressive states—especially those rooted in unresolved intrapsychic conflicts—may act as indirect risk factors for somatic disease. These findings support the implementation of integrative psycho-oncological models that include the assessment of conflictual dynamics, personality structure, and depression in both cancer prevention and treatment.

Toxic Family Dynamics, Insecure Attachment and Psychosomatic Vulnerability

The family is a relational framework in which the affective and identity structure of the individual develops, and from this perspective, the dynamics of family relationships have an essential role in shaping long-term psychological and somatic health, contributing significantly to shaping the emotional balance and psychological regulation patterns of the individual [52,53]. When the family, the primary source of safety, becomes a conflictive, emotionally abusive environment with verbal or physical violence, critical or chaotic, a toxic dynamic appears that can produce chronic psychological conflicts, identity distortions and long-term emotional stress, leading to the emergence of psychosomatic vulnerabilities.

A toxic family dynamic is characterized by dysfunctional relationships between family members, in which either excessive control generated by the lack of psychological boundaries prevails, or constant criticism with emotional invalidation or emotional neglect through the lack of empathy and support; Also with harmful effect in the family environment can appear reversed parental roles (the child becomes the caregiver), unresolved tensions or chronic family secrets. This atmosphere produces in family members, including children, a latent psychological tension, often internalized as self-blame, shame, fear of rejection and emotional hyper-vigilance, defining elements of the ongoing psychological conflict.

An essential aspect in understanding psychosomatic vulnerability is the link between toxic relationship patterns in childhood and emotional regulation difficulties in adulthood. People raised in conflictive family environments frequently develop insecure attachment styles, of the anxious or avoidant type, which are associated with difficulties in emotional processing and stress regulation.

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In the oncological context, these psychological traits can negatively affect the quality of life, the capacity for adaptation and therapeutic compliance [54,55]. For example, studies show that patients with breast or lung cancer who exhibit avoidant or anxious attachment styles experience increased levels of psychological distress and significant decreases in quality of life [55,56]. Insecure attachment is also correlated with dysfunctional communication within the couple, with a reluctance to share emotional experiences, which negatively influences perceived social support and acceptance of the disease [57].

Furthermore, low self-compassion and difficulties in emotional integration, mediated by attachment styles, may affect post-treatment psychological adjustment [58]. Thus, we can conclude that a key element in understanding the long-term impact of toxic family dynamics is the direct relationship between these early experiences and the emergence of major emotional regulation difficulties in adulthood. Parental relationships marked by affective inconsistency, hostility, excessive criticism, or lack of emotional support often generate a disorganized or insecure attachment (anxious or avoidant type), which affects the individual's ability to manage stress, recognize, and express one's own emotions in a coherent and adaptive manner [59]. Difficulties in emotional regulation are often manifested by impulsivity, a tendency to suppress or dissociate intense emotions, affective hypervigilance, or an inability to tolerate emotional discomfort. These maladaptive mechanisms may function as mediating factors between early relationship trauma and the development of psychiatric or psychosomatic disorders, including vulnerability to chronic diseases such as cancer [60,61].

In addition, oncological psychology studies highlight the fact that oncological patients who have histories of abusive or invalidating relationships have an increased probability of developing accentuated somatic symptoms, sleep disorders, stress symptoms posttraumatic and affective reactions organized in the context of the disease [62].

This fact suggests that psychotherapeutic interventions in oncology should include the assessment of time relations and patterns of emotional regulation, in order to facilitate an integrative and personalized approach to the patient.

Regarding the psychosomatic implications of a dysfunctional family environment, numerous studies have shown that a hostile family environment in childhood and beyond, with prolonged exposure to conflictual relationships, can generate activation of the HPA stress system and immune system disorders; these changes favor chronic inflammation, with increased levels of systemic inflammation (interleukina 6 (IL-6), C-reactive protein(CRP) and the establishment of a biological terrain conducive to the development of some somatic pathologies, including oncological ones [18,63]. Dysfunctional family relationships are also frequently associated with the internalization of anxiety, depression, and the emergence of maladaptive defense mechanisms such as repression, dissociation, and somatization; all of these can generate vulnerability to affective and behavioral disorders such as dysfunctional behaviors (denial of one's own needs, self-sacrifice), associated with maladaptive coping styles in the face of illness. A significant example in this sense is the study by Brown et al. [64] who analyzed the correlation between adverse childhood experiences (including family conflicts) and the occurrence of certain forms of cancer in adulthood. The results showed a significantly higher incidence of cancer among people who experienced early family trauma, especially in the absence of an emotional support system.

Also, longitudinal studies on ACEs have shown that individuals exposed to abuse and family dysfunction in childhood are at increased risk of chronic diseases, psychiatric disorders and health-harming behaviors [38]. In conclusion, toxic family dynamics do not only have immediate psychological consequences but can become a profound etiological factor of psychosomatic imbalances and oncological vulnerability. By altering attachment style, emotional regulation capacity and stress system functions, these early experiences create a biological and psychological terrain susceptible to chronic diseases. Thus, investigating family relationships in oncological anamnesis should become an integral part of psycho-oncological practices.

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Toxic Marital Relationships and Their Impact on Psychosomatic and Oncological Health

Marital relationships, considered one of the most significant emotional and psychological support frameworks in adulthood, can also become a profound source of chronic stress when it is marked by toxic dynamics. These include controlling behaviors, emotional or physical abuse, constant invalidation, infidelity, dysfunctional communication, pathological addiction, or passive-aggressive hostility. Prolonged exposure to such relationships can lead to significant psychological and somatic imbalances.

According to attachment theory and models of couple affect regulation, a partner perceived as hostile, unstable, or distant activates stress reactions similar to existential threats, which keeps the neuroendocrine system in a state of hyperactivation [65]. These effects are particularly exacerbated in relationships where the person cannot escape the dysfunctional dynamic (e.g., for financial, social, religious, or fear reasons), leading to a form of chronic relational trauma, described in the psycho-traumatology literature as one of the most dangerous forms of persistent stress [66].

Recent studies have highlighted a correlation between toxic marital relationships and depression, anxiety, and somatic disorders. For example, in a study by Whisman et al. [67], low marital satisfaction was associated with marked depression and higher levels of systemic inflammation (e.g., CRP, IL-6), factors known to be involved in the etiology of chronic diseases and cancer [68]. In particular, women in abusive or invalidating marital relationships are at increased risk of emotional dysregulation, unexplained somatic symptoms, marital burnout, and even a diminished ability to cope with cancer [69,70].

Furthermore, recent studies [71,72] have shown that the perception of hostility from a partner correlates with higher long-term cortisol levels and impaired immune function, especially in women. These biological mechanisms contribute to chronic immunosuppression, persistent inflammation, and hormonal dysfunction, creating an internal environment conducive to tumor development and reduced efficacy of cancer treatments.

In conclusion, toxic marital relationships can act as a chronic stressor with a profound impact on mental and physical health. In particular, in the case of women, these dysfunctional dynamics amplify the risk of depression, immunological dysfunctions and hormonal imbalances, essential elements in oncological vulnerability. Identifying these factors in relational anamnesis could represent a crucial step in personalizing oncological and psychotherapeutic care.

Parental Toxic Relationships and the Impact on Psychosomatic Health

The parent–child relationship is one of the most formative and influential relationships in an individual's life, with profound effects on attachment development, emotional regulation, and self-formation. When this relationship is disrupted by emotional, verbal, or physical abuse, or chronic invalidation (expressed through excessive criticism, intrusive control, or emotional neglect), the psychological and somatic consequences can be long-lasting. Such dynamics can shape vulnerable personality traits, dysfunctional relationships, and maladaptive defense mechanisms, including self-sabotaging behaviors [73]. Instead of providing support, acceptance, and emotional security, a toxic parent becomes a major source of chronic relational stress, generating persistent feelings of shame, guilt, self-doubt, and relational anxiety in the child. This creates an insecure attachment style (avoidant or disorganized), with direct implications for the capacity for emotional self-regulation and the way of relating in adult life, including psychosomatic and oncological vulnerability [74,75].

The specialized literature shows that dysfunctional relationships with parents significantly increase the risk for depressive and anxiety disorders, personality disorders (e.g. borderline) and maladaptive stress management strategies [76]. In particular, hypercritical, narcissistic, or passive-aggressive mothers may induce a chronic sense of inadequacy and guilt, associated with hyperactivation of the HPA axis and disruptions in the neuro-immuno-endocrine balance, as well as chronic low-grade inflammation [77–79]. Recent studies in the field of PNI indicate that early relational traumas – including parental ones – can influence stress epigenetics and immune

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regulation, contributing to the development of chronic diseases or to reduced efficacy of treatment responses [80,81].

This specific form of relational stress is clinically underappreciated, but recent studies have begun to document its somatic implications. For example, a study published in Health Psychology identified higher levels of inflammatory markers and increased incidence of psychosomatic symptomatology among women with persistent toxic relationships with their mothers [82]. In another study of cancer patients, a history of dysfunctional maternal relationships was associated with higher scores of posttraumatic stress, sleep disturbances, and passive coping styles, with negative effects on treatment compliance and overall prognosis [83]. Unresolved parent–child relationships can become sources of chronic relational trauma, especially when cancer reactivates old dynamics: blame, lack of support, destructive comparisons, or ignoring emotional needs. Women with a history of toxic maternal relationships are at increased risk of depression, anxiety disorders, self-defeating behaviors, and greater difficulties in adapting to cancer stress [84]. These difficulties are reflected in decreased motivation for therapy, difficulty accessing social support, and a reduced capacity for emotional self-regulation [85]. As part of the oncological process, these women may encounter major obstacles in accessing the emotional resources necessary for coping, effective social support and maintaining therapeutic motivation [85]. Another relevant aspect is the phenomenon of unconscious loyalty to the maternal figure, in which the daughter may internalize toxic messages such as “I don’t deserve to be cured” or “I’m not good enough”, thus indirectly influencing the course of the disease and attitude towards treatment.

In the context of cancer, the parent-child relationship can become a trigger or maintainer of chronic relational trauma, especially when the disease brings to the fore unresolved dynamics from the past: lack of support, destructive comparisons, blaming or ignoring emotional needs. Furthermore, studies show that women who have had toxic relationships with their mothers have higher rates of depression, anxiety disorders, self-defeating behaviors, and difficulties in coping with major stressors, such as a cancer diagnosis [84].

Increasing empirical evidence suggests that strained or dysfunctional family relationships may be a significant psychosocial factor in shaping cancer vulnerability. Studies show that women from families marked by conflict, criticism, or lack of emotional support have a heightened tendency to develop maladaptive coping strategies, such as suppressing affect and avoiding emotional confrontation, mechanisms associated with increased psychological distress and reduced immune reactivity [86]. Also, oncology patients from dysfunctional family backgrounds report difficulties in accessing emotional support and in positively integrating the diagnosis, which may affect their psychological adjustment and response to treatment [87].

Furthermore, negative marital dynamics have been correlated with a pro-inflammatory physiological profile, in particular an increased production of inflammatory cytokines, as well as with a slowdown in healing processes after medical interventions, indicating a direct link between chronic relational stress and immune dysregulation [88]. These data strengthen the hypothesis that chronic relational conflicts may constitute a significant link between psychosocial stress and biological impairment, contributing to a fertile ground for the initiation and maintenance of oncological processes.)

One of the psychodynamic explanations frequently invoked in the specialized literature regarding the link between family conflict and somatic illness is the formation of a “false self” – a concept introduced by D.W. Winnicott, through which the individual, in an attempt to maintain family cohesion or to avoid rejection, ends up internalizing relational tensions and living according to the expectations of others, repressing his own emotions and needs. This chronic psychic incongruity, between what is expressed and what is experienced internally, becomes fertile ground for unresolved intrapsychic conflicts. In the long term, these internal tensions can generate an increased level of persistent psychological stress, with a direct impact on the functioning of the neuroendocrine and immune systems. Thus, the internalization of family conflicts not only affects mental health but can contribute to the installation of general biological vulnerabilities, favoring the

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emergence of chronic diseases, including cancer, especially in contexts where genetic and environmental factors converge. In this sense, the repressed psyche becomes not only a reservoir of tension, but also a possible catalyst for somatic dysfunctions [89,90].

Unprocessed Emotional Losses and Profound Psychological Stress

Experiences of emotional loss through death, separation, rejection, or emotional abandonment are events that have a profound impact on an individual's psychological well-being. Whether it is the death of a parent in childhood, traumatic separations, or chronic lack of affection, these experiences can generate ruptures in the emotional continuity of the self. When the natural process of mourning is blocked by defensive mechanisms such as denial, avoidance, or repression, emotional pain becomes "unresolved grief," with persistent effects on mental and physical health [91,92].

In the psychosomatic context, this form of latent emotional distress can lead to chronic hyperactivation of the HPA axis, continuous stimulation of inflammatory pathways, increased "allostatic load," and immune dysregulation—biological mechanisms well documented to be involved in the onset and maintenance of chronic diseases, including cancer [93,94]. For example, studies show that the loss of a life partner is associated with increased levels of IL-6 and CRP (inflammatory markers), persistently elevated salivary cortisol, decreased T-lymphocyte activity, and increased risk of cardiovascular and cancer mortality [95–97].

The concept of "complicated grief" describes situations in which the person remains stuck in a state of deep emotional suffering, marked by prolonged sadness, insomnia, guilt, social isolation and a lack of existential meaning. When the expression of emotions is inhibited, somatic manifestations such as headache, gastrointestinal disorders or diffuse pain may appear – all reflecting the conversion of the psychic into the somatic. In the view of psychosomaticians, elaborated grief can become a "zone of psychic silence" in which repressed emotional energy is transformed into somatic symptoms. In this sense, Gabor Maté emphasizes that "repressed pain" and systematic suppression of needs can constitute the emotional basis of chronic diseases, including cancer [26]. People who perceive themselves as "strong", who "must be pushed aside", risk ignoring their own signals of inner suffering, a major factor of psychosomatic vulnerability.

For example, in a longitudinal study conducted on adolescents who lost a parent to cancer, it was found that, 6–9 years after the event, over 50% of the participants had not "processed" their grief, and they presented increased rates of insomnia, chronic fatigue and depressive symptoms – psychosocial risk factors for poor adaptation to stress and somatic vulnerability [98].

A relevant contribution in this field is also the review carried out by Paula et al. [99]. which analyzes the relationship between emotional loss and breast cancer risk. Although the results of the studies are heterogeneous, the authors propose a possible explanatory model: loss → chronic stress → HPA dysregulation → immunosuppression → tumor susceptibility. They emphasize the importance of longitudinal studies that also evaluate other involved factors, such as risk behaviors, smoking/alcohol, lifestyle or social support [98]. Incorporating this perspective allows us to argue that unresolved emotional loss may represent not only a psychological vulnerability, but also an element of the biological terrain predisposing to the disease. In this context, processed emotional losses are not only an emotional vulnerability, but can also become a biological risk factor, favoring an internal climate of identity fragility and resilience dysregulation. This "emotional fracture" may impair the ability to adapt to subsequent traumas, including major traumas associated with cancer diagnosis (e.g., shock of diagnosis, invasive treatments, fear of relapse). People with elaborated grief may have difficulty accessing social support, a tendency to avoid emotional confrontation, and reduced treatment compliance, factors associated with poor oncological prognosis [100,101].

Therefore, in modern oncological etiology, it is necessary to include unresolved emotional "residues", such as unexpressed emotional losses, which can contribute to chronic psychological stress, maladaptive behavior, and systemic biological vulnerability. The integration of this perspective adds depth to the bio-psycho-social model of disease, in which the unexamined emotional dimension becomes a potentially modifiable risk factor.

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Adverse Childhood Experiences and Cancer Vulnerability

ACEs are defined as traumatic or destabilizing events experienced in the early years of life, such as physical, emotional, or sexual abuse, neglect, domestic violence, parental separation, substance use in the family, or parental mental illness. These early traumatic events are not just isolated episodes, but can generate lingering psychological conflicts – chronic, persistent intrapsychic tensions that latently influence personality development and emotional regulation capacity. In the absence of adequate processing mechanisms and symbolization, the child internalizes the conflict, resulting in a fragmentation of the self and an imbalance between contradictory parts of the personality (e.g., the need for protection vs. fear of abandonment, the desire for autonomy vs. separation anxiety). These conflicts may remain unconscious but continue to act as underlying forces that shape perceptions, relational choices, and reactions to stress, constituting a long-term vulnerability to psychological and somatic disorders.

In addition, persistent psychological conflicts may be accompanied by rigid defense mechanisms, such as emotional suppression, dissociation, or denial, which prevent the emotional integration of the trauma and perpetuate latent psychological stress. In this context, not only the trauma itself, but also the chronic inability to process, express, and resolve the psychological conflict generated by the ACE contributes to the deterioration of health. This indirect causality between childhood trauma, persistent psychological conflict, and somatic illness, including cancer, represents an emerging direction of research in psychosomatic psychiatry and psychoneuroimmunology [102,103].

These early traumas have been increasingly associated with long-term risks to adult physical and mental health, with a profound impact on the individual's development. The classic study by Felitti and Anda [38] established a paradigm for understanding adult morbidity, demonstrating a dose-effect relationship between the number of ACEs and the risk of adult chronic diseases, including cancer. In fact, systematic reviews indicate that individuals with a high score on ACEs have a higher risk of developing cancer later in life. This meta-analysis by Hu et al [104] showed that physical abuse (OR ≈1.23), sexual abuse (OR ≈1.26) and exposure to domestic violence (OR ≈1.26) were associated with an increased risk of cancer. At the same time, the study by Brown et al. [105] highlights a significant correlation between childhood trauma and cancer risk in adulthood, with the number of adverse events being proportional to the subsequent incidence of cancer.

From the perspective of biological and psychosocial mechanisms, there are several relevant explanatory lines, which could not outline the causal relationship between ACE and cancer. The "developmental dysregulation" model: childhood adversity produces chronic stress ("toxic stress") that affects the HPA axis, leading to altered cortisol secretion, persistent inflammatory activation, and increased allostatic load, biological factors implicated in carcinogenesis [106]. The authors also emphasize that behavioral transmission of risks can occur, with ACEs being linked to early adoption of cancer risk behaviors (smoking, alcohol consumption, sedentary lifestyle, obesity) which, in turn, increase cancer incidence.

Another mechanism may be related to compromised emotional regulation and social support, with children exposed to adverse events developing emotional and relational regulation difficulties (e.g., insecure attachment, repression, dissociation), which can affect adaptation to major life stresses, including cancer diagnosis, and reduce biological and psychological resilience resources [107].

In the oncological context, these connections are of practical importance: people with a history of ACEs may not only have a higher risk of developing cancer, but may also have a more difficult therapeutic response, delayed healing, and poor psychological adjustment after the disease. Recent studies on cancer survivors show that ACEs are associated with more persistent fatigue, increased psychological distress, sleep disturbances, and posttraumatic symptoms [108].

However, it is crucial to mention that literature still has significant gaps: heterogeneity in ACE definitions, outcome measures, insufficient adjustment for confounders (genetics, risk behaviors, environment), and the fact that only a few studies have directly examined the relationship between ACEs and cancer incidence [109].

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In conclusion, the integration of ACEs into the oncological vulnerability model adds an essential dimension: not only biological factors or lifestyle matter, but also the early emotional and relational load. Early identification of people with a history of ACEs and integrated psychosocial interventions could contribute to oncological prevention and to improving the prognosis of cancer patients. From a psychological point of view, a series of mechanisms can be triggered as a result of childhood trauma, with repercussions on somatic health. First of all, attachment dysregulation, children raised in unsafe or abusive environments develop anxious or disorganized attachment patterns, which negatively influence the capacity for emotional regulation, according to attachment theory [110,111]. These individuals tend to overexert their stress systems and interpret the environment as constantly threatening, favoring the emergence of chronic psychological conflicts and sustained emotional distress. Also at the psychological level, repression and dissociation may appear as defense mechanisms induced by early traumas, through which negative emotions are "blocked" from consciousness. These processes do not eliminate tension, but "store" it somatically, contributing to the appearance of inexplicable physical symptoms (somatization, chronic pain) and, in the long term, to neuroendocrine dysfunctions [112].

Another trait that these children may develop throughout life is a hypersensitivity to stress and anticipatory anxiety, with hyperactivation of the amygdala and alteration of the prefrontal cortex, becoming hypervigilant, with catastrophic thinking and being prone to generalized anxiety, depression and prolonged intrapsychic conflicts [113,114].

In the context of early trauma, internalizing behaviors of guilt and shame may appear, especially in abused or neglected children, who often end up internalizing a negative self-image ("there is something wrong with me") and associating suffering with personal guilt. This process generates chronic psychological conflicts between the desire for affirmation and the fear of rejection, between the desire for intimacy and the fundamental distrust of others, and over time the formation of an "unconscious illness scenario" may take shape. According to dynamic psychosomatics [115], trauma can generate an unconscious structure in which illness is "accepted" as a symbolic solution to inner conflict. These "unconscious scenarios" can manifest themselves through self-sabotaging behaviors, lack of self-care, denial of the need for help, or passively absorbing suffering.

Childhood trauma can also affect the process of self-integration, a disturbance in practical identity development, and create a persistent sense of lack of control over one's life, which leads to high stress reactivity and low frustration tolerance, psychological elements relevant to cancer vulnerability.

Recent evidence from population studies supports the idea that adverse childhood experiences may constitute an independent risk factor for the development of cancer. Hovdestad et al. [116], analyzing data from a representative sample of Canadian adults, showed that physical, sexual abuse, and exposure to violence in childhood are associated with a higher incidence of cancer in adulthood, even after controlling for behavioral risk variables. The relationship was more pronounced among women, highlighting a possible gender-differentiated vulnerability. These data strengthen the hypothesis that early trauma not only disrupts psycho-emotional development but also modulates in the longterm biological reactivity to stress and the functioning of the neuroendocrine and immune systems, mechanisms relevant in carcinogenesis.

In detailing this robust population study, which confirms the link between childhood trauma and cancer risk, we note several valuable ideas as main results: (1) participants who reported at least one form of childhood abuse had a significantly higher probability of being diagnosed with cancer in adulthood compared to those without such antecedents, (2) the risk was cumulative, increasing proportionally to the number of types of abuse suffered and (3) women showed a more pronounced association between childhood sexual abuse and cancer, compared to men. Also, what is very important, the fact that the results remained significant even after adjusting for factors such as age, socioeconomic status, smoking, alcohol consumption and other predictors of cancer risk. The authors offered several explanatory mechanisms, intensely debated in similar studies, such as chronic physiological dysregulations induced by early stress (hyperactivation of the HPA axis, persistent

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systemic inflammation), risky health behaviors (smoking, alcohol abuse, sedentary lifestyle), frequent among people with a history of trauma and deficient emotional regulation and psychological stress, with a negative impact on immune function. Thus, the study demonstrates that the impact of childhood abuse extends beyond mental health, having serious somatic consequences, including oncological ones, and reiterates the idea that screening for ACEs should be integrated into medical and oncological practice, especially for preventive and trauma-informed interventions.

In this sense, the study by Oppegaard et al. [117] adds a current clinical-psychological dimension to the discussion of how trauma and stress can influence the subjective experience of onco-therapeutic illness. In a cohort of 1,332 patients undergoing chemotherapy, the authors assessed combined cancer-related cognitive impairment (CRCI) and anxiety, along with measures of global stress, disease-specific stress, cumulative stress, and resilience. Through latent analysis, three distinct symptom classes were found: from "no CRCI + low anxiety" to "high CRCI + high anxiety". Participants in the most severe classes showed significantly higher levels of stress and reported higher rates of adverse childhood experiences (emotional, physical abuse, sexual harassment). By supporting a dose-effect relationship, the study suggests that early traumatic-stressful experiences can "set the stage" for a maladaptive interaction between cancer-related stress and cognitive and emotional vulnerabilities. This work serves as a modern example of how early trauma can shape not only cancer risk, but also how patients experience and respond psychologically to the therapeutic process. It follows that childhood emotional vulnerabilities (ACEs) are not just passive components but can mediate cognitive and anxiety reactions in cancer patients, and therefore may have implications for quality of life, adherence to treatment, and, indirectly, disease progression.

Preliminary conclusions, supported by epidemiological evidence, show a robust link between early adversarial trauma and oncological risk, stronger in women, and the pathophysiological mechanisms involved include chronic stress, inflammation, immunosuppression and epigenetics. Thus, childhood trauma generating chronic psychological conflicts configures an oncological predisposing terrain, justifying early preventive psychosocial and psycho-oncological interventions. Historical assessment of early traumas should be integrated into the psychological history of the oncological patient. Early interventions on individuals at high psychosocial risk (e.g. girls with a history of abuse, institutionalized children) may reduce the risk of oncological comorbidity. Trauma-focused psychotherapeutic approaches (e.g. Eye Movement Desensitization and Reprocessing, Acceptance and Commitment Therapy, Interpersonal Psychotherapy) may contribute to reducing systemic stress and improving oncological prognosis.

Therefore, the systematic inclusion of childhood trauma history in oncological evaluation and the implementation of trauma-focused psychotherapeutic interventions may represent essential steps in the holistic approach to the vulnerable oncological patient.

PTSD, Chronic Psychological Trauma and Oncological Vulnerability: Biopsychosocial and Clinical Implications

Posttraumatic stress disorder (PTSD) is a severe psychological condition with major systemic implications—neurobiological, immunological, and behavioral. Although initially associated with acute traumatic events (such as natural disasters, physical assaults, or war experiences), contemporary literature also recognizes PTSD as a result of chronic psychological trauma, such as emotional neglect, childhood rejection, repetitive verbal abuse, or persistent relationship stress encountered in family or professional contexts. These forms of trauma can be conceptualized as lingering psychological conflicts with a profound impact on psychosomatic balance.

From a biological perspective, PTSD is not just a mental disorder but reflects a complex systemic dysfunction. Persistent activation of the hypothalamic-pituitary-adrenal (HPA) axis is noted, along with hyperactivation of the amygdala and hypoactivation of the prefrontal cortex, leading to chronic release of cortisol and other stress hormones. These processes contribute to immune dysregulation, low-level but persistent systemic inflammation, increased oxidative stress, inhibition of cellular apoptosis, and disruption of cell proliferation control mechanisms, all of which have been implicated

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in carcinogenesis [118,119]. Studies conducted over the past two decades indicate that PTSD is associated with epigenetic changes, including DNA methylation in immune-related genes and DNA repair, which may facilitate malignant development. Yang and Jiang [120], in a landmark meta-analysis, found a statistically significant association between PTSD and cancer incidence, especially in women. Other studies, such as the one conducted by Boscarino [17], support the existence of a relationship between PTSD and serious somatic diseases, including breast, colorectal, and lung cancer.

Beyond these biological mechanisms, the behavioral dimension of PTSD cannot be ignored. Affected individuals tend to adopt behaviors harmful to health — excessive smoking, alcohol abuse, unbalanced diet — and to avoid medical contact (e.g., oncological screenings or treatment follow-up), indirectly but significantly contributing to the increase in oncological risk.

In addition, the impact of psychotrauma on the immune system is particularly relevant in the oncological context. Studies show that PTSD is associated with decreased natural killer (NK) cell activity and impaired T-lymphocyte function, which are essential factors in the recognition and destruction of incipient tumor cells [121–123].

From an integrative perspective, PTSD resulting from interpersonal psychological trauma—such as emotional abuse, rejection, or loss—is not just an isolated psychological phenomenon, but a systemic risk factor. A transdisciplinary understanding of PTSD as an interface between the mind, the endocrine system, and the immune system is needed within a broader biopsychosocial paradigm.

Traumatic Cyclicity and Vulnerability to Disease

An essential aspect in understanding the relationship between psychological stress and oncological vulnerability is the cyclical and self-replicative nature of psychic trauma. According to psychoanalyst Donald Kalsched, in his work "The Inner World of Trauma" [124], the traumatized psyche tends to unconsciously expose itself to contexts similar to the original trauma, reliving the pain in a reactivated and often somatized form. This retraumatization is not just a passive repetition, but a failed attempt by the psyche to "repair" or to confer the initial trauma, which leads to the consolidation of rigid defense mechanisms, hyperactivation of the stress system and, in time, to the depletion of psychophysiological resources. In this context, reliving trauma can take on relational (choosing abusive partners), professional (toxic environments), but also somatic forms, by accentuating neuroimmune imbalances. Repeated exposure to situations of emotional vulnerability maintains a high level of hypervigilance and autonomic reactivity, which, according to psychoneuroimmunological models, favors chronic systemic inflammation and homeostatic instability, conditions conducive to the development of oncogenic processes [125].

Reactivation of trauma is not only a psychological phenomenon, but a biopsychic cycle that involves the entire organism. Thus, in the case of a person with unresolved emotional traumas for a long time, the risk of re-experiencing and somatization is increased, and the body can become, in time, the scene on which the psychic conflict is expressed — sometimes in chronic, degenerative or even oncological forms. This dynamic of "retraumatization" emphasizes the need for oncological treatments to include not only screening for previous traumas, but also psychotherapeutic interventions focused on the original trauma, in an integrative vision of health.

A crucial aspect in understanding psychological trauma is its tendency to manifest in a cyclical, self-replicating pattern. People who have experienced significant adverse events in childhood or early adulthood find themselves unconsciously re-entering relational or existential contexts similar to the traumatic ones, thus perpetuating an internal climate of psychological and physiological vulnerability. This chronic "retraumatization" weakens emotional resilience and can lead to the development of persistent disorders such as PTSD. Recent research suggests that these psychological manifestations are not only the result of life context but may also be genetically modulated.

The study by Johnson et al. [126] provides important evidence in this sense, identifying genetic variants associated with PTSD symptoms in patients diagnosed with gynecological cancer. These data support the idea of bidirectional links between psychological vulnerability, genetic expression,

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and oncological trajectory, marking an essential step in understanding the psychogenetics of cancer risk in recurrent traumatic contexts. In this study, Johnson and colleagues investigate the role of genetic variants in the manifestation of PTSD symptoms in gynecological cancer survivors (the sample included patients with ovarian, uterine/endometrial, cervical, or vaginal/vulvar cancer). In the cohort of 181 patients (recruited between 2017 and 2020 at the University of Minnesota), who completed DSM-V PTSD questionnaires and provided genetic samples (saliva samples), two mutations (SNPs) were significantly associated with high levels of symptoms: rs622337 in the HTR2A gene, involved in the serotonin pathway, and rs510769 in OPRM1, related to opioid receptors. These genetic variants indicate a biological predisposition to more severe PTSD manifestations in the oncological context, suggesting that not only external and psychological factors matter, but also internal vulnerability related to cancer. of genetic variations. This suggests that biological predisposition, through genetic variations, mediates the psychological response to cancer trauma and illness stress.

Although limited by the sample size and the self-reported nature of PTSD symptoms, the study provides an important step toward understanding how genotype interacts with psychosocial factors to generate persistent symptoms of post-traumatic stress. From a clinical perspective, these data argue for integrated genetic and psychological screening, as well as early interventions in patients with gynecological cancer who have predisposing genes or prior traumatic exposures.

The study by Johnson et al. highlights not only the role of PTSD symptoms in gynecological cancer patients, but also the complex interaction between genetic predisposition and persistent psychological trauma. These findings support the idea that severe trauma, especially that of interpersonal or sexual nature, can leave a deep mark not only on the psyche, but also on the biological expression of the individual. In particular, sexual trauma, with its profound implications on bodily integrity, self-esteem and emotional regulation, has been associated in multiple studies with an increased risk of chronic psychological disorders, hormonal disorders and immune modifications relevant to oncological pathogenesis. This relationship becomes even more important in the context of gynecological cancers, where the body becomes simultaneously the site of trauma and disease.

We will now focus on the literature exploring the link between sexual trauma and cancer vulnerability in women, bringing into discussion recent studies that support this biopsychosocial connection.

The meta-analysis by Yang & Jiang [120] discusses a possible association between PTSD and an increased risk of cancer, with the authors arguing that this study starts from contradictory clinical and epidemiological premises regarding the link between PTSD and cancer. Their aim was to clarify whether PTSD increases cancer risk, using rigorous statistical models and data from relevant observational studies. The researchers filtered 3,129 articles from the literature, until they were left with only 8 articles totaling 11 distinct studies (cohort, case–control). Meta-analysis estimated the relative risk (RR) for cancer and specific cancers (e.g. ovarian, breast, lung), based on statistically correct volumes (random effects models) and heterogeneity (I^2) values. Main results indicated that regarding overall cancer risk: PTSD was not associated with a significant overall risk of cancer (RR = 1.05; 95% CI: 0.90–1.22), with moderate heterogeneity ($I^2 \approx 57\%$, p = 0.01). Regarding ovarian cancer, two analyzed studies showed a significant increase in risk among women with PTSD (RR = 2.05; 95% CI: 1.24–3.39), with low heterogeneity ($I^2 = 0\%$), and for breast cancer the association was not significant (RR = 1.19; 95% CI: 0.66–2.13), with high heterogeneity ($I^2 = 78.8\%$), and similarly for gastrointestinal and lung cancer, no significant association was detected (GI: RR = 0.94, $I^2 = 7.1\%$; Lung: RR = 0.98, $I^2 = 58.6\%$).

We can therefore state that PTSD does not seem to be a general predictor of cancer but may be involved only in certain types (e.g. ovarian). The authors recommend investigating the specific neurophysiological mechanisms and differences between cancer types in relation to PTSD. They summarize the need for additional studies with large samples, extended follow-up, and adjustments for confounding factors, including risk behaviors and inappropriate lifestyles associated with PTSD.

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However, we note that this is the first meta-analysis to suggest a specific and relevant link between PTSD and ovarian cancer, confirming the hypothesis that severe emotional behavior may facilitate oncogenesis in a hormone-sensitive context. They also highlight the importance of differentiating between cancer types in psychosomatic studies (no general impact, but specific effect), and clinicians may consider screening for PTSD in the context of oncological predisposition in women with complex trauma. The authors also emphasize the fact that sexual abuse is one of the main causes of PTSD in women, which may have implications for physical health, sexual abuse, as an extreme form of violation of psychic and bodily integrity, being one of the main predictors of PTSD among women. In this meta-analysis, although the data are not dissociated according to the type of trauma, the authors explicitly recognize that sexual abuse is a major trigger of PTSD, with physiological implications on the HPA axis, chronic inflammation and possible hormonal dysregulation. These mechanisms may create a vulnerable biological terrain for the development of certain forms of cancer, especially hormone-sensitive ones, such as ovarian and breast cancer.

In conclusion, this meta-analysis reinforces the hypothesis of a significant connection between PTSD and cancer risk, highlighting the fact that people exposed to major, unresolved psychological trauma may have an increased susceptibility to developing cancer.

This association is reinforced by the results of the systematic review carried out by Pereira [119] which extends the perspective on the influence of psychological factors such as chronic stress, depression, hostility or loss of social support, on the risk of breast and lung cancer. If the study by Yang and Jiang offers a quantitative view of the PTSD–cancer relationship, the analysis by Pereira et al. deepens the qualitative dimension of the affective psychodynamics that accompany and may contribute to the oncogenic process. Together, these two studies highlight the essential role of severe psychological stress—either acute or persistent—in the equation of cancer vulnerability and reinforce the need to integrate psychosocial variables into cancer risk prediction models.

This systematic review of the literature, published in 2022 in Frontiers in Psychology by Pereira et al., constitutes an important plea for further research into the mechanisms and researchers regarding the involvement of psychological factors and PTSD in oncogenesis. The main aim of the study was to explore the relationship between psychological trauma, bereavement, and depression in relation to the risk of breast and lung cancer, before diagnosis. The protocol was rigorous, conducted according to the PRISMA guidelines, and included only cohort or case–control studies that assessed psychological factors antecedent to cancer diagnosis. In total, 26 studies with over 2.5 million participants from various countries were analyzed, with average follow-up of up to 36 years. The main findings indicated that there is partial evidence that emotional trauma may be associated with an increased risk of breast cancer, especially among women and in relevant situations of loss (grief) formulated as adverse events. Interestingly, in the case of lung cancer, no significant association with psychological trauma was identified. However, depression was a consistent and significant risk factor in most of the studies analyzed. Regarding grief and lung cancer, no relevant studies were detected, signaling a clear gap in the current literature.

The review adds theoretical weight to the hypothesis that psychological factors - especially emotional trauma and depression - may contribute to the etiology of certain types of cancer, especially those with a hormonal or somatic-cognitive substrate (e.g. breast). The connection between prolonged grief and breast cancer, although not consensual, indicates the need for future studies focused on different phases of emotional pain. The results confirm the tendency to expand models of oncological vulnerability by including psychological factors such as complex trauma, depression and pre-existing internal conflict.

The conclusions of the systematic review by Pereira highlight the breadth and complexity of the influence of psychological factors on the risk of cancer, especially in the case of frequently studied forms such as breast and lung cancer. These factors include not only perceived stress, but also persistent depression, repressed hostility and alterations in the social support network.

Also in this line is the study carried out by Abate et al. [127] which provides additional and current evidence regarding the close link between psychological stress and oncogenic processes,

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focusing on the pathophysiological mechanisms through which chronic stress, especially emotional and relational stress, contributes to tumor development and progression. Thus, the two works converge towards a new integrative paradigm, in which the psychological component becomes not just an adjacent factor, but a determinant in the etiology and evolution of oncological diseases. Abate and collaborators propose a comprehensive analysis of how psychological stress can influence the initiation and progression of cancer. The authors highlight the fact that, although carcinogenesis is traditionally explained by genetic factors and exogenous exposure (radiation, toxins, infectious agents), in recent years a relationship between chronic psychological stress and oncological susceptibility has become increasingly clear. The work synthesizes experimental and clinical evidence showing how stress repeatedly activates the sympathetic nervous system and releases hormones such as adrenaline and noradrenaline, which can promote systemic inflammation, immune dysfunction and even changes in the tumor microenvironment. Thus, stress not only alters the body's immune response, but can also stimulate essential processes in oncogenesis such as angiogenesis, cell invasion and resistance to apoptosis.

Furthermore, the authors draw attention to the effects of psychological stress on the efficiency of oncological treatments, especially immunological therapies, by reducing lymphocyte activity and the function of NK (natural killer) cells. These observations suggest that stress may contribute not only to the onset of the disease, but also to treatment refractoriness.

At the same time, the article highlights a series of methodological limitations in the studies analyzed: variability in the definition and measurement of stress, lack of standardization of assessment instruments, absence of adjustment for confounding factors such as lifestyle or comorbidities, and the small number of longitudinal studies.

The authors' conclusion is firm: there is growing evidence that psychological stress is a relevant factor in the etiology of cancer and that integrating the psycho-emotional dimension into oncological medicine should become a priority in both prevention and intervention.

In the same area, a recent meta-analysis by Geng et al. [128] systematically investigates the relationship between psychological factors and ovarian cancer incidence. Eight cohort and two case-control studies were used, selected from an extensive literature database (PubMed, Web of Science) up to August The authors report a relative risk in the analyzed cohorts, suggesting a significant association between exposure to psychological stress or psychosocial adversity and ovarian cancer. However, the case-control studies indicate a slight reverse effect, which highlights the possible presence of selection bias, retrospective measurement errors and methodological differences.

From a clinical and theoretical point of view, these findings support the hypothesis that psychological stress, especially when chronic and associated with other indicators of vulnerability (trauma, adverse psychosocial factors), may have an active role in ovarian carcinogenesis. This fact justifies the interest in psychological screening in women, psychosocial risk assessment and the development of preventive interventions. The limitations analyzed are useful for guiding future studies: standardized definitions of psychological stress, prospective-longitudinal data, control for hormonal and lifestyle factors. A strong argument for the involvement of psychological factors in cancer is provided by the work carried out by Roberts et al. [129], which concludes that PTSD may be an etiological factor in ovarian cancer. The study is based on data from the Nurses' Health Study II, with a follow-up of 26 years and over 50,000 women. PTSD symptoms were assessed in 2008, and the diagnosis of ovarian cancer was confirmed by medical records. Women with high levels of symptoms (6-7) had approximately double the risk compared to women without trauma, even after adjusting for environmental and behavioral factors. The relationship was even stronger among premenopausal women. Although it has limitations such as the relatively small number of cases and the self-reported nature of symptoms, this study provides robust clinical evidence of how PTSD may contribute to cancer vulnerability, supporting the hypothesis of ongoing psychological conflicts as significant risk factors. PTSD symptom assessment was based on a questionnaire administered in 2008, including history of trauma exposure and number of PTSD symptoms. Self-reports of ovarian cancer were validated by reviewing medical records. Incidence rates of ovarian cancer among women

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with varying levels of PTSD symptoms were analyzed, adjusting for known risk factors (hormonal factors, use of oral contraceptives, smoking, etc.). The main results of the study showed that women with 6-7 PTSD symptoms had an approximately double risk of developing ovarian cancer compared with those without trauma exposure. After additional adjustment for gynecological and health risk factors, the risk decreased slightly but remained high. In the prospective analysis (i.e. only incidents occurring after the PTSD assessment in 2008), an increased risk was observed for those with high PTSD symptoms.

A very important aspect revealed by the study is that premenopausal women had an even higher risk, among those with high levels of PTSD symptoms. There are limitations of the study related to the relatively small number of ovarian cancer cases in the subgroups analyzed (110 cases), which reduces the statistical power for some analyses (e.g.: prospective vs retrospective). PTSD symptoms are self-reported and measured at one point in time (2008), which may imply retrospective bias for those with older trauma. Adjustments for all hormonal and other behavioral risk factors are not identical between the substudies, which may influence the estimates. The relationship between menopause and increased risk is explored, but not all biological layers (e.g.: menopausal hormones) are clearly demarcated. The implications of the study are even greater as it provides strong evidence that PTSD is not just a secondary psychological factor, but may contribute to the etiology of ovarian cancer, particularly in young and premenopausal women. It suggests that psychological prevention and interventions for PTSD should be considered in public health strategies for women and provides a good model for investigating the biological mechanisms of how posttraumatic stress affects hormones, immunity and, potentially, the ovarian microenvironment.

Complementing the evidence on the influence of psychological stress on the risk of cancer occurrence and progression, the study by Batty [130] makes a valuable contribution through a robust quantitative approach, using data from 16 prospective cohorts. The authors were able to highlight a clear association between psychological distress and mortality from localized cancer, demonstrating that persistent emotional suffering not only influences oncological incidence, but can have a significant impact on the evolution and prognosis of the disease. This research supports the idea that psychological factors cannot be ignored in explanatory models of cancer and, in addition, validates the need for an integrated psychosocial intervention within oncological care, with the potential to improve survival and quality of life of patients. By combining data from 16 prospective studies with 163,363 participants, using the GHQ-12 score to assess anxiety and depression, the team identified that people in the group with the highest level of distress had a significantly higher risk of death from cancer, compared to the group with the lowest distress. This association was also present for nonsmoking-related cancers, and for cancers of the colon, pancreas, esophagus, prostate, and leukemia, among others. This study reinforces the view that psychological distress—through biological and behavioral mechanisms—may have a pronounced influence on cancer mortality and serves as population-wide evidence supporting the hypothesis that chronic psychological conflict not only predisposes to cancer but may also affect its progression and prognosis. All of these studies provide support for the hypothesis that psychological trauma, prolonged stress, and affective disorders are not only comorbidities but may also become etiological risk factors in carcinogenesis.

The convergence of clinical research, meta-analyses, and biological models strongly supports the integration of PTSD and psychological trauma into the broader model of cancer vulnerability. Thus, mental health becomes not only a component of cancer quality of life, but an essential determinant of disease etiopathogenesis and prognosis. They emphasize the need for an integrative bio-psycho-social model and suggest that psychological interventions should not be viewed as ancillary, but as an essential part of modern cancer prevention.

Trauma–Cancer–Trauma Cyclicality

A cancer diagnosis is often experienced by patients as an "existential shock" with high traumatic potential. Numerous studies have shown that a significant percentage of cancer patients develop

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symptoms of posttraumatic stress disorder (PTSD) or partial PTSD after diagnosis and during treatment [131,132].

The prevalence of PTSD in cancer varies between 3% and 30%, depending on the type of cancer, severity of the disease, psychological history and quality of social support [62,120]. Patients with a history of previous trauma are significantly more likely to develop a posttraumatic response after diagnosis [133], which supports the idea of a cumulative vulnerability model.

The traumatic impact of cancer is not limited to the moment of diagnosis. The stages of treatment (surgery, chemotherapy, radiotherapy) can reactivate deep fears related to death, loss of bodily integrity or identity. Furthermore, the post-treatment phase is marked by the fear of relapse, a central symptom in the picture of posttraumatic stress disorder [134]. Thus, in the case of patients with unresolved traumas or old psychological conflicts, cancer may function as a traumatic reactivator, intensifying latent symptoms and psychological vulnerability. In patients with unresolved conflicts, childhood abuse or chronic trauma, the disease may amplify latent psychological symptomatology by reactivating the fear of abandonment or loss of control, intensifying the feeling of helplessness and repressed somatic suffering and the emergence of regressive defense mechanisms.

Thus, we can discuss the trauma–cancer–trauma cycle, a model of cumulative vulnerability, in which paradoxical trauma may be both cause and effect.

Contemporary psychosomatic and oncological psychiatry literature increasingly highlights a bidirectional relationship between psychological trauma and oncological vulnerability. On the one hand, previous traumatic experiences – such as childhood abuse, chronic relational trauma or major emotional loss – can lead to persistent dysregulation of the HPA axis, chronic systemic inflammation and immune dysfunction, thus creating a favorable terrain for the initiation of oncogenetic processes [38,119,120]. This first level of trauma thus becomes a possible biological and psychological "trigger" for the onset of cancer.

On the other hand, however, a cancer diagnosis itself represents a major trauma, capable of reactivating previous traumas or generating de novo PTSD. Studies show that a significant percentage of cancer patients develop trauma-like symptoms, such as hypervigilance, avoidance of stimuli associated with the disease, flashbacks, or derealization [129,132]. This stage marks the second traumatic peak in a cycle that profoundly affects psychic identity, self-coherence, and coping capacity.

The trauma–cancer–trauma cycle has major clinical implications, as it indicates a cumulative vulnerability: patients with a history of unresolved trauma are more susceptible to developing severe posttraumatic stress disorder after diagnosis, and the lack of early psychological intervention may lead to worsening of psychological symptoms and even poor compliance with treatment [126,127]. In this context, it is necessary to integrate specialized psychological support protocols, focused on complex trauma, into all stages of oncology care, not only as psychological support, but as an essential part of integrative medicine.

Psychological Trauma, Chronic Stress and the Persistence of HPV Infection: A Psychoneuroimmunological Mechanism

In this dynamic of the relationship between psyche and oncogenesis, an often underestimated but majorly important aspect is represented by precancerous states — silent phases in which psychological stress and trauma can decisively influence susceptibility to oncogenic infections and progression to cancer. A conclusive example is infection with human papillomavirus (HPV), considered the main precursor of cervical cancer. Infection with human papillomavirus (HPV) is one of the most frequent sexually transmitted viral infections and is the main cause of cervical cancer, as well as other anogenital cancers. Although most HPV infections are transient and cleared by an immune-competent system, a subset of women develop persistent infections and precancerous lesions, which raises the question of immunological and psychosocial factors that can modulate this pathological transition. Increasing evidence supports the hypothesis that psychological trauma,

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chronic stress, and emotional dysfunction play a significant role in impairing the cellular immune response, increasing the risk of viral persistence and oncogenic progression.

Recent studies suggest that chronic stress, unresolved psychological trauma, and severe emotional imbalances can weaken the body's immune response, reducing its ability to eliminate the virus and increasing the risk of persistent infection and development of dysplastic lesions [135,136]. This perspective requires an extension of psychosomatic analysis not only to oncological diseases themselves, but also to the subtle mechanisms that favor the transition from viral infection to malignant transformation in psychologically vulnerable contexts.

In this sense, the work by Lugović-Mihić et al. [135] explores how psychological stress affects the manifestations of human papillomavirus (HPV) infection and contributes to the progression of carcinogenesis. The article highlights that patients with a high level of perceived stress, a history of negative life events or maladaptive coping mechanisms are at increased risk of persistent HPV infection, progression to dysplastic lesions and reactivation of latent infections. At the biological level, the authors describe many stress-mediated mechanisms, including: alteration of the Th1 immune response, decreased natural killer (NK) cell activity, increased Th2 response (less antivirally effective), as well as chronic cortisol release, which may modulate the expression of the viral E6/E7 oncogenes involved in malignant transformation. This immunological dysfunction has direct implications for the body's ability to clear the virus and for the risk of developing HPV-associated neoplasia, especially cervical cancer. The authors also highlight the role of contextual factors, such as gender, age, socioeconomic status, and access to social support, in mediating this relationship. Women with HPV lesions have higher levels of perceived psychological distress, suggesting a possible emotional vulnerability that deserves to be explored in cancer screening. The work contributes to the consolidation of the idea that chronic psychological stress may be an indirect but significant risk factor in the pathogenesis of cancer, through its interference with immune function and viral control. Consequently, psychological and social interventions, aimed at reducing stress and improving coping strategies, could represent an important adjunct in the prevention and management of HPV lesions, with the potential to reduce progression to cancer.

A study by Kuebler et al. [136] directly investigated the relationship between psychological stress and the presence/persistence of HPV in young women, demonstrating that high levels of perceived stress were associated with an increased likelihood of persistent HPV infection, even after adjusting for other behavioral risk factors. The authors propose as the main mechanism the impairment of cellular immunity – in particular the decrease in the activity of NK (natural killer) cells and the alteration of the T lymphocyte response – essential processes in the control of viral infections, advancing the idea that perceived stress may be associated with the persistence of HPV infection in young women, which suggests an interference of stress in the mechanisms of viral elimination.

The authors explore the association between chronic psychological stress and diurnal cortisol variations with the presence and persistence of high-risk HPV (HR-HPV) infection in young women (mean age ~25 years). An increased level of stress, expressed through excessive demands at work and family care, was significantly associated with HR-HPV positivity, independent of sexual and behavioral factors such as smoking. This study contributes significantly to the understanding of psychological stress and HPA axis dysfunction, which may be involved in HPV-associated carcinogenesis: persistence of infection is a critical factor in the progression to cervical dysplasia and cervical cancer. Thus, interventions aimed at reducing stress and regulating the hormonal response (e.g., mindfulness, stress management, social support) could have a preventive role in populations of young women with HPV infections.

Also, a large epidemiological study by Lu et al. [137] provides important evidence regarding the influence of psychological stress on cervical cancer-specific mortality. The analysis was based on data from the Swedish national registry and included 4,245 women diagnosed with cervical cancer between 2002 and 2011, with a mean age of approximately 54 years. The researchers assessed the presence of stress-related psychiatric disorders (e.g., adjustment disorders, anxiety, depression) or extremely stressful life events, occurring before or at the time of cancer diagnosis. The results

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indicated that women with such a psychological history had a significantly increased risk of specific mortality compared with those without a similar history. Specifically, the overall risk was 33% higher among those exposed to severe stress. Women with psychiatric diagnoses related to stress had an approximately 55% higher risk, and those who had experienced significant stressful events without a formal psychiatric diagnosis had a 20% higher risk. These associations were maintained even after adjusting for key clinical variables such as tumor stage, histological type, treatment administered, and associated comorbidities.

This study highlights the fact that severe psychological stress is not only a possible cofactor in the etiology of cancer, but also an important determinant of oncological prognosis. Therefore, the authors advocate for the integration of psychological assessment and emotional support interventions into the oncological treatment plan, especially for patients newly diagnosed with cervical cancer. The relevance of this study lies in strengthening the hypothesis that mental health is a direct determinant of somatic evolution and survival in oncological diseases.

In addition, Cvitanović et al. [138] analyzed a sample of HPV-positive patients and identified increased serum cortisol values, changes in immunological parameters and significant psychological disorders (anxiety, depression, posttraumatic stress) compared to the control group. The results support the theory of a psychoneuroimmunological model in which chronic stress modulates the neuroendocrine immune response, facilitating the persistence of the virus and possible oncological complications [139].

An eloquent example of the impact of psychological trauma on the prevention and early detection of cervical cancer is provided by the study by Kohler et al. [140], which investigates the experiences of women in situations of housing instability or homelessness. The results highlight that previous trauma, including sexual abuse, domestic violence and childhood neglect, has a direct impact on the avoidance of cervical cancer screening, either due to difficulties in relating to medical personnel or due to flashbacks during the gynecological examination. Furthermore, the authors argue that standardized health systems are often not equipped to recognize or adequately respond to the needs of traumatized patients, which leads to distrust in the medical act and delays in accessing preventive services. In this context, the need for a trauma-informed approach in gynecological and oncological services, which should include psychological counseling, empathetic communication and emotionally adapted screening options, is becoming increasingly clear. The article is a convincing call for the integration of psychosocial factors into cancer prevention protocols, especially for vulnerable categories of the population.

Several key findings emerge from this study. First, they identified frequent traumatic histories, with many women reporting stories of trauma, including sexual abuse, in childhood or adulthood. These experiences create heightened sensitivity to invasive medical procedures. They also found adverse physical and psychological reactions to screening, with the Pap test perceived as potentially retraumatizing—positioning, genital exposure, loss of erectile control, and touching can be triggers for anxiety, physical discomfort, shame, and stress. These negative expectations lead to delaying or refusing the test. In fact, because of trauma, many women avoid screening in order to avoid being exposed to situations that remind them of their traumatic experiences. Even if they have been screened at some point, mental preparation, fear, and anticipated fear affect screening fidelity and regularity. The study is highly relevant because it shows how psychological conflicts, deep trauma, and PTSD can affect not only the risk of developing cancer, but also early detection through refusal, delay, or avoidance of screening, which worsens the prognosis. These vulnerable populations (homeless, marginalized) combine structural factors (access to services, resources) with psychological factors, making unresolved trauma and intrapsychic conflicts “invisible” risk elements that translate into health decisions. Taken together, these studies support the idea that psychological stress has multiple implications for HPV infection and cervical oncogenesis—through hormonal, immune, and behavioral mechanisms.

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An integrated approach that includes psychological support, hormonal screening, and trauma-informed interventions could contribute not only to reducing the risk of cervical cancer, but also to improving adherence to prevention programs.

Studies on Chronic Stress and Oncological Therapies - PTSD and the Impact on Oncological Evolution

Beyond its role in triggering oncogenic processes, chronic psychological stress and PTSD can profoundly influence the efficacy of oncological treatment and the patient's overall prognosis. The mechanisms involved are varied – from changes in the tumor microenvironment and functional immunosuppression, to molecular chemoresistance, systemic inflammation and medical avoidance behaviors. This subsection synthesizes recent evidence from literature that supports the need to reevaluate the therapeutic paradigm in oncology, integrating the psychological dimension not only as support, but as a strategic therapeutic intervention [141–143].

The study by Chen et al. [144] highlighted the fact that chronic psychological stress can reduce the efficacy of radiotherapy by inducing an immunodepressed tumor microenvironment and by increasing the expression of cellular radiation resistance mechanisms. These changes have been associated with activation of the HPA axis and increased cortisol secretion, which affects the recruitment of cytotoxic T cells and the production of proinflammatory cytokines necessary for the destruction of malignant cells. Thus, at the molecular level, psychological stress activates the HPA axis, causing increased secretion of glucocorticoids (such as cortisol), which inhibit the cellular immune response and modify the tumor microenvironment. This phenomenon facilitates: polarization of macrophages towards the M2 phenotype, which promotes angiogenesis and suppresses antitumor immunity, reduced recruitment of CD8+ T cells, increased expression of DNA repair mechanisms in tumor cells subjected to radiation. Under these conditions, in the presence of chronic stress, radiotherapy becomes less effective, requiring rethinking of therapeutic protocols depending on the psychological state of the patient. The study strongly supports the need to integrate stress assessment and psychological support into the overall oncological plan, underlining the importance of a holistic approach to the patient.

In a comprehensive review, Flaherty et al. [145] analyze in depth how chronic psychological stress can compromise the efficacy of anticancer treatments, favoring resistance to chemotherapy and immunotherapy. The authors show that stress hormones—glucocorticoids and catecholamines—influence critical cellular pathways involved in cell survival, DNA repair, suppression of apoptotic mechanisms, and modulation of the immune response. In addition, the administration of synthetic glucocorticoids, frequently used as supportive therapy, can exacerbate these effects by activating resistance agents. Also, β-adrenergic signaling induced by catecholamines can stimulate cellular proliferation and invasion processes, decreasing sensitivity to cytotoxic drugs. At the molecular level, it is possible that under conditions of chronic stress, the expression of efflux transporters (e.g. P-gp/ABCB1) increases, proteins that actively eliminate cytotoxic drugs from tumor cells, conferring chemoresistance, influencing the expression of oncogenic genes and those involved in apoptosis, especially by activating signaling pathways such as PI3K/Akt, NF-κB and STATOverall, the article provides theoretical and empirical support for the concept that psychological stress not only contributes to the occurrence of cancer but can be an essential factor in the failure of oncological therapy, significantly influencing the prognosis of the oncological patient. The paper proposes a paradigm shift in the therapeutic approach to the oncological patient, considering that the assessment of chronic stress should be integrated into the treatment plan. Thus, psychological interventions can become complementary to oncological therapy, increasing its effectiveness and reducing the risk of relapse, with therapeutic potential in pharmacological blockade of stress-activated pathways, in parallel with standard chemotherapy.

Both studies highlight the major impact of chronic psychological stress on cancer treatments, but from complementary perspectives: Chen et al. focuses on the immunosuppressive effects of stress on the response to radiotherapy, while Flaherty et al. explores the molecular and epigenetic

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modifications that increase cellular resistance to cancer drugs. This complementarity supports the idea that an integrative psychological approach is not just an additional support, but can be crucial for optimizing cancer response, regardless of the nature of the treatment. At the same time, perioperative stress should be mentioned with its possible repercussions on cancer prognosis. Psychological and physiological stress associated with cancer surgery is an often underestimated factor, but with major implications on postoperative evolution and long-term prognosis. Recent studies suggest that activation of the sympathetic nervous system and HPA axis in the perioperative period may lead to transient immunosuppression, reduced natural killer cell activity, and favoring microdissemination of residual tumor cells [146–149]. Furthermore, increased psychological stress before and after surgery is associated with slower recovery, increased postoperative complications, and even a higher risk of tumor recurrence. These findings support the need for targeted psychological interventions in the perioperative period, with the aim of optimizing the physiological response to stress and improving long-term oncological outcomes.

This is supported by the remarkable study by Hanalis-Miller et al. [150], which provides concrete evidence regarding the effectiveness of personalized psychological intervention in the perioperative period in breast cancer patients. The individually tailored intervention led not only to significant improvements in psychological indicators – such as reduced anxiety and emotional distress – but also to beneficial changes at the biological level, reflected in molecular biomarkers of metastases identified in excised tumor tissues. The results suggest a direct correlation between effective psychological support and regulation of the immune response, reduction of systemic inflammation and decreased metastatic potential. This research supports the hypothesis that perioperative stress can profoundly influence the tumor microenvironment, and well-calibrated psychological interventions can play an essential adjunct role in integrative oncology treatment.

Posttraumatic stress that is not addressed clinically influences: adherence to treatment (hospital avoidance, refusal of therapy), immune dysregulation through chronically elevated cortisol, and amplified somatic symptoms (pain, fatigue, insomnia). In a systematic review, Oh and Son [151] evaluated the relationship between psychological stress and the risk of cancer recurrence, pooling data from 6 clinical and observational studies. The results provide a consistent picture: chronic psychological stress is associated with a significant increase in the risk of recurrence in most types of cancer, including breast, colorectal, and liver. The authors analyze in detail the biological mechanisms involved – such as activation of the HPA axis, elevated cortisol levels, and inhibition of NK (natural killer) cell function – which may contribute to the survival of residual tumor cells. Furthermore, studies that included psychological interventions have suggested that stress reduction may have a protective effect against recurrence. The paper also draws attention to existing limitations: methodological heterogeneity of the included studies, the lack of standardized stress measures, and the difficulty of establishing a clear causal relationship. However, this paper provides significant empirical support for the hypothesis that psychological stress is not only a prognostic factor but may be actively involved in the release of biological factors that favor tumor reactivation. The review supports the idea that psychological stress, and not only biological factors, may play a significant role in the risk of tumor recurrence, especially in cancers with a hormonal or immune-sensitive profile (e.g., breast cancer).

Psychological interventions, especially those that reduce anxiety, depression, and hostility, may have an adjunct role in reducing recurrence, at least for breast cancer. The study provides a theoretical and empirical framework for including psychological interventions in therapeutic plans, not only as support, but as a preventive strategy in the "post-diagnosis, post-treatment stage".

Limitations of the Review

This narrative review is conceptual in design and does not follow a systematic selection protocol, which may limit the reproducibility and exhaustiveness of the included evidence. The cited studies vary in their methodological rigor, outcome definitions, and sample characteristics, which may introduce bias or limit the generalizability of the findings.

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Furthermore, while the review highlights plausible psychoneuroimmunological mechanisms linking prolonged psychological conflicts with cancer vulnerability, a direct causal relationship remains difficult to establish based on the current evidence. Gender-specific susceptibilities and trauma subtypes are discussed, but not quantitatively analyzed, which opens directions for future studies.

Additionally, most of the literature originates from Western populations, and the cultural variability in trauma processing and illness narratives remains underexplored.

Future Research Recommendations

Future studies should adopt longitudinal, transdisciplinary designs to clarify the causal relationship between prolonged psychological conflicts and oncogenesis. Special attention is needed to explore the psychoneuroimmunological mechanisms that mediate the impact of unresolved emotional trauma on immune function, inflammation, and hormonal dysregulation.

Particular focus should be placed on hormone-sensitive cancers (such as breast, ovarian, and cervical cancer), where the biological consequences of chronic stress and trauma may be amplified by endocrine vulnerability. Integrating trauma-informed psychological assessments into oncology protocols could help identify patients at greater psychosomatic risk and improve treatment personalization.

Moreover, future research should investigate the efficacy of psychotherapeutic interventions (e.g., EMDR, ACT, trauma-focused CBT) in modulating stress-related biomarkers and enhancing treatment adherence, immune resilience, and overall quality of life. Addressing current gaps in the standardized measurement of chronic stress and psychological conflict will be crucial for advancing evidence-based psycho-oncological care.

Conclusions, Interpretation of Benefits, and Recommendations

Interpretation of Benefits

This review contributes to a growing body of literature exploring how chronic psychological conflicts, specially unresolved trauma and emotional repression, may influence oncological vulnerability.

By synthesizing data from psychoneuroimmunology, clinical psycho-oncology, and trauma psychology, the paper illustrates how persistent stressors and unprocessed emotional wounds can act as indirect, but significant, biological co-factors.

The main benefit of this integrative approach lies in shifting the biomedical model toward a more holistic framework, where psychological history becomes relevant not only for mental health outcomes, but for somatic disease trajectories as well.

Recommendations

Given empirical and theoretical evidence, we recommend integrating systematic psychological screening, especially for trauma, prolonged grief, and early adverse experiences, into routine oncological assessments. Psycho-oncological interventions, particularly those trauma-informed, should be offered early in the cancer care process, potentially improving both psychological coping and biological treatment responsiveness. Multidisciplinary teams should include psychologists trained in trauma and somatic medicine, and future oncology protocols should incorporate mind–body mechanisms as part of therapeutic planning.

Conclusions

Prolonged psychological conflicts can no longer be viewed as merely emotional burdens. When left unresolved, they may shape physiological pathways that predispose individuals to immune dysregulation, chronic inflammation, and oncogenic processes. Furthermore, these conflicts can

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interfere with treatment efficacy and recovery if unaddressed. This review supports the inclusion of psychological dynamics, especially trauma, stress, and maladaptive coping patterns, as integral factors in cancer vulnerability models and survivorship frameworks.

Final Reflection

In an era of precision medicine, the inclusion of emotional history as a prognostic and therapeutic variable marks a critical evolution in cancer care. The body remembers what the mind tries to suppress. Healing must therefore address not only the tumor, but the story of the person behind the diagnosis. Integrating psychodynamic insight, trauma healing, and emotional resilience strategies into standard oncological care may redefine what it means to treat the whole patient and not just the disease.

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Abbreviations

The following abbreviations are used in this manuscript:

HPA	hypothalamic–pituitary–adrenal
HPV	human Papillomavirus
PTSD	posttraumatic stress disorder
ACEs	adverse childhood experiences
PNI	psychoneuroimmunology
IPNB	interpersonal Neurobiology
IL-6	interleukina 6
CRP	C-reactive protein
CRCI	cancer-related cognitive impairment

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