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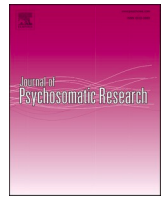
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Review article

Demoralization in suicide: A systematic review

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ABSTRACT

Objective: In psychiatric literature, few original studies exist on the topic of demoralization in suicide. In this review, we aim to identify original studies on suicidal ideation (SI)/suicidal behavior (SB) and demoralization in populations of community-dwellers and patients with somatic or psychiatric disorders.

Methods: We employed a systematic approach that followed PRISMA guidelines, searching through four major electronic databases (PubMed/MEDLINE, Scopus, Science Direct, and PsychINFO) for relevant titles/abstracts published from January 1980–June 2021. We included original studies that explicitly mentioned the investigation of a potential association between SI/SB and demoralization.

Results: A total of 18 studies met our inclusion criteria. Their synthesis revealed that demoralization can be associated with SI/SB in a wide range of populations (community dwellers, patients with somatic or psychiatric disorders) and lead to significantly higher suicide risk (odds ratios of >6 were encountered in community dwellers experiencing financial hardship or isolation). Moreover, demoralization alone (about half the patients who were demoralized did not meet the criteria for an affective disorder nor were they clinically depressed) or together with depression has been identified as a major risk factor for SI/SB. Regarding the crucial issue of progression from SI to SA, in the context of the “ideation-to-action” frame, some authors found that the interaction of demoralization and over-arousal could be a useful predictor for this progression, while others found that depression alone was sufficient to differentiate attempters from non-attempters or the interaction with shutdown (helplessness and low positive emotions).

Conclusion: These results emphasize the possibility to identify demoralization as an independent risk factor for suicide. In patients with psychiatric disorders, the association between demoralization and SI/SB may be transnosographic. Overall, from the clinical implications perspective, our findings highlight that: i. Assessment of demoralization may contribute to a more comprehensive suicide risk detection. This appears particularly relevant in Emergency Departments (EDs) where heterogeneous population typologies are usually admitted and a clinical diagnosis of depression is often difficult to be defined. ii. Additionally, since meaninglessness is considered one of the demoralization subcomponents, meaning-centered psychotherapeutic approaches prove to be indicated and they can be initiated already at the EDs upon first contact with the patient. Further studies are necessary to confirm these findings.

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1. Introduction

The term demoralization was first mentioned in the psychiatric literature by J.D. Frank [1] who saw it as resulting from a “persistent failure to cope with internally or externally induced stresses that the person and those close to him expect him to handle. Its characteristic features, not all of which need to be present in any one person, are feelings of impotence, isolation, and despair”. Demoralization was initially observed in American soldiers who repeatedly had been exposed to unfamiliar diseases [2] and subsequently documented in many other demographic groups, including holocaust survivors, immigrants, college students, health professionals, and patients with somatic or psychiatric diseases. According to De Figueiredo [3] demoralization is a syndrome of distress with “subjective incompetence”, defined as “a state of self-perceived incapacity to act at some minimal level according to some internalized standard in a specific stressful situation”, this latter being its clinical hallmark. Fava and a number of Italian authors [4–7] extensively investigated this construct in patients with various somatic disorders and defined a set of diagnostic criteria for demoralization including helplessness and sense of failure or inability to cope, hopelessness, and giving up. These criteria, based on Engel’s “giving-up/given-up complex” [8], designate the presence of some psychological characteristics: a feeling of giving up experienced as helplessness or hopelessness, a depreciated image of the self, loss of gratification from relationships or roles in life, disruption of the sense of continuity between past, present, and future, and a reactivation of memories of earlier periods of giving-up. Furthermore, these authors formally brought the concept of demoralization into the psychosomatic research domain [4–7] and proposed to introduce demoralization into the Diagnostic and Statistical Manual of Mental Disorders (DSM) [5]. In Kissane and Clarke’s model [9–11], initially conceptualized in patients with advanced diseases near the end of life, demoralization is identified by the presence of five sub-dimensions: hopelessness or disheartenment, loss of meaning in life, helplessness, sense of failure, and dysphoria. In this model, while existential distress is present in a spectrum of mental states, only a subset of its extreme forms is potentially pathological and constitutes the demoralization syndrome [9].

A possible association between demoralization and the development of suicidal ideation (SI)/suicidal behavior (SB), covering the entire range from suicide attempts, SA, to completed suicides) was first noted by Slavney [12] in patients who had undergone general medical treatment or surgeries: “people differ in their vulnerability to demoralization, but even the most resilient persons have their breaking point — a phenomenon observed in soldiers in combat”. However, he considered demoralization a normal response to adversity, instead of a condition with specific pathological features or a psychiatric disorder [12,13]. De Figueiredo [14] subsequently connected the possible development of SI/SB in demoralized community-dwellers experiencing an overlap between distress and subjective incompetence. SI/SB in demoralization was thoroughly investigated by Kissane [15,16], who approached demoralization because of a specific interest in suicide. He observed a predictable progression toward a desire to die or to make suicide in patients with somatic diseases, particularly those in palliative care [15,16]. Notably, while these patients were demoralized, they were not necessarily depressed [9,11,17]. Similarly, in cancer patients, demoralization has been associated with SI/SB development, both as co-occurring with depression [18] and as an independent factor [18–20]. Drake [21] described a model of demoralization syndrome in patients with schizophrenia in which repeated exacerbations of psychotic symptoms and functional deterioration compared with premorbid abilities can precipitate suicide, particularly during periods of clinical improvement following a relapse, in individuals with good premorbid adjustment and residual insight. Despite these pivotal works, the role of demoralization in the development of SI/SB in individuals with somatic or psychiatric disorders, as well in community-dwellers, has only been scarcely investigated.

The association between demoralization and SI/SB also needs to be critically analyzed with respect to the relationships between demoralization and both depression and hopelessness, as the latter two conditions are highly associated with suicide risk.

Depression and demoralization are described as two different entities because of a number of phenomenological distinctions. E.g., Schildkraut and Klein [22] noted that while a depressed person loses their capacity to feel pleasure (anhedonia), a demoralized individual loses their sense of effectiveness (i.e., mastery). Additionally, de Figueiredo [23] emphasized that the main problem in demoralization is the subjective incompetence experienced by the subject, caused by uncertainty about the appropriate direction of action, while the major concern in depression is a decreased motivation, even when the appropriate direction of action is known. Clarke and Kissane [9–11,24] characterized demoralization by a loss of meaning and hope, while considering the presence of anhedonia as the hallmark of depression [9,24]. In patients with cancer [10,17–19,25,26] and other diseases [6], there may be a frequent overlap or co-occurrence of demoralization and depression without any hierarchical connection.

Regarding hopelessness, further research is needed to improve our understanding of the relationship between demoralization and hopelessness, which was been found by Beck’s crucial works to be associated with suicide risk, independently from depression [27]. In their theoretical model, Clarke and Kissane [9–11] suggested that hopelessness was a sub-component of demoralization. However, it is still unclear whether demoralization with hopelessness as a sub-component is of higher predictive value than hopelessness alone [28]. To the best of our knowledge, there is only one prior one systematic review that discussed the role of demoralization and hopelessness in SI/SB, although limited to the context of schizophrenia [29].

Finally, although SI and SB are intrinsically linked, individuals with SI do not necessarily progress to SB. Klonsky and May [30] stated that predictors and explanations for suicide should be classified as to whether they address (a) risk of SI, (b) risk of SA among those with SI, or (c) both. Analogously, in their seminal paper appeared in *Lancet Psychiatry*, O’Connor and Nock [31] emphasized the urgent need to understand the psychological mechanisms involved in both the development of SI and in the transition from SI to SB and to promote pragmatic and innovative interventions to prevent them. However, such models and interventions remain scarce [32]. Therefore, this crucial issue also needs to be considered in the context of demoralization.

Here, we provided a systematic literature review to identify original studies that investigated possible associations between demoralization and SI/SB in three population typologies (community-dwellers, patients with somatic disorders, and patients with psychiatric disorders) to evaluate whether demoralized participants had a higher risk of SI/SB. In addition, in this context, we examined the role of demoralization with respect to depression and hopelessness. Finally, we discussed the “ideation-to-action” frame. In conclusion, we looked at the possible clinical implications of the demoralization construct, linked to the assessment of suicide risk and the possible psychotherapeutic approaches.

2. Methods

This review has been prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [33] and Cochrane collaboration guidelines [34].

2.1. Information sources and search strategy

We performed a systematic search in four major electronic databases (PubMed/MEDLINE, Scopus, Science Direct, and PsychINFO) for relevant titles and abstracts published between January 1980 and June 2021. Although J.D. Frank [1] introduced the construct of demoralization in the 1970s, we limited our search to studies published after

January 1980 by which time the construct had become more standardized and established. Additional articles were retrieved from the reference lists of relevant publications. Additional articles were retrieved from the reference lists of relevant publications. The following terms were combined to search the Pubmed/MEDLINE database either in Medical Subject Headings terms [MeSH] or in titles/abstract [TA]: “Demoralization” AND “Suicidal ideation” [MeSH] OR “Suicide, attempted” [MeSH] OR “Suicide” [MeSH] OR “Suicidal Behavior” [TA] OR “Suicidality” [TA]. The same combination of search terms was used to search the other databases (adapting the search fields accordingly).

2.2. Eligibility criteria

We included original articles that explicitly mentioned a potential association between demoralization (and not just one of its sub-components e.g., hopelessness or meaninglessness) [4–7,9–11,35,36] and SI/SB. Articles with seemingly eligible because of their titles/abstracts were read in full to determine the real relevance. Studies were excluded if: (a) published before 1980, (b) not peer-reviewed, (c) not in English, and (d) either meta-analytical, systematic, or narrative reviews, or book chapters.

2.3. Study selection and data collection

The authors independently extracted and reviewed the studies using a two-step process: (1) screening and selecting based on title and abstract, (2) screening and selecting based on the full-text. Author(s), publication year, study design, sample characteristics (population type, sample size, and psychiatric diagnosis when appropriate), instrument(s) used to assess demoralization and SI/SB, and impact of demoralization on suicide hopelessness-related variables (SI, SA, completed suicide, other SB-related variables, and/or main commentaries) were entered into a spreadsheet [33]. Potential disagreements regarding article inclusion and data collection were resolved by consensus meetings of all senior authors.

2.4. Study quality assessment

We assessed included articles for quality using the following criteria [37,38]: (1) representativeness of the sample of the general population, (2) presence and representativeness of a control group, (3) presence of longitudinal follow-up, (4) evidence-based measures of demoralization, (5) presence of raters who independently identified demoralization, (6) statistical evaluation of inter-rater reliability, and (7) evidence-based measures of SI or SA. Each criterion was scored between 0 and 2 points yielding an overall quality score between 0 and 14. In general, we awarded higher marks if: (i) the study employed a case-control study design, (ii) demoralization was measured through Demoralization Scale (DS) or other validated psychometric instruments, (iii) the presence/severity/risk of SI and SB were determined either through Beck's Hopelessness and Suicide Ideation (SSI) Scales, the Columbia Suicide Severity Rating (C-SSR) Scale, or other validated psychometric instruments, (iv) the study employed more sophisticated statistical methods (e.g., logistic regression or latent class analysis), and (v) the study targeted the role of depression vs demoralization or individual components of demoralization (e.g., the crucial role of hopelessness). Studies were divided into 3 groups: (1) good quality (10–14 points), (2) moderate quality (5–9 points), or (3) low quality (0–4 points). Findings reported by the latter group were interpreted with caution. Articles were initially scored independently by all co-authors who would meet to reach a consensus score.

3. Results

3.1. Included studies

Our initial search yielded 764 articles, 200 of which were duplicates and 546 met at least one exclusion criterion, leaving 18 included publications (17 articles and 1 abstract) (Fig. 1).

3.2. Characteristics of included studies

All 18 included studies were cross-sectional while three had case-control designs (Table 1). Three studies used non-clinical populations, namely income support recipients aged 18 years and above ($n = 10,641$) [39], community-dwelling elderly women aged 65 and above ($n = 62$) [40], and college students ($n = 18,527$) [41]. The remaining 15 studies included adult and older patient groups: clinical populations with a somatic disorder (9 studies), namely patients with different stages of cancer [17,19,20,42–45], Parkinson's disease (PD) [46], and cluster headache [47] (total $n = 3347$); clinical populations with a psychiatric disease (5 articles and one abstract), namely schizophrenia [48,49] and psychiatric outpatients [50], patients attending an adult Emergency Department (ED) [51], and psychiatric inpatients [52,53] with various psychiatric diagnoses (total $n = 1288$).

Ten studies [17,19,20,40,43–45,48,50,51] utilized DS only [10], three studies [42,46,47] combined DS with a Criteria of Psychosomatic Research-Demoralization interview (DCPR-D) [5]. Three studies [41,50,53] used the Restructured Clinical scale for demoralization (RCd) of the Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF) [54]. One study [39] utilized the Composite International Diagnostic Interview (CIDI) [55] and one study [48] employed the Global Assessment Scale (GAS) [48,56]. A total of 6 studies attempted separate assessments of associations between demoralization and SI and between demoralization and SA [46–48,50,51,53].

In order to assess SI and SB, two studies [52,53] utilized the Columbia Suicide Severity Rating Scale (C-SSRS) [57]; two studies [46,47] combined the C-SSRS with the Suicidal Behavior Questionnaire revised (SBQ-R); three studies [19,50,51] used the Scale for Suicidal Ideation (SSI) [58]; three studies [42–44] used the Patient Health Questionnaire-9 (PHQ-9) [59]; two studies [20,39] used the Composite International Diagnostic Interview (CIDI) [55]; one study [41] used the Mini International Neuropsychiatric Interview (M.I.N.I.) [60]; one study [48] used the modified version of the Harkavy Asnis Suicide Survey (HASS) [61], one study [17] used the Schedule of Attitudes Toward Hastened Death (SAHD) [62]; one study [45] used the Self-rating Idea of Suicide Scale (SIOSS) [63]; one study investigated anamnesis [40].

Most included studies (13) are recent, i.e., published after 2016 [17,20,41–47,50–53]. Five studies are from the United States [46–48,50,53], five from Europe [20,42,43,50,51], three from Australia [17,39,40], two from China [44,45], and one each from Taiwan [19] and Korea [41].

3.3. Quality assessment

Studies were scored based on our quality scoring system (see Methods, Table 1). The mean score of all included studies was 8.88.

3.4. Primary findings

3.4.1. Studies involving community-dwellers

In subjects receiving income support all psychological measures of demoralization were concurrently elevated with measures of SI and SA, such that those reliant on welfare payments had approximately 3 to 9 times higher odds of SI/SA associated with about 3 times higher odds of demoralization [39]. In elder women with either SI or SA, the demoralization score was three times higher compared to non-suicidal

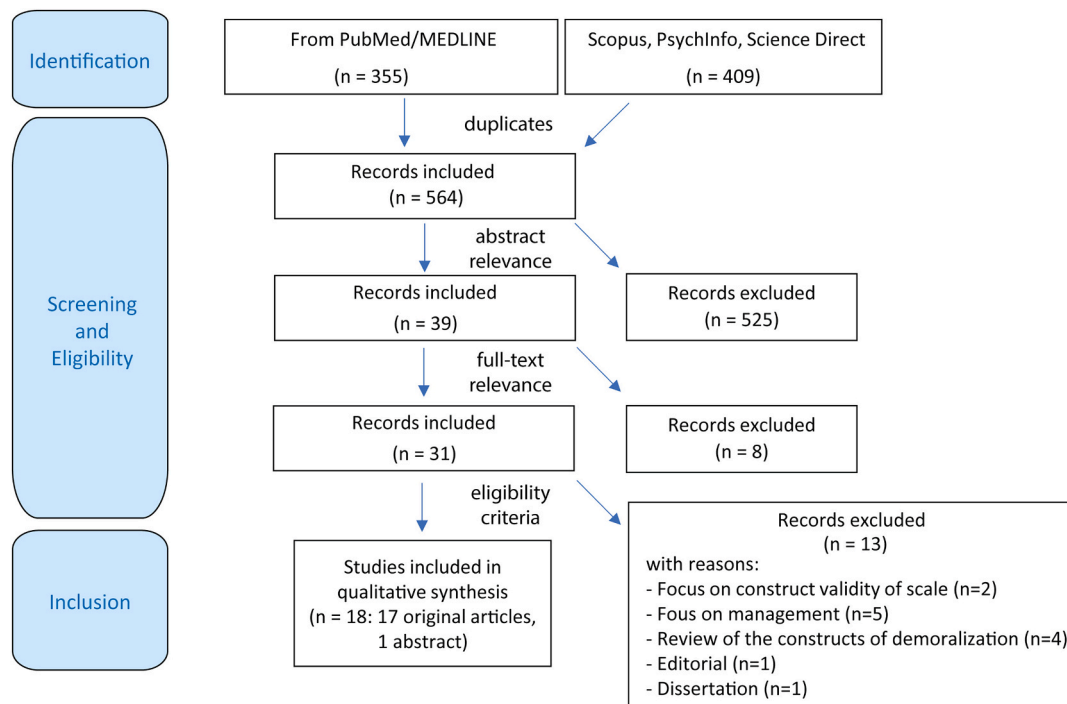


Fig. 1. Flow chart illustrating the search and selection process [32].

controls, after adjusting for financial status and presence of social support [40]. Classifying college students as high-, moderate-, or low-risk for suicide one study found that higher suicide risk was associated with higher scores in demoralization compared to healthy (no-risk) controls [41].

3.4.2. Studies involving patients with somatic disorders

In patients with cancer or other somatic disorders such as PD or cluster headache, demoralization was significantly associated with SI or SB in eight out of nine studies [19,20,42–47]. As an effect modifier, there were significant differences in frequency of SI between patients with high demoralization compared with low/no demoralization: individuals that scored >30 on the DS-Mandarin Version (MV) were about six times more likely to exhibit SI compared to those with DS-MV scores <30 [44]. In three studies, demoralization together with depression represented a major risk for SI and SB [42,44,45]. While three studies demonstrated that demoralization influenced SI or SB more than depression [19,20,47], one study found the opposite result but identified high demoralization as an independent risk factor for SI [44]. Hopelessness, a demoralization sub-component [4–7,9–11,35,36], was only investigated as a separate factor in two studies [42,45]. While demoralization and depression appeared to synergistically promote the direct and indirect effects of this factor on SI, depression alone had no significant impact on the relationship between hopelessness and SI [42,45]. Meaninglessness, another demoralization sub-component [9–11,35,36], appeared to modulate the direct effect of a person's global quality of life on their desire to hasten death [64]. In summary, while all studies identified demoralization and some of its components as independent risk factors for SI/SB in subjects with somatic diseases, these effects were not the same for SI and SB (Table 1).

3.4.3. Studies involving patients with psychiatric disorders

Two studies among patients with schizophrenia [48,49] showed that demoralized patients with schizophrenia exhibited a higher suicide risk. Restifo et al. [48] found that demoralization may lead to an elevated risk for SA in patients with schizophrenia/schizoaffective disorders and that the psychological symptoms of associated depression significantly

differentiated attempters from non-attempters was feelings of guilt. Boursier et al. [49] demonstrated that 94% of patients in their cohort were demoralized and the degree of demoralization was significantly and positively correlated with the intensity of schizophrenia symptoms like depression, despair, poor quality of life, low self-esteem, and suicidality (without specifying whether this meant SI, SB, or both). Stanley et al. [50] showed that the interaction between demoralization and over-arousal (hypomanic activation or activation) was a predictor of SA history in psychiatric outpatients. Furthermore, the combination of elevated demoralization and over-arousal was a predictor for progression from SI to SA. Rufino et al. [53] were unable to replicate these results in a sample of psychiatric inpatients where shutdown (represented by low positive emotions and hopelessness/helplessness) but not over-arousal was a predictor of SA history. Low scores on shutdown, social isolation, and self-alienation indicators were predictors of SA [53]. In a heterogeneous cohort of psychiatric patients attending a psychiatric ED, Costanza et al. [51] found that demoralization was positively correlated with SI and represented a more sensitive risk factor for suicidality than depression, although SA, as an inclusion criterion, was negatively correlated with both SSI and DS scores. In addition, hopelessness, as a demoralization sub-component, only accounted for a small portion of the variance in SI compared to demoralization. In psychiatric inpatients, Berardelli et al. [52] found that psychiatric inpatients with higher illness insight had 1.35 times greater odds of elevated suicide risk, while those with lifetime SA had 7.45 times greater odds of elevated suicide risk. Demoralization was not significantly associated with elevated suicidal risk and greater illness insight was found to be involved in suicide risk regardless of demoralization (Table 1).

4. Discussion

We presented a systematic review of original clinical studies investigating possible associations between demoralization and suicide in three different populations: community-dwellers, patients with somatic illnesses, and patients with psychiatric illnesses. In all populations, demoralization was found to be associated with suicide risk (Table 1).

Table 1Studies analyzing association between demoralization and suicidality ($n = 18$).

Authors	Study design	Sample		Instruments used to assess		Separate assessment of demoralization role with respect to SI and SB	Main findings (including roles of hopelessness and depression)	Quality assessment score
		Participant characteristics	Size (n)	Demoralization	SI/SB			
Studies of association in community-dwellers								
Butterworth et al., 2006 [39]	Cross-sectional	Income support recipients living in private dwellings	10,641	CIDI	CIDI	No, although they provide separate OR for SI and SA with regard to receiving welfare.	Three groups of income support recipients (unemployed, lone mothers, and disability payment recipients) reported significantly elevated levels on all psychological measures related to demoralization (hopelessness, worthlessness, and dissatisfaction with life) compared to non-recipients. These groups exhibited a similar pattern for measures of SI and reported SA, with OR increased by factors between 3 and 9. 48% of participants classified as demoralized did not meet criteria for affective disorder.	5
Lau et al., 2010 [40]	Cross-sectional, case-control	Elderly women, suicidal and non-suicidal	62, (n = 31 for each group)	DS	Anamnesis: reported history of SI and SA in the past 5 years	No. While they consider both SI and SA, results are lumped together.	Elderly women who reported SI or SA in the past 12 months reported higher demoralization: mean DS of 38.65 ± 20.3 [SD] vs. 13.35 ± 12.3 [SD] for non-suicidal women (p < 0.0001) (after adjusting for social support and presence of networks, good physical health, and good financial status).	8
Kim et al., 2020 [41]	Cross-sectional, Case control	College students, suicidal and non-suicidal	Suicidal (n = 964); healthy (n = 7660)	RCd of MMPI-2 RF	M.I.N.I.	No. They consider SI and SA but through the proxy of "risk level".	Suicidal subjects were classified in three suicide risk groups (high-, moderate-, and low-risk). Scores for demoralization were significantly elevated in all three suicide risk groups (p < 0.0001) compared to healthy subjects.	11
Studies of association in patients with somatic disorders								
Fang et al., 2014 [19]	Cross-sectional	Patients with cancer	200	DS-MV	SSI	No. Only SI.	Higher demoralization was correlated with hospitalization status, continued treatment, lung cancer, and diagnosis during 1 to 2 years. Tobit regression analysis showed that demoralization influenced SI more than depression (t = 2.84, p < 0.01). Regarding psychological distress and SI, both depression and demoralization played a mediating role	9

(continued on next page)

Table 1 (continued)

Authors	Study design	Sample		Instruments used to assess		Separate assessment of demoralization role with respect to SI and SB	Main findings (including roles of hopelessness and depression)	Quality assessment score
		Participant characteristics	Size (n)	Demoralization	SI/SB			
Vehling et al., 2017 [20]	Cross-sectional	Patients with cancer	430	DS	CIDI-O	No. Only SI.	with the latter having a greater effect. Considered together in the mediation model, demoralization maintained a greater role. Clinically relevant levels of demoralization were present in 21% of participants. Demoralization co-occurred with a mood/anxiety. Disorder in 7% of participants. Demoralization was associated with a 2.8-times higher risk of SI compared to depression; after adjusting for mental disorders, the effect remained significant (RR = 2.0; 95% CI: 1.1–3.5).	11
Robinson et al., 2017 [17]	Cross-sectional	Patients requiring palliative care	162	DS-II	SAHD	No. Only SI.	Depressive symptoms, loss of Meaning-Purpose, loss of control, and low self-worth mediated the direct effect of global quality of life on desire to hasten death. The Distress-Coping Ability component of demoralization was not a significant mediator. 25% prevalence (95% CI: 0.19–0.31) of clinically relevant demoralization. About half the participants who were demoralized were not clinically depressed. Self-reported SI (PHQ-9, item 9) was found in a minority of patients (8.2%), most of whom (77%) were depressed, while nearly one-quarter (23%) were not depressed but moderately/severely demoralized. SI was associated with DS-Hopelessness ($p < 0.001$) and DS-loss of meaning-purpose ($p < 0.001$) more than DS-Failure ($p < 0.01$) and DS-Dysphoria ($p < 0.05$). Demoralization and demoralization with depression mediated the direct and indirect effects of hopelessness on SI. Depression alone did not mediate the effect of hopelessness on SI.	8
Nanni et al., 2018 [42]	Cross-sectional	Cancer outpatients from two countries (Portugal and Italy)	195	DS, DCPR-D	PHQ-9, item 9	No. Only SI.		11
			1527	German DS		No. Only SI.		10

(continued on next page)

Table 1 (continued)

Authors	Study design	Sample		Instruments used to assess		Separate assessment of demoralization role with respect to SI and SB	Main findings (including roles of hopelessness and depression)	Quality assessment score
		Participant characteristics	Size (n)	Demoralization	SI/SB			
Bobeviski et al., 2018 [43]	Cross-sectional	Early or advanced cancer			PHQ-9, Item 9		Using latent class analysis to identify discrete subgroups of participants based on symptoms of demoralization, depression, anxiety, (4-class model), demoralization was significantly associated with SI ($p < 0.001$)	
Xu et al., 2019 [44]	Cross-sectional	Patients with cancer	303	DS-MV	PHQ-9, item 9	No. Only SI.	14.5% of participants reported SI and 49% high demoralization. Logistic regression identified high demoralization as an independent risk factor for SI. Depression (OR = 6.68) had a stronger influence on SI than demoralization (OR = 5.85). Patients with both depression and demoralization were most likely to experience SI. As an effect modifier, there were significant differences in SI frequency between patients with high demoralization compared with low/no demoralization: individuals that scored >30 on the DS-MV were about six times more likely to exhibit SI compared to those with DS-MV scores <30	8
Liu et al., 2020 [45]	Cross-sectional	Patients with cancer	244	DS-MV	SIOSS	No. Only SI.	Bootstrap analyzes indicated direct and indirect effects of hopelessness on SI mediated solely by demoralization ($B = 2.3074$, $SE = 0.1724$, $p < 0.001$ or by demoralization with depression ($B = 0.1605$, $SE = 0.0303$, $p < 0.001$, 95% CI). The mediation of depression alone in the relationship between hopelessness and SI was non-significant ($B = 0.1541$, $SE = 0.0519$, 95% CI). Exploratory graph analysis suggested that the dimension with the strongest edge between demoralization and SI was hopelessness.	9
Elfil et al., 2020 [46]	Cross-sectional, Case-control	Patients with PD; controls matched with age, gender, race/ethnicity, income, marital	PD Patients ($n = 186$); Control, $n = 177$	DS, DCPR-D	C-SSRS, SBQ-R	Yes. They also distinguish between “passive” (death wish) and “active” (suicide wish) SI. However,	Patients with PD were more likely than controls to have lifetime depression history (34.4% vs. 20.9%; $p =$	10

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Table 1 (continued)

Authors	Study design	Sample		Instruments used to assess		Separate assessment of demoralization role with respect to SI and SB	Main findings (including roles of hopelessness and depression)	Quality assessment score
		Participant characteristics	Size (n)	Demoralization	SI/SB			
		status, and education.				outcomes “plan” and “attempt” are lumped together.	0.004) and demoralization (19.9% vs. 10.7%; $p = 0.02$) but not more likely than controls to have high suicide risk (SBQ-R ≥ 7) (7.5% vs. 11.3%; $p = 0.22$) or a lifetime suicide plan or SA (2.7% vs. 5.1%; $p = 0.24$), and were less likely to have had lifetime SI (23.1% vs. 35.0%; $p = 0.01$). However, patients with PD with high vs. normal suicide risk had higher Non-Motor Aspects of Experiences of Daily Living scale (nM-EDL) scores (16.5 ± 6.8 vs. 10.7 ± 5.9 ; $p = 0.002$), and more demoralization (71.4% vs. 21.5%; $p < 0.0001$). Across the entire cohort, demoralization was associated with higher suicide risk and demoralization was significantly more likely among those with high suicide risk ($p < 0.0001$) and those with past suicide attempts or plans ($p = 0.004$).	
Koo et al., 2021 [47]	Cross-sectional, case-control	Patients with cluster headache, healthy subjects comparable for age, sex, Caucasian race, current marital status, current employment, and income	Participants with cluster headache ($n = 100$); and controls ($n = 135$)	DS, DCPR-D	C-SSRS, SBQ-R	Yes. While SI was slightly more common in cluster headache with high DS, SA was the same between cluster headache and controls.	In patients with cluster headache, lifetime SI was associated more with demoralization (OR = 6.66) than with depression (OR = 1.89), while the reverse was true in control subjects.	10
<i>Studies of association in patients with psychiatric disorders</i>								
Restifo et al., 2009 [48]	Cross-sectional	Patients with schizophrenia or schizoaffective disorder	164	GAS	Modified version of the HASS	Yes. The psychological symptoms of associated depression that most strongly differentiated attempters from non-attempters was feelings of guilt.	This study provided the first multivariate test of Drake's demoralization model in individuals with schizophrenia and schizoaffective disorder with past SA. Patients with schizophrenia who also presented with a constellation of depressive symptoms reflecting demoralization may have an increased risk for suicidality, irrespective of whether they meet the full criteria for major depression. Presence of insight may increase demoralization. >94% of patients were demoralized, 16.36%	7
Boursier et al., 2013	Cross-sectional	Patients with schizophrenia	55	DS	Not specified	No. Only SA.		3

(continued on next page)

Table 1 (continued)

Authors	Study design	Sample		Instruments used to assess		Separate assessment of demoralization role with respect to SI and SB	Main findings (including roles of hopelessness and depression)	Quality assessment score
		Participant characteristics	Size (n)	Demoralization	SI/SB			
<div>[49] – abstract</div>								
Stanley et al., 2018 [50]	Cross-sectional	Psychiatric outpatients	189	RCd of MMPI-2 RF	SSI	Yes. Concluded simultaneously high demoralization and over-arousal was good predictive indicator of progression from SI to SA.	severely. The degree of demoralization correlated with the intensity of positive symptoms ($p = 0.016$), depression ($p < 0.001$), despair ($p = 0.015$), suicidality ($p < 0.01$), poor quality of life ($p = 0.007$), and low self-esteem ($p < 0.000$). 46.6% reported a past SA. The interaction of demoralization and over-arousal (measured by RC9 or ACT) predicted increased history of SA.	9
Costanza et al., 2020 [51]	Cross-sectional	Patients with various psychiatric diagnoses attending an ED	199	DS	SSI	Yes. While SI was strongly correlated with demoralization, SA as an inclusion criterion was negatively correlated with SSI and DS scores.	Demoralization was strongly and positively correlated with SI ($p < 0.001$). Demoralization was related to major depressive episodes but was confirmed to be a different and probably more sensitive construct for suicidality, validating its specificity in relation to depression. Hopelessness (considered as a sub-component of demoralization) only accounted for a small portion of the variance in SI, compared to demoralization.	10
Berardelli et al., 2021 [52]	Cross-sectional	Psychiatric inpatients	100	DS	C-SSRS	No. Used “suicide risk” as proxy.	Demoralization was not significantly associated with high suicidal risk. Patients with higher illness insight had 1.35 times greater OR of having a higher suicide risk, and those with lifetime SA had 7.45 times greater OR of having a higher suicide risk. Greater illness insight was found to be involved in suicide risk regardless of demoralization.	11
Rufino et al., 2021 [53]	Cross-sectional	Psychiatric inpatients	581	RCd of MMPI-2 RF	C-SSRS	Yes. They could not replicate the findings of [30] but found that shutdown was a good predictor of SI to SA progression.	The study could not replicate the results in [38]. Shutdown (represented by low RC2 and HLP) but not over-arousal (RC9, or ACT) predicted SA history. Low scores on shutdown, social isolation and self-alienation indicators provided an additional prediction of SA.	10

Legend: ACT = activation; CIDI=Composite International Diagnostic Interview; CIDI-O=Computer-assisted Composite International Diagnostic Interview–Oncology; C-SSRS=Columbia-Suicide Severity Rating Scale; DCPR-D = The Diagnostic Criteria for Psychosomatic Research Demoralization interview; DS=Demoralization Scale; DS-II=Demoralization Scale-II; DS-MV=Demoralization Scale Mandarin Version; ED = Emergency Department; HASSS=Harkavy Asnis Suicide Survey; GAS = Global Assessment Scale; HLP = hopelessness/helplessness; M.I.N.I. = Mini International Neuropsychiatric Interview; MMPI-2 = Minnesota Multiphasic Personality Inventory-2 Restructured Form; nM-EDL = Non-Motor Aspects of Experiences of Daily Living scale; OR = odds ratio; PD=Parkinson's disease; PHQ-9 = Patient Health Questionnaire-9; RC2 = low mood; RC9 = hypomanic activation; RC9SA = suicide attempt; RCd = Restructured Clinical scale for demoralization; SAHD=Schedule of Attitudes Toward Hastened Death; SBQ-R = The Suicidal Behavior Questionnaire revised; SI = suicidal ideation; SIOSS = Self-rating idea of suicide scale; SSI=Scale for Suicidal Ideation.

Particularly in Emergency Departments (EDs), typically attended by heterogeneous populations with SI or SB [65–67], psychiatric diagnoses of depression based on the Diagnostic and Statistical Manual of mental disorders (DSM) or the International Classification of Diseases (ICD) may not be possible and the construct of demoralization can be used instead to facilitate a more inclusive detection and mitigation of suicide risk.

While the studies focusing on community dwellers considered populations with various socio-economic backgrounds and life stages (individuals in precarious economic conditions [39], elder women [40], and college students [41]), all three studies found significant associations between demoralization and suicide risk. Their findings on demoralization and economic insecurity highlight the impact of the latter on mental health, particularly suicide, as evidenced by studies examining the effects of the economic crises of 2008 [68–70] and related to the Covid-19 pandemic [71]. Historically, psychotherapy had a significant relevance to demoralized patients, often without a psychiatric diagnosis, i.e. community dwellers: J.D. Frank argued that it was precisely demoralization that often prompted patients to seek psychotherapeutic help [72,73]. He noted that these patients used similar expressions to describe their suffering: “The chief problem of all patients who come to psychotherapy is demoralization” and “the effectiveness of all psychotherapeutic schools lies in their ability to restore patient morale” [72]. In this regard, “demoralized individuals responded readily to help and encouragement, as they were at a heightened state of suggestibility that interacted with expectations of improvement in the psychotherapeutic context” [73]. Further work [74] demonstrated the importance of promoting a sense of mastery and a return of hope in demoralized patients. Specifically, encouragement, support, and education are essential to restore a feeling of mastery and achieve a reduction in helplessness [74]. Social integration may also be important as isolation and social breakdown are linked to demoralization [75,76]. An additional rationale behind psychotherapy focusing on social integration lies in the notion that distress and subjective incompetence are less likely to co-occur in the presence of adequate social bonds [3]. An inverse relationship between the extent of demoralization and the degree of socio-cultural integration has been documented [77]. People who are less integrated in their social groups are more demoralized even if they have fewer stressful life events than those that are more integrated [78] and their risk of suicide is higher [79].

About half the included studies involved patients with somatic illnesses and demoralization has indeed been investigated extensively in such patients, although, historically, this construct was first mentioned in the context of psychotherapy [72,73]. It could be hypothesized that this construct shifted to patients with severe somatic diseases because the psychiatric criteria of depression did not fit them and the more existentialist concepts of hopelessness and meaningless (both sub-components of demoralization) were more relevant. This hypothesis, e. g., has been proposed as a characteristic feature of serious neurologic diseases and may be associated with the unpredictable course of the disease (relapses, progression, or chronicity), the unavailability of curative treatments, loss of autonomy, deterioration or loss of identity and status, a sense of uselessness, as well as social isolation and stigma [80–83].

In patients with a psychiatric diagnosis, insight appears crucial. While several studies found that demoralization was associated with increased SI/SB risk in schizophrenia patients, particularly when disease

insight was present [21], this could not be confirmed in psychiatric in-patients where only illness insight but not demoralization was significantly associated with elevated suicide risk [52]. This mismatch was attributed to the fact that the latter sample consisted of psychiatric patients hospitalized for symptomatic worsening rather than suicidal risk, while previous studies having found a link between demoralization and suicide risk had focused on somatic illnesses in patients presenting suicide risk [52]. Our findings in patients with different psychiatric diagnoses indicate that the association between demoralization and SI/SB may be transnosographic, as previous suggested [52].

While there is an overlap between depression and demoralization [10,17–19,25,26], demoralization can occur independently. It has been theorized that demoralization and depression differ in that depression is often associated with anhedonia and a loss of motivation, while a demoralized individual loses their sense of effectiveness (i.e., mastery) [22], hope and meaning [4–7,9–11,24,35,36], and may experience a sense of incompetence [23]. The studies reviewed here found that across all three populations (community-dwellers, patients with somatic disorders, and patients with psychiatric disorders) about half the patients who were demoralized did not meet the criteria for an affective disorder nor were they clinically depressed (Table 1). Four out of five studies involving patients with a somatic disorder found that demoralization led to a more significant increase in both SI and SB compared to depression [17,19,20,47], while one study [44] found no significant differences between the two but identified high demoralization as an independent risk factor for SI. In patients admitted to a psychiatric ED with various psychiatric disorders, demoralization was found to be a different and, probably, more sensitive construct for suicidality, thus validating its specificity in relation to depression [51]. With regard to psychological distress and SI, both depression and demoralization seem to play a mediating role with the latter having a greater effect, even when considered together in the mediation model [19]. Two studies suggested that demoralization and depression may have a synergistic effect on the development of SI and SB [42,44].

Using network and exploratory graph analyses, Belvederi Murri et al. [84] examined the strength of association between symptoms such as life feeling pointless, low mood/discouragement, hopelessness, feeling trapped, and SI in four identified communities: (1) Neurovegetative depression, (2) Loss of purpose, (3) Frustrated isolation, and (4) Low mood and morale. They found that features of depression and demoralization were independent except for low mood and self-reproach. However, anhedonic symptoms of depression separated into a discrete cluster with SI being located in the same cluster as demoralization symptoms, where SI loaded at a probability of nearly 1 while hopelessness loaded at 0.86 for the same community [84]. Similarly, using latent class analysis, Bobevski et al. [43] found a 75.5% probability of SI in individuals with anhedonia and 81.3% probability in individuals with “adjustment disorder with demoralization”. Both studies further characterize demoralization with regard to depression and provide additional evidence for the association of demoralization and SI.

Regarding hopelessness role (considered as a demoralization sub-component), it remains unclear whether demoralization is of higher predictive value than hopelessness alone [26]. The studies reviewed here (Table 1) found that in demoralized patients with somatic disorders, depression alone did not mediate the effect of hopelessness on SI [42,45]. In psychiatric patients admitted to an ED, hopelessness accounted only for a small portion of the variance in SI compared to

demoralization [51]. However, the dimension with the strongest edge between demoralization and SI was hopelessness [45]. A recent systematic review suggested that demoralization was prevalent in patients with schizophrenia and supported the hypothesis that the association between depression and suicide was moderated by hopelessness [29]. These somewhat inconsistent findings clearly demonstrate the complexity of the issue and the necessity for additional studies to improve our understanding of how the different dimensions of demoralization and hopelessness interact.

In the “ideation-to-action” frame, hopelessness and most psychiatric disorders are characterized as predictors of SI [30,85]. In contrast, lower social support, reduced pain sensitivity, fearlessness, and substance abuse (e.g. alcohol) appear to specifically characterize SA but not SI [86–88], although this may be age-dependent. For example, in geriatric patients with mood disorders Pompili et al. [89] found that while attempters and ideators had similar risk factors for SB, attempters reported lower social support compared with ideators. This corroborates findings that social isolation can exacerbate the impact of demoralization in community-dwellers and psychiatric inpatients [53]. Neither the SSI nor BSI scale can discriminate between SI and SA [90]. Some studies investigated the role of demoralization separately in ideators and attempters. During the most severe episode of depressed mood, all but one of the psychological symptoms of depression (feelings of guilt) significantly differentiated attempters from non-attempters in patients with schizophrenia or schizoaffective disorder whereas the somatic symptoms did not [48]. This is consistent with the hypothesis that cognitive rather than somatic symptoms of depression can discriminate attempters from non-attempters [48]. Stanley et al. [50] found that the interaction of demoralization and over-arousal was a useful predictor for the progression from SI to SA. A high over-arousal score indicated absence of lethargy as a mitigating factor, indicating a higher probability of progression from SI to SA. This agrees with Binford & Liljequist [91] who showed that demoralization significantly correlated with SI but not SA, possibly because demoralization is often accompanied by apathy and lethargy (also clinical features of major depression), making SB physically and emotionally more difficult, even in the presence of serious SI. Rufino et al. [53] were unable to replicate the Stanley et al. [50] results in a psychiatric inpatient sample and found that shutdown (low positive emotions and hopelessness/helplessness) was a predictor for progression from SI to SA but not over-arousal. Costanza et al. [51] found that demoralization and SI positively correlated with the number of psychiatric diagnoses and current diagnosis of major depressive episode, although lifetime SA, as an inclusion criterion, was negatively correlated with SSI and DS scores, which they attribute to a possible mitigating effect of a lifetime SA on later SI.

None of the included studies considered “completed suicide” and it is therefore difficult to draw any conclusions here. Nevertheless, we could hypothesize an association between demoralization and completed suicide if we consider that hopelessness, a sub-component of demoralization, is closely related to both SI and SB, even in its most severe forms, i.e., completed suicide [27,92,93]. Moreover, the subject is highly complex: since demoralization is often investigated in patients with severe or terminal somatic diseases, the question arises whether assisted suicides (euthanasia), legal in some countries, should be considered completed suicides.

Considering demoralization as a risk factor for suicide should be understood neither as an effort to minimize the role of psychiatric pathologies (one of the most relevant risk factor [94]) nor as the basis of biological vulnerability. For the latter, in addition to well-known authoritative models [95–99], other biological aspects, are emerging, such as neuroinflammation [100], to improve biomarkers detection and refine prevention in possible high-risk subgroups of vulnerable patients.

To elucidate the clinical significance and practical implications of these findings, we must consider two aspects: their contributions to suicide risk assessment and to treatment.

Demoralization can be useful for the early detection of SI/SB,

particularly in an urgent care setting as EDs where heterogeneous population typologies (non-clinical and clinical somatic/psychiatric populations) are admitted [65–67,101]. Demoralization could complement a more comprehensive preventive and therapeutic approach, especially if psychiatric diagnoses are difficult to define clinically. One prime example is the evaluation of elderly admitted to EDs with somatic conditions, where suicide risk can easily go undetected [102].

With regard to treatment, psychotherapies first considered stress and emotion-/problem-based coping models [103] to arrive more recently at meaning-centered approaches [104–106]. As mentioned above, meaningless is one of the demoralization sub-components. Folkman [103–105] added meaning-based approaches in the late 1990's to the original emotion-/problem-based coping models by Lazarus and Folkman [106]. It saw two pathways from a harmful or threatening event, one leading to a favorable resolution and positive emotion while the second leading to an unfavorable resolution and distress, with a loop back to the appraisal process [103]. This model was revised in 1984 [107] by extending the unfavorable resolution pathway including impacts of positive emotion as individuals deal with unfavorable outcomes. Positive emotion affects event reappraisal, the energy and the resources individuals have available for coping, and the meaning they derive from unfavorable outcomes [104,106]. Meaning-focused coping was defined as “appraisal-based coping in which the person draws on his or her beliefs (e.g., religious, spiritual, or beliefs about justice), values, and existential goals (e.g., purpose in life or guiding principles) to motivate and sustain coping and well-being during a difficult time” [105]. Such recognition of meaning ushered in a body of meaning-centered therapies that focus on the value, meaning, and fulfillment that can be derived from life. Simultaneously, demoralization studies about psychotherapeutic interventions matured [108–110], often with a focus on patients affected by severe somatic disease, cancer, or receiving palliative care [111,112]. Meaning-centered interventions would lead to lower demoralization scores, e.g., with Rodin's CALM therapy (RCT) [113] and Ross's psilocybin-assisted psychotherapy RCT [114,115], illustrating the value of existentially-oriented and meaning-centered psychotherapy for treating demoralized patients with SI/SB. These treatment options could already be employed starting in EDs on patients with SI/SB [79,116,117]. Especially in situations where antidepressants are not indicated because the suicide attempt was not associated with anhedonic depression, meaning-centered therapies can become a brief and focused model of intervention that psychiatric services need to develop, study, and learn to appreciate.

4.1. Limitations

The results should be treated with a certain amount of caution because (i) all included articles used a cross-sectional study design, (ii) some had to rely on relatively small sample sizes, and (iii) the overall mean score of the included studies was only 8.88 (out of 14) with no study scoring higher than 11, indicating the presence of at least some flaws in all studies. Only one of the studies involving patients with psychiatric illnesses [52] examined the role of demoralization on SI/SB according to different diagnoses, and while most were limited to schizophrenia, other disorders (e.g., bipolar) also are highly associated with suicide risk; both issues can introduce biases. Furthermore, there was a certain degree of heterogeneity in the measurement of both demoralization and SI/SB, which may lead to classification bias. In addition, we excluded articles in non-English languages. Lastly, most studies focused on SI and SA rather than completed suicides.

4.2. Conclusions

Our findings emphasize the importance of recognizing demoralization in both non-clinical and clinical somatic and psychiatric populations. Demoralization emerged as a relevant risk factor for SI/SB. Furthermore, hopelessness is not only a sub-component of

demoralization but represents an independent dimension that is frequently and highly associated with suicide risk [27,92,93]. Future research should focus on evaluating the association between demoralization and suicidality in more extensive populations as well as dissecting the roles of demoralization and hopelessness, especially considering that hopelessness may be pivotal for determining the development of SI/SB related to demoralization.

In clinical practice, demoralization should be considered as a complementary factor to arrive at a more comprehensive approach that is both preventive and therapeutic. Demoralization, being more inclusive, could be useful for the early detection of SI/SB, particularly in individuals who do not meet the clinical diagnosis of depression [118] but may still be at high risk for depression due to certain situational or existential characteristics, e.g., in the urgent care settings at EDs and their heterogeneous population typologies [65–67,101]. Whenever possible, demoralization should be assessed by administering the demoralization scale (DS), even in its short forms [119]. Otherwise, interviews should touch upon the five DS sub-components and patients should be offered glimmers of hope through the possibility of psychotherapy interventions (meaning-centered models) or by exploring aspects from the patients everyday life that can be approached from a pragmatic perspective (e.g., with the support of a social worker or other professional figures). Finally, in our experience, patients highly appreciated a combination of risk assessment and basic beginning of psychotherapy, even initiated already at the EDs upon first contact, as long as time, attention, and extended listening was devoted to them [51]. Moreover the DS offers cues for expanded discourse (not necessarily part of standard psychiatric interviews/scales) involving existential points close to the patient's suffering and concerns.

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Declaration of Competing Interest

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References

- [1] J.D. Frank, Psychotherapy: the restoration of morale, *Am. J. Psychiatry* 131 (1974) 271–274, <https://doi.org/10.1176/ajp.131.3.271>.
- [2] J.D. Frank, Emotional reactions of American soldiers to an unfamiliar disease, *Am. J. Psychiatry* 102 (1946) 631–640, <https://doi.org/10.1176/ajp.102.5.631>.
- [3] J.M. de Figueiredo, J.D. Frank, Subjective incompetence, the clinical hallmark of demoralization, *Compr. Psychiatry* 23 (1982) 353–363, [https://doi.org/10.1016/0010-440x\(82\)90085-2](https://doi.org/10.1016/0010-440x(82)90085-2).
- [4] G.A. Fava, H.J. Freyberger, P. Bech, G. Christodoulou, T. Sensky, T. Theorell, T. N. Wise, Diagnostic criteria for use in psychosomatic research, *Psychosom.* 63 (1995) 1–8, <https://doi.org/10.1159/000288931>.
- [5] G.A. Fava, S. Fabbri, L. Sirri, T.N. Wise, Psychological factors affecting medical condition: a new proposal for DSM-V, *Psychosomatics* 48 (2007) 103–111, <https://doi.org/10.1176/appi.psy.48.2.103>.
- [6] L. Mangelli, G. Fava, S. Grandi, L. Grassi, F. Ottolini, P. Porcelli, C. Rafanelli, C. Rigatelli, N. Sonino, Assessing demoralization and depression in the setting of medical disease, *J. Clin. Psychiatry* 66 (2005) 391–394, <https://doi.org/10.4088/jcp.v66n0317>.
- [7] L. Grassi, R. Caruso, S. Sabato, S. Massarenti, M.G. Nanni, The UniFe psychiatry working group coauthors, psychosocial screening and assessment in oncology and palliative care settings, *Front. Psychol.* 5 (2014) 1485, <https://doi.org/10.3389/fpsyg.2014.01485>.
- [8] G.L. Engel, A life setting conducive to illness: the giving-up–given-up complex, *Ann. Intern. Med.* 69 (1968) 293–300, <https://doi.org/10.7326/0003-4819-69-2-293>.
- [9] D.M. Clarke, D.W. Kissane, Demoralization: its phenomenology and importance, *Aust. N. Z. J. Psychiatry* 36 (2002) 733–742, <https://doi.org/10.1046/j.1440-1614.2002.01086.x>.
- [10] D.W. Kissane, S. Wein, A. Love, X.Q. Lee, P.L. Kee, D.M. Clarke, The demoralization scale: a report of its development and preliminary validation, *J. Palliat. Care* 20 (2004) 269–276, <https://doi.org/10.1177/082585970402000402>.
- [11] D.W. Kissane, D.M. Clarke, A.F. Street, Demoralization syndrome - a relevant psychiatric diagnosis for palliative care, *J. Palliat. Care* 17 (2001) 12–21, <https://doi.org/10.1177/082585970101700103>.
- [12] P.R. Slavney, Diagnosing demoralization in consultation psychiatry, *Psychosomatics* 40 (1999) 325–329, [https://doi.org/10.1016/S0033-3182\(99\)71227-2](https://doi.org/10.1016/S0033-3182(99)71227-2).
- [13] Slavney, Letter to the editor: reply to Dr. de Figueiredo, *Psychosomatics* 41 (2000) 450–452.
- [14] J.M. de Figueiredo, Diagnosing demoralization in consultation psychiatry, *Psychosomatics* 41 (2000) 449–450, <https://doi.org/10.1176/appi.psy.41.5.449>.
- [15] D.W. Kissane, Distress, demoralization and depression in palliative care, *Curr. Ther.* 6 (2000) 14–19.
- [16] D.W. Kissane, B.J. Kelly, Demoralisation: depression and the desire for death: problems with the Dutch guidelines for euthanasia of the mentally ill, *Aust. N. Z. J. Psychiatry* 34 (2000) 325–333, <https://doi.org/10.1080/j.1440-1614.2000.00692.x>.
- [17] S. Robinson, D.W. Kissane, J. Brooker, C. Hempton, S. Burney, The relationship between poor quality of life and desire to hasten death: a multiple mediation model examining the contributions of depression, demoralization, loss of control, and low self-worth, *J. Pain Symptom Manag.* 53 (2017) 243–249, <https://doi.org/10.1016/j.jpainsymman.2016.08.013>.
- [18] P.L. Tang, H.H. Wang, F.H. Chou, A systematic review and meta-analysis of demoralization and depression in patients with cancer, *Psychosomatics* 56 (2015) 634–643, <https://doi.org/10.1016/j.psym.2015.06.005>.
- [19] C.K. Fang, M.C. Chang, P.J. Chen, C.C. Lin, G.S. Chen, J. Lin, R.K. Hsieh, Y. F. Chang, H.W. Chen, C.L. Wu, K.C. Lin, Y.J. Chiu, Y.C. Li, A correlational study of suicidal ideation with psychological distress, depression, and demoralization in patients with cancer, *Support Care Cancer* 22 (2014) 3165–3174, <https://doi.org/10.1007/s00520-014-2290-4>.
- [20] S. Vehling, D.W. Kissane, C. Lo, H. Glaesmer, T.J. Hartung, G. Rodin, A. Mehnert, The association of demoralization with mental disorders and suicidal ideation in patients with cancer, *Cancer* 123 (2017) 3394–3401, <https://doi.org/10.1002/cncr.30749>.
- [21] R.E. Drake, C. Gates, A. Whitaker, P.G. Cotton, Suicide among schizophrenics: a review, *Compr. Psychiatry* 26 (1985) 90–100, [https://doi.org/10.1016/0010-440x\(85\)90053-7](https://doi.org/10.1016/0010-440x(85)90053-7).
- [22] J.J. Schildkraut, F.D. Klein, The classification and treatment of depressive states, in: R.I. Shader (Ed.), *Manual of Psychiatric Therapeutics*, Little, Brown & Co, Boston, MA, 1975.
- [23] J.M. de Figueiredo, Depression and demoralization: phenomenologic differences and research perspectives, *Compr. Psychiatry* 34 (1993) 308–311, [https://doi.org/10.1016/0010-440x\(93\)90016-w](https://doi.org/10.1016/0010-440x(93)90016-w).
- [24] D.M. Clarke, D.W. Kissane, T. Trauer, G.C. Smith, Demoralization, anhedonia and grief in patients with severe physical illness, *World Psychiatry* 4 (2005) 96–105.
- [25] A.F. Angelino, G.J. Treisman, Major depression and demoralization in cancer patients: diagnostic and treatment considerations, *Support Care Cancer* 9 (2001) 344–349, <https://doi.org/10.1007/s005200000195>.
- [26] J.C. Jacobsen, L.C. Vanderwerker, S.D. Block, R.J. Friedlander, P.K. Maciejewski, H.G. Prigerson, Depression and demoralization as distinct syndromes: preliminary data from a cohort of advanced cancer patients, *Indian J. Palliat. Care* 12 (2006) 8–15, <https://doi.org/10.4103/0973-1075.25913>.
- [27] A.T. Beck, M. Kovacs, A. Weissman, Hopelessness and suicidal behavior. An overview, *J.A.M.A.* 234 (1975) 1146–1149, <https://doi.org/10.1001/jama.1975.03260240050026>.
- [28] J.C. Jacobsen, G. Maytal, T.A. Stern, Demoralization in medical practice, *Prim. Care Companion J. Clin. Psychiatry* 9 (2007) 139–143, <https://doi.org/10.4088/pcc.v09n0208>.
- [29] I. Berardelli, S. Sarubbi, E. Rogante, M. Hawkins, G. Cocco, D. Erbutto, D. Lester, M. Pompili, The role of demoralization and hopelessness in suicide risk in schizophrenia: a review of the literature, *Medicina (Kaunas)* 55 (2019) 200, <https://doi.org/10.3390/medicina55050200>.
- [30] E.D. Klonsky, A.M. May, Differentiating suicide attempters from suicide ideators: a critical frontier for suicidology research, *Suicide Life Threat. Behav.* 44 (2014) 1–5, <https://doi.org/10.1111/sltb.12068>.
- [31] R.C. O'Connor, M.K. Nock, The psychology of suicidal behavior, *Lancet, Psychiatry* 1 (2014) 73–85, [https://doi.org/10.1016/S2215-0366\(14\)70222-6](https://doi.org/10.1016/S2215-0366(14)70222-6).
- [32] A. Costanza, J. Ambrosetti, K. Wyss, et al., Prevention of suicide at emergency room: from the “interpersonal theory of suicide” to the connectedness [Prévenir le suicide aux urgences: de la “Théorie Interpersonnelle du suicide” à la connectedness], *Rev. Med. Suisse* 14 (2018) 335–338.
- [33] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, PRISMA group, preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, *BMJ* 339 (2009), b2535, <https://doi.org/10.1136/bmj.b2535>.
- [34] P.T. Higgins, S. Green, *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0*, Cochrane Collaboration, London, UK, 2014.
- [35] L. Tecuta, E. Tomba, S. Grandi, G.A. Fava, Demoralization: a systematic review on its clinical characterization, *Psychol. Med.* 45 (2015) 673–691, <https://doi.org/10.1017/S0033291714001597>.

- [36] S. Robinson, D.W. Kissane, J. Brooker, S. Burney, A systematic review of the demoralization syndrome in individuals with progressive disease and cancer: a decade of research, *J. Pain Symptom Manag.* 49 (2015) 595–610, <https://doi.org/10.1016/j.jpainsymman.2014.07.008>.
- [37] G. Serafini, C. Muzio, G. Piccinini, E. Flouri, G. Ferrigno, M. Pompili, P. Girardi, M. Amore, Life adversities and suicidal behavior in young individuals: a systematic review, *Eur. Child Adolesc. Psychiatry* 24 (2015) 1423–1446, <https://doi.org/10.1007/s00787-015-0760-y>.
- [38] A. Costanza, M. Prelati, M. Pompili, The meaning in life in suicidal patients: the presence and the search for constructs. A systematic review, *Medicina* 55 (2019) 465, <https://doi.org/10.3390/medicina55080465>.
- [39] P. Butterworth, et al., Hopelessness, demoralization and suicidal behaviour: the backdrop to welfare reform in Australia, *Aust. N. Z. J. Psychiatry* 40 (2006) 648–656, <https://doi.org/10.1080/j.1440-1614.2006.01864.x>.
- [40] R. Lau, C.A. Morse, S. Macfarlane, Psychological factors among elderly women with suicidal intentions or attempts to suicide: a controlled comparison, *J. Women Aging* 22 (2010) 3–14, <https://doi.org/10.1080/08952840903488831>.
- [41] S. Kim, H.K. Lee, K. Lee, Assessment of suicidal risk using Minnesota multiphasic personality inventory-2 restructured form, *B.M.C. Psychiatry* 20 (2020) 81, <https://doi.org/10.1186/s12888-020-02495-2>.
- [42] M.G. Nanni, R. Caruso, S. Sabato, L. Grassi, Demoralization and embitterment, *Psychol. Trauma* 10 (2018) 14–21, <https://doi.org/10.1037/tra0000326>.
- [43] I. Bobevski, D.W. Kissane, S. Vehling, D.P. McKenzie, H. Glaesmer, A. Mehnert, Latent class analysis differentiation of adjustment disorder and demoralization, more severe depressive and anxiety disorders, and somatic symptoms in patients with cancer, *Psychooncology* 27 (2018) 2623–2630, <https://doi.org/10.1002/pon.4761>.
- [44] K. Xu, D. Hu, Y. Liu, Y. Han, X. Guo, F. Teng, Y. Zhou, Relationship of suicidal ideation with demoralization, depression, and anxiety: a study of cancer patients in mainland China, *J. Nerv. Ment. Dis.* 207 (2019) 326–332, <https://doi.org/10.1097/NMD.0000000000000974>.
- [45] S.T. Liu, X. Wu, N. Wang, Q.Q. Zhao, L. Xiao, C.K. Fang, Y. Yu, D.M. Lin, L. L. Zhang, Serial multiple mediation of demoralization and depression in the relationship between hopelessness and suicidal ideation, *Psycho-Oncology* 29 (2020) 1321–1328, <https://doi.org/10.1002/pon.5439>.
- [46] M. Elfil, N. Ahmed, A. Alapat, R. Bahekar, M. Kandil, C. Kim, S. Schaefer, S. Tinaz, A.S. Patel, J.M. de Figueiredo, E.D. Louis, B.B. Koo, Suicidal risk and demoralization in Parkinson disease, *J. Neurol.* 267 (2020) 966–974, <https://doi.org/10.1007/s00415-019-09632-2>.
- [47] B.B. Koo, A. Bayoumi, A. Albanna, M. Abusuliman, L. Burrone, J.J. Sico, E.A. D. Schindler, Demoralization predicts suicidality in patients with cluster headache, *J. Headache Pain* 22 (2021) 28, <https://doi.org/10.1186/s10194-021-01241-7>.
- [48] K. Restifo, et al., Suicidal behavior in schizophrenia: a test of the demoralization hypothesis, *J. Nerv. Ment. Dis.* 197 (2009) 147–153, <https://doi.org/10.1097/NMD.0b013e318199f452>.
- [49] S. Boursier, F. Jover, D. Pringuey, Relevance of the concept of demoralization in schizophrenic patients, *Eur. Psychiatry* 28 (Suppl. 1) (2020) 1 (Abstract of the 21th European Congress of Psychiatry).
- [50] I.H. Stanley, J.R. Yancey, C.J. Patrick, T.E. Joiner, A distinct configuration of MMPI-2-RF scales RCd and RC9/ACT is associated with suicide attempt risk among suicide ideators in a psychiatric outpatient sample, *Psychol. Assess.* 30 (2018) 1249–1254, <https://doi.org/10.1037/pas0000588>.
- [51] A. Costanza, M. Baertschi, H. Richard-Lepouriel, K. Weber, I. Berardelli, M. Pompili, et al., Demoralization and its relationship with depression and hopelessness in suicidal patients attending an emergency department, *Int. J. Environ. Res. Public Health* 17 (2020), <https://doi.org/10.3390/ijerph17072232>.
- [52] I. Berardelli, M. Innamorati, S. Sarubbi, E. Rogante, D. Erbutto, E. De Pisa, A. Costanza, A. Del Casale, M. Pasquini, D. Lester, M. Pompili, Are demoralization and insight involved in suicide risk? An observational study on psychiatric inpatients, *Psychopathology* 54 (2021) 127–135, <https://doi.org/10.1159/000515056>.
- [53] K.A. Rufino, S.E. Daruwala, J.C. Anestis, Predicting suicide attempt history in a psychiatric inpatient sample: a replication and extension, *Psychol. Assess.* 33 (2021) 685–690, <https://doi.org/10.1037/pas0001026>.
- [54] Y.S. Ben-Porath, A. Tellegen, The Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF): Manual for Administration, Scoring, and Interpretation, University of Minnesota Press, Minneapolis, MN, 2008.
- [55] L.N. Robins, et al., The composite international diagnostic interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures, *Arch. Gen. Psychiatry* 45 (1988) 1069–1077, <https://doi.org/10.1001/archpsyc.1988.01800360017003>.
- [56] J. Endicott, R.L. Spitzer, J.L. Fleiss, J. Cohen, The global assessment scale. A procedure for measuring overall severity of psychiatric disturbance, *Arch. Gen. Psychiatry* 33 (1976) 766–771, <https://doi.org/10.1001/archpsyc.1976.01770060086012>.
- [57] K. Posner, G.K. Brown, B. Stanley, D.A. Brent, K.V. Yershova, M.A. Oquendo, G. W. Currier, G.A. Melvin, L. Greenhill, S. Shen, J.J. Mann, The Columbia-suicide severity rating scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults, *Am. J. Psychiatry* 168 (2011) 1266–1277, <https://doi.org/10.1176/appi.ajp.2011.10111704>.
- [58] A.T. Beck, M. Kovacs, A. Weissman, Assessment of suicidal intention: the scale for suicide ideation, *J. Consult. Clin. Psychol.* 47 (1979) 343–352, <https://doi.org/10.1037/0022-006x.47.2.343>.
- [59] K. Kroenke, R.L. Spitzer, J.B.W. Williams, The PHQ-9: validity of a brief depression severity measure, *J. Gen. Intern. Med.* 16 (2001) 606–613, <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>.
- [60] D.V. Sheehan, Y. Lecrubier, K.H. Sheehan, P. Amorim, J. Janavs, E. Weiller, T. Hergueta, R. Baker, G.C. Dunbar, The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10, *J. Clin. Psychiatry* 59 (Suppl. 20) (1998) 22–33 (quiz 34).
- [61] J.M.H. Friedman, G.M. Asnis, Assessment of suicidal behavior: a new instrument, *Psychiatr. Ann.* 19 (1989) 382–387, <https://doi.org/10.3928/0048-5713-19890701-11>.
- [62] B. Rosenfeld, W. Breitbart, M. Galieta, M. Kaim, J. Funesti-Esch, H. Pessin, C. J. Nelson, R. Brescia, The schedule of attitudes toward hastened death: measuring desire for death in terminally ill cancer patients, *Cancer* 88 (2000) 2868–2875, [https://doi.org/10.1002/1097-0142\(20000615\)88:12<2868::aid-cnrc30>3.0.co;2-k](https://doi.org/10.1002/1097-0142(20000615)88:12<2868::aid-cnrc30>3.0.co;2-k).
- [63] C.Y. Xia, D.B. Wang, S.Q. Wu, J.H. Ye, Primary development of self-rating idea of suicide scale, *J. Clin. Psychiatr.* 12 (2002) 100–102.
- [64] S. Robinson, D.W. Kissane, J. Brooker, C. Hempton, S. Burney, The relationship between poor quality of life and desire to hasten death: a multiple mediation model examining the contributions of depression, demoralization, loss of control, and low self-worth, *J. Pain Symptom Manag.* 53 (2017) 243–249, <https://doi.org/10.1016/j.jpainsymman.2016.08.013>.
- [65] G.L. Larkin, A.L. Beautrais, Emergency departments are underutilized sites for suicide prevention, *Crisis* 31 (2010) 1–6, <https://doi.org/10.1027/0227-5910/a000001>.
- [66] A. Costanza, V. Mazzola, M. Radomska, A. Amerio, A. Aguglia, P. Prada, G. Bondolfi, F. Sarasin, J. Ambrosi, Who consult an adult psychiatric emergency department? Pertinence of admissions and opportunities for telepsychiatry, *Medicina (Kaunas)* 56 (2020) 295, <https://doi.org/10.3390/medicina56060295>.
- [67] L. Ostertag, P. Golay, Y. Dorogi, S. Brovelli, M. Bertran, I. Cromec, B. Van Der Vaeren, R. Khan, A. Costanza, K. Wyss, A. Edan, F. Assandri, R. Barbe, S. Lorillard, S. Saillant, L. Michaud, The implementation and first insights of the French-speaking Swiss programme for monitoring self-harm, *Swiss Med. Wkly.* 149 (2019), w20016, <https://doi.org/10.4414/smw.2019.20016>.
- [68] M. Economou, M. Madianos, L.E. Peppou, C. Theleritis, A. Patelakis, C. Stefanis, Suicidal ideation and reported suicide attempts in Greece during the economic crisis, *World Psychiatry* 12 (2013) 53–59, <https://doi.org/10.1002/wps.20016>.
- [69] S.S. Chang, D. Stuckler, P. Yip, D. Gunnell, Impact of 2008 global economic crisis on suicide: time trend study in 54 countries, *BMJ* 347 (2013), f5239, <https://doi.org/10.1136/bmj.f5239>.
- [70] M. Pompili, M. Vichi, M. Innamorati, D. Lester, B. Yang, D. De Leo, P. Girardi, Suicide in Italy during a time of economic recession: some recent data related to age and gender based on a nationwide register study, *Health Soc. Care Commun.* 22 (2014) 361–367, <https://doi.org/10.1111/hsc.12086>.
- [71] A. Costanza, A. Amerio, A. Aguglia, G. Serafini, M. Amore, E. Macchiarulo, F. Branca, R. Merli, From “the interpersonal theory of suicide” to “the interpersonal trust”: an unexpected and effective resource to mitigate economic crisis-related suicide risk in times of Covid-19? *Acta Biomed* 92 (2021), e2021417 <https://doi.org/10.23750/abm.v92i6.12249>.
- [72] J.D. Frank, Psychotherapy of bodily disease. An overview, *Psychother. Psychosom.* 26 (1975) 192–202, <https://doi.org/10.1159/000286930>.
- [73] J.D. Frank, J.B. Frank, *Persuasion and Healing*, third ed., Johns Hopkins University Press, Baltimore, 1991.
- [74] R.I. Shader, Demoralization revisited, *J. Clin. Psychopharmacol.* 25 (2005) 291–292, <https://doi.org/10.1097/01.jcp.0000172072.58388.74>.
- [75] J.D. Frank, *Persuasion and Healing*, Johns Hopkins University Press, Baltimore, 1961.
- [76] E.M. Gruenberg, The social breakdown syndrome – some origins, *Am. J. Psychiatry* 123 (1967) 1481–1489, <https://doi.org/10.1176/ajp.123.12.1481>.
- [77] J.M. de Figueiredo, The law of sociocultural demoralization, *Soc. Psychiatry* 18 (1983) 73–78, <https://doi.org/10.1007/BF00583991>.
- [78] J.M. de Figueiredo, Demoralization and psychotherapy: a tribute to Jerome D. Frank, MD, PhD (1909–2005), *Psychother. Psychosom.* 76 (2007) 129–133, <https://doi.org/10.1159/000099839>.
- [79] A. Costanza, A. Amerio, A. Aguglia, G. Serafini, M. Amore, Meaning in life and demoralization constructs in light of the interpersonal theory of suicide: a trans-theoretical hypothesis for a cross-sectional study, *Psychol. Res. Behav. Manag.* 13 (2020) 855–858, <https://doi.org/10.2147/PRBM.S279829>.
- [80] A. Costanza, M. Baertschi, K. Weber, A. Canuto, Neurological diseases and suicide: from neurobiology to hopelessness, (*Maladies neurologiques et suicide: de la neurobiologie au manque d'espoir*), *Rev. Med. Suisse* 11 (2015) 402–405.
- [81] V. Chytas, A. Costanza, V. Piquet, C. Cedraschi, G. Bondolfi, Demoralization and meaning in life in suicidal ideation: a role for patients suffering from chronic pain? (*Démoralisation et sens dans la vie dans l'idéation suicidaire: un rôle chez les patients douloureux chroniques?*), *Rev. Med. Suisse* 15 (2019) 1282–1285.
- [82] A. Costanza, A. Amerio, A. Aguglia, A. Escelsior, G. Serafini, I. Berardelli, M. Pompili, M. Amore, When sick brain and hopelessness meet: some aspects of suicidality in the neurological patient, *CNS Neurol. Disord. Drug Targets* 19 (2020) 257–263, <https://doi.org/10.2174/1871527319666200611130804>.
- [83] L. Balogh, M. Tanaka, N. Török, L. Vécsei, S. Taguchi, Crosstalk between existential phenomenological psychotherapy and neurological sciences in mood and anxiety disorders, *Biomedicine* 9 (2021) 340, <https://doi.org/10.3390/biomedicine9040340>.

- [84] M. Belvederi Murri, R. Caruso, H. Ounalli, L. Zerbinati, E. Berretti, S. Costa, E. Recla, F. Folesani, D. Kissane, M.G. Nanni, L. Grassi, The relationship between demoralization and depressive symptoms among patients from the general hospital: network and exploratory graph analysis, *J. Affect. Disord.* 276 (2020) 137–146, <https://doi.org/10.1016/j.jad.2020.06.074>.
- [85] A. Apter, N. Horeish, D. Gothelf, H. Graffi, E. Lepkifker, Relationship between self-disclosure and serious suicidal behavior, *Compr. Psychiatry* 42 (2001) 70–75, <https://doi.org/10.1053/comp.2001.19748>.
- [86] P.N. Smith, K.C. Cukrowicz, E.K. Poindexter, V. Hobson, L.M. Cohen, The acquired capability for suicide: a comparison of suicide attempters, suicide ideators, and non-suicidal controls, *Depress. Anxiety* 27 (2010) 871–877, <https://doi.org/10.1002/da.20701>.
- [87] S. Stack, Differentiating suicide ideators from attempters: violence—a research note, *Suicide Life Threat. Behav.* 44 (2014) 46–57, <https://doi.org/10.1111/sltb.12054>.
- [88] A. Costanza, S. Rothen, S. Achab, G. Thorens, M. Baertschi, K. Weber, A. Canuto, H. Richard-Lepouriel, N. Perroud, D. Zullino, Impulsivity and impulsivity-related endophenotypes in suicidal patients with substance use disorders: an exploratory study, *Int. J. Ment. Heal. Addict.* 19 (2021) 1729–1744, <https://doi.org/10.1007/s11469-020-00259-3>.
- [89] M. Pompili, M. Innamorati, C. Di Vittorio, L. Sher, P. Girardi, M. Amore, Sociodemographic and clinical differences between suicide ideators and attempters: a study of mood disordered patients 50 years and older, *Suicide Life Threat. Behav.* 44 (2014) 34–45, <https://doi.org/10.1111/sltb.12051>.
- [90] M. Baertschi, A. Costanza, A. Canuto, K. Weber, The dimensionality of suicidal ideation and its clinical implications, *Int. J. Methods Psychiatr. Res.* 28 (2019), e1755, <https://doi.org/10.1002/mpr.1755>.
- [91] A. Binford, L. Liljequist, Behavioral correlates of selected MMPI-2 clinical, content, and restructured clinical scales, *J. Pers. Assess.* 90 (2008) 608–614, <https://doi.org/10.1080/00223890802388657>.
- [92] D. Erbutto, M. Innamorati, D.A. Lamis, I. Berardelli, A. Forte, E. De Pisa, M. Migliorati, G. Serafini, X. Gonda, Z. Rihmer, A. Fiorillo, M. Amore, P. Girardi, M. Pompili, Mediators in the association between affective temperaments and suicide risk among psychiatric inpatients, *Psychiatry* 81 (2018) 240–257, <https://doi.org/10.1080/00332747.2018.1480251>.
- [93] J.D. Ribeiro, X. Huang, K.R. Fox, J.C. Franklin, Depression and hopelessness as risk factors for suicide ideation, attempts and death: meta-analysis of longitudinal studies, *Br. J. Psychiatry* 212 (2018) 279–286, <https://doi.org/10.1192/bjp.2018.27>.
- [94] E.D. Klonsky, A.M. May, B.Y. Saffer, Suicide, suicide attempts, and suicidal ideation, *Annu. Rev. Clin. Psychol.* 12 (2016) 307–330, <https://doi.org/10.1146/annurev-clinpsy-021815-093204>.
- [95] K. Hawton, K. van Heeringen, Suicide, *Lancet* 373 (2009) 1372–1381, [https://doi.org/10.1016/S0140-6736\(09\)60372-X](https://doi.org/10.1016/S0140-6736(09)60372-X).
- [96] J.J. Mann, D.M. Currier, Stress, genetics and epigenetic effects on the neurobiology of suicidal behavior and depression, *Eur. Psychiatry* 25 (2010) 268–271, <https://doi.org/10.1016/j.eurpsy.2010.01.009>.
- [97] K. van Heeringen, J.J. Mann, The neurobiology of suicide, *lancet, Psychiatry* 1 (2014) 63–72, [https://doi.org/10.1016/S2215-0366\(14\)70220-2](https://doi.org/10.1016/S2215-0366(14)70220-2).
- [98] G. Turecki, D.A. Brent, Suicide and suicidal behaviour, *Lancet* 387 (2016) 1227–1239, [https://doi.org/10.1016/S0140-6736\(15\)00234-2](https://doi.org/10.1016/S0140-6736(15)00234-2).
- [99] G. Turecki, D.A. Brent, D. Gunnell, R.C. O'Connor, M.A. Oquendo, J. Pirkis, B. H. Stanley, Suicide and suicide risk, *Nat. Rev. Dis. Primers* 5 (2019) 74, <https://doi.org/10.1038/s41572-019-0121-0>.
- [100] G. Serafini, V.M. Parisi, A. Aguglia, A. Amerio, G. Sampogna, A. Fiorillo, M. Pompili, M. Amore, A specific inflammatory profile underlying suicide risk? Systematic review of the main literature findings, *Int. J. Environ. Res. Public Health* 17 (2020) 2393, <https://doi.org/10.3390/ijerph17072393>.
- [101] A. Costanza, S. Di Marco, M. Burroni, F. Corasaniti, P. Santinon, M. Prelati, V. Chytas, C. Cedraschi, J. Ambrosetti, Meaning in life and demoralization: a mental-health reading perspective of suicidality in the time of COVID-19, *Acta Biomed* 91 (2020), e2020163, <https://doi.org/10.23750/abm.v91i4.10515>.
- [102] A. Costanza, A. Amerio, M. Radomska, J. Ambrosetti, S. Di Marco, M. Prelati, A. Aguglia, G. Serafini, M. Amore, G. Bondolfi, L. Michaud, M. Pompili, Suicidality assessment of the elderly with physical illness in the emergency department, *Front. Psychiatry* 11 (2020), 558974, <https://doi.org/10.3389/fpsy.2020.558974>.
- [103] R.S. Lazarus, *Psychological Stress and the Coping Process*, McGraw Hill, New York, 1966.
- [104] S. Folkman, J.T. Moskowitz, Positive affect and the other side of coping, *Am. Psychol.* 55 (2000), <https://doi.org/10.1097/NCC.0000000000000628>, 647–654–340.
- [105] S. Folkman, The case for positive emotions in the stress process, *Anxiety Stress Coping* 21 (2008) 3–14.
- [106] S. Folkman, Stress, coping, and hope, *Psychooncology* 19 (2010) 901–908, <https://doi.org/10.1002/pon.1836>.
- [107] R.S. Lazarus, S. Folkman, *Stress, Appraisal, and Coping*, Springer, New York, 1984.
- [108] J.M. de Figueiredo, Demoralization and psychotherapy: a tribute to Jerome D. Frank, MD, PhD (1909–2005), *Psychother. Psychosom.* 76 (2007) 129–133, <https://doi.org/10.1159/000099839>.
- [109] J.M. de Figueiredo, S. Gostoli, Culture and demoralization in psychotherapy, *Adv. Psychosom. Med.* 33 (2013) 75–87, <https://doi.org/10.1159/000348735>.
- [110] G. da Ponte, J.E. Santo, H. Santos, et al., Meaning centered psychotherapy: the state of the art, *Curr. Psychiatr. Rev.* 14 (2018) 152–159.
- [111] J. Vos, D. Vitali, The effects of psychological meaning-centered therapies on quality of life and psychological stress: a metaanalysis, *Palliat Support Care* 16 (2018) 608–632, <https://doi.org/10.1017/S1478951517000931>.
- [112] K.A. Kang, S.J. Han, Y.S. Lim, S.J. Kim, Meaning-centered interventions for patients with advanced or terminal cancer: a meta-analysis, *Cancer Nurs.* 42 (2019) 332.
- [113] G. Rodin, C. Lo, A. Rydall, C. Malfitano, A. Chiu, T. Panday, S. Watt, E. An, R. Nissim, M. Li, C. Zimmermann, S. Hales, Managing cancer and living meaningfully (CALM): a randomized controlled trial of a psychological intervention for patients with advanced cancer, *J. Clin. Oncol.* 36 (2018) 2422–2432, <https://doi.org/10.1200/JCO.2017.77.1097>.
- [114] S. Ross, A. Bossis, J. Guss, G. Agin-Liebes, T. Malone, B. Cohen, S.E. Mennenga, A. Belser, K. Kalliontzis, J. Babb, Z. Su, P. Corby, B.L. Schmidt, Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial, *J. Psychopharmacol.* 30 (2016) 1165–1180, <https://doi.org/10.1177/0269881116675512>.
- [115] S. Ross, G. Agin-Liebes, S. Lo, R.J. Zeifman, L. Ghazal, J. Benville, S. Franco Corso, C. Bjerre Real, J. Guss, A. Bossis, S.E., Mennenga SEAcute and sustained reductions in loss of meaning and suicidal ideation following psilocybin-assisted psychotherapy for psychiatric and existential distress in life-threatening cancer, *ACS Pharmacol. Transl. Sci.* 4 (2021) 553–562, <https://doi.org/10.1021/acspstci.1c00020>.
- [116] A. Costanza, M. Baertschi, H. Richard-Lepouriel, K. Weber, M. Pompili, A. Canuto, The presence and the search constructs of meaning in life in suicidal patients attending a psychiatric emergency department, *Front Psychiatry* 11 (2020) 327, <https://doi.org/10.3389/fpsy.2020.00327>.
- [117] A. Costanza, A. Amerio, A. Odone, M. Baertschi, H. Richard-Lepouriel, K. Weber, S. Di Marco, M. Prelati, A. Aguglia, A. Escelsior, G. Serafini, M. Amore, M. Pompili, A. Canuto, Suicide prevention from a public health perspective. What makes life meaningful? The opinion of some suicidal patients, *Acta Biomed* 91 (2020) 128–134, <https://doi.org/10.23750/abm.v91i3-S.9417>.
- [118] L. Costantini, C. Pasquarella, A. Odone, M.E. Colucci, A. Costanza, G. Serafini, A. Aguglia, M. Belvederi Murri, V. Brakoulis, M. Amore, S.N. Ghaemi, A. Amerio, Screening for depression in primary care with patient health Questionnaire-9 (PHQ-9): a systematic review, *J. Affect Disord.* 279 (2021) 473–483, <https://doi.org/10.1016/j.jad.2020.09.131>.
- [119] M. Belvederi Murri, L. Zerbinati, H. Ounalli, D. Kissane, B. Casoni, M. Leoni, G. Rossi, R. Dall'Olio, R. Caruso, M.G. Nanni, L. Grassi, Assessing demoralization in medically ill patients: factor structure of the Italian version of the demoralization scale and development of short versions with the item response theory framework, *J. Psychosom. Res.* 128 (2020), 109889, <https://doi.org/10.1016/j.jpsychores.2019.109889>.