

**Relationship between spirituality, meaning in life, psychological distress, wish for hastened death, and their influence on quality of life in palliative care patients**

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## **Abstract**

### **Context**

Spiritual, existential, and psychological issues represent central components of quality of life (QOL) in palliative care. A better understanding of the dynamic underlying these components is essential for the development of interventions tailored to the palliative context.

### **Objectives**

The aims were to explore (i) the relationship between spirituality, meaning in life, wishes for hastened death and psychological distress in palliative patients, and (ii) the extent to which these non-physical determinants influence QOL.

### **Methods**

A cross-sectional study involving face-to-face interviews with Swiss palliative patients was performed, including the *Schedule for Meaning in Life Evaluation* (SMILE), the Spiritual Subscale of the *Functional Assessment of Chronic Illness Therapy* (FACIT-Sp), the *Idler Index of Religiosity* (IIR), the *Hospital Anxiety and Depression Scale* (HADS) and the *Schedule of Attitudes toward Hastened Death* (SAHD). QOL was measured with a single item visual analogue scale (0-10).

### **Results**

206 patients completed the protocol (51.5% female; mean age=67.5 yrs). The results indicated a significant negative relationship between FACIT-Sp/SMILE and HADS total scores ( $p=.000$ ). The best model for QOL explained 32.8 % of the variance ( $p=.000$ ) and included the FACIT-Sp, SMILE, and SAHD total scores, the IIR “private religiosity” subscale, as well as the HADS “depression” score.

### **Conclusion**

Both spiritual well-being and meaning in life appear to be potential protective factors against psychological distress at the end of life. Since non-physical determinants play a major role in shaping QOL **at the end of life**, there is a need for the development of meaning-oriented and spiritual care interventions tailored to the fragility of palliative patients.

**Key words:** meaning in life, spirituality, quality of life, wish to hasten death, psychological distress

## Introduction

The World Health Organization definition of quality of life (QOL) focuses on the general perception of the individuals' position in life, in relation to their goals, expectations, standards and concerns (1). This construct includes all the significant areas of life that allow people to satisfy their needs, including the psychological and spiritual domains. The latter have been shown to be particularly relevant for QOL in palliative care patients (2, 3, 4). In the palliative care context, spirituality has been defined as “the aspect of humanity that refers (i) to the way individuals seek and express meaning and purpose, and (ii) the way they experience their connectedness to the moment, to self, to others, to nature and to the significant and sacred” (5). In line with this definition, meaning in life (MIL) represents a core element of spirituality, while religiosity may or may not be related to an individual's spiritual dimension (6).

Little is known about the dynamic underlying the relationship between spirituality and MIL as well as their significance in the context of wishes to hasten death (WTHD) and their **interaction** with depression and anxiety at the end of life. Previous results suggest that spirituality may represent a protective factor against the development of psychological distress, in particular depression and anxiety (7, 8). Given the relatively high prevalence of these forms of distress in palliative care (25% for depression and 10% with anxiety (9); 5-17% with high WTHD (10)), and their clinical relevance, the degree of association between these non-physical determinants of QOL warrants a detailed investigation. In particular, it would be interesting to know to which extent these determinants contribute to QOL in the palliative care context.

The aims of this study were therefore to explore:

- (i) the relationship between spirituality and meaning in life with wishes for hastened death and psychological distress in palliative patients (**for the purpose of this study, the term “psychological distress” refers to symptoms of depression and anxiety**).
- (ii) the extent to which these non-physical determinants can be considered as significant predictors of subjectively perceived QOL in palliative care patients.
- iii) whether differences occur in three geographically and linguistic diverse regions (German, French, Italian) of Switzerland.

## Methods

We performed an exploratory, cross-sectional study in palliative care patients, based on structured face-to-face interviews, in the German, French, and Italian regions of Switzerland. Inclusion criteria were (i) 18 years or older, (ii) treated by one of the specialized palliative care teams involved and (iii) <6 months life expectancy according to the treating physician. Exclusion

## Non-physical predictors of quality of life

criteria were (i) psychiatric disease, (ii) significant cognitive impairment, and (iii) insufficient knowledge of the local language.

**Patients** hospitalized in a palliative care unit or cared for by a palliative home care team, who fulfilled the inclusion criteria were asked to participate in the study by a research collaborator who was not part of the palliative care team. After obtainment of informed consent, a meeting was scheduled with the research collaborator in order to complete the case report form. The project was approved by the three regional ethics committees.

### *Instruments*

#### ➤ *The Schedule for Meaning in Life Evaluation (SMILE)*

This instrument was developed and validated by Fegg et al. (11). Respondents are first asked to indicate three to seven areas that actually provide meaning to their lives. Next, the importance and the current level of satisfaction associated to each area are rated on a Likert scale. An index of weighting (“IoW” ranging from 20 to 100) and an index of satisfaction (“IoS” ranging from 0 to 100) indicate the mean weighing score and the mean satisfaction score for the areas mentioned, respectively (**higher scores reflecting higher importance and satisfaction scores**). A SMILE total score (0-100) indicates the global MIL satisfaction by taking into account the level of importance attached to each area (**with higher scores reflecting higher global satisfaction**).

#### ➤ *The Functional Assessment of Chronic Illness Therapy-Spiritual Well-being Scale (FACIT-Sp)*

The FACIT system is a collection of QOL questionnaires targeted to the management of chronic illness. The FACIT-Sp was specially developed to assess the spiritual wellbeing (12) and comprises several different aspects (meaning, faith peace). The total score for spiritual wellbeing (0-48 **with higher scores reflecting higher spiritual wellbeing**) was assessed in this study (13).

#### ➤ *The Idler Index of Religiosity (IIR)*

This is a four-item instrument that measures public (range 2-10) and private (range 2-7) religiosity (14). The IIR total score ranges from 4 (least religious) to 17 (most religious).

#### ➤ *The Hospital Anxiety and Depression Scale (HADS)*

The HADS consists of 14 items rated on a Likert scale (15) yielding a “HADS total score” (0-42), a “HADS depression score (0-21) and a “HADS anxiety score” (0-21), **with higher scores reflecting higher psychological distress**.

#### ➤ *The Schedule of Attitudes towards Hastened Death (SAHD)*

The questionnaire aims to evaluate the wish to hasten death among terminally ill patients and was developed by Rosenfeld et al. (16). It is a self-response scale consisting of 20 true/false items (range 0-20 with higher scores reflecting higher WTHD).

## Non-physical predictors of quality of life

### ➤ *Single-item Quality of Life Scale – Numeric Rating Scale 0 -10 (SQOLS)*

Subjective QOL was measured on a visual analogue scale (VAS) from 0 (worst imaginable quality of life) to 10 (best imaginable quality of life). The question is worded: “By considering all the aspects of your life, how would you judge your quality of life at the present moment?” This approach to measuring quality of life was evaluated by de Boer et al. (17).

All instruments which were not already validated in French, German or Italian were translated using good practice principles for translation (including forward-backward translation) and cultural adaptation of patient-reported outcomes (18). SMILE, SAHD, IIR were translated in Italian; and SAHD and IIR in French.

### *Statistical analyses*

Considering the first aim of this study, regression analyses were performed successively variable by variable. The psychological issues (HADS and SAHD score) were included as dependent variables. The “spiritual/existential” dimensions (FACIT-Sp and SMILE total scores) and their interactions between the three linguistic regions were included as independent variables. Linear regressions using the least squares method were calculated for the HADS scores (close to normal distribution), and Poisson regressions were calculated for the SAHD score (close to log-normal distribution; logarithmic transformation impossible given the presence of zero).

Considering the second aim of this study, multivariate analyses were realized in order to test psychological issues (HADS and SAHD scores) and “spiritual/existential” variables (FACIT-Sp, SMILE and IIR scores). In a first step, univariate regression analyses were performed successively variable by variable. All the variables with a p-value <0.1 (including also variables showing a tendency towards significance) were then considered for a multivariate regression model forming a full model. The latter was reduced by dropping a variable at a time in a backward selection procedure, starting by the variable with highest p-value. Each time a variable was dropped, the Akaike Information Criteria (AIC) and the adjusted R<sup>2</sup> were compared with those of the preceding model. The backward selection was stopped after finding a model that minimised AIC and maximised the adjusted R<sup>2</sup>. Bonferroni correction for multiple comparisons was performed.

Regarding the missing data management, HADS scores with 14% or more of missing data (two or more missing responses on a 14 item questionnaire), SAHD scores with 20% or more of missing data (four or more missing responses on a 20 items questionnaire), and finally FACIT-Sp scores with 17% or more of missing data (two or more missing responses on a 12 items questionnaire) were not included in the analysis.

### *Sample Size*

Sample size was estimated based on the planned use of multivariate analyses. According to the literature, 20 observations are needed for each independent variable considered in the regression analyses (19). In our case, the minimum sample size was 140.

## Results

### *Sociodemographic and medical characteristics*

In the three Swiss linguistic regions, 588 participants met the inclusion criteria. Due to the reasons listed in fig. 1, 138 patients could not meet the research team and 234 did not participate after meeting the team. 206 participants consented and completed the CRF between September 2012 and January 2015.

*[Insert figure 1]*

Table 1 indicates the demographic and medical characteristics of the patient population. Cancer is by far the most common diagnosis among the participants.

*[Insert table 1]*

### *Scales: descriptive results*

Table 2 indicates the descriptive statistics (means, SD) for each questionnaire used.

*[Insert table 2]*

### ***Relationship between (i) MIL/spiritual wellbeing and WTHD/psychological distress***

#### *➤ Relationship between WTHD (SAHD) and spiritual wellbeing (FACIT-Sp)*

The results of the Poisson regression model showed that 2.2 % of the variance was explained (pseudo  $R^2=.022$ ,  $p=.007$ ) with a significant negative relationship between WTHD and spiritual wellbeing (see table 3).

#### *➤ Relationship between WTHD (SAHD) and MIL (SMILE total score)*

The results of the Poisson regression model showed that the total model explained 0.2 % of the variance (pseudo  $R^2=.002$ ,  $p=.375$ ), with no significant relationship between WTHD and MIL (see table 3).

*[Insert table 3]*

#### *➤ Relationship between psychological distress (HADS) and spiritual wellbeing (FACIT-Sp)*

The results of the linear regression model showed that 19% of the variance of the psychological distress (HADS total score) was explained (adjusted  $R^2=.185$ ;  $p<.001$ ), with a significant negative relationship between psychological distress and spiritual wellbeing (see table 4 and figure 2).

## Non-physical predictors of quality of life

When considering separately the depression and anxiety dimensions of psychological distress (subscales of the HADS), the results indicate that (i) 18.1% of the variance of depression ( $\beta = -.219$ ,  $p < .001$ ), and (ii) 8.9% of the variance of anxiety ( $\beta = -.141$ ,  $p < .001$ ) are explained by the spiritual wellbeing.

### ➤ *Relationship between psychological distress (HADS) and MIL (SMILE total score)*

The linear regression model showed that 10.1 % of the variance of psychological distress (HADS total score) was explained (adjusted  $R^2 = .096$ ;  $p < .001$ ), with a significant negative relationship between psychological distress and MIL (see table 4). In particular, MIL explained 3.6% of the variance of depression ( $\beta = -.053$ ,  $p = .005$ ) and 11.6% of the variance of anxiety ( $\beta = -.081$ ,  $p < .001$ ).

[Insert table 4]

[Insert figure 2]

### *Predictors of perceived QOL*

After successive univariate regression analyses, the following parameters were considered for a first regression model: FACIT-Sp total score, IIR “public”, IIR “private”, SMILE total score, HADS “anxiety”, HADS “depression”, SAHD total score. This first model explained 32.4% of the variance of the perceived QOL (adjusted  $R^2 = .324$ ,  $AIC = 694.108$ ,  $p = .000$ ). Only the FACIT-Sp total ( $\beta = .084$ ,  $p = .002$ ) and the HADS “depression” ( $\beta = -.208$ ,  $p = .000$ ) appeared as significant predictors of QOL (details of the model can be obtained from the first author).

Subsequent multivariate models were performed in order to obtain the most parsimonious model. The most parsimonious model explained 32.8 % of the variance of the perceived QOL (adjusted  $R^2 = .328$ ,  $AIC = 691.194$ ,  $p = .000$ ) and included FACIT-Sp total score, IR “private”, SMILE total score, HADS “depression”, and SAHD total score. Among these variables, the FACIT-Sp total score and the HADS “depression” appeared again as the variables the most strongly associated with perceived QOL after Bonferroni correction (see table 5).

[Insert table 5]

### *Differences between linguistic regions*

Overall, we found generally homogeneous results between the three Swiss linguistic regions, which are therefore presented together in this paper. A detailed analysis of the differences observed between the three regions will be published separately.

## **Discussion**

Regarding the first aim of this study, the main results are the significant negative relationships found between spiritual wellbeing and (i) psychological distress and (ii) WTHD. Our data also indicate that MIL is significantly and negatively associated with psychological distress, but not with WTHD. Regarding the second aim, spiritual wellbeing and depression represent strong predictors of perceived QOL in palliative care patients.

*Relationship between spirituality/MIL and psychological issues*

Why is spiritual wellbeing significantly associated with WTHD in our study, while MIL is not? Firstly, the spiritual wellbeing construct (as measured by the FACIT-Sp) appears to be more inclusive than the MIL construct, as it comprises MIL but also other aspects, such as peace and faith. Secondly, the FACIT-Sp assesses the presence or absence of spiritual wellbeing from an intensity perspective (nomothetic approach), while the SMILE instrument captures the satisfaction level with individual life areas named by the respondents as contributing to their personal MIL (idiographic approach) (20). These two approaches are not contradictory but represent complementary ways of addressing this issue.

Another interesting finding is that the negative relationship was much stronger between spiritual wellbeing and psychological distress than between spiritual wellbeing and WTHD. This result is also valid, but to a lesser extent, for the relationship between MIL and psychological distress and WTHD. This difference may be explained by the complexity of the WTHD concept. According to a recent review (21), WTHD can be considered as a possible response to several dimensions of suffering. Existential, psychological, and social aspects do seem to play a major role underlying WTHD (21, 22, 23), but an important part of the variance of WTHD remains unexplained. We can therefore assume that WTHD may also refer to a “letting-go” attitude. The latter would be the expression of the acceptance of one’s illness and imminent death, possibly associated with the feeling that one’s life was meaningful (22). Such a non-suffering dimension of WTHD could explain why the negative relationship between spirituality and WTHD is weaker than the corresponding relationship between spirituality and psychological distress.

Our data also show that spiritual wellbeing and MIL are both significantly and negatively associated with psychological distress, with a stronger association between spiritual wellbeing and psychological distress (18.5% vs 9.6% of variance explained). Globally, these findings are consistent with those of a recent meta-analysis on the relations between MIL and psychological distress in cancer patients which demonstrated a total effect-size of  $r=-0.41$  without differentiating anxiety, depression and other specific psychological variables (24). Our data show that the variance of anxiety is explained quite similarly by spiritual wellbeing and MIL (8.9% and 11.6%, respectively). On the other side, the magnitude of variance explained is more important when considering depression: 18.1% by spiritual wellbeing and only 3.6% by MIL. We assume that these differences may be explained by same reasons mentioned above for the relationship between spiritual well-being, MIL and WTHD.

Based on our data, we hypothesize that spirituality may represent a potential protective factor against the development of psychological distress. This is in line with recent work (7, 8), which highlighted the coping role of MIL with respect to the development of psychological distress, particularly depression, in a longitudinal study with cancer patients. The ability to maintain or redefine a sense of MIL, by either integrating the trauma of a fatal disease in their own life story or accommodating themselves to this new reality (meaning-making model), seems to almost guarantee a preserved psychological wellbeing (25). Of note, the concept of MIL has largely been developed in the context of research on coping with traumatic events (25).

The observed strong negative relationship between depression and spirituality poses the question of the exact nature of the relationship between these dimensions. In the literature, terms such as hopelessness, helplessness, worthlessness, guilt (26, 27) have been proposed to substitute somatic symptoms as indicators of depression in terminally ill patients, and this terminology is closely related to spiritual distress (28). However, recent research on this issue based on a longitudinal methodology showed an increase in existential distress at the end of life without a parallel increase in psychiatric disorders (7), suggesting that these two dimensions are likely to be independent. De Figueiredo (29), as well as Kissane and Clarke (30) described the concept of “demoralization” in the specific context of terminal illness as a syndrome of existential distress distinct from depression that should be considered as a relevant differential diagnosis in palliative care.

### *The non-physical determinants of perceived QOL*

Concerning the second aim of this research, our results highlighted the importance of the non-physical determinants for the patients' QOL, with almost one-third of the QOL variance being explained by these determinants. Among all the predictors, depression was the most influential factor for QOL, followed by spiritual wellbeing. Interestingly, private religiosity also figures in the final model, while public religiosity does not. It is possible that the “private” dimension of religiosity as a source of personal strength and support may be more determinant for QOL than “public” religious practice.

The influence of depression on QOL was stressed in other studies (31). Cramarossa et al. (32) and Kawaguchi et al. (33) identified emotional functioning as one of the most significant predictors of worse overall QOL in cancer patients. It is worth mentioning that depression was also highlighted as the greatest determinant on QOL in a general older population when considering a large panel of psychosocial and health factors (34). In our sample, almost 40% of our participants presented a moderate or high level of depression, even if caution is warranted in interpreting the prevalence of depression based only the HADS, given his poor specificity (35). A meta-analysis (36) showed that the rate of major and minor depression according to DSM-IV was around 25% in onco-haematological and palliative care settings.

## Non-physical predictors of quality of life

It is worth reminding that the systematic screening and surveillance of depression in the palliative care context remains highly challenging. Up to now, pharmacotherapy and psychotherapy of depression in palliative care patients seem to have only limited benefits (37, 38). Since our results indicate that spiritual wellbeing may protect against depression, it is not surprising that several manualized psychotherapeutic interventions specifically targeting existential issues also demonstrated to have a positive impact on depression and anxiety (39, 40, 41, 42, 43, 44). A recent meta-analysis on the impact of existential therapies confirmed their positive global impact on psychological indicators (45). Unfortunately, most of these interventions are rather time-consuming, thus making their implementation in late-stage palliative care difficult, due to the patients' frailty.

Another important challenge is related to the identification of spiritual/existential distress. In a systematic review of tools assessing spirituality in clinical research, Monod et al. (46) found that only two instruments appeared to adequately assess the patient's spirituality (FACIT-Sp and the Spiritual Well-Being Scale). However, these tools measure spiritual well-being, while it would appear to be more clinically relevant to identify patients with spiritual distress. They therefore developed the Spiritual Distress Assessment Tool, a semi-structured interview based on the Spiritual Needs model (47). While this tool has been validated in hospitalized elderly patients (48), its use in palliative care settings still needs further testing.

Some limitations of this study need to be mentioned. First, several elements may contribute to a selection bias: (i) the fact that the participants screening was not systematic in all the palliative care units; (ii) the fact that only palliative care patients with less than six months of life expectancy were considered for the study, and finally (iii) the fact that more than half of the patients who met the inclusion criteria could not participate in the study, which points to the great fragility of palliative care patients. Secondly, concerning the variance of QOL explained by the non-physical determinants, it would be important to also consider and include in the same regression model some indicators of the health and functional status. While the high level of variance explained by the model leaves little doubt about the importance of the existential and psychological variables considered in this study, further studies will have to include specific health indicators, as well as other psychological dimensions (self-esteem, optimism), and markers of social and familial support. Thirdly, the measurement of QOL by a single item scale does not allow an in-depth assessment of QOL. The selection of this instrument was led by the wish to be the least time consuming for the patients while using a single validated tool that has been confirmed as relevant in a clinical context (49, 50, 51). In addition, this way of assessing QOL relates to the WHO definition, which focuses on the individual's general perception of QOL (1). Finally, the cross-sectional design of this study does not allow for an in-depth exploration of the dynamic nature of the relationship between spirituality, psychological distress, and QOL.

### *Conclusion*

## Non-physical predictors of quality of life

Our data reinforce the notion of the importance of non-physical determinants such as spiritual well-being and meaning in life for the development of psychological distress and thus for QOL in palliative patients. Specific short-term interventions aimed at enhancing these dimensions and tailored to the needs and the fragility of this patient population are required. Research in positive psychology may provide some guidance (52), given the relatively ease for the implementation of these interventions and their proven impact on depression and existential dimensions of wellbeing. Taken together, the data underscore the pivotal role of psychological and spiritual support for palliative care patients.

### **Competing interests**

The authors declare that they have no competing interests.

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## References

1. Saxena S, Orley J. Quality of life assessment: The World Health Organization perspective. *European Psychiatry* 1997; 12(Suppl 3): 263s-66s.
2. World Health Organization (2002) *National cancer control programmes: Policies and managerial guidelines*, 2 ed. Geneva: World Health Organisation.
3. Albers G, Echteld MA, de Vet HCW, et al. Content and spiritual items of quality of life instruments appropriate for use in palliative care: a review. *J Pain Symptom Manage* 2010; 40: 290-300.
4. Stewart AL, Teno J, Patrick DL, Lynn J. The concept of quality of life of dying persons in the context of health care. *J Pain Symptom Manage* 1999; 17: 93-108.
5. Puchalski C, Ferrell B, Virani R. Improving the quality of spiritual care as a dimension of palliative care: the report of a consensus conference. *J Palliat Med* 2009; 12: 885-904.
6. Brennan J A conflation of existential and spiritual beliefs. *Psycho-oncol* 2006; 15: 933-934.
7. Vehling S, Lehmann C, Oechsle K, et al. Global meaning and meaning related life attitudes: exploring their role in predicting depression, anxiety, and demoralization in cancer patients. *Support Care Cancer* 2011; 19: 513-520.
8. Vehling S, Lehmann C, Oechsle K, Bokemeyer C, Krüll A, Koch U, Mehnert A. Is advanced cancer associated with demoralization and lower global meaning? The role of tumor stage and physical problems in explaining existential distress in cancer patients. *Psychooncology* 2012; 21: 54-63.
9. Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011; 12: 160-174.
10. Rodin G, Zimmermann C, Rydall A, et al. The desire for hastened death in patients with metastatic cancer. *J Pain Symptom Manage* 2007; 33: 661-675.
11. Fegg MJ, Kramer M, L'hoste S, Borasio GD. The Schedule for Meaning in Life Evaluation (SMiLE): Validation of a new instrument for meaning-in-life research. *J Pain Symptom Manage* 2008; 35: 356-364
12. Peterman AH, Fitchett G, Brady M, Hernandez L, Cella D. Measuring spiritual well-being in people with cancer: The Functional Assessment of Chronic Illness Therapy / Spiritual Well-Being Scale (FACIT-Sp). *Ann Behav Med* 2002; 24: 49-58.
13. Peterman AH, Reeve CL, Winford EC, et al. Measuring meaning and peace with the FACIT–Spiritual Well-Being Scale: Distinction without a difference? *Psychol Assessment*, 2014; 26: 127-137.
14. Idler EL. Religious involvement and the health of the elderly: some hypotheses and an initial test. *Soc Forces* 1987; 66: 226-38.

15. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
16. Rosenfeld B, Breitbart W, Galietta M, et al. The schedule of attitudes toward hastened death: Measuring desire for death in terminally ill cancer patients. *Cancer* 2000; 88: 2868-75.
17. de Boer A, van Lanschot J, Stalmeier P, et al. Is a single-item visual analogue scale as valid, reliable and responsive as multi-item scales in measuring quality of life? *Qual Life Res* 2004; 13: 311-320.
18. Wild AG, Grove A, Martin M, et al. Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) measures: Report of the ISPOR task force for translation and cultural adaptation. *Value Health* 2005; 8: 94-104.
19. Bressoux P. *Modélisation statistique appliquée aux sciences sociales*. Paris: De Boeck, 2010.
20. Brandstätter M, Baumann U, Borasio GD, Fegg M. Systematic review of meaning in life assessment instruments. *Psychooncology* 2012; 10:1034-52.
21. Monforte-Royo C, Villavicencio-Chavez C, Tomas-Sabado J, Balaguert A. The wish to hasten death: a review of clinical studies. *Psychooncol* 2011; 20: 795-804.
22. Rodin G, Lo C, Mikulincer M, et al. Pathways to distress: the multiple determinants of depression, hopelessness, and the desire for hastened death in metastatic cancer patients. *Soc Sci Med* 2009; 68: 562-569.
23. Breitbart W, Rosenfeld B, Pessin H, et al. Depression, hopelessness, and desire for death in terminally ill cancer patients. *JAMA* 2000; 284: 2907-2911.
24. Winger JG, Adams RN, Mosher CE. Relations of meaning in life and sense of coherence to distress in cancer patients: a meta-analysis. *Psychooncol* 2016; 25: 2-10.
25. Park CL. Making sense of the meaning literature: an integrative review of meaning making and its effect on adjustment to stressful life events. *Psychol Bull* 2010; 136: 257–301.
26. Asghar-Ali AA, Wagle KC, Braun UK. Depression in Terminally ill patients: dilemmas in diagnosis and treatment. *J Pain Symptom Manage* 2013; 45: 926-933.
27. Block SD. Assessing and managing depression in the terminally ill patient. ACP-ASIM End-of-Life Care Consensus Panel. American College of Physicians - American Society of Internal Medicine. *Ann Internal Med* 2000; 132: 209-18.
28. Boston P, Bruce A, Schreiber A. Existential suffering in the palliative care setting: an integrated literature review. *J Pain Symptom Manage* 2011; 41: 604-618.
29. de Figueido JM. Depression and demoralization: phenomenologic differences and research perspectives. *Compr Psychiatry* 1993; 34: 3018-311.
30. Clarke DM, Kissane DW. Demoralization: its phenomenology and importance. *Aust N Z J Psychiatry* 2002; 36: 733-742.

## Non-physical predictors of quality of life

31. Hermann CP, Looney SW. Determinants of quality of life in patients near the end of life: a longitudinal perspective. *Oncol Nurse Forum* 2011; 38: 23-31.
32. Cramarossa, G, Chow, E, Zhang, et al. Predictive factors for overall quality of life in patients with advanced cancer. *Support Care Cancer* 2013; 21: 1709-1716.
33. Kawaguchi T, Iwase S, Koinuma M, et al. Determinants affecting quality of life: implications for pharmacist counseling for patients with breast cancer in Japan. *Biol Pharm Bull* 2012; 35: 59-64.
34. Brett C, Gow AJ, Corley J, et al. Psychosocial factors and health determinants of quality of life in community-dwelling older adults. *Qual Life Res* 2012; 21:505-516.
35. Mitchell AJ, Meader N, Symonds P. Diagnostic validity of the Hospital Anxiety and Depression Scale (HADS) in cancer and palliative settings: A meta-analysis. *J Affect Disord* 2010; 126: 335-48.
36. Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *Lancet Oncol* 2011; 12:160-174.
37. Gelenberg AJ, Chesen CL. How fast are antidepressants? *J Clinical Psychiatry* 2000; 61: 712-21.
38. Akechi T, Okuyama T, Onishi J, Morita T, Furukawa TA. Psychotherapy for depression among incurable cancer patients. *Cochrane Database Syst Rev* 2008; CD005537.
39. Breitbart W, Rosenfeld B, Pessin H, et al. Meaning-centered group psychotherapy: an effective intervention for improving psychological well-being in patients with advanced cancer. *J Clin Oncol* 2015; 33: 749-754.
40. Lo C, Hales S, Jung J, et al. Managing cancer and living meaningfully (CALM): Phase 2 trial of a brief individual psychotherapy for patients with advanced cancer. *Palliat Med* 2014; 28: 234-242.
41. Chochinov HM, Kristjanson LJ, Breitbart W, et al. Effect of dignity therapy on distress and end of life experience in terminally ill patients: a randomised controlled trial. *Lancet Oncol* 2011; 12: 753-762.
42. Breitbart W, Poppito S, Rosenfeld B, et al. Pilot randomized controlled trial of individual meaning-centered psychotherapy for patients with advanced cancer. *J Clin. Oncol* 2012; 30: 1304-1309.
43. Henry M, Cohen SR, Lee V, et al. The meaning-making intervention (MMi) appears to increase meaning in life in advanced ovarian cancer: a randomized controlled pilot study. *Psychooncology* 2010, 19:1340-1347.
44. Breitbart W, Rosenfeld B, Gibson C, et al. Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. *Psychooncol* 2010; 19: 21–28.

45. Vos J, Craig M, Cooper M. Existential therapies: A meta-analysis of their effects on psychological outcomes. *J Consul Clin Psychol* 2015; 83: 115-128.
46. Monod S, Brennan M, Rochat E, et al. Instruments measuring spirituality in clinical research: a systematic review. *J Gen Intern Med* 2011; 26: 1345-57.
47. Monod S, Rochat E, Bula C, et al. The Spiritual Needs Model: Spirituality assessment in the geriatric hospital setting. *J Relig Spiritual Aging* 2010; 22: 271-82.
48. Monod S, Martin E, Spencer B, et al. Validation of the Spiritual Distress Assessment Tool in older hospitalized patients. *BMC Geriatr* 2012; 12:13.
49. Locke DE, Decker PA, Sloan JA, et al. Validation of single-item linear analog scale assessment of quality of life in neuro-oncology patients. *J Pain Symptom Manage* 2007; 34: 628-38.
50. Sloan JA, Cella D, Frost M, et al. Assessing clinical significance in measuring oncology patient quality of life: introduction to the symposium, content overview, and definition of terms. *Mayo Clin Proc* 2002; 77: 367-70.
51. Stewart AL, Teno J, Patrick DL, Lynn J. The concept of quality of life of dying persons in the context of health care. *J Pain Symptom Manage* 1999; 17: 93–108.
52. Sin NL, Lyubomirsky S. Enhancing well-being and alleviating depressive symptoms with positive psychology interventions: A practice-friendly meta-analysis. *J Clin Psychol* 2009; 65: 467-487.