Psychological Medicine (2015), **45**, 673–691. © Cambridge University Press 2014
doi:10.1017/S0033291714001597

REVIEW ARTICLE

Demoralization: a systematic review on its clinical characterization

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Background. Demoralization has been described as a psychological state characterized by helplessness, hopelessness, a sense of failure and the inability to cope.

Methods. We conducted a systematic review with qualitative data analysis following PRISMA criteria with the following aims: to review validated assessment instruments of the demoralization syndrome, report main findings regarding demoralization as measured by validated instruments that emerge in the literature, compare and report evidence for the clinical utility of the identified instruments. Utilizing the key word 'demoralization' in PubMed and PsycINFO databases, an electronic search was performed, supplemented by Web of Science and manual searches. Study selection criteria included the assessment of medical patients and use of instruments validated to assess demoralization. Seventy-four studies were selected.

Results. Four instruments emerged in the literature. Main findings concern prevalence rates of demoralization, evidence of discriminant validity from major depression, factors associated with demoralization and evidence of clinical utility. The instruments vary in their definition, the populations they aim to assess, prevalence rates they estimate and their ability to discriminate between different conditions. Nonetheless, demoralization appears to be a distinctive psychological state characterized by helplessness, hopelessness, giving up and subjective incompetence. It is not limited to life-threatening diseases such as cancer, but may occur in any type of clinical situation. It is associated with stress and adverse health outcomes.

Conclusions. Studies addressing the incremental value of demoralization in psychiatry and psychology are needed. However, demoralization appears to entail specific clinical features and may be a distinct condition from major depression.

Received 7 March 2014; Revised 12 June 2014; Accepted 13 June 2014; First published online 17 July 2014

Key words: Demoralization, depression, helplessness, hopelessness, medical illness.

History of demoralization

Various definitions of demoralization have been proposed since it was introduced. Frank (1961) first introduced the term demoralization as a definite cluster of symptoms, a state akin to the 'giving up–given up' complex, in which one primarily experiences persistent feelings of subjective incompetence or failure to meet one's own or others' expectations, an inability to cope and problem solve. An inability to cope is understood in Frank's works as feelings of being overwhelmed and defeated by one's circumstances and of being unable to effectively engage in problem-solving and perform tasks. According to the author, this state characterized psychotherapy clients seeking treatment who had exhausted personal resources, and were no longer able to cope with their personal problems. For this reason the demoralized individual responded readily to help and encouragement, as they were at a heightened state of suggestibility which interacted with expectations of improvement in the psychotherapeutic context (Frank & Frank, 1991).

Schmale & Engel (1967) subsequently identified a psychological state which may precede illness characterized by helplessness or hopelessness, feelings of being at a loss and 'at the end of one's rope' and unable to cope, naming it the 'giving up–given up' complex. An inability to cope, an essential element of the 'giving up–given up' complex, was described by Engel (1968) as the sense of psychological impotence in which previously used strategies, whether psychological or social, seem no longer effective in dealing with changes in the environment.

'Giving up' or demoralization indicated a complex state that included both helplessness and hopelessness.

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Sweeney *et al.* (1970) provided a differentiation of these giving up affects. The qualitative differences between the two affects were postulated to have distinct and underlying developmental bases. Helplessness was defined as a feeling of being left out or abandoned where loss of gratification is perceived as caused by external events or objects and cannot be regained by active self-intervention. Hopelessness was hypothesized to develop instead when the individual feels that he/she alone is responsible for the loss and that there is nothing that he or anyone else can do to overcome it. Helplessness is thus more active than hopelessness because of the orientation toward the environment. Further, the individual feels no personal responsibility for the events leading to the feeling. Hopelessness entails a self-perception of inadequacy and a sense of responsibility for the event, associated with the perception that it will last forever (Sweeney *et al.* 1970).

This intermittent and transient state, in the presence of vulnerability to organic diseases, was hypothesized to be able to alter and compromise one's biological economy and consequently disrupt one's ability to counteract pathogenic processes (Schmale & Engel, 1967). Klein & Davis (1969) viewed it as a state characterized by the pervasive change in self-image rather than anhedonia. Subsequently, utilizing Frank's (1973) conceptualization as a starting point, de Figueiredo & Frank (1982) further elaborated demoralization as a syndrome with two main distinct components: personal distress and subjective incompetence.

Fava *et al.*'s (1995) definition of demoralization integrates Schmale & Engel's giving up–given up complex (Schmale & Engel, 1967) and Frank's (1973) demoralization syndrome. The authors introduced this conceptualization within the Diagnostic Criteria for Psychosomatic Research (DCPR), in an effort to translate psychosocial variables derived from psychosomatic research into an operational diagnostic framework. Demoralization was subsequently suggested to become a part of the 'Psychological Factors Affecting Medical Conditions' category of the DSM as a clinical specifier (Fava *et al.* 2007).

Clarke & Kissane (2002) in an attempt to operationalize existential distress in the medical context, elaborated a definition of the demoralization syndrome characterized by hopelessness, helplessness and meaninglessness. Demoralization is a frightening sense of hopelessness, meaninglessness, not coping and essentially 'not knowing what to do' (p. 737).

Previous narrative reviews on the demoralization syndrome have focused primarily on the phenomenological differentiation of the syndrome from major depressive disorder (MDD) (de Figueiredo, 1993), in addition to providing suggestions for future research and treatment considerations (Angelino & Treisman, 2001; Clarke & Kissane, 2002). Clarke & Kissane's (2002) and Rickelman's (2002) reviews instead have presented theoretical models which highlight the role of stressors in the emergence of demoralization symptoms. While these previous reviews have provided valuable phenomenological considerations and comprehensive theoretical models of the demoralization syndrome, to the best of our knowledge no systematic review of demoralization has been attempted.

The aims of the present systematic review with qualitative data analysis which follows Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria (Moher *et al.* 2009) are to first provide a review of the available assessment instruments of the demoralization syndrome which have been validated. Second, the review aims to report main findings regarding the demoralization syndrome that emerge in the literature. Such main findings will be qualitatively analyzed and presented in major themes. Third, the review aims to compare and report evidence for the clinical utility of the demoralization instruments based on findings. The review aims to also provide clinical implications of the differentiation of demoralization from mood disorders. A conceptual synthesis which compares existing literature with interpretive models regarding the demoralization syndrome and its components will be provided (Table S1) (all Tables appear in the Supplementary online material).

Methods

Eligibility criteria

Eligible articles were in the English language and published in peer-reviewed journals. Studies were selected for inclusion if the psychological assessment consisted of validated demoralization instruments and if they were conducted in a medical setting and/or evaluated medical patients as participants. Studies assessing demoralization in community samples were included as well to be able to compare prevalence rates between medical patients and the general population. Studies which assessed 'demoralization' with measures typically reserved for depressive symptomatology were excluded as they seem to consider demoralization as a single component of major depression rather than considering demoralization as a distinct syndrome. Furthermore, studies that used demoralization scales that are part of a larger instrument and cannot be administered independently of that instrument were also excluded.

Information sources and searches

Medline and PsycINFO were systematically searched from inception to January 2014 utilizing the sole key word *demoralization*. The use of *demoralisation* as key

https://doi.org/10.1017/S0033291714001597 Published online by Cambridge University Press

word yielded substantially fewer results that in any case overlapped with the results found using the key word 'demoralization'. Using variants such as *demoralized, demoralizing*, or *demoralised, demoralising* also led to fewer results containing references to demoralization in lay terms rather than to a well-defined psychological state. Titles and abstracts were screened by one reviewer (L.T.). Articles that appeared potentially relevant were retrieved, and two reviewers (L.T. and E.T.) independently assessed each of the full reports, arriving at a consensus regarding eligibility. The methods described here fulfilled PRISMA guidelines (Moher *et al.* 2009). During the electronic search, for each excluded study we determined which elements of the eligibility criteria were not fulfilled. At this stage of selection, studies were excluded for the following reasons: the sample was not medically ill or not a community sample, the context was non-medical, the study did not include assessment of demoralization. Case studies were excluded as well. Remaining studies received full-text review to verify the inclusion of a validated demoralization instrument among the assessment measures. Web of Science was subsequently used to supplement the search. The review was supplemented by a manual search of the literature and references of selected studies. The study selection methodology is reported in the flow diagram (see Fig. 1). Data were extracted about: participant characteristics, study characteristics and context, instruments used, and the authors' main findings regarding demoralization and evidence for the clinical utility of the instruments.

Presentation and synthesis of results

First, the results concerning selection of articles and study characteristics will be presented. Second, the assessment instruments which were identified will be described and discussed as well as their validation. Subsequently, a qualitative analysis which gathers main findings that emerge in the literature on demoralization into themes will be presented. Furthermore, evidence of the clinical utility of the instruments will be reported.

Results

Selection of articles and study characteristics

The literature search of Medline and PsycINFO databases yielded a total of 772 abstracts, 445 after exclusion of duplicates. A citations search of Web of Knowledge yielded 238 citations, of which 188 remained after removal of duplicates. In this first stage of selection, a total of 633 abstracts resulted in the search. Screening based on titles and of 482 abstracts resulted in the exclusion of 397 articles using the inclusion criteria. Full-text review of the resulting 82 articles led to the exclusion of 12 studies which did not contain validated methods to assess demoralization. A total of 70 studies were identified in the electronic search. Four studies were found through supplementary manual search of the literature and references of selected studies for a total of 74 studies included in the review.

Among the 74 studies, 19 used the Psychiatric Epidemiological Research Interview – Demoralization Scale (PERI-D; Dohrenwend *et al.* 1980), 40 used the DCPR (Fava *et al.* 1995), 13 used the Demoralization Scale (DS; Kissane *et al.* 2004), and two used the Subjective Incompetence Scale (SIS; Cockram *et al.* 2009). Main findings across studies and across instrument use generally fell within the following themes: validation of the measures, prevalence rates of the demoralization syndrome, differentiation from mood disorders, factors or characteristics associated with presence of demoralization (sociodemographic factors, stress, somatization, and pain, illness behavior, psychological well-being), and health outcomes associated with demoralization.

Assessment methods and validation data

Of the four main instruments that assess demoralization that were identified, three are self-report questionnaires yielding a dimensional assessment while one is a structured interview which yields a categorical diagnosis. The three scales will be described, followed by the DCPR interview.

PERI-D

The PERI-D (Dohrenwend *et al.* 1980) is a multidimensional self-report questionnaire comprising 27 items which constitute eight dimensions or subscales of the PERI, developed to screen psychopathology in epidemiological and community settings. The items are constructed with a 5-point response scale ranging from *never*, a score of 0, to *very often* corresponding to a score of 4. A total score is calculated by adding all item scores and dividing by 27. The PERI-D dimensions are anxiety, sadness, hopelessness-helplessness, dread, confused thinking, poor self-esteem, psychophysiologic symptoms and perceived physical health.

PERI-D has been validated in a New York City sample, demonstrating a high concurrent validity with the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) and the Bradburn Negative Affect Scale (Bradburn, 1969; Vernon & Roberts, 1981). The measure has demonstrated high reliability coefficients in community samples (Dohrenwend *et al.* 1980; Vernon & Roberts, 1981; Page & Cole, 1992;

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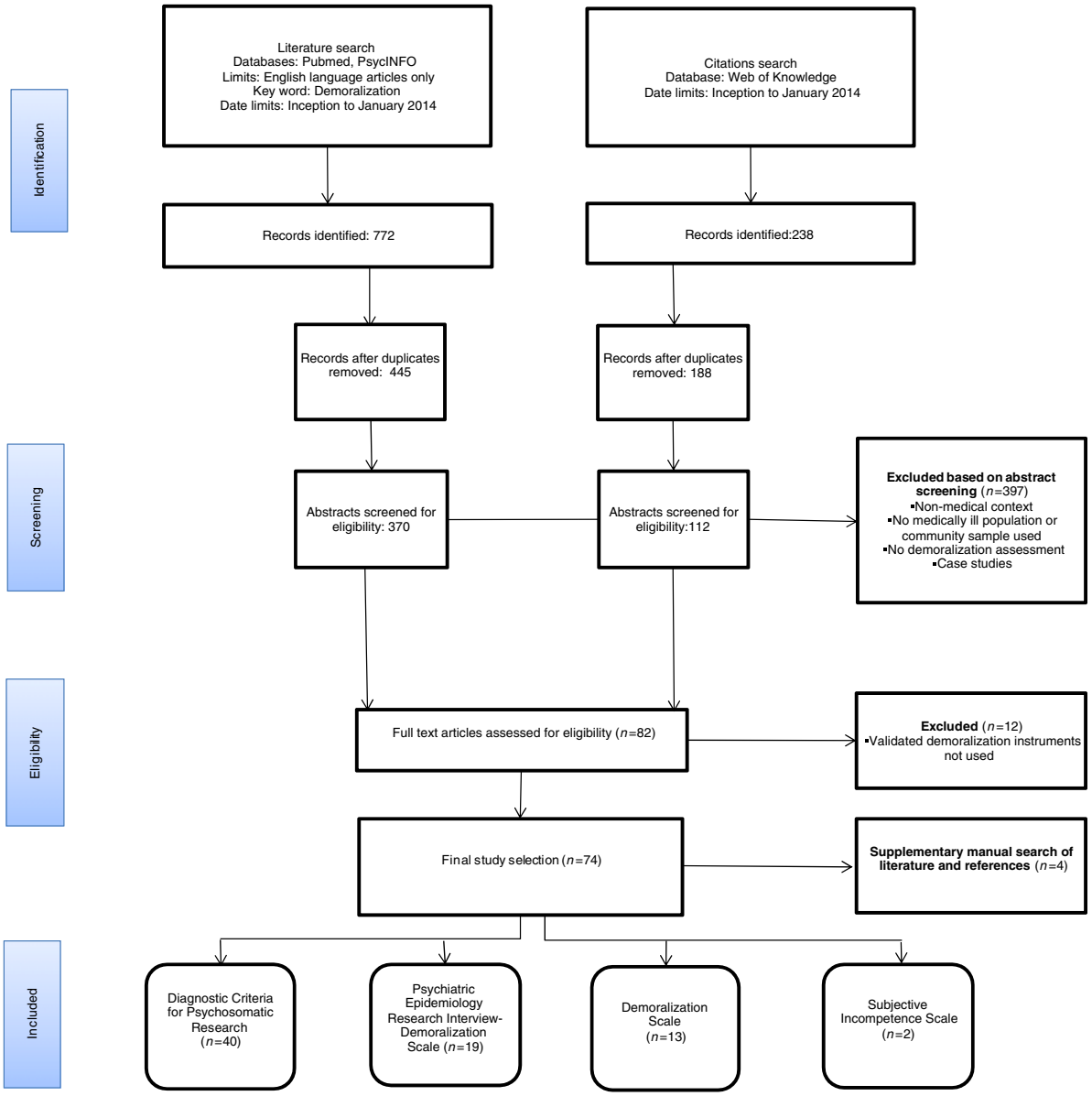

Fig. 1. PRISMA flow diagram. Identification, screening, eligibility and inclusion of data sources for the study.

Reyes *et al.* 2011), in medical patients with pain experiences (Lennon *et al.* 1990; Gallagher *et al.* 1995) and healthy controls (Gallagher *et al.* 1995). It has been used in psychiatric samples as well (Jackson & Tessler, 1984; Fichter *et al.* 1993; Ritsner *et al.* 1996; Fichter & Quadflieg, 2001).

The instrument has been applied to US ethnically diverse samples containing not only white participants, but also participants of African and Latin American descent (Vernon & Roberts, 1981; Page & Cole, 1992; Reyes *et al.* 2011; Wallace *et al.* 2003) and has also been used in Poland (Perera *et al.* 2013), Israel (Feldman *et al.* 1995; Ritsner *et al.* 1996), and Germany (Fichter *et al.* 1993; Fichter & Quadflieg, 2001). It has never been validated in non-Western populations. In a few studies (Roberts & Vernon, 1981; Feldman *et al.* 1995; Reyes *et al.* 2011) cut-off scores have been applied to determine 'caseness'. Please see Table S2 for details.

DS

Kissane *et al.* (2004) developed the self-report DS to assess existential distress in advanced cancer patients. The measure contains 24 items and five factors: loss of meaning and purpose, dysphoria, disheartenment, helplessness, and sense of failure. The measure is a multidimensional instrument used primarily as a unidimensional measure of demoralization. The 24-item self report scale has a 5-point scale of response, from 0 (*never*) to 4 (*all the time*) with a maximum score of 96.

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A score >30 is suggested as a cut-off for the presence of demoralization. The scale asks the patient to consider their state in the 2 weeks preceding assessment (Kissane *et al.* 2004). The DS demonstrated good internal consistency in several validation studies (Kissane *et al.* 2004; Mullane *et al.* 2009; Mehnert *et al.* 2011). While the instrument is dimensional, authors have applied cut-offs to establish a categorical evaluation of presence of demoralization.

In the preliminary validation study (Kissane *et al.* 2004), 'loss of meaning and purpose' was found to correlate strongly with the Beck Hopelessness Scale (Beck *et al.* 1974), and with the desire for hastened death as measured by the Schedule of Attitudes towards Hastened Death (Rosenfeld *et al.* 2000). Dysphoria, factor 2, strongly correlated with the Beck Depression Inventory – II (BDI-II; Dozois *et al.* 1998) and moderately correlated with the Patient Health Questionnaire (PHQ; Kroenke *et al.* 2001). The third factor, disheartenment, correlated highly with the McGill Quality of Life Questionnaire (McGill QOL; Cohen *et al.* 1995). Factor 4, helplessness, also correlated well with the PHQ, while sense of failure, factor 5, was correlated moderately with the McGill QOL. The total DS score demonstrated a statistically significant correlation with all scales used to validate the concurrent validity of individual scale factors. The DS has been validated in several different countries in advanced cancer patient samples and palliative settings, including Ireland (Mullane *et al.* 2009), Germany (Mehnert *et al.* 2011), Taiwan (Lee *et al.* 2012) and Australia (Kissane *et al.* 2004), where the measure was developed. Details of DS studies are listed in Table S3.

Several peculiarities emerge in all validation studies. Different cut-off scores have been used to create 'demoralized' and 'non-demoralized' categories. A score >30 has been used to identify demoralized cases in some studies including the preliminary one (Kissane *et al.* 2004; Lee *et al.* 2012) while others have used the sample mean (Mullane *et al.* 2009) or both (Vehling *et al.* 2011). Cross-tabulation frequency methods were used to establish divergent validity from PHQ and BDI measures (applied to determine depression diagnoses), a method which is generally considered weak evidence and has been questioned (Mullane *et al.* 2009). Indeed χ^2 analyses reveal that divergent validity of the DS from the PHQ is not statistically supported (Mullane *et al.* 2009; Lee *et al.* 2012). Moreover, the PHQ and BDI-II were used to confirm both divergent validity of the categorical DS diagnosis and concurrent validity of individual DS factors (disheartenment and dysphoria) as well as the concurrent validity of the DS as dimensional measure (total score) through use of correlational analyses.

SIS

The SIS is a measure developed by Cockram *et al.* (2009) whose aim is to measure what is thought by the authors to be the clinical hallmark feature of demoralization. It is a 12-item self-report unidimensional questionnaire which asks subjects to consider the week preceding the day of assessment. The SIS demonstrates high internal consistency with a reliability coefficient of 0.90. The authors confirmed statistically significant positive correlations between several Brief COPE subscales (denial, behavioral disengagement, self-blame) (Carver, 1997) and the SIS scale. The authors underline the limitations of this preliminary study of a cancer patient sample, mainly the homogeneity of the study group, the lack of validation with other demoralization scales and diagnostic criteria, and unknown levels of perceived stress and social support in the sample (Cockram *et al.* 2009). In a subsequent study, subjective incompetence and depression were found to correlate negatively when both perceived stress was low and social support was high, while they were found to converge when perceived stress and social support were both low or both high (Cockram *et al.* 2010). The questionnaire has been used in only two studies thus far including the preliminary validation (see Table S4).

Structured Interview for the DCPR

The Structured Interview for the DCPR (Mangelli *et al.* 2007) contains 58 questions with a 'yes/no' response. The primary aim of the DCPR is to provide a conceptual framework and assessment strategy for psychosomatic syndromes commonly encountered in the medical setting (Sirri & Fava, 2013). The interview identifies 12 psychosomatic syndromes including demoralization. The authors base their demoralization operationalization on Schmale & Engel's giving up–given up complex (Schmale & Engel, 1967) and Frank's (1973) demoralization syndrome as detailed in Table S1. All three criteria are required to receive a diagnosis of demoralization. The DCPR operationalization of demoralization is the first to explicitly specify its duration (at least 1 month) and the chronology of symptoms to distinguish the syndrome from similar psychiatric disorders (Mangelli *et al.* 2005).

The structured interview has demonstrated high inter-rater reliability and Cohen's kappa values ranging from 0.69 to 0.97 for the 12 syndromes. Cohen's kappa for demoralization was found to be 0.90 (Galeazzi *et al.* 2004). The DCPR interview has been validated and applied in the Italian context in numerous studies across varying medical diagnoses (see Table S5) with the exclusion of one study (Chaturvedi & Goswami, 2012). A multitude of validation studies

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have focused on establishing divergent validity from the Diagnostic and Statistical Manual for Psychiatric Disorders – IV (DSM-IV; APA, 1994) using the Structured Clinical Interview for DSM disorders (Spitzer *et al.* 1992), finding evidence for incremental clinical utility in the psychological assessment of medical patients (Porcelli *et al.* 2000, 2009; Grandi *et al.* 2001; Rafanelli *et al.* 2003, 2005, 2010; Sonino *et al.* 2004, 2006, 2011; Grassi *et al.* 2005, 2007; Mangelli *et al.* 2005, 2006; Ottolini *et al.* 2005; Picardi *et al.* 2005, 2006; Tossani *et al.* 2013). One study has validated the DCPR with the International Classification of Diseases (Sartorius *et al.* 1993) in a sample of consultation liaison psychiatry patients (Galeazzi *et al.* 2004).

Characterization and content overlap

One question emerges in the review of available validated demoralization instruments. How do the instruments differ and how are they similar? First, the instruments differ in the time reference of the assessment. The PERI-D asks participants to consider the preceding year, the DS the preceding 2 weeks, the SIS the preceding week. The DCPR instead requires the presence of symptoms for at least 1 month duration. Second, the instruments differ in structure and type of assessment. The DCPR is a clinician-administered interview while the PERI-D, DS, and SIS are self-report questionnaires. While the PERI-D and DS are multi-dimensional scales containing nine and five factors, respectively, the SIS is a unidimensional scale. However, all three of these measures yield a total score. Despite the differences present between the instruments, there is substantial overlap in content and characterization of the demoralization syndrome (see Table S1).

Subjective incompetence remains a common factor among all instruments. It is presented as a sense of failure and/or inability to cope in both the DS and in the DCPR demoralization criteria and as low self-esteem in the PERI-D. Helplessness and hopelessness are common to most instruments, i.e. the PERI-D, the DCPR, and the DS. Psychological distress is present in two measures; in the PERI-D as sadness and anxiety items and in the DS as dysphoria and disheartenment factor items. Only the DS contains an existential component, that is, loss of meaning and loss of purpose of one's life. It is very closely associated with the common loss of mastery and independence that the severely physically ill experience (Clarke & Kissane, 2002).

Demoralization prevalence

One of the main types of data present in the literature on demoralization is prevalence of the syndrome in the study samples. The prevalence of demoralization depends on the instrument used and the type of population assessed. First, we will discuss prevalence rates found in community samples and healthy control participants. These data concern the DCPR and PERI-D studies as no SIS and DS studies have investigated the prevalence of demoralization in non-medical populations. Second, we will discuss the prevalence rates of demoralization in medical samples which were available for studies using the DCPR, the DS and the PERI-D.

Non-medical settings

Few studies have investigated presence of demoralization in non-medical settings. In community samples, demoralization as defined by the PERI-D appears particularly prevalent with 20–30% of the sample reporting demoralization symptoms (Vernon & Roberts, 1981; Feldman *et al.* 1995; Reyes *et al.* 2011). Demoralization in healthy controls evaluated with the DCPR appears to be relatively rare. DCPR studies report a prevalence of 2–5% in healthy participants (Sonino *et al.* 2007; Ferrari *et al.* 2008; Tomba *et al.* 2012) and a prevalence rate of 3% in a community sample (Mangelli *et al.* 2006).

Medical settings

Demoralization as defined by the DCPR emerged as particularly prevalent in the medical context with roughly one third or more of patients meeting criteria across medical diagnoses including: cardiac illness (Ottolini *et al.* 2005; Rafanelli *et al.* 2009; Porcelli *et al.* 2012; Sirri *et al.* 2012; Guidi *et al.* 2013), cardiac transplantation (Grandi *et al.* 2001, 2011; Sirri *et al.* 2010), essential hypertension (Rafanelli *et al.* 2012), endocrine diseases (Sonino *et al.* 2004, 2007), primary aldosteronism (Sonino *et al.* 2006, 2011), oncological diseases (Grassi *et al.* 2004, 2005), primary care (Ferrari *et al.* 2008), consultation liaison psychiatry patients (Galeazzi *et al.* 2004; Porcelli *et al.* 2009), medical outpatient samples with a wide variety of medical diagnoses (Mangelli *et al.* 2005; Grassi *et al.* 2007; Guidi *et al.* 2011), and cyclothymic disorder (Tomba *et al.* 2012). Patients with vasovagal syncope and medically unexplained syncope also report relatively high rates (around 20%) (Rafanelli *et al.* 2013).

The highest prevalence has been reported in psychiatric patients with roughly half of the samples suffering from the syndrome (Abbate-Daga *et al.* 2013; Tossani *et al.* 2013). DCPR studies have been able to ascertain a higher presence of demoralization in medical (Sonino *et al.* 2007; Ferrari *et al.* 2013) and psychiatric (Tomba *et al.* 2012) samples compared to healthy controls.

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The applicability of the demoralization syndrome and the DCPR is beginning to be explored in the Indian population as well, with a preliminary study reporting 15% of a psychiatric sample suffering from the syndrome (Chaturvedi & Goswami, 2012). However, considering the socio-cultural differences between the cultural context in which the instrument has been developed and validated (Italy) and the Indian context, further studies are needed to validate the measure. Moreover, DCPR demoralization also seems to be stable in individuals over time. In patients assessed after coronary artery bypass surgery, prevalence of demoralization did not change significantly over the course of 6–8 years' follow up (Rafanelli *et al.* 2006).

Prevalence rates of demoralization using the DS varied according to the use of cut-off scores as can be seen in Table S3. When the sample mean score and S.D.s were used to distinguish cases of low, moderate and high demoralization, moderate demoralization was found to be present in 70% of cancer patients. High demoralization was found in about 15% of cancer patients (Mullane *et al.* 2009; Mehnert *et al.* 2011). Demoralization prevalence rates around 50% were reported when median scores or a score >30 were used as cut-offs (Kissane *et al.* 2004; Lee *et al.* 2012).

Link & Dohrenwend (1980) reported a median prevalence in 14 local community studies of around 24.6%. From the PERI-D studies included for review, a prevalence between roughly 20–30% also emerged in community samples (Roberts & Vernon, 1981) including a sample of inner-city low-income mothers (Reyes *et al.* 2011), while in a military outpatient clinic 26.4% of males and 16.3% of females reported being demoralized.

Differential diagnosis

Demoralization and depression

DCPR and DS studies have focused on differentiating demoralization from depression. Presence of the DCPR demoralization syndrome did not necessarily coincide with diagnoses of MDD in an extensive medical patient sample with varying diagnoses (Guidi *et al.* 2011), in medical outpatients (Mangelli *et al.* 2005), in inpatients (Galeazzi *et al.* 2004), in the context of primary care (Ferrari *et al.* 2008), cardiac transplantation (Grandi *et al.* 2001, 2011; Sirri *et al.* 2010), endocrine conditions (Sonino *et al.* 2004, 2007), primary aldosteronism (Sonino *et al.* 2006, 2011), myocardial infarction (Ottolini *et al.* 2005), hypertension (Sonino *et al.* 2011; Rafanelli *et al.* 2012), congestive heart failure (Rafanelli *et al.* 2009), acute heart disease (Rafanelli *et al.* 2005), cardiac rehabilitation (Rafanelli *et al.* 2003), functional gastrointestinal disorders (Porcelli *et al.* 2000), dermatology (Picardi *et al.* 2005) and oncology (Grassi *et al.* 2005). The aforementioned studies documented cases of demoralization without depression and of depression without demoralization, indicating that the psychological states are different clinical phenomena and are independent. Of note, DCPR demoralization emerged as more prevalent than major depression in all studies which assessed both states further indicating their differentiability. Only two studies constitute exceptions (Rafanelli *et al.* 2005; Sonino *et al.* 2011), but the reasons for the discrepancy appear to be unclear.

Demoralization as defined by the DCPR was found to be distinguishable from minor depression as well in patients with cardiovascular diseases (Rafanelli *et al.* 2003, 2006, 2009, 2010) and hypertensive patients (Rafanelli *et al.* 2012). Dysthymia and demoralization could also be differentiated in two studies (Rafanelli *et al.* 2010, 2012).

The DS was also used to identify cases of demoralization in absence of major depression in several studies assessing advanced cancer patients (Kissane *et al.* 2004; Mullane *et al.* 2009; Mehnert *et al.* 2011; Lee *et al.* 2012) with varying prevalence depending on the cut-off used (see Table S3 for reported percentages).

Most PERI-D studies and the validation study of the SIS contained little to no concomitant assessment of DSM-defined psychopathology, thereby haltering the possibility of validating the demoralization syndrome and divergent validity with psychiatric categorizations of psychological distress such as minor depression, dysthymia, major depression and adjustment disorders.

Demoralization and adjustment disorder

Jacobsen *et al.* (2007) argued that demoralization could be distinguishable from an adjustment disorder considering the quantitative differences rather than qualitative ones, with the two conditions being different in severity. The substantial overlap of adjustment disorder diagnoses with other psychiatric categorizations, especially in the medical setting, has contributed significantly to critiques on its questionable clinical utility (Semprini *et al.* 2010).

DCPR demoralization syndrome is more prevalent than adjustment disorders in both psychiatric and medical outpatient samples (Mangelli *et al.* 2005; Guidi *et al.* 2011; Fava *et al.* 2012*a*), dermatological inpatients (Picardi *et al.* 2005, 2006), cardiac disease and heart transplantation (Sirri *et al.* 2010, 2012), consultation liaison psychiatry (Porcelli *et al.* 2009) and endocrine disorder (Sonino *et al.* 2004, 2007) patients. Moreover, almost identical prevalence rates of

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demoralization and adjustment disorder have been reported in oncological patients (Grassi *et al.* 2005) and functional gastrointestinal disorder (FGID) patients (Porcelli *et al.* 2000). In a sample of medical patients with adjustment disorders, about a third was also suffering from demoralization syndrome (Grassi *et al.* 2007).

A large overlap of 'non-specific psychological distress,' or demoralization as measured by the PERI-D, and adjustment disorder was also reported by Marchesi & Maggini (2007), in a cancer patient sample.

Associated features

Sociodemographic factors

Several sociodemographic factors were found to be significantly correlated with demoralization. Being female was associated with higher PERI-D scores (Page & Cole, 1992; Marchesi & Maggini, 2007; Mehnert *et al.* 2011) and with a DCPR demoralization syndrome diagnosis (Grandi *et al.* 2011; Ferrari *et al.* 2013) in several studies. Being female was associated with higher DS scores in the Vehling *et al.* study (2012) as well, although not significantly, while it was found to be a significant predictor of demoralization in a previous study (Vehling *et al.* 2011). In contrast, Feldman *et al.* (1995) found higher PERI-D scores in males in a military primary-care setting, although the difference in mean scores did not reach statistical significance. No gender differences in DCPR demoralization diagnoses were found in an oncology patient sample (Grassi *et al.* 2005).

The evidence for an association between measures of demoralization and age was contradictory. Positive (Vehling *et al.* 2012), negative (Page & Cole, 1992; Clarke *et al.* 2005; Cockram *et al.* 2009; Mehnert *et al.* 2011; Vehling *et al.* 2013), or no associations (Grassi *et al.* 2005; Lee *et al.* 2012) with age have been reported. However, most of the samples in these studies had a relatively high mean age of patients with most patients being middle-aged or older.

Family and social factors may play a role in demoralization. Low social support is a significant predictor of demoralization (Vehling *et al.* 2013). Demoralized medical patients report poorer family support and scarcer positive relationships compared to both their non-demoralized counterparts (Marchesi & Maggini, 2007) and to healthy controls (Lennon *et al.* 1990; Grandi *et al.* 2011). Low social support is particularly prevalent in demoralization syndrome diagnoses in cancer patients (Grassi *et al.* 2004). Furthermore, living alone (Mehnert *et al.* 2011) as well as being jobless or having a low income (Lee *et al.* 2012) was found to be significantly associated with DS-demoralization in cancer patients

Stress

An association between stress and demoralization was found in the literature. It is important to first distinguish between objective measures of stress and subjective measures which assess perceived stress. While the use of objective stress measures such as event checklists has clear advantages, their use implies a direct relationship between stressful life events and pathology, while minimizing cognitive evaluations and subjective experience. The impact of stressful life events is always in some degree determined by the subjective perception of their stressfulness (Cohen *et al.* 1983).

Regarding objective stress, more stressful life events (Marchesi & Maggini, 2007) and more negative life changes following negative events (Lennon *et al.* 1990) were significantly correlated with PERI-D scores in medical patients. Elderly women with a history of suicidality in the past 5 years (suicidal attempts or ideation), found to have high DS scores, reported more important stressful life events in the prior 12 months compared to controls without recent history of suicidality (Lau *et al.* 2010). Patients who reported allostatic overload (Fava *et al.* 2010*a*; Tomba & Offidani, 2012), that is, a condition in which an identifiable stressor(s) exceeds an individual's ability to cope, reported significantly higher frequency of DCPR demoralization than those who did not present with such stressful characterization (Porcelli *et al.* 2012).

Subjective or perceived stress related to dignity (Sautier *et al.* 2014), shame and stigma (Kissane *et al.* 2013) in cancer patients were found to be correlated significantly and positively with DS-demoralization scores. The role of perceived stress along with social support may be considered to better understand the convergence of demoralization with depression (Cockram *et al.* 2010).

Somatization and pain

Somatization, understood as the tendency to communicate and experience psychological distress through physical symptoms while seeking medical attention for them (Lipowski, 1988), was found to be associated with demoralization in its various conceptualizations. The co-occurrence of demoralization with physical symptomatology is also suggested by the substantial overlap rates of DSM somatoform diagnoses and DCPR demoralization diagnosis. In the Picardi *et al.* (2006) study of dermatological inpatients, a large overlap of somatoform diagnoses with demoralization syndrome was reported. Similar overlap of demoralization and somatoform disorders was found in gastrointestinal patients (Porcelli *et al.* 2000). In addition, the high prevalence of demoralization in

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frequent attenders of a primary-care clinic (Ferrari *et al.* 2008) may indicate a somatization tendency in this subset of patients. A recent cluster analysis study underlined the associations between demoralization, somatization processes, anxiety and mood disorders (Fava *et al.* 2012*a*).

Several findings indicate a possible relationship between demoralization and pain experience. Greater pain intensity was found to be associated with presence of DCPR demoralization syndrome (Porcelli *et al.* 2009). PERI-D demoralization has been found to be associated with phantom tooth pain (Marbach, 1993) and myofascial pain (Gallagher *et al.* 1995). Pain events (compared to other negative events) were associated with greater negative change in patients with myofascial pain syndromes which was in turn associated with high PERI-demoralization (Lennon *et al.* 1990).

Other facets of painful illness may certainly be involved such as functional disability, also found to correlate with demoralization in a sample of inpatients independently of illness severity (Marchesi & Maggini, 2007). Existential factors such as loss of sense of dignity may also account partially for the association between physical problems and demoralization specifically in advanced cancer patients (Vehling & Mehnert, 2013).

Illness behavior

Illness behavior emerged in association with demoralization. DCPR demoralization syndrome was found to be associated with frequent attender behavior in a primary-care setting while controlling for other sociodemographic factors (Ferrari *et al.* 2008). Furthermore, demoralization was found to overlap with illness denial in consultation liaison psychiatry (Galeazzi *et al.* 2004). Patients with substance use disorders exhibit a substantial overlap between demoralization syndrome and illness denial (Tossani *et al.* 2013). A cluster characterized by demoralization and abnormal illness behaviors (including health anxiety, illness denial) was identified in a large sample of medically ill patients (Fava *et al.* 2012*a*). High rates of demoralization (96%) characterized a severe psychosomatic cluster (high rates of illness denial, irritable mood, health anxiety, and alexithymia) in a sample of anorexia nervosa inpatients (Abbate-Daga *et al.* 2013). In a sample of patients with temporomandibular pain and dysfunction syndrome, higher demoralization scores were related to over-reporting of children's illness even after controlling for illness attitudes (Raphael *et al.* 1990). In cancer patients (Cockram *et al.* 2009), subjective incompetence, the clinical hallmark of demoralization, has also been found to significantly correlate with denial and behavioral disengagement as measured by the COPE scale (Carver, 1997).

Psychological well-being

Psychological well-being (Ryff, 1989) represents a dimensional model which considers the various psychological dimensions which are conducive to an individual's development of optimal functioning: positive evaluation of one's self, the belief that life is purposeful and meaningful, the possession of quality relationships with others, a sense of continued growth and development, a sense of mastery over one's environment, and a sense of self-determination. Sense of autonomy, environmental mastery, positive relations, self-acceptance and purpose in life were found to be significantly worse in demoralized patients compared to non-demoralized patients in the setting of cardiac transplantation. Additionally, cases of co-morbid demoralization and depression reported significantly lower autonomy, positive relations with others, and self-acceptance than patients who were only depressed (Grandi *et al.* 2011). Identified by cluster analysis, a group of hypertensive patients was found to be characterized by worse psychological well-being scores and significantly higher rates of demoralization, minor depression and generalized anxiety disorder (Rafanelli *et al.* 2012). These findings underline that among demoralized patients, there is also a lack of positive functioning characteristics, which is not always the flip-side of the presence of psychological distress (Ryff *et al.* 2006).

A poor sense of coherence (Antonovsky, 1987) in gynecological cancer was also found to correlate with higher DS scores (Boscaglia & Clarke, 2007), Similarly, a lack of global meaning, which comprises both a sense of personal coherence and of purpose, was found to predict DS scores (Vehling *et al.* 2011).

Demoralization and health outcomes

Adverse health outcomes have also been reported in association with DCPR demoralization syndrome, specifically in cardiac conditions. In a follow-up study of myocardial infarction survivors, patients with joint presence of dysthymia and demoralization were found to be at risk 3.67 times more than patients without dysthymia for developing cardiac events, such as cardiac death or re-hospitalization (Rafanelli *et al.* 2010). Demoralization was found to be a prodromal symptom of cardiac events, indicating the possibility that a poor psychological state may be indicative of vulnerability to coronary artery disease (Ottolini *et al.* 2005; Rafanelli *et al.* 2005). In cardiac transplant patients with concomitant depression and demoralization, acute rejection episodes were more frequent than

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in patients with demoralization in absence of depression, although this result may be due to lower pharmacological compliance (Grandi *et al.* 2011).

Altered immune function was found to be associated with PERI-demoralization. Specifically, concanavalin A and pokeweed mitogen responses (measures of decreased lymphocyte activity) in patients with temporo-mandibular pain and dysfunction syndrome were decreased in relation to the level of demoralization. Interestingly, depression scores (Hamilton, 1967) did not seem to be associated with altered mitogen responses (Marbach *et al.* 1990). However, the aforementioned studies had small sample sizes, therefore results must be interpreted with caution.

High maternal PERI-D scores were associated with offspring's adverse health outcomes. More specifically, maternal demoralization scores were found to correlate significantly with both persistent and transient wheeze, significant predictors of clinical childhood asthma, in children of inner-city low-income mothers (Reyes *et al.* 2011), as well as with adverse neurobehavioral outcomes in offspring exposed to high levels of air pollutants (Perera *et al.* 2013). An indirect association between body mass index and both maternal PERI-D scores and economic deprivation emerged in low-income mothers exposed to high community stress. However, the relationship between stress, poverty, dietary behaviors and psychological distress is complex requiring further investigation (Wallace *et al.* 2003).

As one would expect, poorer quality of life and functioning was found to be associated with demoralization in medically ill patients. Quality of life negatively correlated with DS scores in cancer patients (Kissane *et al.* 2004; Lee *et al.* 2012). Similarly, cancer patients with DCPR demoralization syndrome fared worse on quality of life measures than other psychosomatic DCPR syndrome groups, reporting more physical symptoms, poorer leisure activity, poorer adjustment and poorer social support (Grassi, *et al.* 2004). Demoralized cardiac transplant patients and demoralized consultation liaison psychiatry (CLP) inpatients also reported significantly worse quality of life and poorer psychosocial functioning than their non-demoralized counterparts (Porcelli *et al.* 2009; Grandi *et al.* 2011). In CLP patients, DCPR demoralization was found to be a better predictor of impaired psychosocial functioning than any DSM diagnosis, even while controlling for medical and demographic variables (Porcelli *et al.* 2009).

Poorer quality of life, in terms of number of physical problems, predicted DS scores in cancer patients (Vehling *et al.* 2012, 2013) which in turn were correlated with complaints of fatigue, mobility constraints, breathing problems, constipation, concentration or memory problems (Vehling *et al.* 2012). Furthermore, demoralized cancer patients were more likely to report physical problems than non-demoralized cancer patients (Mehnert *et al.* 2011).

Clinical utility of the instruments

PERI-D

The PERI-D may be useful to screen for depressive symptomatology in community samples as indicated by several studies (Roberts & Vernon, 1981; Vernon & Roberts, 1981; Marbach *et al.* 1990; Marchesi & Maggini, 2007). Additionally, the instrument has demonstrated the ability to distinguish psychiatric cases from non-cases (Fichter *et al.* 1993; Ritsner *et al.* 1996) and to differentiate groups of patients with various pain syndromes (Lennon *et al.* 1990; Marbach *et al.* 1990; Marbach, 1993; Gallagher *et al.* 1995). However, it does not seem to be sensitive to changes over time (Lennon *et al.* 1990; Reyes *et al.* 2011) and does not capture the severity of distress symptoms (Ritsner *et al.* 1996; Marchesi & Maggini, 2007).

DS

The DS appears to be sensitive to suicidality (Catanese *et al.* 2009; Lau *et al.* 2010). The instrument has also been found to be associated with illness-related variables such as cancer type and treatment strategies of anti-cancer treatments in one study (Lee *et al.* 2012), but not to stage of cancer and illness duration, type of treatment and cancer site in another sample (Boscaglia & Clarke, 2007; Vehling *et al.* 2012). Furthermore, in one study the DS did not capture changes over time (Vehling *et al.* 2012). However, a strong relationship between DS demoralization, physical problems and loss of global meaning in advanced cancer patients may indicate its utility in capturing illness-related distress related to such symptoms (Vehling *et al.* 2012). Sensitivity to treatment response of the DS has been demonstrated in patients presenting to the emergency room with suicidal intentions (Catanese *et al.* 2009).

SIS

The SIS requires further validation, but preliminary data suggests that it may be useful to assess medical patients for possible abnormal illness behaviors or attitudes, as SIS scores correlated significantly with denial and behavioral disengagement (Cockram *et al.* 2009).

Structured Interview for the DCPR

The DCPR interview appears to be a sensitive tool with which to assess the demoralization syndrome in the

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clinical context. Studies have been able to ascertain a higher presence of demoralization in medical and psychiatric samples compared to healthy controls (Sonino *et al.* 2007, 2011; Tomba *et al.* 2012; Ferrari *et al.* 2013) and compared to the general population (Mangelli *et al.* 2006) which present a much lower prevalence. Additionally, DCPR demoralization was found to differentiate frequent attenders of primary care from controls (Ferrari *et al.* 2008).

Sensitivity to changes over time has yet to be explored across varying diagnoses. Nonetheless, prevalence rates did not differ greatly between baseline and follow-up in coronary artery bypass surgery patients (Rafanelli *et al.* 2006) and coronary heart disease inpatients (Rafanelli *et al.* 2005, 2010). The DCPR demoralization criteria show sensitivity in discriminating presence of psychological distress specifically in the form of allostatic overload syndrome (Fava *et al.* 2010*a*). The condition presents an identifiable stressor or stressors that exceed the individual's ability to cope which precipitates psychosomatic or psychopathological symptomatology (Porcelli *et al.* 2012).

Discussion

Differences between instrument use, prevalence rates, and associated features

The assessment instruments have been used for different purposes and populations. The differing prevalence rates differ greatly across instruments which may be due to the different definitions of demoralization, participant characteristics, and methods of assessment. While the instruments overlap in content as previously discussed, they may be capturing slightly different psychological states due to their variations in definitions, format and time reference. Several considerations must be made to determine whether the instruments constitute valid methods for the assessment of demoralization understood as a distinct condition.

Interestingly, the PERI-D seems to be a useful tool for assessing distress in patients with medical conditions characterized by chronic pain (Lennon *et al.* 1990; Marbach *et al.* 1990; Marbach, 1993; Gallagher *et al.* 1995). It is highly present in association with chronic distress strongly correlated with household economic deprivation (Wallace *et al.* 2003) which may account for its correlation with adverse health outcomes in offspring of mothers in moderate to low socio-economic stressful conditions (Reyes *et al.* 2011; Perera *et al.* 2013). The high rates of demoralization (20–30%) in community samples (Roberts & Vernon, 1981; Reyes *et al.* 2011) may indicate that the PERI-D captures non-specific psychological distress associated with living in stressful conditions.

The usefulness of the PERI-D in screening community samples for depressive symptomatology may underscore the lack of discriminant validity of PERI-D demoralization from depression. Its association with general psychopathology (Fichter & Quadflieg, 2001) and perceived lack of control (Jackson & Tessler, 1984) in psychiatric patients suggest it does indeed capture general psychological distress associated with chronic psychopathology (Kohn, 2013). Indeed the PERI-D has been questioned as a valid measure of demoralization by de Figueiredo (1993) and Marchesi & Maggini (2007) for its lack of subjective incompetence assessment, despite the developers' drawing of parallelisms between their scale and Frank's construct. Indeed The PERI-D considers the past year, a time-frame which is scarcely useful in the clinical context. A clear strength of the PERI-D is its validation across ethnically diverse samples.

The data that emerged from the review of studies that applied the DS indicate that the scale may be capturing a specific type of existential psychological distress related to end of life and distress associated with physical suffering associated with terminal and life-threatening illness. The measure has been used primarily to assess advanced cancer samples. This may account for the high prevalence rates reported which are also the highest among all the reviewed studies assessing medical patients (see Table S3).

Furthermore, the evidence of discriminant validity from depression may not be entirely reliable as the use of a dimensional scale to create diagnostic categorizations presents methodological inadequacies. Additionally, the cut-off scores vary across studies, creating confusion and difficulties in interpretation and comparisons of results, specifically of prevalence rates. The measure's sensitivity to suicidality (Catanese *et al.* 2009; Lau *et al.* 2010) may indicate that the measure's utility goes beyond capturing end of life distress and may prove to be useful in psychiatric populations and for screening suicidality. On the other hand, this may indicate that DS demoralization greatly overlaps with depression. Indeed DS scores have been found to correlate with depression scores (Vehling *et al.* 2011). While these findings may underline known associations between hopelessness, depression and suicidality (Chioqueta & Stiles, 2003; Stewart *et al.* 2005), longitudinal associations between hopelessness, depressive symptoms, and suicidality are inconsistent (Shahar *et al.* 2006). Demoralization, suicidality, and depression may be correlated but distinct psychological states.

The majority of the data from DCPR studies indicate that demoralization, as defined by the instrument, is a relatively rare occurrence in healthy participants who do not have medical illnesses (Sonino *et al.* 2007;

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Ferrari *et al.* 2008; Tomba *et al.* 2012) and in community samples (Mangelli *et al.* 2006). It may be that DCPR demoralization criteria captures a specific psychological state associated with the experience of illness (see prevalence rates in Table S5) as also suggested by associations with somatization (Porcelli *et al.* 2000; Picardi *et al.* 2006; Fava *et al.* 2012*a*; Abbate-Daga *et al.* 2013; Guidi *et al.* 2013), allostatic overload (Porcelli *et al.* 2012) and abnormal illness behavior (Galeazzi *et al.* 2004; Ferrari *et al.* 2008; Fava *et al.* 2012*a*; Abbate-Daga *et al.* 2013; Tossani *et al.* 2013) and quality of life (Grassi *et al.* 2004; Mangelli *et al.* 2006; Grandi *et al.* 2011).

A large percentage of illnesses present in the DCPR samples were of a chronic nature and non life-threatening in the immediate future (i.e. functional gastrointestinal disorders, hypertension, psychiatric disorders, endocrine disorders) indicating that DCPR demoralization may be regarded as a manifestation of dealing with stress of a chronic nature, rather than a reaction to acute or life-threatening stressors. Indeed there are no significant differences in the prevalence of demoralization across different medical settings, such as oncology and gastroenterology (Mangelli *et al.* 2005). The use of DCPR as an integrative tool for DSM criteria is a strength of the instrument.

The SIS (Cockram *et al.* 2009) has not been used to gather information on prevalence or differentiability from major depression or other psychiatric disorders. Further studies may elucidate such relationships and provide such information. The possible relationship between demoralization, understood as subjective incompetence and distress, and coping deficits (Cockram *et al.* 2009) may have extremely useful implications in the medical setting.

One consistent result emerges across instrument type and across studies. Demoralization is associated with stress experiences whether acute, severe or chronic. Furthermore, in the medical setting, demoralization emerges as a psychological state associated with adverse health outcomes.

Conceptual synthesis

There have been various definitions and conceptualizations of demoralization. Demoralization has been seen as a normal reaction to adversity (Jacobsen *et al.* 2007). Slavney (1999) and Parker (2004) had proposed to consider demoralization as a normal dysphoric condition, akin to grief, in which, upon removal of the stressor and improvement of psychosocial protective factors (i.e. family support) improvement of the condition is observed. More importantly, according to those authors, while the social and functional impairment or excessive reactive distress in adjustment disorders is defined as unjustified by the nature of the circumstances, in demoralization the stress reaction should be considered natural. The literature on demoralization discussed in the current review calls such views into question.

The demoralization syndrome that was discussed in works by Schmale & Engel (1967) and Frank (1973), that formed the basis of DCPR criteria (see Table S1) appears to be more in line with the data that are available from this systematic review. Further, there are overlaps between DCPR criteria and the scales that have been used that may further specify the clinical picture. In the late 1960s, Schmale & Engel (1967) described the characteristics which may be related to the concept of subjective incompetence: feelings of helplessness and hopelessness; perception of diminished competence and control in one's own functioning; impairment in relationships with significant others; external environment and one's performance do not fulfil the subject's expectations given by previous experiences; loss of sense of continuity between past and future, with diminished hope and confidence in projecting oneself into the future; proneness to revive previous unsuccessful or frustrating experiences. Such formulation has been confirmed in a study using Ryff's Psychological Well-Being Scales (1989), outlining impairments with autonomy, environmental mastery, purpose in life, positive relations, and self-acceptance (Grandi *et al.* 2011).

Other findings support de Figueiredo's (1993) definition of demoralization as the convergence of psychological distress and subjective incompetence (Grandi *et al.* 2001; Marchesi & Maggini, 2007). Indeed, demoralization does not appear to simply represent subthreshold psychological distress (Porcelli *et al.* 2004; Ottolini *et al.* 2005; Ferrari *et al.* 2008; Grandi *et al.* 2011).

In the theoretical framework of the cognitive reformulation of the learned helplessness theory (Seligman, 1975), that is, the hopesslessness theory of depression (Abramson *et al.* 1989) hopelessness is seen as a cognitive vulnerability to depression. Demoralization in this sense may be viewed as a state characterized by a tendency to attribute negative life events to causes which are internal (i.e. subjective incompetence) and stable (i.e. hopelessness). In this view, some demoralized individuals may develop depression if attributions of negative outcomes become global rather than remain specific to a stressful situation and current coping abilities.

Clinical implications

The DCPR Structured Interview has been applied in a greater variety of medical contexts, contributing to its generalizability across medical and psychiatric

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settings. The studies which employed the DCPR provide the most amount of information on the differentiability of demoralization from depression and other psychiatric mood disorders (i.e. dysthymia, minor depression, cyclothymia, anxiety disorders). While the DCPR criteria provide a very helpful basis for the identification of demoralization, monitoring of the syndrome, particularly throughout the course of medical illness, requires additional instruments that may provide incremental information (Tomba & Bech, 2012).

Specifically, results obtained with DCPR criteria (Mangelli *et al.* 2005; Grandi *et al.* 2011) confirm previous phenomenological observations (de Figueiredo, 1993) on the differentiation between demoralization and major depression. Several authors (de Figueiredo & Frank, 1982; de Figueiredo, 1993, 2013; Cockram *et al.* 2009) have argued that low motivation to action in demoralization is thought to be caused by a sense of subjective incompetence, while in depression there is an outright decreased magnitude of motivation. Major distinctions between demoralization and 'endogenomorphic' depression in alteration of appetite and sleep cycle have also been underscored by the authors. According to Klein *et al.* (1980), in demoralization, anticipatory pleasure, the ability to derive pleasure from the anticipation of an event, is negatively affected, while consummatory pleasure, the ability to enjoy the event itself, has been observed to remain intact. In the depressed individual, however, both anticipatory and consummatory pleasures are adversely affected.

Not only is the distinction between demoralization and major depression feasible, but the addition of depression to demoralization does not alter the psychobiological features of the latter. Indeed, the co-occurrence of demoralization significantly worsens the clinical status of patients (Grandi *et al.* 2011). In factor analytic studies (Kissane *et al.* 2001; Clarke *et al.* 2005; Jacobsen *et al.* 2006) demoralization has been shown to be distinguishable from depression. Specifically, the syndrome has been shown to be distinct from anhedonia, a core feature of MDD and grief (Clarke *et al.* 2005).

Differentiating demoralization and depression may especially be important in the psychiatric setting. For instance, demoralization was found to frequently occur in association with anxiety disorders (Fava *et al.* 2010*b*), but it is frequently subsumed under the rubric of major or minor depression. It is conceivable, even though yet to be tested, that demoralization that occurs in the course of cognitive behavioral treatment may improve during the continuation of therapy (Emmrich *et al.* 2012) or respond to specific cognitive strategies, whereas depressive features may require pharmacological treatment.

A possible collocation for the demoralization syndrome in the Diagnostic Manual of Mental Disorders (APA, 2013) is in the 'psychological factors affecting medical condition' category, as a useful clinical specification (Fava *et al.* 2007; Wise, 2009).

Suggestions for further research

A number of research needs emerge from our analysis of the literature.

Differentiation from mood disorders

Further evidence of the differentiation of demoralization from mood disorders is needed. While the differentiation of demoralization from major depression has been supported in DCPR studies, further evidence of the differentiation of the syndrome from minor depression and dysphoria is needed. Several studies in the current review have reported differential prevalence rates from demoralization syndrome and minor depression and dysthymia. However, sample sizes were small and limited to cardiovascular patients (Rafanelli *et al.* 2003, 2006, 2009, 2010, 2012).

Furthermore, the temporal relationship between demoralization and major depression remains unclear and longitudinal studies are needed. Several authors have described demoralization as a possible prodromal state to depression or suicidality (Kissane *et al.* 2001; Rickelman, 2002; de Figueiredo, 2013). Indeed there is evidence for a continuum between hopelessness and major depression (Haslam & Beck, 1994; Iacoviello *et al.* 2013). Once a basic formulation of demoralization is confirmed and divergent validity from mood disorders is adequately supported, future studies may explore other aspects and applications of the demoralization syndrome as well as its treatment.

Determination of incremental validity

Little is known about the correlations among different instruments measuring demoralization and their differential sensitivity. A high correlation is often regarded as evidence that two scales measure the same factor. Common content of two scales may ensure a high positive correlation between them, but the items they do not share may be important in determining their sensitivity (Fava *et al.* 2012*b*; Tomba & Bech, 2012).

Demoralization in psychiatric settings

There is very little research on the role of demoralization in the setting of psychiatric disease (Chaturvedi & Goswami, 2012; Tomba *et al.* 2012; Abbate-Daga *et al.* 2013; Kohn, 2013; Tossani *et al.* 2013). Adamson & Schmale (1965) pioneered the studies on the role of

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demoralization and giving up in the prodromal phase of psychiatric disorders. The high prevalence of demoralization in anorexia nervosa (Abbate-Daga *et al.* 2013) and substance use disorders (Tossani *et al.* 2013) underline the importance in considering the role of demoralization in the maintenance of compulsive behaviors. Indeed a perceived lack of control has been found to be associated with demoralization in psychiatric patients (Jackson & Tessler, 1984).

Demoralization as a risk factor

Schmale (1972) postulated that giving up may increase vulnerability to the development of medical disease. It has been found to be a prodromal symptom of serious illness (Ottolini *et al.* 2005; Rafanelli *et al.* 2005) Furthermore, demoralization may also constitute a risk factor for psychiatric disorders (Kohn, 2013). Demoralization may be examined as a risk factor in longitudinal studies.

Interaction with other psychological variables

This analysis of the literature underscores the need of further research on the impact of demoralization on important clinical phenomena such as allostatic load (McEwen & Stellar, 1993), illness behavior (Pilowsky, 1997; Sirri *et al.* 2013), psychological well-being (Ryff, 1989), perceived stress (Cohen *et al.* 1983) and suicidality.

Validation of demoralization measures in other populations

A few DCPR and PERI-D studies have investigated the presence of demoralization in the general population or in healthy controls. Future studies that explore the possibility that demoralization develops in the absence of physical illness or mental illness are recommended for all four assessment instruments.

Moreover, there is a lack of validation of the available demoralization instruments in non-Western cultures which is warranted for all instruments. The DCPR, DS, and SIS may be further validated in ethnically diverse community samples as well.

Neurobiologic correlates

The neurobiologic correlates of demoralization are virtually unexplored and the physiological functioning that may potentially differentiate it from depression may unravel important insights. Future investigations may help elucidate the relationship between demoralization syndrome and the learned helplessness state which is known to induce neurochemical depletion and exaggerated activity in the raphe and amygdala (Forgeard *et al.* 2011).

Treatment

No randomized controlled trial of a pharmacological or psychological nature has been performed on demoralization patients. According to de Figueiredo (1993) the distress component can be effectively treated with symptom removal, whereas subjective incompetence requires a more in-depth modification of subjects' attitudes. This includes the hypothesis that demoralization may require the promotion of well-being and positive functioning (Fava & Tomba, 2009) and emphasizing of hope and empowerment (Frank, 2013). Demoralization may require psychotherapeutic support specifically aimed at increasing a sense of mastery and self-competence (de Figueiredo & Slavney, 2000).

Conclusions and limitations

Using validated instruments, there is evidence that demoralization appears to be a distinctive clinical presentation characterized by hopelessness, helplessness, giving up, and subjective incompetence. Furthermore, there is mounting support that demoralization may be an independent condition distinguishable from MDD. Demoralization appears to be common in the medical setting as well as associated with specific clinical aspects and adverse health outcomes. However, several limitations of the current systematic literature review must be considered. First, the different instruments used in the literature contain common features, but also distinct ones. The different definitions and instruments of demoralization that continue to be used make comparison of existing data on the prevalence and construct validity of demoralization open for discussion and further validation.

Nonetheless these findings give rise to several clinical implications. First, the demoralization syndrome warrants careful consideration in the clinical and medical context through valid assessment procedures that permit identification of cases in medical patients. Second, demoralization as a distinct condition may require the development of tailored and targeted treatment approaches.

The majority of studies reviewed are cross-sectional in nature which presents a clear limitation in interpretation of the reported results. Future research would benefit from longitudinal studies. The interactive nature of physical and psychological processes is evident in the literature, supporting the need for a more integrative and multifactorial model.

Supplementary material

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0033291714001597.

https://doi.org/10.1017/S0033291714001597 Published online by Cambridge University Press

Declaration of Interest

None.

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