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Illness Denial in Medical Disorders:

Systematic Review

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Abstract

Introduction: Illness denial pertains to medical patients who do not acknowledge the presence or severity of their disease or the need of treatment. ***Objective:*** This systematic review was performed to clarify the clinical role and manifestations of illness denial, its impact on health attitudes and behavior, as well as on short- and long-term outcomes in patients with medical disorders. ***Methods:*** The systematic search according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines was conducted on PubMed, Scopus, and Web of Science. ***Results:*** The initial search yielded a total of 14098 articles; 176 studies met the criteria for inclusion. Illness denial appeared to be a relatively common condition affecting a wide spectrum of health attitudes and behavior. In some cases, it may help a person cope with various stages of illness and treatment. In other situations, it may determine delay in seeking treatment, impaired adherence and reduced self-management, leading to adverse outcomes. The Diagnostic Criteria for Psychosomatic Research (DCPR) were found to set a useful severity threshold for the condition. An important clinical distinction can also be made based on the DCPR for illness denial, which require the assessment of whether the patient has been provided with an adequate appraisal of the medical situation. ***Conclusions:*** This systematic review indicates that patients with medical disorders experience and express illness denial in many forms and with varying degrees of severity. The findings suggest the need for a multidimensional assessment and provide challenging insights into the management of medical disorders.

Introduction

The term "denial" has a Greek origin and derives from the word "apóphasis", which results from the combination of "apó" meaning "away" or "far off" and "phasis" meaning "statement" or "proposition". Consistent with the Greek origin of the term, the verb "to deny" means "to declare untrue" or "to assert the contrary of" [1]. Based on these etymological roots, attention has been initially focused on the behavioral components of denial (i.e., the direct negation of a problem in words) and the term "denial" was used essentially to refer to the conscious or unconscious tendency of some individuals to verbal repudiation or minimization of part or all of the total available meaning of an event [2, 3]. This definition relied on a psychodynamic framework, where the concept of denial, usually described as the psychological process of disavowal of reality, indicated an immature and pathological defense mechanism, mainly of patients with mental (i.e., psychotic and neurotic) disorders [4, 5]. On this background, researchers have come to conceive denial as a primitive defense, and to view its presence as a signal of serious underlying psychopathology [3]. This view of denial as a dysfunctional defense mechanism was endorsed by other psychoanalytic investigators [6-8]. Shelp and Perl [1] noted, however, that the term "denial" and the psychoanalytic concept it represents have often been used improperly and provided a partial consideration of the complex clinical phenomena related to this construct.

It was David Mechanic [9] who linked denial to the concept of illness behavior, which refers to the ways in which given symptoms may be differentially perceived, evaluated, and acted (or not acted) upon by different kinds of persons. He noted that some individuals have the tendency to minimize symptoms, to shrug them off, and avoid seeking medical care because of their inclination to ignore illnesses [9]. Illness denial was subsequently included in Pilowsky's [10] concept of abnormal illness behavior, which was defined as the persistence of a maladaptive mode of experiencing, perceiving, evaluating, and responding to one's own health status, despite the fact that a doctor has provided a lucid and accurate appraisal of the situation and management to be followed (if any), with opportunities for discussion, negotiation and clarification, based on adequate

assessment of all relevant biological, psychological, social and cultural factors. Over the years, other conceptual frameworks were used to describe the several (i.e., affective, cognitive, and interpersonal) components of illness denial and many definitions were introduced to define this construct [1, 2, 11-20].

Fava et al. [21] developed the first diagnostic criteria for illness denial of having a physical disorder and of the need for treatment as part of the Diagnostic Criteria for Psychosomatic Research (DCPR). An updated version of these criteria was published in 2017 [22] and is displayed in Table 1. Denial was associated with characteristic health-damaging attitudes and behavior such as lack of compliance, delayed seeking of medical attention for serious and persistent symptoms, and counterphobic behavior as a reaction to the symptoms, signs, diagnosis, or medical treatment of a physical illness. Many other definitions of illness denial are available in the literature [1, 2, 12, 14, 19, 20]. The one suggested by Rainer Goldbeck [16] is very comprehensive and applies to patients with different medical conditions presenting with one or more of the following tendencies: (1) not accepting diagnosis or appearing oblivious to it; (2) minimizing the implications of their illness; (3) delay to seek medical advice; (4) refusal or poor compliance with treatment; (5) tendency to apparent detachment in the face of their illness. Thomas P. Hackett and his research group at the Massachusetts General Hospital [3, 23-31] paved the ground for a concept of illness denial which did not necessarily involve negative outcomes and a maladaptive response to illness (e.g., delay in seeking medical help, reduced treatment compliance and/or critical attitude toward hospital/physician), but might have an important adaptive and/or protective value, particularly in the early stages of disease, when illness denial was found to allay fear, anxiety and other unpleasant affects.

There is thus the need for a systematic review of the literature to outline the complex manifestations of illness denial in patients with medical disorders. The major aim of this systematic review of studies was to clarify the clinical role of illness denial and its impact on a wide spectrum of health attitudes and behavior, as well as on short- and long-term outcomes in patients with

different medical disorders. The multiple manifestations of denial in the setting of psychiatric disorders [32] were not included in this systematic review.

Methods

Search Strategy

The present systematic review was conducted in accordance with the updated version of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines [33, 34]. The systematic search was performed in the following databases: PubMed, Scopus, and Web of Science. Each database was searched from inception to March 2023. A manual search of the literature was also performed, and reference lists of the included articles, as well as relevant review articles were examined for further studies not yet identified. Search terms were "denial", "disease", "disorder", and "illness" that were combined using "AND" and "OR" as Boolean operators. A reference management software (Mendeley Desktop) was used to merge results from all searches and remove duplicates.

Eligibility Criteria

To be included in this systematic review, studies had to meet the following criteria: 1) English-language article published in a peer-review journal; 2) the full-text of the article was available online or after request to the authors; 3) illness denial was adequately defined and appropriately evaluated with patient-reported outcome measures (PROMs) [35] and/or with the use of clinician-rated instruments, including open-ended questions; 4) the article was an original investigation reporting quantitative data on illness denial in a clinical population of adult patients (i.e., older than 18 years) with medical disorders (e.g., acute coronary syndrome, diabetes, cancer). Single case reports, general population studies or those where qualitative data were only available (e.g., commentaries, opinion articles), as well as studies involving pediatric or adolescent populations were excluded. Neurological and psychiatric investigations (for instance, those involving

Alzheimer's disease and/or psychotic patients) were also excluded, since they might reflect the spurious effects of lack of insight, as the result of the disease (i.e., neurodegenerative or psychopathological) process. Neuropsychological studies on anosognosia, a term originally coined by Babinski [36] to describe organically based forms of unawareness affecting patients with localized or diffuse brain damage, were also excluded. There were no restrictions regarding the year of publication and the study design.

Study Selection and Data Extraction

Two authors (C.P. and D.C.) independently performed the search, screened titles and abstracts for inclusion, evaluated the full-text of articles appearing potentially relevant, selected studies meeting the eligibility criteria and extracted data on illness denial. In case of disagreement, a consensus was reached through discussion with the senior author (G.A.F.). Data that are concerned with illness denial as a clinical factor affecting health attitudes and behavior in patients with different medical disorders, as well as those regarding the prevalence and impact of illness denial on several clinical outcomes, were extracted, analyzed, and discussed.

Results

The initial search of the literature yielded a total of 14098 articles, of which 2600 on PubMed, 8590 on Scopus, and 2908 on Web of Science. After removing 6743 duplicates using the reference management software, the remaining 7355 articles were screened for evaluation. Excluding 4638 records on the basis of title and abstract, the full-text of the remaining 2717 articles was assessed for potential inclusion. By removing a total of 2541 records on the basis of eligibility criteria, 176 research studies were included in this systematic review. The selection/screening process of studies is described in detail in the PRISMA flowchart (shown in Fig. S1). The results are presented according to manifestations of illness denial in different medical settings. Each section is subdivided according to its relationships with other health attitudes and behavior, prevalence and

clinical implications. The main characteristics (e.g., medical diagnosis, number of participants, methods of assessment of illness denial) of included studies are provided in the online supplementary material (Table S1).

Cardiology

Health Attitudes and Behavior

In evaluating the way in which patients with a diagnosis of acute myocardial infarction responded to symptoms of chest pain, Olin and Hackett [30] showed that the most common initial response was illness denial associated with the tendency to delay seeking medical help. In a subsequent study involving patients with a diagnosis of suspected or proved acute myocardial infarction, Hackett and Cassem [27] did not find a statistically significant relationship between illness denial and the tendency to delay seeking medical care. They showed that patients who denied minimally did not require outside help to seek medical attention [27]. Only patients with major denial (i.e., those who stated unequivocally that they felt no fear at any time throughout their hospitalization) had the tendency to delay seeking medical help unless someone else forced them into action [27]. A more recent study supported these findings showing that myocardial infarction patients with illness denial exhibited only minimally longer overall delay times to reach the coronary care unit compared to myocardial infarction patients without illness denial [37]. Different results were, however, obtained in other studies [38-42]. In a clinical investigation involving consecutive patients with a diagnosis of acute myocardial infarction or coronary artery bypass surgery, Ades et al. [43] observed that those assessed by clinicians as denying the severity of their illness were significantly less likely to enter the cardiac rehabilitation program. In a study with myocardial infarction patients, O'Carroll et al. [40] demonstrated that those who waited over 4 hours prior to seeking medical help had significantly higher levels of illness denial. Similarly, in a cross-sectional investigation examining patients with a first-time myocardial infarction, Stenström et al. [42] found that those with illness denial were more likely to delay seeking medical help and not to attend a cardiac rehabilitation

program. In another cross-sectional study with acute coronary syndrome patients, Perkins-Porras et al. [41] showed that those who had greater levels of illness denial were more likely to have long pre-hospital delay (i.e., defined as the interval between symptom onset and the time of hospital admission recorded in the patients' medical records). Other studies were concerned with the relationship between illness denial and treatment adherence [44, 45]. White et al. [45] conducted a cross-sectional study with congenital heart disease patients and found that illness denial was a significant predictor of nonadherence to cardiac care follow-up. Ganasegeran and Rashid [44] reported similar results in a cross-sectional study with post-myocardial infarction patients demonstrating that a 1-unit increase in the illness denial score was associated with a 20% increase in the odds of being non-adherent to medications.

Prevalence

Prevalence rates of illness denial according to DCPR criteria are reported in Table 2 [46-49]. They ranged from 3.3% in patients with first myocardial infarction to 23.9% in those with suspected vasovagal syncope [48, 49]. Two studies estimated the prevalence rates of illness denial in cardiology with other assessment methods [45, 50]. White et al. [45] showed that a large percentage of patients (42.5%) with congenital heart disease had illness denial. Hoschar et al. [50] found that more than half (i.e., 53.2%) of patients with acute myocardial infarction exhibited illness denial in the prodromal phase of the disease.

Clinical Outcome

Olin and Hackett [30] found that the majority of acute myocardial infarction patients with illness denial were aware of the seriousness of their condition but none of them showed signs of severe anxiety during the interview. A number of studies reported similar results [25, 51, 52]. Gentry et al. [52] and Froese et al. [25] showed that myocardial infarction patients with illness denial experienced less situational anxiety than did those without illness denial. Similarly, Fang et al. [37]

demonstrated that patients with higher illness denial were not only less likely to suffer from anxiety and depression but they were also more likely to report optimal levels of psychological well-being in the six months prior to the onset of an ST-segment-elevation myocardial infarction. In a study involving patients with a diagnosis of acute myocardial infarction, Havik and Mæland [53] consistently found that illness denial was significantly correlated to optimal health attitudes (i.e., more positive views of the consequences of the myocardial infarction, lower levels of hopelessness, and greater satisfaction with the hospital staff). In another study, a negative relationship between illness denial and mortality was found [26]. Illness denial was also found to predict favorable outcomes in patients with cardiovascular disorders [54-58]. In a longitudinal study investigating the relationship between illness denial and the course of recovery in patients who were hospitalized for myocardial infarction or for coronary bypass surgery, Levine et al. [57] found that those with higher levels of illness denial spent fewer days in the intensive care unit and had fewer signs of cardiac dysfunction during their hospitalization compared to patients with lower levels of illness denial. The authors also found that, in the year following discharge, patients with higher levels of illness denial were more noncompliant with medical recommendations and required more days of rehospitalization than those with lower levels of illness denial [57]. Levenson et al. [56] showed that, compared to patients with unstable angina without illness denial, those with high levels of illness denial had half as many episodes of angina during hospitalization and were more likely to reach medical stabilization. In a longitudinal study with a follow-up period of 12 months, Julkunen and Saarinen [59] found that illness denial was a significant predictor of good recovery (i.e., return to work and self-rated health status) in myocardial infarction patients.

Chronic Pain Patients

Health Attitudes and Behavior

Pilowsky and Spence [60] were among the first to show that illness denial was a common coping strategy for patients with chronic pain, particularly for those who minimized the seriousness of their

condition and also tended not to feel sad, anxious or irritable despite the fact that their pain has persisted on average for over 10 years. In a study with chronic low back pain patients, Turner and Clancy [61] found that the denial of pain was significantly and positively correlated to downtime, meaning that those who reported greater use of illness denial spent more time lying down or in a reclining position during the day and evening. High denial was found to be associated not only with lower distress but also with reduced risk of maladaptive cognitions that can have a negative impact on patients' adherence and response to treatment [62]. Mann et al. [63] showed that patients with chronic pain with neuropathic characteristics used illness denial as a coping strategy to reduce the emotional impact of chronic pain.

Prevalence

In a study including patients with pain-prone disorder (defined as persistent/continuous pain associated with a desire for surgery), Blumer and Heilbronn [64] showed that 52% of them denied having had any emotional difficulties because of their condition. In a subsequent study involving consecutive patients with chronic pain, Bouckoms et al. [65] found that the denial of feelings about suffering was documented in 44% of the sample. Holmes et al. [66] found that illness denial was present in 10 of 31 chronic pain patients (32%) with intractable nonmalignant pain.

Clinical Outcome

In patients with chronic pain, Osborne and Swenson [67] found that those with high levels of muscle tension were more likely to use illness denial. Exploring whether coping strategies predicted adjustment in patients with chronic low back pain, higher scores on the subscales of denial of pain and persistence (reflecting the patients' tendency to ignore their pain sensations and continue, where possible, with their normal everyday functioning) were found to be associated with lower levels of disability [68].

Dermatology

Health Attitudes and Behavior

Goldsmith et al. [69] observed attitudes of denial in psoriatic patients who were generally uncooperative in following an outpatient treatment regimen. In a subsequent cross-sectional study with patients having a dermatologist-confirmed diagnosis of psoriasis, Fortune et al. [70] found that those who used alcohol and drugs as a way of coping with their illness were more likely to be in denial and to report greater disability as a result of their psoriasis.

Prevalence

Using the DCPR, illness denial was detected in 10 of the 545 patients (1.8%) with various forms of skin disease undergoing a comprehensive psychosomatic assessment [71] and thus found to be relatively uncommon compared to other medical disorders (Table 2).

Clinical Outcome

In patients with psoriasis, Cvitanović and Jančić [72] found that illness denial was significantly correlated with higher levels of stress and greater disease severity. The same research group replicated these findings in a subsequent study [73]. Similar findings were also observed in patients with melanoma, where correlation analyses revealed that illness denial was significantly associated to higher levels of psychological distress [74]. In patients with plaque psoriasis, Jankowiak et al. [75] showed that denial, defined as a lower level of illness acceptance, was significantly associated with impaired quality of life.

Diabetology and Endocrinology

Health Attitudes and Behavior

Several studies have been performed to evaluate attitudes of denial in patients with diabetes [76-82]. In particular, Hyphantis et al. [77] showed that illness denial was a significant predictor of poor

adherence (defined as delayed engagement to treatment) in outpatients with type 2 diabetes. In evaluating patients' attitudes towards insulin therapy in adults with type 2 diabetes, Rajab et al. [79] found similar results.

Prevalence

In patients with a diagnosis of type 1 diabetes mellitus, high levels of illness denial were found in 22% of the sample [83]. Karlsen and Bru [84] showed that 13% of their sample of patients with both types of diabetes responded to diabetes-related problems by illness denial. In a study with diabetes patients, of which 1261 with type 2 diabetes, illness denial was detected in 7% of the sample [85]. Rajab et al. [79] reported the tendency to deny the severity of disease in 67.5% of patients with type 2 diabetes. A high prevalence of illness denial (33.8%) was also detected in a recent study involving patients with type 2 diabetes mellitus [86]. In a study investigating reasons for failure to achieve disease control in a group of 120 patients with long-standing acromegaly, illness denial was detected in 23.3% of the sample [87].

Clinical Outcome

Several studies have been conducted to assess the extent to which illness denial affected clinical outcomes and recovery in patients with various forms of diabetes [85, 88-92]. Peyrot and McMurry [90] showed a statistically significant relationship between illness denial and poor glucose control in a small sample of insulin-treated diabetic adults. Mühlhauser et al. [89] found that illness denial was a significant risk factor of severe hypoglycemia in a large sample of patients with type I (insulin-dependent) diabetes. Garay-Sevilla et al. [88] reported similar findings in a cross-sectional study involving patients with type 2 diabetes mellitus. They found that illness denial was a significant predictor of poor metabolic (i.e., glycemic) control [88].

Gastroenterology and Hepatology

Prevalence

Kiernan and Powers [93] were among the first to detect inappropriate reactions of illness denial in hepatitis B patients. They showed that 30% of patients denied the possibility of disease transmission [93]. The same authors reported similar prevalence rates in a subsequent study [94]. In a more recent study illness denial was detected in 13.7% of patients with hepatitis B [95]. Using the DCPR, illness denial was found in 7 of the 190 patients (3.7%) with functional gastrointestinal disorders [96].

Clinical Outcome

In a research study investigating the role of biological (e.g., immune parameters such as interferon-a and soluble interleukin-2) and psychological factors in determining disease progression, Rose et al. [97] concluded that illness denial may have a negative impact on recovery processes of patients with hepatitis A.

Infectious Diseases

Health Attitudes and Behavior

Several studies have been performed to assess the clinical role of illness denial in human immunodeficiency virus (HIV) patients [98-103]. In a case-control study comparing patients with HIV and HIV-negative controls, Perkins et al. [102] found that in HIV patients, those with a personality disorder showed significantly greater use of illness denial and helplessness as mental and behavioral strategies to cope with the threat of acquired immune deficiency syndrome (AIDS). Commerford et al. [98] reported similar findings in a subsequent study with female patients with HIV/AIDS infection. Illness denial and problem-focused threat minimization were found to be associated with measures of anxiety and depression, meaning that the greater the use of these coping strategies, the higher were anxiety or depression [98]. In patients with HIV, illness denial was found to be associated with poor quality of life and with perceived stress [100, 103]. The use of

illness denial as a form of coping was found to be associated with lower levels of physical and mental health-related quality of life [100]. Kiyingi et al. [101] showed that the initial denial of HIV infection was a significant predictor of delayed initiation of the therapy.

Prevalence

Prevalence rates of illness denial in HIV greatly varied across studies, from 9% of cases [104] to 74% [105], with intermediate results such as in 33% [106] and 28% of the samples [107]. In a prospective study of HIV patients who were enrolled in a tuberculosis preventive therapy program, illness denial (defined as the denial of the HIV infection status) was found in 11 of the 72 (15.3%) patients who demonstrated poor treatment adherence [108].

Clinical Outcome

In a 2-year longitudinal study involving patients with AIDS, Ironson et al. [109] found that illness denial and poor adherence to behavioral interventions were significant predictors of disease progression, meaning that the higher the increase of illness denial and the lower the treatment adherence, the greater the likelihood of having symptoms at 2-year follow-up. Illness denial was also found to be significantly associated with a decline in the number of CD4 cells, which are immune markers of disease progression in the spectrum of HIV-related disorders [109]. In a subsequent prospective study involving patients with HIV type-1 infection without AIDS or symptoms at baseline, Leserman et al. [110] reported similar results and demonstrated that those who cope with the threat of AIDS by using illness denial have faster disease progression when followed for up to 7.5 years. Patients who used illness denial as a strategy of coping with HIV/AIDS were significantly more likely to report greater pain severity [111]. More recent studies were also conducted to evaluate the clinical role of illness denial in other infectious diseases [112, 113]. In a cross-sectional survey examining levels of perceived stress and coping mechanisms related to COVID-19, illness denial was found to be positively associated with optimal levels of

psychological well-being [113]. In another cross-sectional investigation, illness denial was found to be significantly associated with an increase in levels of COVID-19-related stress [112].

Nephrology

Health Attitudes and Behavior

Several studies evaluated the clinical role of illness denial in patients with various forms of renal disease [114-117]. Short and Wilson [116] were among the first to show that illness denial may serve as an effective mental mechanism helping patients with chronic renal failure to cope with a continuing unsatisfactory situation. In a retrospective study, Richmond et al. [118] demonstrated that higher levels of illness denial were positively correlated with increased probability of success on home hemodialysis. In a subsequent cross-sectional investigation involving hemodialysis patients, Jadoulle et al. [119] reported similar findings. They found that illness denial was an efficient coping style having a protective effect against negative emotions, particularly against anxiety and depression [119]. The authors, however, showed that illness denial can reduce treatment compliance [119]. In a retrospective study of patients with chronic kidney disease, Obialo et al. [120] found that illness denial was a significant determinant of late and ultra-late referral and presentation for renal replacement therapy.

Prevalence

Jungers et al. [121] found that 40% of their late referral patients failed not only to acknowledge the existence of their chronic kidney disease but also to appear for follow-up visits with their nephrologist. Obialo et al. [120] reported similar results showing that illness denial, which was detected in 45% of their retrospective sample of patients with chronic kidney disease, was the predominant reason for delayed referral for renal replacement therapy. In a subsequent study involving patients with chronic kidney disease, illness denial was detected in 35.24% of the sample [122]. In kidney transplant recipients, DCPR illness denial was detected in 13.4% of the sample

[123], with a high prevalence compared to other medical disorders (Table 2). In a cross-sectional investigation involving hemodialysis patients, Shamasneh et al. [124] found that 17.8% of patients denied their disease or even their need for hemodialysis. Alfarhan et al. [125] conducted a similar study reporting higher prevalence rates of denial of chronic kidney disease and of the need of hemodialysis that were detected in 76.4% of the sample.

Clinical Outcome

In a research study involving chronic hemodialysis outpatients, Yanagida et al. [117] demonstrated that the higher was the level of denial, the lower were feelings of depression and a sense of helpless dependence. Similarly, in a study with end-stage renal disease patients, Fricchione et al. [126] showed that those with low levels of illness denial were more sensitive, had more anxiety and depression, and also reported greater sleep disturbances than patients with high levels of illness denial. In a more recent study involving pre-dialysis patients with chronic kidney disease, Pugi et al. [127] found that illness denial was a significant predictor of higher levels of health-related quality of life. The authors showed that chronic kidney disease patients with illness denial were not bothered by the effects of the kidney disease on daily life, did not perceive high levels of frustration and interference of kidney disease in their life, did not report any concentration problems or mental confusion [127]. In a cross-sectional investigation involving hemodialysis patients, however, Carvalho et al. [128] showed that illness denial was associated with impaired health-related quality of life. In a study of patients with peritoneal dialysis, the intensity of illness denial correlated with end-stage renal disease-related anxiety [129].

Oncology

Health Attitudes and Behavior

Many studies have been conducted to assess whether illness denial was a determinant of health attitudes and behavior in patients with cancer [28, 130-148]. In particular, Lynch and Krush [138]

showed that factors contributing to delay (defined as an interval of three months or longer between the time an individual first notices signs or symptoms of cancer and the time he/she seeks medical attention) in a heterogeneous sample of patients with various forms of cancer included attitudes of denial. In a more recent study, Panzarella et al. [149] found that illness denial was a significant predictor of diagnostic delay in patients with oral squamous cell carcinoma. Similarly, in a cohort study of newly diagnosed patients with lung cancer, Kotecha et al. [150] found that illness denial was one of the most significant patient-related causes of delay (defined as the time from first symptoms of lung cancer to contacting primary care). Contrasting results were also reported. For instance, Watson et al. [151] did not observe a statistically significant relationship between illness denial and increased delay in seeking medical treatment in a newly diagnosed group of patients with breast cancer.

Prevalence

Aitken-Swan and Easson [11] detected the initial reaction of illness denial to the diagnosis of cancer in 19% of the sample. In assessing why patients with various forms of cancer (e.g., breast, cervix, and lung cancer) delayed seeking medical advice, Henderson [152] found that the most common reason was denying the seriousness of symptoms (39.4% of the sample). Lebovits et al. [153] found similar prevalence rates. In a study conducted in patients with a diagnosis of lung cancer, denial was detected in 15% of the sample [154]. Evaluating cancer patients with the use of DCPR [21], Grassi et al. [155] documented illness denial in 8.2% of the sample. Vos et al. [156] investigated the prevalence of illness denial over time in newly diagnosed lung cancer patients. They found that most patients displayed a low (65%) or moderate (21.5%) level of illness denial at baseline, while only a small number (3%) showed a high level of illness denial [156]. They also found that the majority of patients continued to exhibit a low level of illness denial at subsequent assessments [156]. In evaluating the reasons for delayed diagnosis and treatment in a cohort of consecutive patients with non-melanoma skin cancer, Alam et al. [130] found that patients waited to see their

doctor because of their illness denial. Specifically, the authors showed that the two most commonly reported reasons why patients delayed seeking medical care were thought it would go away (36% of patients) and thought it wasn't important (24% of the sample) [130]. Beesley et al. [157] detected illness denial in 74% of patients with ovarian cancer.

Clinical Outcome

Several studies have been performed to evaluate the impact of illness denial on clinical outcomes and recovery in patients with various forms of cancer [151, 158-173]. Greer et al. [161] conducted a prospective study involving consecutive patients with early breast cancer to examine whether particular coping responses affected long-term prognosis. They showed that recurrence-free survival at 5-year follow-up was significantly more common among patients who had initially reacted to cancer by denial than among those who had responded with stoic acceptance or with feelings of helplessness and hopelessness [161]. In a subsequent study using the same design and sample, Pettingale et al. [173] found that patients with psychological responses of denial to the diagnosis of cancer had significantly higher levels of serum immunoglobulins IgM than either those who responded with fighting spirit or stoic acceptance. Findings demonstrating the protective effect of illness denial were replicated in other longitudinal studies with follow-up evaluations of 10 and 15 years, where it was found that breast cancer patients who responded with illness denial were significantly more likely to be alive and free of recurrence than those with fatalistic or helpless responses [162, 174]. Watson et al. [151] reported that breast cancer patients who denied the seriousness of their diagnosis experienced significantly less mood disturbances and less anxiety than those who accepted the implications of their diagnosis, thus suggesting that denial rather than a confrontation-coping-response may effectively reduce psychological distress, particularly during the initial phase of hospitalization. Dean and Surtees [159] revealed that breast cancer patients employing a coping strategy of illness denial had a better chance of remaining recurrence-free during the follow-up period than those adopting other coping strategies. They also found that there

was a statistically significant tendency for breast cancer patients with illness denial, at three months postoperatively, to have more chances of survival than those exhibiting other coping strategies [159]. Lehto et al. [175] reported similar findings showing that illness denial was a significant predictor of longer survival in patients with localized melanoma. They also found that illness denial was the only protective factor that predicted survival independent from other psychological variables [175]. Vos et al. [176] investigated the relationship between illness denial and clinical outcomes in a longitudinal investigation with newly diagnosed lung cancer patients: those displaying moderate or increasing denial reported better physical functioning, less nausea and vomiting, less appetite loss, and less dyspnea. They also found that moderate deniers suffered less from fatigue than low deniers and increasing deniers reported less fatigue over time [176]. In a subsequent study of newly diagnosed lung cancer patients, the authors prospectively investigated the relationship between illness denial and psychological outcomes [177]. They not only found that moderate deniers reported better emotional functioning, less anxiety, and less depression than low deniers but also showed that overall quality of life was significantly better among lung cancer patients who displayed either moderate or increasing levels of denial [177].

Primary Care

Prevalence

In a case-control study involving primary care patients who were assessed using the DCPR, illness denial was a frequent psychosomatic syndrome, which was detected in 68% of frequent attenders [178]. In a trial using the DCPR to assess psychosocial problems in primary care patients, illness denial was found to occur in 3.5% of the sample [179].

Respiratory Diseases

Health Attitudes and Behavior

In evaluating psychological reactions of patients following a life-threatening attack of asthma, Yellowlees and Ruffin [180] observed that patients responded to this adverse event by either decompensating psychiatrically and developing symptoms of anxiety, or by increasing their levels of illness denial. In a subsequent study with consecutive patients who presented to the emergency hospital with a near fatal attack of asthma, Campbell et al. [181] found that those with higher levels of illness denial were less likely to describe the presentation of asthma attacks as a progressive respiratory distress and more likely to report the presentation of these symptomatic episodes as a sudden respiratory collapse. The authors thus concluded that high levels of illness denial may be life-threatening since they may be an obstacle to the adoption of appropriate self-management strategies to control asthma and reduce the severity of attacks [181]. In patients with a diagnosis of asthma, illness denial and the level of adherence to asthma medication were not significantly correlated [182, 183].

Prevalence

In a study with consecutive cases of near fatal asthma attacks, illness denial was detected in 57% of patients [181]. In a subsequent study with near fatal asthma, illness denial was detected in 42% of the sample [184]. Gamble et al. [185] found that 160 of 182 patients (88%) with difficult asthma admitted poor adherence with inhaled therapy after initial denial. In a comparative study involving patients with end-stage chronic obstructive pulmonary disease, 26% of them appeared to be in denial [186].

Clinical Outcome

In a prospective, randomized controlled trial of patients with moderate-to-severe asthma who did not have evidence of poor perception of bronchoconstriction on histamine challenge testing, Adams et al. [187] showed that those who had emergency hospitalizations were more likely to have higher baseline levels of illness denial, and more anxiety on both trait-anxiety, and state-anxiety scales. In

patients with a diagnosis of asthma, illness denial was a significant predictor of poor outcomes [188, 189]. In a cross-sectional study of patients with chronic obstructive pulmonary disease, higher levels of illness denial were found to be associated with impaired health-related quality of life [190].

Rheumatology

Health Attitudes and Behavior

In a comparative study examining differences in reactions to disability between a group of patients with early rheumatoid arthritis and a sample of patients with advanced rheumatoid arthritis, Treharne et al. [191] showed that illness denial may be an adaptive strategy to cope with disability, particularly in the early stages of this rheumatological condition.

Prevalence

Illness denial was found in 44.5% of subjects with rheumatoid arthritis [192]. Tesio et al. [193] conducted a comparative study investigating the prevalence rates of DCPR syndromes in patients with fibromyalgia compared with a group of rheumatoid arthritis patients. Illness denial was detected in 32.7% of patients with fibromyalgia and in 20.4% of those with rheumatoid arthritis [193].

Traumatology

Health Attitudes and Behavior

In an exploratory cross-sectional study of spinal cord injury patients, Livneh and Martz [194] found that those with recent-onset spinal cord injury had higher levels of illness denial. In a subsequent study, emotional attitudes of denial were related to lower levels of adaptation to disability [195, 196]. Kortte et al. [197] found that greater rehabilitation engagement in patients with spinal cord injury was significantly related to lower levels of illness denial.

Prevalence

In a study with spinal cord injury patients, Cook [198] found that 34% of the sample had illness denial. In a subsequent study of patients with spinal cord injury, Fukunishi et al. [199] reported prevalence rates of illness denial (defined as disappearance of consciousness of disability) ranging from 13% to 31%.

Clinical Outcome

In patients with a traumatic spinal cord injury, those with illness denial were more likely not only to be less depressed but also to reject the sick role [200]. Similar findings were reported in a subsequent longitudinal investigation involving patients with traumatically acquired spinal cord injury [201]. Opposite results were also observed [202, 203]. In a cross-sectional analysis of patients with traumatic spinal cord injury, the denial of illness was found to be significantly correlated with anxiety, depression and hopelessness [202]. In another study, higher levels of illness denial were associated with lower levels of affective well-being [203]. In patients with paraplegia due to traumatic long-term spinal cord injury, illness denial was found to be negatively correlated to measures of posttraumatic growth [204]. In subsequent studies with spinal cord injury patients, illness denial was a significant predictor of higher levels of symptoms of anxiety [205] and was also found to be negatively associated with basic hope and a general sense of self-efficacy [206].

Discussion

The findings of this systematic review indicate that illness denial is a significant determinant of health attitudes and outcomes in different medical disorders. Its prevalence (ranging from 1.8% to 74%) may vary as a function of the measure used, the specific disorder and the medical setting. Illness denial appeared to play a major clinical role in the process of convalescence, in the self-management of chronic conditions such as diabetes, and in determining disease progression and a state of recovery, as well as the likelihood of early recognition of life-threatening diseases (e.g.,

cancer, myocardial infarction, near fatal attacks of asthma) and their prompt treatment. Despite its high prevalence and its influence on the course, therapeutic response, and clinical outcome of several medical disorders, illness denial is not included in the customary taxonomy, particularly in diagnostic classification systems such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) [207] or the International Classification of Diseases (ICD) [208].

The findings of this review also indicate that as a general mechanism denial is not necessarily dysfunctional, but may serve important adaptive functions. It may help a person cope with various phases of illness and treatment by allowing time to process and dilute distressing information at a manageable rate, as was found to occur in cancer [209]. Patients who had low levels of denial did not delay in reporting their symptoms to the medical attention, did not require outside help to seek medical help, were more likely to exhibit health-promoting attitudes and behavior, and had more favorable clinical outcomes [27, 37, 53, 56, 57, 59, 118, 119, 126, 127, 161, 173, 175, 176]. Denying the burden of physical disease may indeed be an adaptive coping mechanism in some circumstances and at certain degrees, as in the early stages of the disease, for example immediately after diagnosis, or in the terminal phase of a life-threatening disease because it may alleviate psychological distress, as well as symptoms of anxiety and depression [25, 37, 49, 52, 210]. Illness denial may also improve clinical outcomes [56, 59, 68, 127, 159, 161, 173, 175]. The following clinical findings exemplify these phenomena: (1) unstable angina pectoris patients with illness denial were more likely to reach medical stabilization [56], (2) illness denial was a significant predictor of good recovery in cardiac patients with myocardial infarction [59], (3) chronic pain patients with illness denial reported lower levels of disability [68], (4) in patients with chronic kidney disease illness denial predicted higher levels of health-related quality of life [127], (5) patients who had initially reacted to cancer by denial were significantly more likely to be alive and free of recurrence at a 5-year follow-up evaluation and had significantly higher levels of serum immunoglobulins IgM than either those who responded with fighting spirit or stoic acceptance [173], (6) illness denial was a significant predictor of longer survival in breast cancer patients and in

those with localized melanoma [159, 161, 175]. In these clinical situations, where illness denial may not only provide protection against painful and distressing experiences but also facilitate coping with difficult situations and improve both short- and long-term outcomes, it can be viewed as an adaptive process [16]. However, high levels of denial may be dysfunctional and associated with delay in seeking treatment, impaired adherence, and treatment refusal [109, 110, 188, 189, 211]. For instance, Campbell et al. [181] demonstrated that illness denial was a significant barrier to the adoption of appropriate self-management strategies to control asthma and reduce the severity of attacks. Garay-Sevilla et al. [88] showed that in patients with type 2 diabetes mellitus illness denial was a significant predictor of poor metabolic (i.e., glycemic) control. In another study with post-myocardial infarction patients, illness denial was found to be associated with an increased risk of being non-adherent to medications [44]. Among patients with lung cancer illness denial was one of the most significant causes of delay in seeking medical help [150]. In these cases, where illness denial inhibits actions of potential importance (e.g., refusal of medical attention or poor compliance with necessary treatment), it should be regarded as maladaptive [16, 19].

Criteria of gradation are thus needed to assess the degree of illness denial and its impact on clinical outcomes. The DCPR criteria [21, 22], with their semi-structured interview [212], may help clinicians and investigators to set a severity threshold for illness denial and other health attitudes and behavior. However, it is not just a matter of grading intensity. The criterion B of the DCPR (Table 1) requires the fact that the patient has been provided with an adequate appraisal of the medical situation and management (if any) to be followed, with opportunity for discussion and clarification [22]. Denial should not be confused with lack of adequate information and or misunderstandings that may occur in the medical system, that may be amenable to improvement through provision of medical information and adequate explanation. This shared decision-making approach, which requires an empathetic and communicative physician-patient relationship, is particularly important in individuals with limited health literacy, who would otherwise be prone to worse self-management, lower use of preventive services, and higher hospitalization rates [211].

The findings of this systematic review disclose that illness denial was frequently associated with other health attitudes and behavior related to disease perception and treatment seeking. As a result, evaluation of illness denial needs to be placed within a unifying spectrum [211]. On one side of the spectrum, there are manifestations that are characterized by anxiety, with particular reference to worries about illness, concern about pain and bodily preoccupations. On the other side of the spectrum, there are various forms of health-damaging behavior, that range from unrealistic optimism to delay in seeking medical care, from partial or total lack of adherence to complete denial of diagnosis and of the need for treatment [211]. As important is relating illness denial to affective disturbances that may influence its expression, such as anxiety, depression, demoralization and irritable mood [22, 213].

The findings of this systematic review also highlight the lack of trials that are concerned with treatment or modification of illness denial. The effectiveness of specific management strategies or intervention procedures needs to be tested in randomized controlled trials (RCT) and this area of research deserves high priority in funding.

The clinical evaluation of illness denial in medical settings is a major health care challenge that requires a unifying conceptual framework for the wide range of attitudes and behavior related to the complex balance between health and disease, adoption of a psychosomatic assessment of its multidimensional characteristics, and use of appropriate clinimetric methodology for its determination [22, 35, 214, 215]. Clinimetric indices such as the DCPR that make full use of the clinical experience and skills of the interviewer may address the psychological mechanisms of denial and the level of communication that has occurred between patient and physician, while self-rated scales have considerable limitations in covering such aspects.

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Statement of Ethics

An ethics statement is not applicable because this study is based exclusively on published literature.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Chiara Patierno and Danilo Carrozzino searched, screened, and selected studies; both authors extracted data. Giovanni A. Fava supervised the study selection and data extraction. All the authors conceived the work and drafted and finalized this paper.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

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Table 1. DCPR criteria for illness denial (criteria A and B are required) **(modified from Fava et al. [22])**

Criterion A	Persistent denial of having a physical disorder and needing treatment (e.g., lack of compliance, delayed seeking of medical attention for serious and persistent symptoms, counterphobic behavior) as a reaction to the symptoms, signs, diagnosis, or medical treatment of a physical illness
Criterion B	The patient has been provided with an adequate appraisal of the medical situation and management (if any) to be followed, with opportunity for discussion and clarification

Table 2. Prevalence rates of illness denial using the Diagnostic Criteria for Psychosomatic Research (DCPR)

Medical setting	Authors	Patients (*n*) and medical diagnosis	Prevalence (%)
Cardiology	Grandi et al. [46]	129 patients who underwent heart transplantation	4.6%
	Guidi et al. [47]	70 outpatients with congestive heart failure	22.9%
	Rafanelli et al. [48]	61 patients with first myocardial infarction	3.3%
	Rafanelli et al. [49]	67 patients with suspected vasovagal syncope	23.9%
Dermatology	Picardi et al. [71]	545 patients with various skin diseases	1.8%
Gastroenterology and Hepatology	Porcelli et al. [96]	190 patients with functional gastrointestinal disorders	3.7%
Nephrology	Battaglia et al. [123]	134 kidney transplant recipients	13.4%
Oncology	Grassi et al. [155]	146 outpatients with various forms of cancer	8.2%
Primary Care	Ferrari et al. [178]	50 frequent attenders in primary care	68%
	Piolanti et al. [179]	200 primary care patients	3.5%
Rheumatology	Tesio et al. [193]	98 patients with fibromyalgia	32.7%
	Tesio et al. [193]	98 patients with rheumatoid arthritis	20.4%

Figure S1. Flowchart of the systematic search

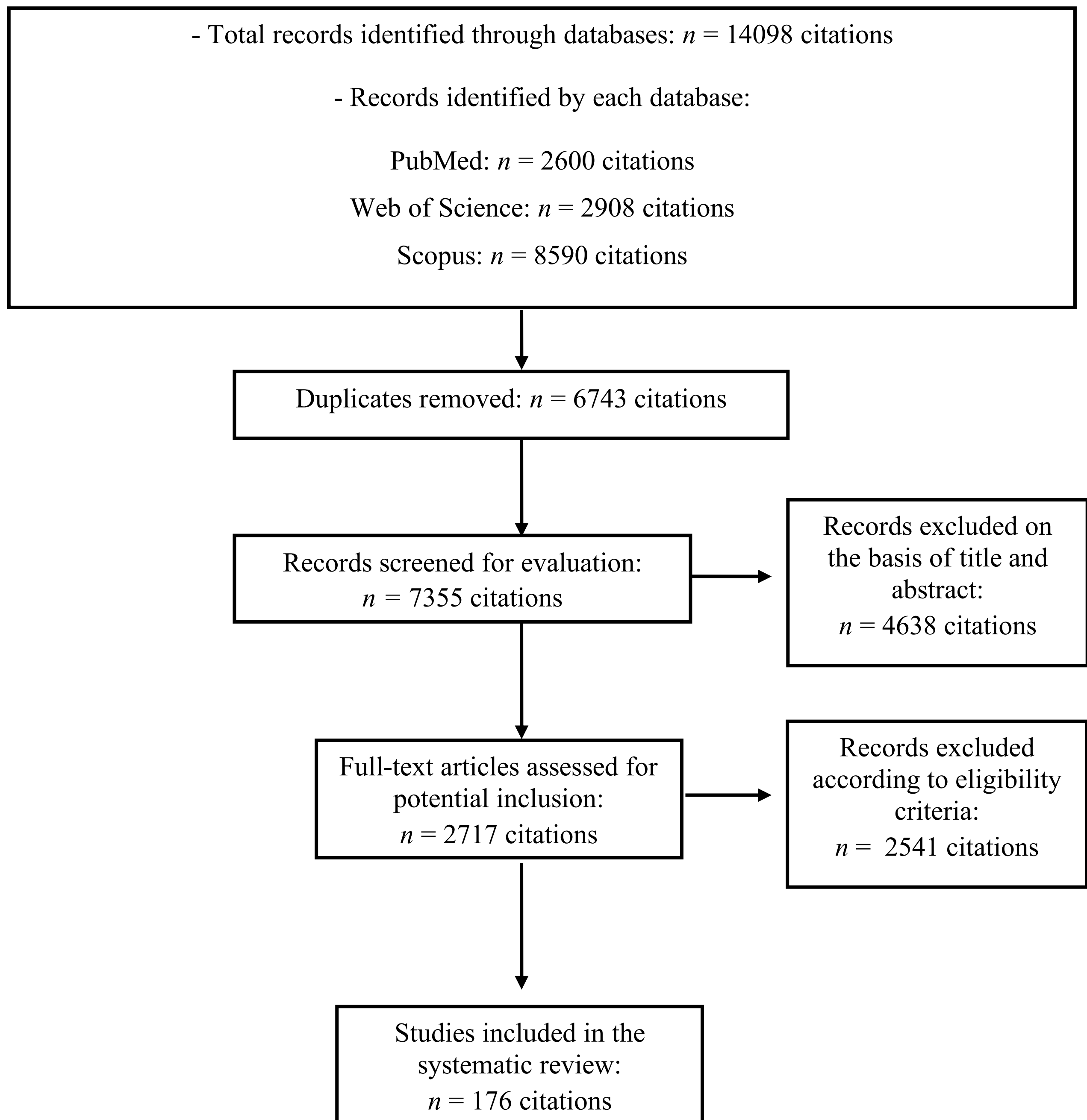

Table S1. The main characteristics of included studies

Authors and year of publication	Title	Patients (*n*) and medical diagnosis	Assessment
Adams et al., 2001 [187]	A randomized trial of peak-flow and symptom-based action plans in adults with moderate-to-severe asthma	134 patients with moderate-to-severe asthma	Illness Behaviour Questionnaire (IBQ)
Ades et al., 1992 [43]	Predictors of cardiac rehabilitation participation in older coronary patients	226 consecutive patients with acute myocardial infarction or coronary artery bypass surgery	Semi-structured interview
Aitken-Swan and Easson, 1959 [11]	Reactions of cancer patients on being told their diagnosis	231 patients with cancer	Semi-structured interview
Alam et al., 2011 [130]	Delayed treatment and continued growth of nonmelanoma skin cancer	982 consecutive patients with nonmelanoma skin cancer	Self-reported questionnaire
Albuquerque et al., 2011 [190]	Ego defense mechanisms in COPD: impact on health-related quality of life and dyspnoea severity	80 patients with chronic obstructive pulmonary disease	40-item Defense Style Questionnaire (DSQ)
Alfarhan et al., 2020 [125]	Causes of the delay in creating permanent vascular access in hemodialysis patients	212 patients with chronic kidney disease	Likert-scale questions
Battaglia et al., 2018 [123]	Abnormal illness behavior, alexithymia, demoralization, and other clinically relevant psychosocial syndromes in kidney transplant recipients: a comparative study of the diagnostic	134 kidney transplant recipients	Diagnostic Criteria for Psychosomatic Research (DCPR)

	criteria for psychosomatic research system versus ICD-10 psychiatric nosology		
Beesley et al., 2018 [157]	Coping strategies, trajectories, and their associations with patient-reported outcomes among women with ovarian cancer	634 patients with ovarian cancer	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Bleeker et al., 1995 [38]	Psychological and knowledge factors related to delay of help-seeking by patients with acute myocardial infarction	300 patients with acute myocardial infarction	Denial Questionnaire
Blumer and Heilbronn, 1981 [64]	The pain-prone disorder: a clinical and psychological profile	234 patients with pain-prone disorder	Minnesota Multiphasic Personality Inventory (MMPI)
Bouckoms et al., 1985 [65]	Denial in the depressive and pain-prone disorders of chronic pain	63 consecutive patients with chronic pain	Semi-structured Interview
Bracken et al., 1981 [200]	Psychological response to acute spinal cord injury: an epidemiological study	190 patients with a traumatic spinal cord injury	Likert-scale questions
Byra, 2016 [204]	Posttraumatic growth in people with traumatic long-term spinal cord injury: predictive role of basic hope and coping	169 patients with paraplegia	Coping Orientations to Problems Experienced (COPE)
Byra and Gabryś, 2023 [206]	Coping strategies of women with long-term Spinal cord injury: the role of beliefs about the world, self-efficacy, and disability	187 women with paraplegia	Coping Orientations to Problems Experienced (COPE)
Campbell et al., 1995 [181]	Psychiatric and medical features of near fatal asthma	77 consecutive cases of near fatal asthma attacks	Illness Behaviour Questionnaire (IBQ)

Carney et al., 2002 [39]	Why people experiencing acute myocardial infarction delay seeking medical assistance	62 patients with acute myocardial infarction	Cardiac Denial of Impact Scale (CDIS)
Carvalho et al., 2013 [128]	The psychological defensive profile of hemodialysis patients and its relationship to health-related quality of life	170 hemodialysis patients	40-item Defense Style Questionnaire (DSQ)
Carver et al., 1999 [158]	How coping mediates the effect of optimism on distress: a study of women with early-stage breast cancer	59 breast cancer patients	Coping Orientations to Problems Experienced (COPE)
Classen et al., 1996 [131]	Coping styles associated with psychological adjustment to advanced breast cancer	101 women with a diagnosis of metastatic or recurrent breast cancer	Mental Adjustment to Cancer
Commerford et al., 1994 [98]	Coping and psychological distress in women with HIV/AIDS	29 female patients with HIV/AIDS infection	Felton Coping Scale
Cook, 1979 [198]	Psychological adjustment to spinal cord injury: incidence of denial, depression, and anxiety	118 spinal cord-injured patients	Mini-Mult Scale
Cook and DeGood, 2006 [62]	The cognitive risk profile for pain: development of a self-report inventory for identifying beliefs and attitudes that interfere with pain management	499 outpatients with chronic pain	68-item version of the Cognitive Risk Profile for Pain (CRPP)
Cooke et al., 2003 [182]	Lung function, adherence and denial in asthma patients who exhibit a repressive coping style	42 patients with asthma	Illness Behaviour Questionnaire (IBQ) - Denial Scale
Cvitanović and Jančić, 2014 [72]	Influence of stressful life events on coping in psoriasis	244 patients with psoriasis	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)

Cvitanović et al., 2020 [73]	How to cope with psoriasis: data from patient tests and surveys	56 patients with psoriasis	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Dean and Surtees, 1989 [159]	Do psychological factors predict survival in breast cancer?	122 women with primary operable breast cancer	Structured interview
Deimling et al., 2006 [160]	Coping among older-adult, long-term cancer survivors	321 long-term cancer survivors	Coping Orientations to Problems Experienced (COPE)
Demi et al., 1997 [107]	Coping strategies used by HIV infected women	264 female patients with HIV	Semi-structured interview
Devins et al., 1987 [114]	Denial as a defense against depression in end-stage renal disease: an empirical test	70 end-stage renal disease	Card sort task
Dougherty and Shaver, 1995 [51]	Psychophysiological responses after sudden cardiac arrest during hospitalization	21 sudden cardiac arrest (SCA) survivors	Distancing Subscale of the Ways of Coping Checklist-Revised
Earl et al., 1992 [106]	Adjustment: denial in the styles of coping with HIV infection	58 HIV positive patients	Structured interview
Elliott and Richards, 1999 [201]	Living with the facts, negotiating the terms: unrealistic beliefs, denial, and adjustment in the first year of acquired physical disability	40 patients with traumatically acquired spinal cord injury	Minnesota Multiphasic Personality Inventory (MMPI)
Erbil et al., 1996 [132]	Cancer patients psychological adjustment and perception of illness: cultural differences between Belgium and Turkey	296 cancer patients	Omega Vulnerability Rating Scale (OVRS)
Escobar Florez et al., 2021 [76]	The relationship between psychosocial factors and adherence to treatment in men, premenopausal and menopausal women with type 2 diabetes mellitus	96 patients with type 2 diabetes mellitus	Levine's Disease Denial Scale

Esteve et al., 1992 [54]	Denial mechanisms in myocardial infarction: their relations with psychological variables and short-term outcome	67 patients with a first myocardial infarction	Structured interview
Fang et al., 2016 [37]	Is denial a maladaptive coping mechanism which prolongs pre-hospital delay in patients with ST-segment elevation myocardial infarction?	533 patients with diagnosis of ST-elevated myocardial infarction (STEMI)	Cardiac Denial of Impact Scale (CDIS)
Ferrari et al., 2008 [178]	Frequent attenders in primary care: impact of medical, psychiatric and psychosomatic diagnoses	100 primary care patients	Diagnostic Criteria for Psychosomatic Research (DCPR)
Fortune et al., 2002 [70]	Patients' strategies for coping with psoriasis	250 patients with psoriasis	Coping Orientations to Problems Experienced (COPE)
Fricchione et al., 1992 [126]	Psychological adjustment to end-stage renal disease and the implications of denial	63 end-stage renal disease patients	Modified Hackett-Cassem Denial Scale
Friedman et al., 1988 [133]	Predictors of psychosocial adjustment to breast cancer	67 women with breast cancer	14-item cancer-specific survey
Froese et al., 1974 [25]	Trajectories of anxiety and depression in denying and nondenying acute myocardial infarction patients during hospitalization	36 acute myocardial infraction patients	Hackett-Cassem Denial Scale
Fukunishi et al., 1995 [199]	Psychological acceptance and alexithymia in spinal cord injury patients	45 patients with spinal cord injury	Open-ended questions
Galvis Aparicio et al., 2021 [205]	Adaptation during spinal cord injury rehabilitation: the role of appraisal and coping	207 spinal cord injury patients	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)

Gamble et al., 2009 [185]	The prevalence of nonadherence in difficult asthma	182 patients with asthma	Open-ended questions
Ganasegeran and Rashid, 2017 [44]	The prevalence of medication nonadherence in post-myocardial infarction survivors and its perceived barriers and psychological correlates: a cross-sectional study in a cardiac health facility in Malaysia	242 post-myocardial infarction patients	Verbal Denial in Myocardial Infarction questionnaire
Garay-Sevilla et al., 1999 [88]	Denial of disease in type 2 diabetes mellitus: its influence on metabolic control and associated factors	160 patients with type 2 diabetes mellitus	Levine Denial of Illness Scale (LDIS)
Gattellari et al., 1999 [134]	Misunderstanding in cancer patients: why shoot the messenger?	244 cancer outpatients	8-item Cardiac Denial of Impact Scale
Gentry et al., 1972 [52]	Denial as a determinant of anxiety and perceived health status in the coronary care unit	16 patients with a diagnosis of myocardial infarction	Structured interview
Ginsburg et al., 1995 [154]	Psychiatric illness and psychosocial concerns of patients with newly diagnosed lung cancer	52 patients with lung cancer	Diagnostic Interview Schedule (DIS)
Girma et al., 2021 [112]	Covid-19 pandemic-related stress and coping strategies among adults with chronic disease in Southwest Ethiopia	613 randomly selected individuals with different chronic conditions including patients with HIV/AIDS	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Goldsmith et al., 1969 [69]	Psychological characteristics of psoriatics: implications for management	13 hospitalized patients with a diagnosis of psoriasis	Minnesota Multiphasic Personality Inventory (MMPI)

Golemati et al., 2013 [192]	Psychological characteristics of systemic sclerosis patients and their correlation with major organ involvement and disease activity	85 patients with systemic sclerosis compared to 120 individuals with rheumatoid arthritis	Ways of Coping (WoC) questionnaire
González-Freire et al., 2010 [189]	Repression and coping styles in asthmatic patients	75 asthmatic patients	Coping Orientation to Problems Experienced Inventory (COPE)
Gore et al., 1997 [186]	Information provision and patients' perceptions in life-threatening respiratory disease	50 patients diagnosed with end-stage chronic obstructive pulmonary disease	Semi-structured interview
Gould et al., 2010 [135]	Psychological adjustment to gynaecological cancer: patients' illness representations, coping strategies and mood disturbance	61 patients with gynaecological cancer	Coping Orientation to Problems Experienced Inventory (COPE)
Grandi et al., 2001 [46]	Psychological evaluation after cardiac transplantation: the integration of different criteria	129 consecutive patients who underwent heart transplant surgery	Diagnostic Criteria for Psychosomatic Research (DCPR)
Grassi et al., 1999 [99]	Illness behavior, emotional stress and psychosocial factors among asymptomatic HIV-infected patients	73 asymptomatic HIV outpatients	Illness Behavior Questionnaire (IBQ)
Grassi et al., 2005 [155]	Use of the diagnostic criteria for psychosomatic research in oncology	146 cancer patients	Diagnostic Criteria for Psychosomatic Research (DCPR)
Greer et al., 1979 [161]	Psychological response to breast cancer: effect on outcome	69 consecutive patients with early breast cancer	Structured interview
Greer et al., 1990 [162]	Psychological response to breast cancer and 15-year outcome	62 patients with non-metastatic breast cancer	Structured interview

Guidi et al., 2013 [47]	Assessing psychological factors affecting medical conditions: comparison between different proposals	70 outpatients with congestive heart failure	Diagnostic Criteria for Psychosomatic Research (DCPR)
Hackett and Cassem, 1969 [27]	Factors contributing to delay in responding to the signs and symptoms of acute myocardial infarction	100 patients with suspected or proved acute myocardial infarction	Hackett-Cassem Scale
Hackett et al., 1968 [26]	The coronary-care unit: an appraisal of its psychologic hazards	50 patients with myocardial infarction	Hackett-Cassem Scale
Hackett and Weisman, 1969 [28]	Denial as a factor in patients with heart disease and cancer	20 patients with acute myocardial infarction and 20 patients with cancer	Hackett-Cassem Scale
Hart et al., 2000 [111]	The relationship between pain and coping styles among HIV-positive men and women	105 patients with HIV	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Hasan et al., 2022 [163]	Gender differences in coping, depression, and anxiety in patients with non-metastatic lung cancer	40 with non-metastatic lung cancer	Coping Orientation to Problems Experienced Inventory (COPE)
Havik and Mæland, 1986 [53]	Dimensions of verbal denial in myocardial infarction: correlates to 3 denial scales	367 patients with acute myocardial infarction	8 ad-hoc items on illness denial
Heim et al., 1997 [164]	Coping and psychosocial adaptation: longitudinal effects over time and stages in breast cancer	74 patients with breast cancer	Bernese Coping Modes
Henderson, 1966 [152]	Denial and repression as factors in the delay of patients with cancer presenting themselves to the physician	50 patients with cancer	Clinical interview

Hinton, 1994 [165]	Which patients with terminal cancer are admitted from home care?	77 patients with cancer	Clinical interview
Holmes et al., 1986 [66]	Covert psychopathology in chronic pain	31 chronic pain patients	Minnesota Multiphasic Personality Inventory (MMPI)
Hoschar et al., 2019 [50]	The MEDEA FAR-EAST Study: conceptual framework, methods and first findings of a multicenter cross-sectional observational study	296 patients with acute myocardial infarction	Cardiac Denial of Impact Score (CDIS)
Hyphantis et al., 2005 [77]	Personality correlates of adherence to type 2 diabetes regimens	71 outpatients with type 2 diabetes	Defense Style Questionnaire (DSQ)
Innes et al., 1998 [184]	Psychosocial risk factors in near-fatal asthma and in asthma deaths	63 patients with asthma	Illness Behavior Questionnaire (IBQ)
Ironson et al., 1994 [109]	Distress, denial, and low adherence to behavioral interventions predict faster disease progression in gay men infected with human immunodeficiency virus	23 patients with AIDS	Coping Orientation to Problems Experienced Inventory (COPE)
Isezuo et al., 2004 [104]	Attitudes of patients towards voluntary human immunodeficiency virus counselling and testing in two Nigerian tertiary hospitals	53 patients with suspected HIV/AIDS	Clinical interview
Islam et al., 2023 [136]	Coping strategy among the women with metastatic breast cancer attending a palliative care unit of a tertiary care hospital of Bangladesh	95 patients with metastatic breast cancer	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Jadoulle et al., 2005 [199]	Anxiety and depression in chronic hemodialysis: some somatopsychic determinants	54 hemodialysis patients	Self-reported questions

Jankowiak et al., 2021 [75]	Illness acceptance as the measure of the quality of life in moderate psoriasis	186 patients with plaque psoriasis	Acceptance of Illness Scale (AIS)
Julkunen and Saarinen, 1994 [59]	Psychosocial predictors of recovery after a myocardial infarction: development of a comprehensive assessment method	243 myocardial infarction patients	Coping with Illness Scale (CILL-26)
Jungers et al., 1993 [121]	Late referral to maintenance dialysis: detrimental consequences	218 patients with renal diseases	Medical records
Kamen et al., 2012 [100]	The impact of denial on health-related quality of life in patients with HIV	65 HIV patients	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Karlsen and Bru, 2002 [84]	Coping styles among adults with type 1 and type 2 diabetes	534 patients with diabetes	Coping Orientation to Problems Experienced Inventory (COPE)
Kennedy et al., 1995 [202]	Traumatic spinal cord injury and psychological impact: a cross-sectional analysis of coping strategies	71 patients with traumatic spinal cord injury	Coping Orientation to Problems Experienced Inventory (COPE)
Khan et al., 2011 [85]	Exploring reasons for very poor glycaemic control in patients with type 2 diabetes	28677 diabetes patients	Clinical interview
Kiernan and Powers, 1979 [93]	Hepatitis B virus: inappropriate reactions to transmission risks	10 patients with hepatitis B virus	Minnesota Multiphasic Personality Inventory (MMPI)
Kiernan and Powers, 1982 [94]	Hepatitis B virus in patients undergoing hemodialysis: transmission risks and psychosocial reactions	13 patients with hepatitis B virus	Self-rated scales

Kiyingi et al., 2023 [101]	Predictors of delayed anti-retroviral therapy initiation among adults referred for HIV treatment in Uganda: a cross-sectional study	312 patients with HIV infection	Semi-structured interview
Konkle-Parker et al., 2011 [105]	Barriers and facilitators to engagement in HIV clinical care in the deep south: results from semi-structured patient interviews	130 consecutive patients with HIV	Clinical interview with open-ended questions
Kortte et al., 2007 [197]	The hopkins rehabilitation engagement rating scale: development and psychometric properties	206 patients with spinal cord injury	Levine's Denial of Illness Scale
Kotecha et al., 2021 [150]	Evaluating the delay prior to primary care presentation in patients with lung cancer: a cohort study	379 newly diagnosed patients with lung cancer	Patient Questionnaire (PQ)
Langford et al., 2020 [137]	Association of personality profiles with coping and adjustment to cancer among patients undergoing chemotherapy	1248 patients undergoing chemotherapy for cancer	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Lebovits et al., 1983 [153]	Exposure to asbestos: psychological responses of mesothelioma patients	38 patients with a diagnosis of malignant mesothelioma	Semi-structured interview
Lehto et al., 2006 [166]	Baseline psychosocial predictors of survival in localised breast cancer	102 patients with breast cancer	Ways of Coping Questionnaire (WOC)
Lehto et al., 2007 [175]	Baseline psychosocial predictors of survival in localized melanoma	59 patients with localized melanoma	Cognitive Escape-Avoidance coping
Lehto et al., 2019 [167]	Early quality-of-life and psychological predictors of disease-free time and survival in localized prostate cancer	81 patients with localized prostate cancer	Ways of Coping Questionnaire (WOC)

Leigh et al., 1980 [168]	Denial and helplessness in cancer patients undergoing radiation therapy: sex differences and implications for prognosis	100 cancer outpatients	Health Awareness Questionnaire
Leserman et al., 2000 [110]	Impact of stressful life events, depression, social support, coping, and cortisol on progression to AIDS	82 patients with HIV type-1 infection without AIDS	Coping Orientation to Problems Experienced Inventory (COPE)
Levenson et al., 1984 [55]	Denial predicts favorable outcome in unstable angina pectoris	26 patients with unstable angina	Hackett-Cassem Denial Scale
Levenson et al., 1989 [56]	Denial and medical outcome in unstable angina	48 patients with unstable angina	Hackett-Cassem Denial Scale
Levine et al., 1987 [57]	The role of denial in recovery from coronary heart disease	45 patients who were hospitalized for myocardial infarction or for coronary bypass surgery	Levine Denial of Illness Scale (LDIS)
Lilja et al., 2003 [169]	Psychological profile in patients with stages I and II breast cancer: associations of psychological profile with tumor biological prognosticators	129 patients with breast cancer	Structured interview
Livneh and Martz, 2003 [194]	Psychosocial adaptation to spinal cord injury as a function of time since injury	317 spinal cord injury patients	Reactions to Impairment and Disability Inventory (RIDI)
Livneh et al., 2006 [195]	Psychosocial adaptation to chronic illness and disability: a preliminary study of its factorial structure	313 patients with spinal cord injury	Reactions to Impairment and Disability Inventory (RIDI)
Lynch and Krush, 1968 [138]	Delay: a deterrent to cancer detection	938 patients with various forms of cancer	Open-ended questions

Mackay et al., 2011 [203]	Goal striving and maladaptive coping in adults living with spinal cord injury: associations with affective well-being	99 patients with spinal cord injury	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Magarey et al., 1977 [139]	Psycho-social factors influencing delay and breast self-examination in women with symptoms of breast cancer	90 women with breast cancer	Clinical interview with open-ended questions
Mann et al., 2018 [63]	A Canadian survey of self-management strategies and satisfaction with ability to control pain: comparison of community dwelling adults with neuropathic pain versus adults with non-neuropathic chronic pain	710 chronic pain patients	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)
Marlow et al., 2016 [122]	Variations in coping stages for individuals with chronic kidney disease: results from an exploratory study with patient navigators	420 patients with chronic kidney disease	Clinical interview
Martz et al., 2002 [78]	Responses to insulin reactions and long-term adaptation to diabetes	41 diabetes patients	Reactions to Impairment and Disability Inventory (RIDI)
Martz et al., 2005 [196]	Predictors of psychosocial adaptation among people with spinal cord injury or disorder	313 patients with various forms of spinal cord injury	Reactions to Impairment and Disability Inventory (RIDI)
McGann et al., 2008 [183]	Denial and compliance in adults with asthma	51 asthmatic patients	Levine Denial of Illness Scale
Merluzzi et al., 2019 [170]	The role of coping in the relationship between stressful life events and quality of life in persons with cancer	662 patients with cancer	Coping Orientation to Problem Experiences Scale-brief version (Brief-COPE)

Mohamed et al., 2005 [140]	Understanding locally advanced breast cancer: what influences a woman's decision to delay treatment?	22 patients with breast cancer	Semi-structured interview
Morris et al., 1992 [171]	Psychological response to cancer diagnosis and disease outcome in patients with breast cancer and lymphoma	88 patients with breast cancer and 50 individuals with lymphoma	Semi-structured interview
Mühlhauser et al., 1998 [89]	Risk factors of severe hypoglycaemia in adult patients with type I diabetes–a prospective population-based study	684 patients with type I diabetes	Structured interview
Nadel and Clark, 1986 [115]	Psychosocial adjustment after renal retransplants	24 patients who underwent more than one kidney transplant	Clinical interview with open-ended questions
Nazarian et al., 2006 [188]	A naturalistic study of ambulatory asthma severity and reported avoidant coping styles	61 patients with a diagnosis of asthma	Coping Orientation to Problems Experienced Inventory (COPE)
Ngamvithayapong et al., 1997 [108]	Adherence to tuberculosis preventive therapy among HIV-infected persons in Chiang Rai, Thailand	412 HIV patients	Clinical interview
Nowak et al., 2015 [129]	Denial defense mechanism in dialyzed patients	55 patients with peritoneal dialysis	Interpersonal Behavior Scale (IBS-R/ED)
Obialo et al., 2005 [120]	Ultralate referral and presentation for renal replacement therapy: socioeconomic implications	460 patients with chronic kidney disease	Open-ended questions
O'Carroll et al., 2001 [40]	Psychological factors associated with delay in attending hospital following a myocardial infarction	72 myocardial infarction patients	Cardiac Denial Scale (CDS)

Olin and Hackett, 1964 [30]	The denial of chest pain in 32 patients with acute myocardial infarction	32 patients with acute myocardial infarction	Interview
Opoku et al., 2012 [141]	Knowledge, attitudes, beliefs, behaviour and breast cancer screening practices in Ghana, West Africa	474 patients with breast cancer	Self-reported questionnaires and semi-structured interview
Osborne and Swenson, 1978 [67]	Muscle tension and personality	68 patients with chronic pain	Minnesota Multiphasic Personality Inventory (MMPI)
Panzarella et al., 2014 [149]	Diagnostic delay in oral squamous cell carcinoma: the role of cognitive and psychological variables	156 patients with oral squamous cell carcinoma	Structured interview
Paredes et al., 2012 [172]	A longitudinal study on emotional adjustment of sarcoma patients: the determinant role of demographic, clinical and coping variables	36 sarcoma patients	Coping Orientation to Problem Experiences Scale - brief version (Brief-COPE)
Peyrot and McMurry, 1985 [90]	Psychosocial factors in diabetes control: adjustment of insulin-treated adults	20 insulin-treated diabetic adults	Coping style scales
Peyrot and McMurry, 1992 [91]	Stress buffering and glycemic control: the role of coping styles	105 insulin-treated adults	Coping style scales
Perkins et al., 1993 [102]	Personality disorder in patients infected with HIV: a controlled study with implications for clinical care	58 patients with HIV	Coping Orientation to Problems Experienced Inventory (COPE)
Perkins-Porras et al., 2008 [41]	Causal beliefs, cardiac denial and pre-hospital delays following the onset of acute coronary syndromes	177 patients with acute coronary syndrome	Cardiac Denial of Impact scale

Pettingale et al., 1981 [173]	The biological correlates of psychological responses to breast cancer	69 consecutive patients with early breast cancer	Clinical interview
Pettingale et al., 1985 [174]	Mental attitudes to cancer: an additional prognostic factor	57 patients with breast cancer	Clinical interview
Phelan et al., 1992 [142]	'I thought it would go away': patient denial in breast cancer	30 patients with breast cancer	Medical records
Picardi et al., 2005 [71]	Psychosomatic assessment of skin diseases in clinical practice	545 patients with various forms of skin disease	Diagnostic Criteria for Psychosomatic Research (DCPR)
Pilowsky and Spence, 1976 [60]	Illness behaviour syndromes associated with intractable pain	100 patients with intractable pain	52-item Illness Behaviour Questionnaire (IBQ)
Piolanti et al., 2019 [179]	A trial integrating different methods to assess psychosocial problems in primary care	200 primary care patients	Diagnostic Criteria for Psychosomatic Research (DCPR)
Porcelli et al., 2000 [96]	Assessing somatization in functional gastrointestinal disorders: integration of different criteria	190 patients with functional gastrointestinal disorders	Diagnostic Criteria for Psychosomatic Research (DCPR)
Pugi et al., 2022 [127]	Health-related quality of life in pre-dialysis patients with chronic kidney disease: the role of big-five personality traits and illness denial	100 pre-dialysis patients with chronic kidney disease	Illness Denial Questionnaire (IDQ)
Rafanelli et al., 2013 [49]	Psychological correlates of vasovagal versus medically unexplained syncope	67 patients with suspected vasovagal syncope	Diagnostic Criteria for Psychosomatic Research (DCPR)
Rafanelli et al., 2003 [48]	Psychological assessment in cardiac rehabilitation	61 patients with first myocardial infarction	Diagnostic Criteria for Psychosomatic Research (DCPR)

Rajab et al., 2020 [79]	Barriers to initiation of insulin therapy in poorly controlled type 2 diabetes based on self-determination theory	151 patients with type 2 diabetes	Clinical interview with open-ended questions
Richmond et al., 1982 [118]	Psychological and physiological factors predicting the outcome on home hemodialysis	136 patients on home hemodialysis	Clinical interview
Rose et al., 2000 [97]	Patients' expressions of complaints as a predictor of the course of acute hepatitis A	47 patients with hepatitis A	Giessen Complaints Questionnaire (GBB)
Roussi et al., 2007 [143]	Patterns of coping, flexibility in coping and psychological distress in women diagnosed with breast cancer	72 patients with breast cancer	Coping Orientation to Problems Experienced Inventory (COPE)
Roy et al., 2005 [144]	The use of denial in an ethnically diverse British cancer population: a cross-sectional study	199 cancer patients	Mental Adjustment to Cancer (MAC) scale
Sanders et al., 1975 [80]	Emotional attitudes in adult insulin-dependent diabetics	60 insulin-dependent diabetic patients	Unstructured interview
Schöfl et al., 2015 [87]	Failure to achieve disease control in acromegaly: cause analysis by a registry-based survey	120 patients with long-standing acromegaly	Self-reported questionnaires
Shamasneh et al., 2020 [124]	Perceived barriers and attitudes toward arteriovenous fistula creation and use in hemodialysis patients in Palestine	156 hemodialysis patients	Structured interview
Sherman et al., 2000 [145]	Coping with head and neck cancer during different phases of treatment	120 patients with advanced cancer	Coping Orientation to Problems Experienced Inventory (COPE)
Short and Wilson, 1969 [116]	Roles of denial in chronic hemodialysis	Hemodialysis patients	Minnesota Multiphasic Personality Inventory (MMPI)

Simonetti et al., 2018 [95]	Quality of life of hepatitis B virus surface antigen-positive patients with suppressed viral replication: comparison between inactive carriers and nucleot(s)ide analog-treated patients	102 patients with hepatitis B	Illness Behaviour Questionnaire (IBQ)
Sircar et al., 2010 [81]	Patients' concepts and attitudes about diabetes	654 patients with diabetes	Structured interview
Spiess et al., 1994 [92]	Psychological moderator variables and metabolic control in recent onset type 1 diabetic patients: a two-year longitudinal study	43 patients with type I diabetes	Hackett Denial Scale
Spiess et al., 1995 [83]	A program to reduce onset distress in unselected type I diabetic patients: effects on psychological variables and metabolic control	23 patients with a diagnosis of type I diabetes mellitus	Hackett Denial Scale
Stenström et al., 2005 [42]	Denial in patients with a first-time myocardial infarction: relations to pre-hospital delay and attendance to a cardiac rehabilitation programme	107 patients with a first-time myocardial infarction	Hackett and Cassem semi-structured interview
Tan et al., 2023 [86]	Severe distress & denial among Asian patients with type 2 diabetes mellitus in the primary care: a prospective, multicentre study.	132 patients with type 2 diabetes mellitus	Problem Areas in Diabetes (PAID) scale
Tesio et al., 2017 [74]	Psychological characteristics of early-stage melanoma patients: a cross-sectional study on 204 patients	204 patients with melanoma	Coping Orientation to Problem Experiences Scale - brief version (Brief-COPE)
Tesio et al., 2019 [193]	Utility of the diagnostic criteria for psychosomatic research in assessing psychological disorders in fibromyalgia patients	98 patients with fibromyalgia and 98 patients with rheumatoid arthritis	Diagnostic Criteria for Psychosomatic Research (DCPR)

Treharne et al., 2004 [191]	Reactions to disability in patients with early versus established rheumatoid arthritis	34 patients with early rheumatoid arthritis and a sample of 84 patients with advanced rheumatoid arthritis	Reactions to Impairment and Disability Inventory (RIDI)
Tuncay et al., 2008 [82]	The relationship between anxiety, coping strategies and characteristics of patients with diabetes	161 patients both types of diabetes	Coping Orientation to Problem Experiences Scale - brief version (Brief-COPE)
Turner and Clancy, 1986 [61]	Strategies for coping with chronic low back pain: Relationship to pain and disability	74 chronic low back pain patients	Coping Strategy Questionnaire (CSQ)
Umucu and Lee, 2020 [113]	Examining the impact of COVID-19 on stress and coping strategies in individuals with disabilities and chronic conditions	269 patients with self-reported disabilities and chronic conditions	Coping Orientation to Problem Experiences Scale - brief version (Brief-COPE)
Vos et al., 2008 [156]	Denial in lung cancer patients: a longitudinal study	195 newly diagnosed lung cancer patients	Denial of Cancer Interview
Vos et al., 2010 [176]	Denial and physical outcomes in lung cancer patients, a longitudinal study	195 consecutive newly diagnosed lung cancer patients	Denial of Cancer Interview
Vos et al., 2011 [177]	Denial and social and emotional outcomes in lung cancer patients: the protective effect of denial	195 newly diagnosed lung cancer patients	Denial of Cancer Interview
Warrenburg et al., 1989 [58]	Defensive coping and blood pressure reactivity in medical patients	29 cardiac patients	Levine Denial of Illness Scale (LDIS)
Watson et al., 1984 [151]	Reaction to a diagnosis of breast cancer relationship between denial, delay and rates of psychological morbidity	24 breast cancer patients	Clinical interview with open-ended questions

Weaver et al., 2004 [103]	Perceived stress mediates the effects of coping on the quality of life of HIV-positive women on highly active antiretroviral therapy	90 patients with HIV	Coping Orientation to Problem Experiences Scale (COPE)
Weinmann et al., 2005 [146]	Characteristics of women refusing follow-up for tests or symptoms suggestive of breast cancer	2694 patients with breast cancer	Medical records
White et al., 2016 [45]	Cardiac denial and psychological predictors of cardiac care adherence in adults with congenital heart disease	80 patients with congenital heart disease	Cardiac Denial of Impact Scale (CDI)
Woby et al., 2005 [68]	Coping strategy use: does it predict adjustment to chronic back pain after controlling for catastrophic thinking and self-efficacy for pain control?	84 patients with chronic low back pain	Coping Strategies Questionnaire
Wool, 1986 [147]	Extreme denial in breast cancer patients and capacity for object relations	50 breast cancer patients	Semi-structured interview
Yanagida et al., 1981 [117]	Denial in dialysis patients: relationship to compliance and other variables	46 chronic hemodialysis outpatients	Marlowe-Crowne Social Desirability Scale (MCSDS)
Yellowlees and Ruffin, 1989 [180]	Psychological defenses and coping styles in patients following a life-threatening attack of asthma	25 patients with asthma	Illness Behaviour Questionnaire (IBQ) Eysenck Personality Inventory
Zijlstra et al., 2023 [148]	Perception of prognosis and health-related quality of life in patients with advanced cancer: results of a multicentre observational study (eQuiPe)	1000 patients with advanced cancer	Denial and Acceptance subscales of the COPE Inventory and the subscales Planning and Active coping of the Brief COPE