



Discrepancy in Patient- and Oncologist-Rated Performance Status on Depression and Anxiety in Cancer: A Prospective Study Protocol

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3 **Discrepancy in Patient- and Oncologist-Rated Performance Status on**
4 **Depression and Anxiety in Cancer: A Prospective Study Protocol**
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Abstract

Objective

Psychological distress is common in patients with cancer. We need a rapid means of screening for and identifying depression and anxiety in patients with cancer. The present study evaluates the potential of the Eastern Cooperative Oncology Group (ECOG) performance status (PS) scoring as a brief screening tool to assess psychological distress in routine cancer care. The ECOG PS is widely used by oncologists and the World Health Organisation as a standardised measure to assess general wellbeing in patients with cancer and quality of life in cancer trials. We examine the discrepancy between patient-rated and oncologist-rated performance status scores on the ECOG in a comparative assessment against the Hospital Anxiety and Depression Scale (HADS).

Methods & Design

This is a prospective evaluation of approximately 500 ambulatory adult cancer patients from a large academic medical centre. Participants will be asked to assess their own ECOG PS on a scale of 0 to 4, which will be compared to ECOG PS as rated by their oncologists. Higher ECOG PS scores indicate poorer daily functioning. Both patient-rated and oncologist-rated ECOG PS and their absolute differences will be tested for predictive and concurrent validity against the HADS. A HADS cut-off ≥ 15 will be used. Ethics approval for this study has been secured from the institutional ethics board. Outcomes are re-evaluated at 4- to 6-week and 1 year follow-up.

Conclusion

This study holds practical significance for rapid screening of psychological distress in the cancer clinic with the use of the ECOG performance status scoring. Given the high prevalence of anxiety and depression in patients with cancer, screening is important to increase its recognition, which will in turn help to direct referrals and deliver appropriate intervention. This study also generates greater insight into the association between psychosomatic complaints and psychological distress.

Keywords

Patient-Rated ECOG, Performance Status, Anxiety, Depression, Cancer.

Introduction

We need a rapid means of screening for and identifying depression and anxiety in patients with cancer. While having patients undergo psychological assessment interviews or complete standardised anxiety and depression questionnaires is ideal, cancer clinics are busy places where oncologists and staff nurses are often overworked.¹ Oncologists are often not sufficiently trained in psychological assessment or testing, nor do they have the time to do so.² Several studies have shown that oncologists are not especially skilled in either discussing psychological problems in general,³ or at recognising anxiety and depression.^{2,4} Published data suggest that the ability of doctors to accurately detect psychiatric morbidity in patients is often little better than that chance.²

As a result psychological distress may go undetected and when recognised, it is more likely to run a more severe and unremitting course, and in some cases to be clearly impacting patients' lives and even cancer treatment in some way. Although tremendous attention has been given to the early detection and treatment of cancer, the issue of psychological distress has lagged behind. There is little consensus with regards to even the criterion and management of anxiety and depression associated with cancer. Early detection is as crucial in the matter of treatment and prognosis in cancer as in anxiety and depression, with greater psychological distress linked to poorer health outcomes.⁵

We lack of adequate screening instruments measuring psychological distress in oncology settings.⁶ For a screening or monitoring tool to be accepted into routine practice, it needs to be brief, relevant in its utility and simple enough to interpret while retaining the necessary specificity and sensitivity.⁵ What we need is to capitalise on an existing tool as a brief form of assessment that can function as a surrogate tool for screening depression and anxiety.⁷ The ECOG PS is one such measure. As a standardised measure of performance status in routine oncology practice, the ECOG bears the potential for widespread usage to psychological distress in this setting due to its high acceptability and ease of use.

Performance status is one of the most widely accepted patient evaluations used in clinical practice and oncology trials. It is typically assessed for all types of cancer due to its demonstrated efficacy in the measurement of treatment responses, survival length, prognostic value as well as a criterion for suitability for chemotherapy and clinical trials.⁸ Yet rarely, if ever, are performance status scores compared across different cancer types. Most commonly reported as part of a randomised clinical trial, the majority of cancer studies or trials where performance status is measured also present data where sample sizes are generally inadequate or moderate at best.⁹ The average cancer trial size wherein performance status is most frequently measured is 200, or an average of 175 for randomised clinical trials.¹⁰

Oncologists have generally found the ECOG easy to use in daily clinic practice. Although traditionally scored by the oncologist, several studies have arrived at rather interesting results when comparing performance status scores as rated by the patients to those rated by their oncologists.⁷ Prior studies in this area already show that there is a significant difference between patient- and oncologist-rated performance status,¹¹ with depression being a confounder where it comes to functional status.³ These previous studies examining discrepancy between patient- and oncologist rated ECOG however are also restricted to patients with cancer in a single site, with most of such studies focusing primarily on non-small cell lung cancer.^{7,11-13} Findings from these studies may not be representative of psychological distress in patients with other types of cancer. It would therefore be interesting to extend this study to include patients with other cancer types.¹²

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3 The main goal of this proposed study is to examine the feasibility of the ECOG PS as a
4 psychological distress screening instrument. We intent to test the predictive and concurrent
5 validity of the ECOG PS against the HADS. The present study is the first to prospectively
6 investigate the use of discrepancy between patient- and oncologist-rated ECOG performance
7 status to gauge psychological distress in patients with cancer.
8

9 10 **Research Questions**

- 11 1. To what extent do patient-rated versus oncologist-rated ECOG PS agree? If
12 discrepant, what is their underlying cause?
- 13 2. To what degree does the ECOG assess psychological distress? Does discrepancy in
14 performance status predict psychological distress at baseline and subsequent 4- to 6-
15 week and 1-year follow-up?
16

17 18 **Hypothesis**

19 It is hypothesised that poorer or discrepant performance status scores are associated with
20 higher levels of psychological distress, rather than the level of activity. It is also posited that
21 discrepancy between patient-rated ECOG at baseline and follow-up is also associated with an
22 increased likelihood of comorbid anxiety or depression in patients with cancer.
23

24 25 **Methods/ Design**

26 This is a prospective single centre study, in the context of patients about to see their
27 oncologist for a consultation in an academic medical centre. Patients will be asked to assess
28 their own ECOG PS score on a scale between 0 and 4. We then compare these to ECOG
29 scores rated by their oncologists (extracted from their medical records). The absolute
30 discrepancy in scores will then subsequently analysed against patient HADS scores.
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32 We will attempt to enroll approximately 500 consecutive patients who have been referred to
33 the adult clinical oncology unit with a diagnosis of cancer from November 2011 to August
34 2012. Patients should be receiving or plan to receive at least one form of treatment (i.e.
35 chemotherapy or radiotherapy) at any point in their disease trajectory. Patients aged less than
36 18 years are excluded, as are those with an incomplete diagnosis and language issues,
37 specifically the inability to understand the instrument language in English or comprehend
38 interviews conducted in all major spoken languages: English, Chinese or the Malay language.
39 We chose not to apply additional exclusion criteria that would limit the applicability of
40 findings to the general cancer patient population unnecessarily.
41

42 43 *Study Variables*

44 A data extraction form that has been specifically developed will be used to obtain relevant
45 demographic and clinical data from patient records. The specific variables and selected
46 outcome variables of interest include age, sex, race, marital status, education and employment
47 status. Relevant clinical information examined includes the primary cancer site and tumour
48 stage. Other variables that will be looked at include treatment planned or received such as
49 surgery, chemotherapy and or radiotherapy.
50

51 52 *Research Tools*

53 The questionnaires used in this study include the ECOG PS as rated by patients themselves
54 and by their oncologists, as well as the Hospital Anxiety and Depression (HADS) scale. All
55 questionnaires used have obtained permission for use from the respective authors and will be
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3 The ECOG PS is highly valid and is one of the most widely used instruments in clinical
4 cancer practice and research (Dajczman, 2008). In this study the single-item score will be
5 rated by both patients and their oncologists on a scale of 0 to 4 (worse scores denoting poorer
6 performance status and higher levels of psychological distress). The ECOG PS score of 5
7 (indicating death) will not be used in the patient version of the scale.
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9
10 The HADS, a 14-item instrument has also been well validated and will be employed for use
11 in the detection of anxiety and depression among cancer patients. Overall scores range from 0
12 to 42, with higher scores indicating greater distress. A cut-off point of greater than or equal to
13 15 will be used. Preliminary testing with 18 patients (male to female ratio = 1:1) conducted in
14 October 2011 for the HADS yielded an alpha of 0.91.

15 *Sample Size Estimation*

16 Using an online sample size calculator (Raosoft),¹⁴ we adopted a 0.05% margin of error
17 which required a minimum of 282 participants to accurately (95% confidence) represent a
18 variable with 50% response distribution in a population of approximately 1050 individuals
19 seen annually.
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21

22 *Procedure*

23 Patients will be directly approached in the waiting room of the adult oncology unit while
24 waiting to see their oncologist. Participants will first be given verbal information on the goal
25 of the study and screened to check if they meet all inclusion and exclusion criteria. Upon
26 assent to participate, informed consent will be obtained and an additional information leaflet
27 be given. Participants will be asked to circle the number that best describes the overall
28 distress that they experienced over the previous week for both the ECOG and HADS. Face to
29 face interviews will be conducted in all major languages (English, Bahasa Malaysia and
30 Chinese). The follow up time ranges from 4 to 6 weeks and 1 year, at which the assessments
31 will be repeated via face-to-face interview, or via telephone interview if necessary.
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34 *Questionnaire administration*

35 The use of a questionnaire design makes this study cost-efficient and allows for rapid yet
36 effective screening of psychological distress in our population. Oncologist-assessed ECOG
37 performance status scores will be extracted from patient oncology records.
38

39 **Analysis of Data**

40 The mean and standard deviations for anxiety and depression for each cancer type will be
41 determined. All data will be coded based on the instructional guidelines as contained in the
42 questionnaire scoring manuals. Responses to the HADS will be analysed according to
43 published recommendations.¹⁵ Two-sided tests will be used, while p-values of ≤ 0.05 will be
44 regarded as statistically significant. For all analyses, a two-sided p -value ≤ 0.05 will be
45 applied. All analyses will be performed using the Statistical Package for Social Sciences
46 (SPSS) version 20.
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49 *Comparison of mean scores*

50 Comparison of baseline scores, change in scores between and within groups, as well as
51 identification of subjects with improved, stable and worsened scores over time will be
52 performed using a t-test, Mann Whitney test, ANOVA or alternately a non-parametric
53 approach such as Kruskal-Wallis as deemed appropriate. Proportions will be compared using
54 chi-squared test or Fisher's exact test.
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56 *Comparison between ECOG and HADS scores*

57 Comparison between the good (0-1), intermediate (2) and poor (3-4) performance status
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3 patient groups will be made using one-way analysis of variance (ANOVA). Pearson
4 correlation coefficient (r) will be used to express the relationship between the psychological
5 distress as measured using the HADS and performance status using the ECOG. Differences
6 in the two subscales of the HADS as well as mean ECOG scores will also be reported.
7 Correlations in each patient group among overall levels of psychological distress and
8 performance status will be measured using Spearman's correlation coefficient.
9

10 Kendall's tau (r) coefficient will be used to measure the portion of ranks that match between
11 patient-rated and oncologist-rated performance status. Additionally, a paired t-test, or the
12 non-parametric Kolmogorov-Smirnov test (KS-test) may be used to determine if there is a
13 significant difference between the patient-rated versus oncologist-rated dataset.
14

15 *Descriptive statistics*

16 Descriptive statistical analysis will be performed for all variables. Continuous variables will
17 be reported using means and standard deviations or median and inter-quartile range. For
18 dichotomous variables, absolute numbers and percentages will be presented. Differences
19 between concordant and discrepant performance status groups in demographic characteristics,
20 clinical variables, anxiety, depression, and performance status will be assessed using *t* test or
21 Mann-Whitney tests for continuous variables, and the X^2 statistic or Fisher's exact test for
22 categorical variables. Linear regression, logistic regression, or the Wilcoxon-Mann-Whitney
23 rank sum test will be used as appropriate to assess the impact of demographic and clinical
24 variables on group differences in depression, anxiety and performance status. Variables
25 included in subsequent analyses include those that demonstrate statistically significant
26 differences between the study groups in univariate analyses.
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29 *Imputation of missing values*

30 All responses with more than 5% missing values will first be removed from the data set. For
31 the remaining items, missing values will be replaced by an imputation process based on an
32 expectation-maximization algorithm using NORM software. This imputation ensures that
33 should subsequent exploratory factor analysis be done, which processes a large number of
34 items, the data set is not reduced too greatly. In order to assess the influence of imputation on
35 the psychometric results, all analyses will additionally be carried out with non-imputed
36 values after the factor analysis. Should differences arise, findings from both imputed and
37 non-imputed data will be presented to allow for comparison. Careful note will be made for all
38 missing data on individual items. Missing data however remains a serious issue for quality of
39 life studies.¹⁵
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43 **Discussion**

44 This is the first study to longitudinally examine the use of discrepancy in ECOG as a
45 predictor of anxiety and depression in cancer patients in a comparative assessment over time.
46 We propose the use of the ECOG as a brief screening instrument for depression and anxiety
47 in cancer patients and hypothesize that poorer or more discrepant patient-rated ECOG scores
48 may be an indicator of greater psychological distress. Given the high prevalence of anxiety
49 and depression in cancer, screening is critical in increasing case recognition to deliver
50 appropriate interventions and prioritise referrals.
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53 While the ECOG was originally developed as a measure of performance status, its brevity
54 and simplicity makes it feasible for widespread adoption as a surrogate tool to detect anxiety
55 and depression. Most oncologists lack familiarity with psychiatric nosology.¹ Screening for
56 anxiety and depression using the ECOG performance status scale does not require special
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3 training because performance status is routinely assessed by oncologists across all cancer
4 types.

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6 There is an emerging trend towards simplifying the assessment of depression and anxiety in
7 outpatient cancer settings,²⁰ particularly as treatment and care has shifted to ambulatory
8 settings. Shorter than any other standard assessment such as the HADS and Beck Depression
9 Inventory, the ECOG functions much like the single-item Distress Thermometer. We predict
10 that the acceptability of the ECOG as a measure would likely be higher and less likely to
11 burden the clinic in terms of time and cost compared to any other form of assessment.
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14 Patients have been shown able to accurately assess their own performance status.¹³ The single
15 item ECOG performance status is also easy for patients to rate, especially with the emergence
16 of different versions of the performance status scale in visual analogue format¹³ suitable for
17 paediatric or illiterate cancer populations, or simply where communication issues might arise
18 from a language barrier.
19

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21 While data which come directly from those experiencing the cancer affords an insightful
22 perspective, there is greater practical value in using the ECOG to comparatively measure
23 discrepancy in performance status scores, rather than solely relying on either patient- or
24 oncologist-rated scores. Discrepancy on the ECOG is also easy to eyeball, while scores can
25 be quickly compare over time when reviewed at each visit.
26

27
28 This study carries several important implications for oncology clinic practice, in that
29 discrepancy in ECOG scores, or patient-rated ECOG can be used as a patient reported
30 outcome measure to raise, discuss as well as routinely monitor psychological concerns.¹²
31 Asking patients to score their own ECOG opens up avenues for discussion of psychological
32 concerns and reduces the likelihood of measurement-, cultural- and educational bias.

33
34 Special attention should be given to cancer patients who demonstrate poorer self rated
35 performance status. As suggested by Ando,¹¹ patients who rate themselves significantly
36 higher on ECOG scores compared to assessment by their oncologist may actually be
37 presenting a subconscious bid for care and reassurance toward their oncologists. This is
38 consistent with the local cultural influence which is not dissimilar to those of other Asian
39 cultures where emotions are suppressed.¹⁸

40
41 Due to indefinite symptomatology such as fatigue, lack of appetite and weight loss,¹⁹
42 differentiating symptoms caused by cancer and its treatment from standard criteria-based
43 syndromes of major depression and clinical grade anxiety is not easy.¹⁷ The use of the ECOG
44 can indicate the presence of psychological distress that does not exclude psychosomatic
45 distress. Multiple sociocultural barriers are inherent in seeking medical and psychosocial
46 information, treatment and care.¹⁸

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48 Regardless of physical disease,²⁰ it is not uncommon for mood disorders to be expressed as
49 somatic rather than psychological symptoms across a number of cultures, partly to avoid the
50 perceived stigma of a psychiatric disorder.¹ Patients from Asian cultures tend to focus on
51 somatising and physiologic symptomatology rather than mental symptoms^{18 21} and to be
52 culturally constrained where it comes to reporting emotional states such as depression.²¹
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55 Physicians too are often reluctant to probe into psychological concerns.² This may be in part
56 due to the biomedical training and orientation of oncologists, who may prove wary of
57 forming attachment to patients, which is also a barrier to supportive care. A rigid biomedical
58 agenda also means oncologists are more comfortable treating somatic symptoms such as pain,
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3 nausea and dyspnea. It is likely that physicians who are trained locally would be even less
4 comfortable addressing distress due to cultural constraints. This gives rise to the question of
5 how likely oncologists are to refer patients for further psychological or psychiatric
6 assessment. Previous studies report the consultation rate from oncologists to consultation-
7 liaison psychiatrists to be only 4-10% among cancer patients.^{5,22}
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10 The majority of cancer patients with (clinically significant) anxiety and depression do not see
11 mental health professionals but do see their oncologists. However relatively few oncologists
12 have sufficient knowledge and expertise to assess and treat psychological distress.³ Prior
13 research in this context shows that oncologists are often unable to detect depression and
14 anxiety, often stemming from a lack confidence in assessing distress and using psychometric
15 instruments.²³
16

17 By no means however should assessment of psychological distress using the ECOG replace
18 comprehensive psychiatric evaluation.⁵ Systematic screening using the ECOG can
19 nonetheless increase case recognition and allow for referral of distressed patients for
20 consultation-liaison or ideally psycho-oncology services.^{2,5,19} Further study is needed to
21 determine if the relationship between performance status and anxiety and depression is
22 predictive, prognostic, causal or merely associative.
23

24 **Implications**

25 Although the ECOG was not developed specifically to detect depression or anxiety, it has
26 good potential to assist in the recognition of distress. Findings from this study would help to
27 validate the surrogate function of an existing clinic tool. Implementation of the ECOG as part
28 of routine systematic screening for psychological distress appears feasible because of its
29 distinct advantage of fundamental use in performance status scoring in oncology, although
30 further validation using criterion-standard structured clinical interviews is still required.
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33 **Ethics**

34 This study is part of a project approved by the ethics committee of the UMMC (MEC Ref.
35 No: 842.2). Individual written informed consent will be obtained following every
36 recommendation in accordance with the ethics of medical research.
37

38 **Abbreviations**

39 PS: Performance status; ECOG: Eastern Cooperative Oncology Group; HADS: Hospital
40 Anxiety and Depression Scale.
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43 **Authors' contributions**

44 CCMH designed and coordinated the study, drafted the manuscript and will conduct the
45 analysis and interpretation. MMY, WAWA, HGF and EK supervised the project, contributed
46 to the design of the study and critically revised the paper for important intellectual content.
47 All authors read and approved the final manuscript.
48

49 **Competing Interests**

50 The authors declare that they have no competing interests.
51

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References

1. Pasquini M & Biondi M. **Depression in cancer patients: a critical review.** *Clinical Pract Epid Mental Health* 2007, **3**:21–30.
2. Fallowfield L, Ratcliffe D, Jenkins V and Saul J. **Psychiatric morbidity and its recognition by doctors in patients with cancer.** *Br J Cancer* 2001; 1011–1015.
3. Sinclair PA, Lyness JM, King DA, Cox C and Caine ED. **Depression and self-reported functional status in older primary care patients.** *Am J Psychiatry* 2001, **158**,416–419.
4. Jefford M, Mileskin L, Richards K, Thomson J, Matthews JP, Zalberg J, Jennens R, McLachlan SA, Wein S, Antill Y, Clarke DM. **Rapid screening for depression-validation of the Brief Case-Find for Depression (BCD) in medical oncology and palliative care patients.** *Br J Cancer* 2004, **91**:900–906.
5. Vodermaier A, Linden W, Siu C. **Screening for emotional distress in cancer patients: a systematic review of assessment instruments.** *J Natl Cancer Inst* 2009, 1464–1488.
6. Krebber AMH, Leemans CR, Bree RD, Straten AV, Smit HFE, Becker A et al. **Stepped care targeting psychological distress in head and neck and lung cancer patients: a randomised clinical trial.** *BMC Cancer* 2012, **12**:173.
7. Dajczman E., Kasymjanova G, Kreisman H, Swinton N, Pepe C & Small D. **Should patient-rated performance status affect treatment decisions in advanced lung cancer?** *J Thorac Oncol* 2008, **3**:1133–1136.
8. Oken MM, Creech RH, Tormey DC, et al. **Toxicity and response criteria of the Eastern Cooperative Oncology Group.** *Am J Clin Oncol* 1982, **5**:649–655.
9. Julious SA, Campbell MJ, Walker SJ, George SL and Machin D. **Sample sizes for cancer trials where Health Related Quality of Life is the primary outcome.** *Br J Cancer* 2000, **83**(7):959–963.
10. Hillner BE. **Trends in clinical trials reports in common cancers between 1989 and 2000.** *J Clin Oncol* 2003, **21**:1850–1858.
11. Ando M, Ando Y, Hasegawa Y, et al. **Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer.** *Br J Cancer* 2001, **85**:1634–1639.
12. Blagden SP, Charman SC, Sharples LD, Magee LR, Gilligan D. **Performance status score: do patients and their oncologists agree?** *Br J Cancer* 2003, **89**:1022–1027.
13. Gralla R, Hollen P, Kuruvialla P. Can performance status (PS) be determined accurately by patients? Results of a prospective trial evaluating ECOG and Karnofsky PS as well as patient-related PS in non-small cell lung cancer (NSCLC). In Proceedings of the 11th World Conference on Lung Cancer. Barcelona, Spain, 2005, pp. 327.

14. Raosoft, Inc. Raosoft sample size calculator. Available from <http://www.raosoft.com/samplesize.html>. Accessed January 10, 2012.
15. Zigmond AS and Snaith RP. **The Hospital Anxiety and Depression Scale.** *Acta Psychiatr Scand* 1983, **67**:361–370.
16. Shrive FM, Stuart H, Quan H & Ghali WA. **Dealing with missing data in a multi-question depression scale: a comparison of imputation methods.** *BMC Med Res Methodol* 2006, **6**:57-67.
17. Fisch M. **Treatment of depression in cancer.** *J Natl Cancer Inst* 2004, 105–111.
18. Hong JJ, Shim EJ, Shin YW, Oh DY, Im SA, Heo DS, Hahm BJ. **Discrepancies in performance status as determined by cancer patients and oncologists: are they influenced by depression?** *Gen Hosp Psychiat* 2007, **29**,555–561.
19. Shimizu K, Akizuki N, Nakaya N, Fujimori M, Fujisawa D, Ogawa A and Uchitomi Y. **Treatment response to psychiatric intervention and predictors of response among cancer patients with adjustment disorders.** *J Pain Symptom Manage* 2011, 684–691.
20. Tsunoda A, Nakao K, Hiratsuka K, Yasuda N, Shibusawa M, Kusano M. **Anxiety, depression and quality of life in colorectal cancer patients.** *IJCO* 2005, 411–417.
21. Bailey RK, Geyen DJ, Scott-Gurnell K, Hipolito MMS, Bailey TA & Beal JM. **Understanding and treating depression among cancer patients.** *Int J Gynecol Cancer* 2005, **15**:203–208.
22. Grassi L, Rossi E, Caruso R, Nanni MG, Pedrazzi S, Sofritti S, Sabatto S. **Educational screening for emotional distress: an observational study.** *Psycho Oncol* 2011, **20**:669–674.
23. Hughes KL, Sargeant H and Hawkes AL. **Acceptability of the Distress Thermometer and Problem List to community-based telephone cancer helpline operators, and to cancer patients and carers.** *BMC Cancer* 2011, **11**:46.



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Abstract

Objective

Psychological distress is common in patients with cancer. We need a rapid means of screening for and identifying depression and anxiety in patients with cancer. The present study evaluates the potential of the Eastern Cooperative Oncology Group (ECOG) performance status (PS) scoring as a brief screening tool to assess psychological distress in routine cancer care. The ECOG PS is widely used by oncologists and the World Health Organisation as a standardised measure to assess general wellbeing in patients with cancer and quality of life in cancer trials. We examine the discrepancy between patient-rated and oncologist-rated performance status scores on the ECOG in a comparative assessment against the Hospital Anxiety and Depression Scale (HADS).

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Conclusion

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Keywords

Patient-Rated ECOG, Performance Status, Anxiety, Depression, Cancer.

Introduction

We need a rapid means of screening for and identifying depression and anxiety in patients with cancer. While having patients undergo psychological assessment interviews or complete standardised anxiety and depression questionnaires is ideal, cancer clinics are busy places where oncologists and staff nurses are often overworked.¹ Oncologists are often not sufficiently trained in psychological assessment or testing, nor do they have the time to do so.² Several studies have shown that oncologists are not especially skilled in either discussing psychological problems in general,³ or at recognising anxiety and depression.^{2,4} Published data suggest that the ability of doctors to accurately detect psychiatric morbidity in patients is often little better than that chance.²

As a result psychological distress may go undetected and when recognised, it is more likely to run a more severe and unremitting course, and in some cases to be clearly impacting patients' lives and even cancer treatment in some way. Although tremendous attention has been given to the early detection and treatment of cancer, the issue of psychological distress has lagged behind. There is little consensus with regards to even the criterion and management of anxiety and depression associated with cancer. Early detection is as crucial in the matter of treatment and prognosis in cancer as in anxiety and depression, with greater psychological distress linked to poorer health outcomes.⁵

We lack adequate screening instruments measuring psychological distress in oncology settings.⁶ For a screening or monitoring tool to be accepted into routine practice, it needs to be brief, relevant in its utility and simple enough to interpret while retaining the necessary specificity and sensitivity.⁵ What we need is to capitalise on an existing tool as a brief form of assessment that can function as a surrogate tool for screening depression and anxiety.⁷ The ECOG PS is one such measure. As a standardised measure of performance status in routine oncology practice, the ECOG bears the potential for widespread usage to screen for psychological distress in this setting due to its high acceptability and ease of use.

Performance status is one of the most widely accepted patient evaluations used in clinical practice and oncology trials. It is typically assessed for all types of cancer due to its demonstrated efficacy in the measurement of treatment responses, survival length, prognostic value as well as a criterion for suitability for chemotherapy and clinical trials.⁸ Yet rarely, if ever, are performance status scores compared across different cancer types. Most commonly reported as part of a randomised clinical trial, the majority of cancer studies or trials where performance status is measured also present data where sample sizes are generally inadequate or moderate at best.⁹ The average cancer trial size wherein performance status is most frequently measured is 200, or an average of 175 for randomised clinical trials.¹⁰

Oncologists have generally found the ECOG easy to use in daily clinic practice.^{7-8,11} Although traditionally scored by the oncologist, several studies have arrived at rather interesting results when comparing performance status scores as rated by the patients to those rated by their oncologists.⁷ Prior studies in this area already show that there is a significant difference between patient- and oncologist-rated performance status,¹² with depression being a confounder where it comes to functional status.³ These previous studies examining discrepancy between patient- and oncologist rated ECOG however are also restricted to patients with cancer in a single site, with most of such studies focusing primarily on non-small cell lung cancer.^{7,11-13} Findings from these studies may not be representative of psychological distress in patients with other types of cancer. It would therefore be interesting to extend this study to include patients with other cancer types.¹¹

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3 The main goal of this proposed study is to examine the feasibility of the ECOG PS as a
4 psychological distress screening instrument. We intent to test the predictive and concurrent
5 validity of the ECOG PS against the HADS. The present study is the first to prospectively
6 investigate the use of discrepancy between patient- and oncologist-rated ECOG performance
7 status to gauge psychological distress in patients with cancer.
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9 10 **Research Questions**

- 11 1. To what extent do patient-rated versus oncologist-rated ECOG PS agree? If
12 discrepant, what is their underlying cause?
- 13 2. To what degree does the ECOG assess psychological distress? Does discrepancy in
14 performance status predict psychological distress at baseline and subsequent 4- to 6-
15 week and 1-year follow-up?
16

17 18 **Hypothesis**

19 It is hypothesised that poorer or discrepant performance status scores are associated with
20 higher levels of psychological distress, rather than the level of activity. It is also posited that
21 discrepancy between patient-rated ECOG at baseline and follow-up is also associated with an
22 increased likelihood of comorbid anxiety or depression in patients with cancer.
23

24 25 **Methods/ Design**

26 This is a prospective single centre study, in the context of patients about to see their
27 oncologist for a consultation in an academic medical centre. Patients will be asked to assess
28 their own ECOG PS score on a scale between 0 and 4. We then compare these to ECOG
29 scores rated by their oncologists (extracted from their medical records). The absolute
30 discrepancy in scores will then subsequently analysed against patient HADS scores.
31

32 We will attempt to enroll approximately 500 consecutive patients who have been referred to
33 the adult clinical oncology unit with a diagnosis of cancer from November 2011 to August
34 2012. Patients should be receiving or plan to receive at least one form of treatment (i.e.
35 chemotherapy or radiotherapy) at any point in their disease trajectory. Patients aged less than
36 18 years are excluded, as are those with an incomplete diagnosis and language issues,
37 specifically the inability to understand the instrument language in English or comprehend
38 interviews conducted in all major spoken languages: English, Chinese or the Malay language.
39 We chose not to apply additional exclusion criteria that would limit the applicability of
40 findings to the general cancer patient population unnecessarily.
41

42 43 *Study Variables*

44 A data extraction form that has been specifically developed will be used to obtain relevant
45 demographic and clinical data from patient records. The specific variables and selected
46 outcome variables of interest include age, sex, race, marital status, education and employment
47 status. Relevant clinical information examined includes the primary cancer site and tumour
48 stage. Other variables that will be looked at include treatment planned or received such as
49 surgery, chemotherapy and or radiotherapy.
50

51 52 *Research Tools*

53 The questionnaires used in this study include the ECOG PS as rated by patients themselves
54 and by their oncologists, as well as the Hospital Anxiety and Depression (HADS) scale. All
55 questionnaires used have obtained permission for use from the respective authors and will be
56 cited.
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3 The ECOG PS is highly valid and is one of the most widely used instruments in clinical
4 cancer practice and research.^{7-8, 11} In this study the single-item score will be rated by both
5 patients and their oncologists on a scale of 0 to 4 (worse scores denoting poorer performance
6 status and higher levels of psychological distress). The ECOG PS score of 5 (indicating
7 death) will not be used in the patient version of the scale. Refer to Appendix 1 for a copy of
8 the ECOG.
9

10 The HADS, a 14-item instrument has also been well validated and will be employed for use
11 in the detection of anxiety and depression among cancer patients. Overall scores range from 0
12 to 42, with higher scores indicating greater distress. A cut-off point of greater than or equal to
13 15 will be used. Preliminary testing with 18 patients (male to female ratio = 1:1) conducted in
14 October 2011 for the HADS yielded an alpha of 0.91.
15

16 *Sample Size Estimation*

17 Using an online sample size calculator (Raosoft),¹⁴ we adopted a 0.05% margin of error
18 which required a total of 306 participants to accurately (95% confidence) represent a variable
19 with 50% response distribution in a population of approximately 1500 cancer patients seen
20 annually. Although an estimated figure of 306 patients would be sufficient to test our
21 hypothesis in a cross-sectional design, a final sample size of 500 was chosen to balance
22 attrition at various follow-ups points (estimated at 20-40%) and to facilitate regression
23 analyses. Pilot testing computed an $r = 0.75$, which following Cohen's conventions can be
24 interpreted as a large effect size. A priori power calculation using an observed effect size of
25 0.75 with the conventional probability level of .05 in a sample size of 306 would result in an
26 observed power of 0.99 (two-tailed).
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29 *Procedure*

30 Patients will be directly approached in the waiting room of the adult oncology unit while
31 waiting to see their oncologist. Participants will first be given verbal information on the goal
32 of the study and screened to check if they meet all inclusion and exclusion criteria. Upon
33 assent to participate, informed consent will be obtained and an additional information leaflet
34 be given. Participants will be asked to circle the number that best describes the overall
35 distress that they experienced over the previous week for both the ECOG and HADS. Face to
36 face interviews will be conducted in all major languages (English, Bahasa Malaysia and
37 Chinese). The follow up time ranges from 4 to 6 weeks and 1 year, at which the assessments
38 will be repeated via face-to-face interview, or via telephone interview if necessary.
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41 *Questionnaire administration*

42 The use of a questionnaire design makes this study cost-efficient and allows for rapid yet
43 effective screening of psychological distress in our population. Oncologist-assessed ECOG
44 performance status scores will be extracted from patient oncology records.
45
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47 **Analysis of Data**

48 The mean and standard deviations for anxiety and depression for each cancer type will be
49 determined. All data will be coded based on the instructional guidelines as contained in the
50 questionnaire scoring manuals. Responses to the HADS will be analysed according to
51 published recommendations.¹⁵ Two-sided tests will be used, while p -values of ≤ 0.05 will be
52 regarded as statistically significant. For all analyses, a two-sided p -value ≤ 0.05 will be
53 applied. All analyses will be performed using the Statistical Package for Social Sciences
54 (SPSS) version 20.
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56 *Comparison of mean scores*

57 Comparison of baseline scores, change in scores between and within groups, as well as
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3 identification of subjects with improved, stable and worsened scores over time will be
4 performed using a t-test, Mann Whitney test, ANOVA or alternately a non-parametric
5 approach such as Kruskal-Wallis as deemed appropriate. Proportions will be compared using
6 chi-squared test or Fisher's exact test.
7

8 *Comparison between ECOG and HADS scores*

9 Comparison between the good (0-1), intermediate (2) and poor (3-4) performance status
10 patient groups will be made using one-way analysis of variance (ANOVA). Pearson
11 correlation coefficient (r) will be used to express the relationship between the psychological
12 distress as measured using the HADS and performance status using the ECOG. Differences
13 in the two subscales of the HADS as well as mean ECOG scores will also be reported.
14 Correlations in each patient group among overall levels of psychological distress and
15 performance status will be measured using Spearman's correlation coefficient.
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18 Kendall's tau (r) coefficient will be used to measure the portion of ranks that match between
19 patient-rated and oncologist-rated performance status. Additionally, a paired t-test, or the
20 non-parametric Kolmogorov-Smirnov test (KS-test) may be used to determine if there is a
21 significant difference between the patient-rated versus oncologist-rated dataset.
22

23 *Descriptive statistics*

24 Descriptive statistical analysis will be performed for all variables. Continuous variables will
25 be reported using means and standard deviations or median and inter-quartile range. For
26 dichotomous variables, absolute numbers and percentages will be presented. Differences
27 between concordant and discrepant performance status groups in demographic characteristics,
28 clinical variables, anxiety, depression, and performance status will be assessed using *t* test or
29 Mann-Whitney tests for continuous variables, and the χ^2 statistic or Fisher's exact test for
30 categorical variables. Linear regression, logistic regression, or the Wilcoxon-Mann-Whitney
31 rank sum test will be used as appropriate to assess the impact of demographic and clinical
32 variables on group differences in depression, anxiety and performance status. Variables
33 included in subsequent analyses include those that demonstrate statistically significant
34 differences between the study groups in univariate analyses.
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37 *Imputation of missing values*

38 All responses with more than 5% missing values will first be removed from the data set. For
39 the remaining items, missing values will be replaced by an imputation process based on an
40 expectation-maximization algorithm using NORM software. This imputation ensures that
41 should subsequent exploratory factor analysis be done, which processes a large number of
42 items, the data set is not reduced too greatly. In order to assess the influence of imputation on
43 the psychometric results, all analyses will additionally be carried out with non-imputed
44 values after the factor analysis. Should differences arise, findings from both imputed and
45 non-imputed data will be presented to allow for comparison. Careful note will be made for all
46 missing data on individual items. Missing data however remains a serious issue for quality of
47 life studies.¹⁵
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50 **Discussion**

51 This is the first study to longitudinally examine the use of discrepancy in ECOG as a
52 predictor of anxiety and depression in cancer patients in a comparative assessment over time.
53 We propose the use of the ECOG as a brief screening instrument for depression and anxiety
54 in cancer patients and hypothesize that poorer or more discrepant patient-rated ECOG scores
55 may be an indicator of greater psychological distress. Given the high prevalence of anxiety
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3 and depression in cancer, screening is critical in increasing case recognition to deliver
4 appropriate interventions and prioritise referrals.
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6 While the ECOG was originally developed as a measure of performance status, its brevity
7 and simplicity makes it feasible for widespread adoption as a surrogate tool to detect anxiety
8 and depression. Most oncologists lack familiarity with psychiatric nosology.¹ Screening for
9 anxiety and depression using the ECOG performance status scale does not require special
10 training because performance status is routinely assessed by oncologists across all cancer
11 types.
12

13 There is an emerging trend towards simplifying the assessment of depression and anxiety in
14 outpatient cancer settings,²⁰ particularly as treatment and care has shifted to ambulatory
15 settings. Shorter than any other standard assessment such as the HADS and Beck Depression
16 Inventory, the ECOG functions much like the single-item Distress Thermometer. We predict
17 that the acceptability of the ECOG as a measure would likely be higher and less likely to
18 burden the clinic in terms of time and cost compared to any other form of assessment.
19

20 Patients have been shown able to accurately assess their own performance status.¹³ The single
21 item ECOG performance status is also easy for patients to rate, especially with the emergence
22 of different versions of the performance status scale in visual analogue format¹³ suitable for
23 paediatric or illiterate cancer populations, or simply where communication issues might arise
24 from a language barrier.
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27 While data which come directly from those experiencing the cancer affords an insightful
28 perspective, there is greater practical value in using the ECOG to comparatively measure
29 discrepancy in performance status scores, rather than solely relying on either patient- or
30 oncologist-rated scores. Discrepancy on the ECOG is also easy to eyeball, while scores can
31 be quickly compare over time when reviewed at each visit.
32

33 This study carries several important implications for oncology clinic practice, in that
34 discrepancy in ECOG scores, or patient-rated ECOG can be used as a patient reported
35 outcome measure to raise, discuss as well as routinely monitor psychological concerns.¹¹
36 Asking patients to score their own ECOG opens up avenues for discussion of psychological
37 concerns and reduces the likelihood of measurement-, cultural- and educational bias.
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40 Special attention should be given to cancer patients who demonstrate poorer self rated
41 performance status. As suggested by Ando,¹² patients who rate themselves significantly
42 higher on ECOG scores compared to assessment by their oncologist may actually be
43 presenting a subconscious bid for care and reassurance toward their oncologists. This is
44 consistent with the local cultural influence which is not dissimilar to those of other Asian
45 cultures where emotions are suppressed.¹⁸
46

47 Due to indefinite symptomatology such as fatigue, lack of appetite and weight loss,¹⁹
48 differentiating symptoms caused by cancer and its treatment from standard criteria-based
49 syndromes of major depression and clinical grade anxiety is not easy.¹⁷ The use of the ECOG
50 can indicate the presence of psychological distress that does not exclude psychosomatic
51 distress. Multiple sociocultural barriers are inherent in seeking medical and psychosocial
52 information, treatment and care.¹⁸
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55 Regardless of physical disease,²⁰ it is not uncommon for mood disorders to be expressed as
56 somatic rather than psychological symptoms across a number of cultures, partly to avoid the
57 perceived stigma of a psychiatric disorder.¹ Patients from Asian cultures tend to focus on
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3 somatising and physiologic symptomatology rather than mental symptoms^{18 21} and to be
4 culturally constrained where it comes to reporting emotional states such as depression.²¹
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6 Physicians too are often reluctant to probe into psychological concerns.² This may be in part
7 due to the biomedical training and orientation of oncologists, who may prove wary of
8 forming attachment to patients, which is also a barrier to supportive care. A rigid biomedical
9 agenda also means oncologists are more comfortable treating somatic symptoms such as pain,
10 nausea and dyspnea. It is likely that physicians who are trained locally would be even less
11 comfortable addressing distress due to cultural constraints. This gives rise to the question of
12 how likely oncologists are to refer patients for further psychological or psychiatric
13 assessment. Previous studies report the consultation rate from oncologists to consultation-
14 liaison psychiatrists to be only 4-10% among cancer patients.^{5 22}
15

16 The majority of cancer patients with (clinically significant) anxiety and depression do not see
17 mental health professionals but do see their oncologists. However relatively few oncologists
18 have sufficient knowledge and expertise to assess and treat psychological distress.³ Prior
19 research in this context shows that oncologists are often unable to detect depression and
20 anxiety, often stemming from a lack confidence in assessing distress and using psychometric
21 instruments.²³
22

23 By no means however should assessment of psychological distress using the ECOG replace
24 comprehensive psychiatric evaluation.⁵ Systematic screening using the ECOG can
25 nonetheless increase case recognition and allow for referral of distressed patients for
26 consultation-liaison or ideally psycho-oncology services.^{2 5 19} Further study is needed to
27 determine if the relationship between performance status and anxiety and depression is
28 predictive, prognostic, causal or merely associative.
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31 **Implications**

32 Although the ECOG was not developed specifically to detect depression or anxiety, it has
33 good potential to assist in the recognition of distress. Findings from this study would help to
34 validate the surrogate function of an existing clinic tool. Implementation of the ECOG as part
35 of routine systematic screening for psychological distress appears feasible because of its
36 distinct advantage of fundamental use in performance status scoring in oncology, although
37 further validation using criterion-standard structured clinical interviews is still required.
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40 **Ethics**

41 This study is part of a project approved by the ethics committee of the UMMC (MEC Ref.
42 No: 842.2). Individual written informed consent will be obtained following every
43 recommendation in accordance with the ethics of medical research.
44

45 **Abbreviations**

46 PS: Performance status; ECOG: Eastern Cooperative Oncology Group; HADS: Hospital
47 Anxiety and Depression Scale.
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50 **Authors' contributions**

51 CCMH designed and coordinated the study, drafted the manuscript and will conduct the
52 analysis and interpretation. MMY, WAWA, HGF and EK supervised the project, contributed
53 to the design of the study and critically revised the paper for important intellectual content.
54 All authors read and approved the final manuscript.
55

56 **Competing Interests**

57 The authors declare that they have no competing interests.
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Role of Funder

Independent of the study sponsors/ funders, the authors retain full authority over all of the following activities: the study design, collection, management, analysis and interpretation of data, as well as the report writing and decision to submit for publication.

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References

1. Pasquini M & Biondi M. Depression in cancer patients: a critical review. *Clinical Pract Epid Mental Health* 2007, **3**:21–30.
2. Fallowfield L, Ratcliffe D, Jenkins V and Saul J. Psychiatric morbidity and its recognition by doctors in patients with cancer. *Br J Cancer* 2001; 1011–1015.
3. Sinclair PA, Lyness JM, King DA, Cox C and Caine ED. Depression and self-reported functional status in older primary care patients. *Am J Psychiatry* 2001, **158**,416–419.
4. Jefford M, Mileskin L, Richards K, Thomson J, Matthews JP, Zalberg J, Jennens R, McLachlan SA, Wein S, Antill Y, Clarke DM. Rapid screening for depression-validation of the Brief Case-Find for Depression (BCD) in medical oncology and palliative care patients. *Br J Cancer* 2004, **91**:900–906.
5. Vodermaier A, Linden W, Siu C. Screening for emotional distress in cancer patients: a systematic review of assessment instruments. *J Natl Cancer Inst* 2009, 1464–1488.
6. Krebber AMH, Leemans CR, Bree RD, Straten AV, Smit HFE, Becker A et al. Stepped care targeting psychological distress in head and neck and lung cancer patients: a randomised clinical trial. *BMC Cancer* 2012, **12**:173.
7. Dajczman E., Kasymjanova G, Kreisman H, Swinton N, Pepe C & Small D. Should patient-rated performance status affect treatment decisions in advanced lung cancer? *J Thorac Oncol* 2008, **3**:1133–1136.
8. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982, **5**:649–655.
9. Julious SA, Campbell MJ, Walker SJ, George SL and Machin D. Sample sizes for cancer trials where Health Related Quality of Life is the primary outcome. *Br J Cancer* 2000, **83**(7):959–963.
10. Hillner BE. Trends in clinical trials reports in common cancers between 1989 and 2000. *J Clin Oncol* 2003, **21**:1850–1858.

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3 11. Blagden SP, Charman SC, Sharples LD, Magee LR, Gilligan D. Performance status
4 score: do patients and their oncologists agree? *Br J Cancer* 2003, **89**:1022–1027.
5
6 Ando M, Ando Y, Hasegawa Y, et al. Prognostic value of performance status assessed by
7 patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. *Br J*
8 *Cancer* 2001, **85**:1634–1639.
9
10 12. Gralla R, Hollen P, Kuruvialla P. Can performance status (PS) be determined accurately
11 by patients? Results of a prospective trial evaluating ECOG and Karnofsky PS as well as
12 patient-related PS in non-small cell lung cancer (NSCLC). In Proceedings of the 11th
13 World Conference on Lung Cancer. Barcelona, Spain, 2005, pp. 327.
14
15 13. Raosoft, Inc. Raosoft sample size calculator. Available from
16 <http://www.raosoft.com/samplesize.html>. Accessed January 10, 2012.
17
18 14. Zigmond AS and Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr*
19 *Scand* 1983, **67**:361–370.
20
21 15. Shrive FM, Stuart H, Quan H & Ghali WA. Dealing with missing data in a multi-
22 question depression scale: a comparison of imputation methods. *BMC Med Res Methodol*
23 2006, **6**:57-67.
24
25 16. Fisch M. Treatment of depression in cancer. *J Natl Cancer Inst* 2004, 105–111.
26
27 17. Hong JJ, Shim EJ, Shin YW, Oh DY, Im SA, Heo DS, Hahm BJ. Discrepancies in
28 performance status as determined by cancer patients and oncologists: are they influenced
29 by depression? *Gen Hosp Psychiat* 2007, **29**,555–561.
30
31 18. Shimizu K, Akizuki N, Nakaya N, Fujimori M, Fujisawa D, Ogawa A and Uchitomi Y.
32 Treatment response to psychiatric intervention and predictors of response among cancer
33 patients with adjustment disorders. *J Pain Symptom Manage* 2011, 684–691.
34
35 19. Tsunoda A, Nakao K, Hiratsuka K, Yasuda N, Shibusawa M, Kusano M. Anxiety,
36 depression and quality of life in colorectal cancer patients. *IJCO* 2005, 411–417.
37
38 20. Bailey RK, Geyen DJ, Scott-Gurnell K, Hipolito MMS, Bailey TA & Beal JM.
39 Understanding and treating depression among cancer patients. *Int J Gynecol Cancer*
40 2005, **15**:203–208.
41
42 21. Grassi L, Rossi E, Caruso R, Nanni MG, Pedrazzi S, Sofritti S, Sabatto S. Educational
43 screening for emotional distress: an observational study. *Psycho Oncol* 2011, **20**:669–
44 674.
45
46 22. Hughes KL, Sargeant H and Hawkes AL. Acceptability of the Distress Thermometer and
47 Problem List to community-based telephone cancer helpline operators, and to cancer
48 patients and carers. *BMC Cancer* 2011, **11**:46.
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Appendix 1

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3 **ECOG Performance Status Score**
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ECOG	Score
Fully active, able to carry on all pre-disease performance without restriction	0
Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	1
Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	2
Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	3
Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	4

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22 Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative
23 Oncology Group. Am J Clin Oncol 1982, 5:649–655.
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7 **Discrepancy in Patient- and Oncologist-Rated Performance Status on**
8 **Depression and Anxiety in Cancer: A Prospective Study Protocol**
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Abstract

Objective

Psychological distress is common in patients with cancer. We need a rapid means of screening for and identifying depression and anxiety in patients with cancer. The present study evaluates the potential of the Eastern Cooperative Oncology Group (ECOG) performance status (PS) scoring as a brief screening tool to assess psychological distress in routine cancer care. The ECOG PS is widely used by oncologists and the World Health Organisation as a standardised measure to assess general wellbeing in patients with cancer and quality of life in cancer trials. We examine the discrepancy between patient-rated and oncologist-rated performance status scores on the ECOG in a comparative assessment against the Hospital Anxiety and Depression Scale (HADS).

Methods & Design

This is a prospective evaluation of approximately 500 ambulatory adult cancer patients from a large academic medical centre. Participants will be asked to assess their own ECOG PS on a scale of 0 to 4, which will be compared to ECOG PS as rated by their oncologists. Higher ECOG PS scores indicate poorer daily functioning. Both patient-rated and oncologist-rated ECOG PS and their absolute differences will be tested for predictive and concurrent validity against the HADS. A HADS cut-off ≥ 15 will be used. Ethics approval for this study has been secured from the institutional ethics board. Outcomes are re-evaluated at 4- to 6-week and 1 year follow-up.

Conclusion

This study holds practical significance for rapid screening of psychological distress in the cancer clinic with the use of the ECOG performance status scoring. Given the high prevalence of anxiety and depression in patients with cancer, screening is important to increase its recognition, which will in turn help to direct referrals and deliver appropriate intervention. This study also generates greater insight into the association between psychosomatic complaints and psychological distress.

Keywords

Patient-Rated ECOG, Performance Status, Anxiety, Depression, Cancer.

Introduction

We need a rapid means of screening for and identifying depression and anxiety in patients with cancer. While having patients undergo psychological assessment interviews or complete standardised anxiety and depression questionnaires is ideal, cancer clinics are busy places where oncologists and staff nurses are often overworked.¹ Oncologists are often not sufficiently trained in psychological assessment or testing, nor do they have the time to do so.² Several studies have shown that oncologists are not especially skilled in either discussing psychological problems in general,³ or at recognising anxiety and depression.^{2,4} Published data suggest that the ability of doctors to accurately detect psychiatric morbidity in patients is often little better than that chance.²

As a result psychological distress may go undetected and when recognised, it is more likely to run a more severe and unremitting course, and in some cases to be clearly impacting patients' lives and even cancer treatment in some way. Although tremendous attention has been given to the early detection and treatment of cancer, the issue of psychological distress has lagged behind. There is little consensus with regards to even the criterion and management of anxiety and depression associated with cancer. Early detection is as crucial in the matter of treatment and prognosis in cancer as in anxiety and depression, with greater psychological distress linked to poorer health outcomes.⁵

We lack ~~of~~ adequate screening instruments measuring psychological distress in oncology settings.⁶ For a screening or monitoring tool to be accepted into routine practice, it needs to be brief, relevant in its utility and simple enough to interpret while retaining the necessary specificity and sensitivity.⁵ What we need is to capitalise on an existing tool as a brief form of assessment that can function as a surrogate tool for screening depression and anxiety.⁷ The ECOG PS is one such measure. As a standardised measure of performance status in routine oncology practice, the ECOG bears the potential for widespread usage to screen for psychological distress in this setting due to its high acceptability and ease of use.

Performance status is one of the most widely accepted patient evaluations used in clinical practice and oncology trials. It is typically assessed for all types of cancer due to its demonstrated efficacy in the measurement of treatment responses, survival length, prognostic value as well as a criterion for suitability for chemotherapy and clinical trials.⁸ Yet rarely, if ever, are performance status scores compared across different cancer types. Most commonly reported as part of a randomised clinical trial, the majority of cancer studies or trials where performance status is measured also present data where sample sizes are generally inadequate or moderate at best.⁹ The average cancer trial size wherein performance status is most frequently measured is 200, or an average of 175 for randomised clinical trials.¹⁰

Oncologists have generally found the ECOG easy to use in daily clinic practice.^{7-8,11} Although traditionally scored by the oncologist, several studies have arrived at rather interesting results when comparing performance status scores as rated by the patients to those rated by their oncologists.⁷ Prior studies in this area already show that there is a significant difference between patient- and oncologist-rated performance status,¹² with depression being a confounder where it comes to functional status.³ These previous studies examining discrepancy between patient- and oncologist rated ECOG however are also restricted to patients with cancer in a single site, with most of such studies focusing primarily on non-small cell lung cancer.^{7,11-13} Findings from these studies may not be representative of psychological distress in patients with other types of cancer. It would therefore be interesting to extend this study to include patients with other cancer types.^{1,12}

Comment [CCMH1]: [1] The word 'of' has been removed.

Comment [CCMH2]: [2] Additional citations have been added.

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7 The main goal of this proposed study is to examine the feasibility of the ECOG PS as a
8 psychological distress screening instrument. We intent to test the predictive and concurrent
9 validity of the ECOG PS against the HADS. The present study is the first to prospectively
10 investigate the use of discrepancy between patient- and oncologist-rated ECOG performance
11 status to gauge psychological distress in patients with cancer.

12 **Research Questions**

- 14 1. To what extent do patient-rated versus oncologist-rated ECOG PS agree? If
15 discrepant, what is their underlying cause?
- 16 2. To what degree does the ECOG assess psychological distress? Does discrepancy in
17 performance status predict psychological distress at baseline and subsequent 4- to 6-
18 week and 1-year follow-up?

19 **Hypothesis**

20 It is hypothesised that poorer or discrepant performance status scores are associated with
21 higher levels of psychological distress, rather than the level of activity. It is also posited that
22 discrepancy between patient-rated ECOG at baseline and follow-up is also associated with an
23 increased likelihood of comorbid anxiety or depression in patients with cancer.

24 **Methods/ Design**

25 This is a prospective single centre study, in the context of patients about to see their
26 oncologist for a consultation in an academic medical centre. Patients will be asked to assess
27 their own ECOG PS score on a scale between 0 and 4. We then compare these to ECOG
28 scores rated by their oncologists (extracted from their medical records). The absolute
29 discrepancy in scores will then subsequently analysed against patient HADS scores.

30
31 We will attempt to enroll approximately 500 consecutive patients who have been referred to
32 the adult clinical oncology unit with a diagnosis of cancer from November 2011 to August
33 2012. Patients should be receiving or plan to receive at least one form of treatment (i.e.
34 chemotherapy or radiotherapy) at any point in their disease trajectory. Patients aged less than
35 18 years are excluded, as are those with an incomplete diagnosis and language issues,
36 specifically the inability to understand the instrument language in English or comprehend
37 interviews conducted in all major spoken languages: English, Chinese or the Malay language.
38 We chose not to apply additional exclusion criteria that would limit the applicability of
39 findings to the general cancer patient population unnecessarily.

40 *Study Variables*

41 A data extraction form that has been specifically developed will be used to obtain relevant
42 demographic and clinical data from patient records. The specific variables and selected
43 outcome variables of interest include age, sex, race, marital status, education and employment
44 status. Relevant clinical information examined includes the primary cancer site and tumour
45 stage. Other variables that will be looked at include treatment planned or received such as
46 surgery, chemotherapy and or radiotherapy.

47 *Research Tools*

48
49 The questionnaires used in this study include the ECOG PS as rated by patients themselves
50 and by their oncologists, as well as the Hospital Anxiety and Depression (HADS) scale. All
51 questionnaires used have obtained permission for use from the respective authors and will be
52 cited.
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The ECOG PS is highly valid and is one of the most widely used instruments in clinical cancer practice and research.^{7-8,11} (Dajezman, 2008). In this study the single-item score will be rated by both patients and their oncologists on a scale of 0 to 4 (worse scores denoting poorer performance status and higher levels of psychological distress). The ECOG PS score of 5 (indicating death) will not be used in the patient version of the scale. [Refer to Appendix 1 for a copy of the ECOG.](#)

The HADS, a 14-item instrument has also been well validated and will be employed for use in the detection of anxiety and depression among cancer patients. Overall scores range from 0 to 42, with higher scores indicating greater distress. A cut-off point of greater than or equal to 15 will be used. Preliminary testing with 18 patients (male to female ratio = 1:1) conducted in October 2011 for the HADS yielded an alpha of 0.91.

Sample Size Estimation

Using an online sample size calculator (Raosoft),¹⁴ we adopted a 0.05% margin of error which required a ~~minimum of 282~~ **total of 306** participants to accurately (95% confidence) represent a variable with 50% response distribution in a population of approximately ~~1050~~ **1500 individuals-cancer patients** seen annually. **Although an estimated figure of 306 patients would be sufficient to test our hypothesis in a cross-sectional design, a final sample size of 500 was chosen to balance attrition at various follow-ups points (estimated at 20-40%) and to facilitate regression analyses. Pilot testing computed an $r = 0.75$, which following Cohen's conventions can be interpreted as a large effect size. A priori power calculation using an observed effect size of 0.75 with the conventional probability level of .05 in a sample size of 306 would result in an observed power of 0.99 (two-tailed).**

Comment [CCMH3]: [3] Justification for sample size of 500 is provided.

Comment [CCMH4]: [5-6] Additional information on pilot testing and effect size are now included.

Procedure

Patients will be directly approached in the waiting room of the adult oncology unit while waiting to see their oncologist. Participants will first be given verbal information on the goal of the study and screened to check if they meet all inclusion and exclusion criteria. Upon assent to participate, informed consent will be obtained and an additional information leaflet be given. Participants will be asked to circle the number that best describes the overall distress that they experienced over the previous week for both the ECOG and HADS. Face to face interviews will be conducted in all major languages (English, Bahasa Malaysia and Chinese). The follow up time ranges from 4 to 6 weeks and 1 year, at which the assessments will be repeated via face-to-face interview, or via telephone interview if necessary.

Questionnaire administration

The use of a questionnaire design makes this study cost-efficient and allows for rapid yet effective screening of psychological distress in our population. Oncologist-assessed ECOG performance status scores will be extracted from patient oncology records.

Analysis of Data

The mean and standard deviations for anxiety and depression for each cancer type will be determined. All data will be coded based on the instructional guidelines as contained in the questionnaire scoring manuals. Responses to the HADS will be analysed according to published recommendations.¹⁵ Two-sided tests will be used, while p-values of ≤ 0.05 will be regarded as statistically significant. For all analyses, a two-sided p -value ≤ 0.05 will be applied. All analyses will be performed using the Statistical Package for Social Sciences (SPSS) version 20.

Comparison of mean scores

Comparison of baseline scores, change in scores between and within groups, as well as identification of subjects with improved, stable and worsened scores over time will be performed using a t-test, Mann Whitney test, ANOVA or alternately a non-parametric approach such as Kruskal-Wallis as deemed appropriate. Proportions will be compared using chi-squared test or Fisher's exact test.

Comparison between ECOG and HADS scores

Comparison between the good (0-1), intermediate (2) and poor (3-4) performance status patient groups will be made using one-way analysis of variance (ANOVA). Pearson correlation coefficient (r) will be used to express the relationship between the psychological distress as measured using the HADS and performance status using the ECOG. Differences in the two subscales of the HADS as well as mean ECOG scores will also be reported. Correlations in each patient group among overall levels of psychological distress and performance status will be measured using Spearman's correlation coefficient.

Kendall's tau (r) coefficient will be used to measure the portion of ranks that match between patient-rated and oncologist-rated performance status. Additionally, a paired t-test, or the non-parametric Kolmogorov-Smirnov test (KS-test) may be used to determine if there is a significant difference between the patient-rated versus oncologist-rated dataset.

Descriptive statistics

Descriptive statistical analysis will be performed for all variables. Continuous variables will be reported using means and standard deviations or median and inter-quartile range. For dichotomous variables, absolute numbers and percentages will be presented. Differences between concordant and discrepant performance status groups in demographic characteristics, clinical variables, anxiety, depression, and performance status will be assessed using *t* test or Mann-Whitney tests for continuous variables, and the X^2 statistic or Fisher's exact test for categorical variables. Linear regression, logistic regression, or the Wilcoxon-Mann-Whitney rank sum test will be used as appropriate to assess the impact of demographic and clinical variables on group differences in depression, anxiety and performance status. Variables included in subsequent analyses include those that demonstrate statistically significant differences between the study groups in univariate analyses.

Imputation of missing values

All responses with more than 5% missing values will first be removed from the data set. For the remaining items, missing values will be replaced by an imputation process based on an expectation-maximization algorithm using NORM software. This imputation ensures that should subsequent exploratory factor analysis be done, which processes a large number of items, the data set is not reduced too greatly. In order to assess the influence of imputation on the psychometric results, all analyses will additionally be carried out with non-imputed values after the factor analysis. Should differences arise, findings from both imputed and non-imputed data will be presented to allow for comparison. Careful note will be made for all missing data on individual items. Missing data however remains a serious issue for quality of life studies.¹⁵

Discussion

This is the first study to longitudinally examine the use of discrepancy in ECOG as a predictor of anxiety and depression in cancer patients in a comparative assessment over time. We propose the use of the ECOG as a brief screening instrument for depression and anxiety in cancer patients and hypothesize that poorer or more discrepant patient-rated ECOG scores

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7 may be an indicator of greater psychological distress. Given the high prevalence of anxiety
8 and depression in cancer, screening is critical in increasing case recognition to deliver
9 appropriate interventions and prioritise referrals.

10 While the ECOG was originally developed as a measure of performance status, its brevity
11 and simplicity makes it feasible for widespread adoption as a surrogate tool to detect anxiety
12 and depression. Most oncologists lack familiarity with psychiatric nosology.¹ Screening for
13 anxiety and depression using the ECOG performance status scale does not require special
14 training because performance status is routinely assessed by oncologists across all cancer
15 types.

16
17 There is an emerging trend towards simplifying the assessment of depression and anxiety in
18 outpatient cancer settings,²⁰ particularly as treatment and care has shifted to ambulatory
19 settings. Shorter than any other standard assessment such as the HADS and Beck Depression
20 Inventory, the ECOG functions much like the single-item Distress Thermometer. We predict
21 that the acceptability of the ECOG as a measure would likely be higher and less likely to
22 burden the clinic in terms of time and cost compared to any other form of assessment.

23 Patients have been shown able to accurately assess their own performance status.¹³ The single
24 item ECOG performance status is also easy for patients to rate, especially with the emergence
25 of different versions of the performance status scale in visual analogue format¹³ suitable for
26 paediatric or illiterate cancer populations, or simply where communication issues might arise
27 from a language barrier.

28
29 While data which come directly from those experiencing the cancer affords an insightful
30 perspective, there is greater practical value in using the ECOG to comparatively measure
31 discrepancy in performance status scores, rather than solely relying on either patient- or
32 oncologist-rated scores. Discrepancy on the ECOG is also easy to eyeball, while scores can
33 be quickly compare over time when reviewed at each visit.

34 This study carries several important implications for oncology clinic practice, in that
35 discrepancy in ECOG scores, or patient-rated ECOG can be used as a patient reported
36 outcome measure to raise, discuss as well as routinely monitor psychological concerns.^{11,2}
37 Asking patients to score their own ECOG opens up avenues for discussion of psychological
38 concerns and reduces the likelihood of measurement-, cultural- and educational bias.

39
40 Special attention should be given to cancer patients who demonstrate poorer self rated
41 performance status. As suggested by Ando,¹²⁺ patients who rate themselves significantly
42 higher on ECOG scores compared to assessment by their oncologist may actually be
43 presenting a subconscious bid for care and reassurance toward their oncologists. This is
44 consistent with the local cultural influence which is not dissimilar to those of other Asian
45 cultures where emotions are suppressed.¹⁸

46 Due to indefinite symptomatology such as fatigue, lack of appetite and weight loss,¹⁹
47 differentiating symptoms caused by cancer and its treatment from standard criteria-based
48 syndromes of major depression and clinical grade anxiety is not easy.¹⁷ The use of the ECOG
49 can indicate the presence of psychological distress that does not exclude psychosomatic
50 distress. Multiple sociocultural barriers are inherent in seeking medical and psychosocial
51 information, treatment and care.¹⁸

52
53 Regardless of physical disease,²⁰ it is not uncommon for mood disorders to be expressed as
54 somatic rather than psychological symptoms across a number of cultures, partly to avoid the

Comment [CCMH5]: [8] The Beck Depression Inventory and Distress Thermometer here as mentioned in comparison as current measures in use only.

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7 perceived stigma of a psychiatric disorder.¹ Patients from Asian cultures tend to focus on
8 somatising and physiologic symptomatology rather than mental symptoms^{18 21} and to be
9 culturally constrained where it comes to reporting emotional states such as depression.²¹

10 Physicians too are often reluctant to probe into psychological concerns.² This may be in part
11 due to the biomedical training and orientation of oncologists, who may prove wary of
12 forming attachment to patients, which is also a barrier to supportive care. A rigid biomedical
13 agenda also means oncologists are more comfortable treating somatic symptoms such as pain,
14 nausea and dyspnea. It is likely that physicians who are trained locally would be even less
15 comfortable addressing distress due to cultural constraints. This gives rise to the question of
16 how likely oncologists are to refer patients for further psychological or psychiatric
17 assessment. Previous studies report the consultation rate from oncologists to consultation-
18 liaison psychiatrists to be only 4-10% among cancer patients.^{5 22}

19 The majority of cancer patients with (clinically significant) anxiety and depression do not see
20 mental health professionals but do see their oncologists. However relatively few oncologists
21 have sufficient knowledge and expertise to assess and treat psychological distress.³ Prior
22 research in this context shows that oncologists are often unable to detect depression and
23 anxiety, often stemming from a lack confidence in assessing distress and using psychometric
24 instruments.²³

25 By no means however should assessment of psychological distress using the ECOG replace
26 comprehensive psychiatric evaluation.⁵ Systematic screening using the ECOG can
27 nonetheless increase case recognition and allow for referral of distressed patients for
28 consultation-liaison or ideally psycho-oncology services.^{2 5 19} Further study is needed to
29 determine if the relationship between performance status and anxiety and depression is
30 predictive, prognostic, causal or merely associative.

32 **Implications**

33 Although the ECOG was not developed specifically to detect depression or anxiety, it has
34 good potential to assist in the recognition of distress. Findings from this study would help to
35 validate the surrogate function of an existing clinic tool. Implementation of the ECOG as part
36 of routine systematic screening for psychological distress appears feasible because of its
37 distinct advantage of fundamental use in performance status scoring in oncology, although
38 further validation using criterion-standard structured clinical interviews is still required.

39 **Ethics**

40 This study is part of a project approved by the ethics committee of the UMMC (MEC Ref.
41 No: 842.2). Individual written informed consent will be obtained following every
42 recommendation in accordance with the ethics of medical research.

43 **Abbreviations**

44 PS: Performance status; ECOG: Eastern Cooperative Oncology Group; HADS: Hospital
45 Anxiety and Depression Scale.

46 **Authors' contributions**

47 CCMH designed and coordinated the study, drafted the manuscript and will conduct the
48 analysis and interpretation. MMY, WAWA, HGF and EK supervised the project, contributed
49 to the design of the study and critically revised the paper for important intellectual content.
50 All authors read and approved the final manuscript.
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Competing Interests

The authors declare that they have no competing interests.

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Role of Funder

Independent of the study sponsors/ funders, the authors retain full authority over all of the following activities: the study design, collection, management, analysis and interpretation of data, as well as the report writing and decision to submit for publication.

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References

1. Pasquini M & Biondi M. Depression in cancer patients: a critical review. *Clinical Pract Epid Mental Health* 2007, **3**:21–30.
2. Fallowfield L, Ratcliffe D, Jenkins V and Saul J. Psychiatric morbidity and its recognition by doctors in patients with cancer. *Br J Cancer* 2001; 1011–1015.
3. Sinclair PA, Lyness JM, King DA, Cox C and Caine ED. Depression and self-reported functional status in older primary care patients. *Am J Psychiatry* 2001, **158**,416–419.
4. Jefford M, Mileschkin L, Richards K, Thomson J, Matthews JP, Zalcborg J, Jennens R, McLachlan SA, Wein S, Antill Y, Clarke DM. Rapid screening for depression-validation of the Brief Case-Find for Depression (BCD) in medical oncology and palliative care patients. *Br J Cancer* 2004, **91**:900–906.
5. Vodermaier A, Linden W, Siu C. Screening for emotional distress in cancer patients: a systematic review of assessment instruments. *J Natl Cancer Inst* 2009, 1464–1488.
6. Krebber AMH, Leemans CR, Bree RD, Straten AV, Smit HFE, Becker A et al. Stepped care targeting psychological distress in head and neck and lung cancer patients: a randomised clinical trial. *BMC Cancer* 2012, **12**:173.
7. Dajczman E., Kasymjanova G, Kreisman H, Swinton N, Pepe C & Small D. Should patient-rated performance status affect treatment decisions in advanced lung cancer? *J Thorac Oncol* 2008, **3**:1133–1136.
8. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982, **5**:649–655.
9. Julious SA, Campbell MJ, Walker SJ, George SL and Machin D. Sample sizes for cancer trials where Health Related Quality of Life is the primary outcome. *Br J Cancer* 2000, **83**(7):959–963.

10. Hillner BE. Trends in clinical trials reports in common cancers between 1989 and 2000. *J Clin Oncol* 2003, **21**:1850–1858.

~~11.~~ 11. Blagden SP, Charman SC, Sharples LD, Magee LR, Gilligan D. Performance status score: do patients and their oncologists agree? *Br J Cancer* 2003, **89**:1022–1027.

~~12.~~ Ando M, Ando Y, Hasegawa Y, et al. Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. *Br J Cancer* 2001, **85**:1634–1639.

~~13.~~ 12. Blagden SP, Charman SC, Sharples LD, Magee LR, Gilligan D. Performance status score: do patients and their oncologists agree? *Br J Cancer* 2003, **89**:1022–1027.

~~14.~~ 13. Gralla R, Hollen P, Kuruvialla P. Can performance status (PS) be determined accurately by patients? Results of a prospective trial evaluating ECOG and Karnofsky PS as well as patient-related PS in non-small cell lung cancer (NSCLC). In Proceedings of the 11th World Conference on Lung Cancer. Barcelona, Spain, 2005, pp. 327.

~~15.~~ 14. Raosoft, Inc. Raosoft sample size calculator. Available from <http://www.raosoft.com/samplesize.html>. Accessed January 10, 2012.

~~16.~~ 15. Zigmond AS and Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983, **67**:361–370.

~~17.~~ 16. Shrive FM, Stuart H, Quan H & Ghali WA. Dealing with missing data in a multi-question depression scale: a comparison of imputation methods. *BMC Med Res Methodol* 2006, **6**:57–67.

~~18.~~ 17. Fisch M. Treatment of depression in cancer. *J Natl Cancer Inst* 2004, 105–111.

~~19.~~ 18. Hong JJ, Shim EJ, Shin YW, Oh DY, Im SA, Heo DS, Hahm BJ. Discrepancies in performance status as determined by cancer patients and oncologists: are they influenced by depression? *Gen Hosp Psychiat* 2007, **29**:555–561.

~~20.~~ 19. Shimizu K, Akizuki N, Nakaya N, Fujimori M, Fujisawa D, Ogawa A and Uchitomi Y. Treatment response to psychiatric intervention and predictors of response among cancer patients with adjustment disorders. *J Pain Symptom Manage* 2011, 684–691.

~~21.~~ 20. Tsunoda A, Nakao K, Hiratsuka K, Yasuda N, Shibusawa M, Kusano M. Anxiety, depression and quality of life in colorectal cancer patients. *IJCO* 2005, 411–417.

~~22.~~ 21. Bailey RK, Geyen DJ, Scott-Gurnell K, Hipolito MMS, Bailey TA & Beal JM. Understanding and treating depression among cancer patients. *Int J Gynecol Cancer* 2005, **15**:203–208.

~~23.~~ 22. Grassi L, Rossi E, Caruso R, Nanni MG, Pedrazzi S, Sofritti S, Sabatto S. Educational screening for emotional distress: an observational study. *Psycho Oncol* 2011, **20**:669–674.

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23. Hughes KL, Sargeant H and Hawkes AL. Acceptability of the Distress Thermometer and Problem List to community-based telephone cancer helpline operators, and to cancer patients and carers. *BMC Cancer* 2011, **11**:46.

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Appendix 1

ECOG Performance Status Score

<u>ECOG</u>	<u>Score</u>
<u>Fully active, able to carry on all pre-disease performance without restriction</u>	<u>0</u>
<u>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</u>	<u>1</u>
<u>Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</u>	<u>2</u>
<u>Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours</u>	<u>3</u>
<u>Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</u>	<u>4</u>

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