PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Protocol for the development and validation of a measure of persistent psychological and emotional distress in cardiac patients: The Cardiac Distress Inventory
AUTHORS	Jackson, Alun; Rogerson, Michelle; Le Grande, Michael; Thompson, David; Ski, Chantal; Alvarenga, Marlies; Amerena, John; Higgins, Rosemary; Raciti, Michela; Murphy, Barbara

VERSION 1 – REVIEW

REVIEWER	Julius Burkauskas Laboratory of Behavioral Medicine. Neuroscience Institute. Lithuanian University of Health Sciences In the past several years I have been working as a consultant at Cogstate, Ltd.
REVIEW RETURNED	21-Dec-2019

GENERAL COMMENTS	In the present research protocol the authors aim to develop and validate a measure of persistent psychological and emotional distress in cardiac patients. It might be a timely and much needed instrument for use in everyday practice of cardiac disease management. However, there are several issues that have to be discussed before recommending the publication of this protocol. First of all, the definition of cardiac distress could be elaborated on. The authors' definition states that cardiac distress is a "persistent negative emotional state rather than a transient state; involving multiple psychosocial domains; that challenges a patient's capacity to cope with living with their heart condition, the treatment of the condition, and the resultant changes to daily living; and challenges the person's sense of self and future orientation". However, it could be explained how this is different from acute stress reaction subsequent to a cardiac event or Cardiac-disease-induced Post-traumatic Stress Disorder (Vilchinsky et al., 2017) The subtle nuances of the specific types of distress might be well known to psychologists and psychiatrists, however, it might be interesting to differentiate the concepts for the general reading audience of the journal. Another important issue which should be addressed in a more elaborate manner is the guidelines for questioning and managing stress related CAD risk factors, which currently exist. For example, the recent guidelines for cardiovascular disease prevention in clinical practice (Piepoli et al., 2016) already contain core questions for the assessment of psychosocial risk factors. These questions already address mental distress issues quite broadly, providing evidence based line of questioning in the topics considering not only anxiety

	and depression, but also post MI PTSD symptoms, hostility, distressed personality characteristics and social isolation. It is suggested that the authors consider what more could be achieved if a measure of persistent psychological and emotional distress were to be created. With regards to methodological issues of the questionnaire concept, there is a chance that patients with CAD might not answer the questionnaire aiming to address emotional difficulties. A study by Ketterer et al. (2018) showed that the use of a significant other in assessing psychosocial/emotional distress in males may confer greater accuracy, and therefore predictive power for clinical endpoints. It also crucially important to methodologically address other aspects of why it is necessary to have such a scale. Is this scale going to predict some sort of stress induced impairment or be a marker of mortality risk or lower HRQoL? Again the impact of stress on patient-oriented outcomes has been quite well investigated in this particular population. The authors of this manuscript are encouraged to provide a broader scope showing how this questionnaire might fit into clinical practice as well as research. This leads to another important issue related to the methodology of the proposed questionnaire. I am not sure the use of an 'Emotional Thermometer' is the best solution for measuring cut-off scores. I understand the logic, however, perhaps some sort of gold standard measure such as the 'MINI Neuropsychiatric Interview' or the 'Sheehan functional impairment scale due to stress' should be used for the cut-off results to show important and clinically significant norms. The authors should also address whether they expect the scale to be multi or uni-dimensional, as this raises issues broadly discussed in the development of other questionnaires (e.g. Riley et al. 2011). It is also mentioned that the questionnaire will be translated into other languages. An explanation of validation and harmonisation of standards to be adhered to during this task is also recommended. I would encourage the authors to consult a recent paper by Boateng et al. (2018) to ensure they adhere to the best practices in testing psychometric properties of a questionnaire. Overall, this is an important and much needed line of research. However, a more detailed explanation of aims would greatly improve the current version of the protocol. References 1. Boateng, Godfred O., et al. "Best practices for developing and validating scales for health, social, and behavioral research: a primer." Frontiers in public health 6 (2018). 2. Vilchinsky, Noa, et al. "Cardiac-disease-induced PTSD (CDI-PTSD): A systematic review." Clinical Psychology Review 55 (2017): 92-106. 3. Ketterer, M. W., et al. "Men deny and women cry, but who dies? Do the wages of "denial" include early ischemic coronary heart disease?." Journal of psychosomatic research 56.1 (2004): 119-123. 4. Piepoli, Massimo F., et al. "2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other

	Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)." European heart journal 37.29 (2016): 2315-2381. 5. Riley WT, Pilkonis P, Cella D. Application of the National Institutes of Health Patient-reported Outcome Measurement Information System (PROMIS) to mental health research. J Ment Health Policy Econ. 2011;14(4):201–208.

REVIEWER	Stefanie Duijndam Tilburg University, the Netherlands
REVIEW RETURNED	13-Feb-2020

GENERAL COMMENTS	The aim and reasoning for the development of the CDI are well described. In my opinion it is an important step to develop such a questionnaire, and the way the authors are planning to conduct the study are well thought of and statistically sound. However, a few minor points come to mind when I read this protocol. - With regard to research ethics, the protocol number is described in the abstract, but not in the main text. Please describe that in the main text as well. - The authors are missing a very important paper in their protocol. The claim that "no currently existing measure would enable a psycho-cardiology professional to identify priority areas clearly enough to offer timely tailored psychosocial intervention for a distressed patient" is in my opinion not completely true, given that a screening tool for psychosomatic problems in cardiac patients already exists: van Montfort et al. 2017. Validity of the European Society of Cardiology's Psychosocial Screening Interview in Patients With Coronary Artery Disease-The THORESCI Study. Psychosomatic Medicine, 79 (4), 404-415. This paper describes the validity of a screening tool, which can be used to assess distress in cardiac patients. Please include this paper in your protocol as well. - In the protocol it says that "No identifying information will be collected as no patient follow-up is required". I understand that no identifying information will be collected, but the reasoning seems odd to me. Especially given that test-retest reliability will be calculated, for which you will need a follow up measure.

REVIEWER	Giada Rapelli Università Cattolica del Sacro Cuore - Milan, Italy
REVIEW RETURNED	20-Feb-2020

GENERAL COMMENTS	The study aims to develop a specific scale on distress for cardiological patients. Although the objective is specific and important to pursue, the authors do not allow access to the choices made step by step in the choice of items and in the validity concurrent with other scales. We recommend following the instructions below to improve the contribution. Lines 29-34: I would also add the fear of disease progression, a construct much investigated in the psychological literature among cardiopaths and even in their caregivers! Line 34: I would also deepen the cardiac-induced post-traumatic symptoms Lines 17-30: I would do a detailed examination of what each scale analyzes, perhaps with a table, and given the scope of the study I would highlight the novelty that the study brings Lines 12-17 having undergone surgery compared to those who have

	not undergone it or who has undergone a less invasive operation (example: coronary stent) can make the difference. How was this variable checked? or, are there any differences in the sub-samples? Lines 16-27: I recommend adding a table with items and factors loading of the scale Lines 23-40: I recommend adding a table with the correlations between CDI and other measures.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Julius Burkauskas	
Comment	**Response**
In the present research protocol the authors aim to develop and validate a measure of persistent psychological and emotional distress in cardiac patients. It might be a timely and much needed instrument for use in everyday practice of cardiac disease management.	Thank you for this comment.
First of all, the definition of cardiac distress could be elaborated on. The authors' definition states that cardiac distress is a "persistent negative emotional state rather than a transient state; involving multiple psychosocial domains; that challenges a patient's capacity to cope with living with their heart condition, the treatment of the condition, and the resultant changes to daily living; and challenges the person's sense of self and future orientation". However, it could be explained how this is different from acute stress reaction subsequent to a cardiac event or Cardiac-disease-induced Post-traumatic Stress Disorder (Vilchinsky et al., 2017) The subtle nuances of the specific types of distress might be well known to psychologists and psychiatrists, however, it might be interesting to differentiate the concepts for the general reading audience of the journal.	The following has been added: "In other chronic conditions such as cancer, diabetes and rheumatic conditions, fear of disease progression has also been identified as an important reason for distress (Herschbach P, Berg P, Dankert A, et al. 2005). This future-oriented component of distress is expressed in an extreme form in cardiac-induced post-traumatic stress disorder (CDI-PTSD) with Vilchinsky and colleagues noting that fear of death dominates the experience of patients with CDI-PTSD (Vilchinsky, Ginzburg, Fait, & Foa, 2017). Traumatic components of a cardiac event are the abruptness of the event, the risk of death, and a strong sense of loss of control and helplessness during the event (Vilchinsky, Ginzburg, Fait, & Foa, 2017). These reactions, coupled with the experience of surgery can lead to significant anxiety associated with death or recurrence, as well as anger, sadness and grief (Vaccarino & Bremner, 2016), all symptoms associated with PTSD (Cotter, Milo-Cotter, Rubinstein, & Shemesh, 2006). Differentiating distress from cardiac disease induced-PTSD (CDI-PTSD), however, are a range of additional psychosocial factors such as challenges to people's coping with daily living, the impact of social isolation, role transitions and challenges, and cognitive issues.
Another important issue which should be addressed in a more elaborate manner is the guidelines for questioning and managing stress related CAD risk factors, which currently exist. For example, the recent guidelines for cardiovascular disease prevention in clinical practice (Piepoli et al., 2016) already contain	Thank you for this suggestion. The section just before the aims now reads: "While the Joint ESC Guidelines psychosocial screen is an excellent start in this regard (Piepoli et al 2016) and provide an indicator for a health professional that psychosocial support is warranted, a measure is

core questions for the assessment of psychosocial risk factors. These questions already address mental distress issues quite broadly, providing evidence based line of questioning in the topics considering not only anxiety and depression, but also post MI PTSD symptoms, hostility, distressed personality characteristics and social isolation. It is suggested that the authors consider what more could be achieved if a measure of persistent psychological and emotional distress were to be created.	needed that enables a cardiac psychology professional to clearly identify priority areas in order to offer a timely tailored intervention for a distressed patient (Pedersen & Andersen 2017; Richards et al 2017). Using the CDI, health professionals will be able to identify key clusters of psychological, eotional and social concern to address with patients, post-cardiac event at a depth not afforded by one or two questions per construct as in the ESC core questions for the assessment of psychosocial risk factors in clinical practice (Piepoli et al 2016). For good clinical intervention, we need to know not just that people are anxious, but they are anxious about. Similarly, what is it that they fear: death, loss of function, loss of role, loss of intimacy? Achieving this degree of granularity to guide intervention is the point of the Cardiac Distress inventory. “
With regards to methodological issues of the questionnaire concept, there is a chance that patients with CAD might not answer the questionnaire aiming to address emotional difficulties. A study by Ketterer et al. (2018) showed that the use of a significant other in assessing psychosocial/emotional distress in males may confer greater accuracy, and therefore predictive power for clinical endpoints.	Thank you for this comment. The Ketterer study is an important one and the observation about the importance of collateral validation is well made. The lead author’s own work on psychological testing of matched pairs of patients and carers in end stage renal failure and on mothers and fathers of children with brain tumours has also shown discrepancies as well as validation, which need to be addressed in couple or family interventions. The present development and validation study will compare male and female responses and it is hoped that the resultant Cardiac Distress Inventory will be used in future studies of carers/ patients or other matched pairs.
It also crucially important to methodologically address other aspects of why it is necessary to have such a scale. Is this scale going to predict some sort of stress induced impairment or be a marker of mortality risk or lower HRQoL? Again the impact of stress on patient-oriented outcomes has been quite well investigated in this particular population. The authors of this manuscript are encouraged to provide a broader scope showing how this questionnaire might fit into clinical practice as well as research.	Thank you for this comment. The clinical applicability of the CDI is canvassed in the Summary. Additions have been made to the beginning of this section to make clearer the point of difference of the CDI. This now reads: “Cardiac distress is complex and various aspects of cardiac distress have been shown to be common among cardiac patients. Before cardiac distress can be treated effectively, it needs to be properly measured by a reliable, valid and sensitive instrument. Stress is increasingly being recognised as a prognostic factor in those with pre-existing cardiovascular or cerebrovascular disease (Kivimaki & Steptoe, 2017) and stress management in cardiac rehabilitation shows promise (Blumenthal et al., 2016). Even so, we are yet to see the totality of cardiac distress, in all of its complexity, being addressed in this way. The primary aim of the project, therefore, is to develop a new clinical measure which health professionals can use to identify and assess cardiac distress.”

This leads to another important issue related to the methodology of the proposed questionnaire. I am not sure the use of an 'Emotional Thermometer' is the best solution for measuring cut-off scores. I understand the logic, however, perhaps some sort of gold standard measure such as the 'MINI Neuropsychiatric Interview' or the 'Sheehan functional impairment scale due to stress' should be used for the cut-off results to show important and clinically significant norms.	Thank you for the opportunity to clarify. The Emotional Thermometers (ET's) are not in themselves being used to determine a cut off score for the CDI. The comparison of cut off scores is exactly that – a comparison, to determine whether the ETs expressed as the sum of the 4 thermometers (ETsum) provides a useful brief measure for use in clinical practice, as has been found in cancer treatment settings and as has been argued, is applicable in CVD settings (Mitchell, A. J., Morgan, J. P., Petersen, D., Fabbri, S., Fayard, C., Stoletniy, L., & Chiong, J. (2012). Validation of simple visual-analogue thermometer screen for mood complications of cardiovascular disease: the Emotion Thermometers. *J Affect Disord, 136*(3), 1257-1263). Once the CDI is finalised we look forward to testing against established gold standard measures, but the comparison above is part of the development of the CDI.
The authors should also address whether they expect the scale to be multi or uni-dimensional, as this raises issues broadly discussed in the development of other questionnaires (e.g. Riley et al. 2011).	The following has been inserted after the section describing item generation: "Consistent with the approach taken to the PROMIS item bank development and testing (Riley et al 2011), and our prior conceptualisation of the primary construct of cardiac distress as a multifactorial construct, we expect that the *Cardiac Distress Inventory* will be a multidimensional measure incorporating emotional, belief, behavioural, cognitive and social domains (Jackson et al 2018) "
It is also mentioned that the questionnaire will be translated into other languages. An explanation of validation and harmonisation of standards to be adhered to during this task is also recommended.	The following text has been added: "Methods for translation vary (Kinzie & Manson 1987; Beaton et al 2000) but we will adopt the following strategy. The CDI will be translated independently by two bilingual cardiac psychologist clinician / researchers. These translations will then be back translated into English by a bilingual psychologist independent of the two original translators and not familiar with the CDI study. These back translations will be reviewed by a subgroup of the investigators. Discrepancies will be resolved by consensus between the original translators and the review subgroup."
I would encourage the authors to consult a recent paper by Boateng et al. (2018) to ensure they adhere to the best practices in testing psychometric properties of a questionnaire.	Thank you for this suggestion. We believe that the scale development and validation protocol conforms to the Boateng et al (2018) standard and this is reflected in the following addition to the text after the Method heading: "The method described in this protocol for development and validation of the *Cardiac Distress Inventory* conforms, we believe, to the

	'best practices' for undertaking such a task, outlined by Boateng and colleagues (Boateng at al 2018)."
Overall, this is an important and much needed line of research. However, a more detailed explanation of aims would greatly improve the current version of the protocol.	Thank you for the comment. We believe that the additions and clarifications now address the need for a stronger rationale.
Reviewer 2: Stefanie Duijndam	
Comment	**Response**
The aim and reasoning for the development of the CDI are well described. In my opinion it is an important step to develop such a questionnaire, and the way the authors are planning to conduct the study are well thought of and statistically sound.	Thank you for this comment.
With regard to research ethics, the protocol number is described in the abstract, but not in the main text. Please describe that in the main text as well.	The sentence "This protocol has been approved by the Monash Health Human Research Ethics Committee (Approval number – RES-19-0000631L-55979 0)" has been added below the aims.
The authors are missing a very important paper in their protocol. The claim that "no currently existing measure would enable a psycho-cardiology professional to identify priority areas clearly enough to offer timely tailored psychosocial intervention for a distressed patient" is in my opinion not completely true, given that a screening tool for psychosomatic problems in cardiac patients already exists: van Montfort et al. 2017. Validity of the European Society of Cardiology's Psychosocial Screening Interview in Patients With Coronary Artery Disease-The THORESCI Study. Psychosomatic Medicine, 79 (4), 404-415. This paper describes the validity of a screening tool, which can be used to assess distress in cardiac patients. Please include this paper in your protocol as well.	Thank you for pointing out this important paper which we inadvertently missed. This measure has been added and components from it not already mentioned have been included. This section now reads: "Examples of cardiac-specific measures include the Cardiac Depression Scale[29] , the Cardiac Event Threat Questionnaire[30], the Cardiac Anxiety Questionnaire[31], the MacNew Quality of Life measure[32] , the Screening Tool for Psychological Distress (STOP–D)[33], the Myocardial Infarction Dimensional Assessment Scale (MIDAS)[34] and the European Society of Cardiology (ESC) brief (15-item) screen of psychosocial risk factors for cardiac patients (REF). These measures collectively assess a range of features associated with cardiac distress such as impaired quality of life, anxiety, depression, fear, death anxiety, illness-related dependency, feeling unable to cope, work and family stress, worrying levels of pain, social isolation and low perceived social support, anger and Type D personality. However, there remains no single comprehensive assessment of the multiple dimensions of cardiac distress as we have defined it (REF). Whie the ESC psychosocial screen is an excellent start in this regard, a measure is needed that would enable a cardiac psychology professional to clearly identify priority areas to offer a timely tailored intervention for a distressed patient[35, 36]." Reference added: van Montfort et al. 2017. Validity of the European Society of Cardiology's Psychosocial Screening Interview in Patients With Coronary Artery

	Disease-The THORESCI Study. Psychosomatic Medicine, 79 (4), 404-415.
In the protocol it says that "No identifying information will be collected as no patient follow-up is required". I understand that no identifying information will be collected, but the reasoning seems odd to me. Especially given that test-retest reliability will be calculated, for which you will need a follow up measure.	Thank you for picking this up. Ethics approval was dependent on there being no identifying information collected as it was a measurement development study rather than an intervention study, therefore there will be no test-retest undertaken. This had remained in the manuscript from an earlier draft and all reference to test-retest has been removed from the abstract, main text and Table 1.
Reviewer 3: Giada Rapelli	
Comment	**Response**
The study aims to develop a specific scale on distress for cardiological patients. Although the objective is specific and important to pursue, the authors do not allow access to the choices made step by step in the choice of items and in the validity concurrent with other scales.	Thank you for the comments, but we need to emphasise that this is a **protocol** paper that describes what we intend to do, i.e. to develop and validate the *Cardiac Distress Inventory (CDI)*. The detailed information on choices made, for example in item selection and validation against other measures in the proposed method such as the K6, will be reported in a follow-up paper. This **results** paper will describe the results of the item generation process, the validation measures and psychometric properties of the resultant CDI, and the development of the short form screener version of the CDI.
Lines 29-34: I would also add the fear of disease progression, a construct much investigated in the psychological literature among cardiopaths and even in their caregivers!	The list is of constructs relate to cardiac-related studies. This is made clearer in the text with additional text in line 29: " A small number of studies *of cardiac patients,* however...". A new sentence has been added: "In other chronic conditions such as cancer, diabetes And rheumatic conditions, fear of disease progression has also been identified as an important reason for distress. This future-oriented component of distress is expressed in an extreme form in cardiac-induced post-traumatic stress disorder (CDI-PTSD) with Vilchinsky and colleagues noting that fear of death dominates the experience of patients with CDI-PTSD ". References added: Herschbach P, Berg P, Dankert A, et al. Fear of progression in chronic diseases: psychometric properties of the Fear of Progression Questionnaire. *J Psychosom Res* 2005; 58: 505-511. Vilchinsky, N., Ginzburg, K., Fait, K., & Foa, E. B. (2017). Cardiac-disease-induced PTSD (CDI-PTSD): A systematic review. *Clinical Psychology Review, 55*(Supplement C), 92-106.
Line 34: I would also deepen the cardiac-induced post-traumatic symptoms	Done. See above

Lines 17-30: I would do a detailed examination of what each scale analyzes, perhaps with a table, and given the scope of the study I would highlight the novelty that the study brings	As this is a **protocol** only, the scales will be reported in a **results** paper (see the 'Statistical analysis for the trial' section Part A- Establishing dimensions of the CDI
Lines 12-17 having undergone surgery compared to those who have not undergone it or who has undergone a less invasive operation (example: coronary stent) can make the difference. How was this variable checked? or, are there any differences in the sub-samples?	When the data analysis is undertaken, event type and procedure will be analysed as subtypes against all measures: Trial version Cardiac Distress Inventory, Emotion Thermometers, PHQ4, K6 and STOP-6. None of these analyses can be reported here as this is a **protocol** paper and not a **results** paper.
Lines 16-27: I recommend adding a table with items and factors loading of the scale	None of these analyses can be reported here as this is a **protocol** paper and not a **results** paper.
Lines 23-40: I recommend adding a table with the correlations between CDI and other measures.	None of these analyses can be reported here as this is a **protocol** paper and not a **results** paper.

VERSION 2 – REVIEW

REVIEWER	Julius Burkauskas Lithuanian University of Health Sciences, Neuroscience Institute, Laboratory of Behavioral Medicine.
REVIEW RETURNED	10-Apr-2020

GENERAL COMMENTS	The authors have done a very good job in describing and helping the reader to better understand their aim to develop and validate a measure of persistent psychological and emotional distress in patients with CAD.

REVIEWER	Stefanie Duijndam Tilburg University, the Netherlands
REVIEW RETURNED	20-Apr-2020

GENERAL COMMENTS	I have reviewed this protocol paper for the second time, and I am satisfied with the changes that are made. The authors clearly elaborate on their ideas and are strong in their arguments for the development of this questionnaire. It is a very important topic and I think this questionnaire will be helpful in identifying cardiac distress in cardiac patients, which in turn helps cardiac/medical psychologists in treating these patients.

REVIEWER	Giada Rapelli Università Cattolica del Sacro Cuore – Milan
REVIEW RETURNED	08-Apr-2020

GENERAL COMMENTS	The aim for developing the CDI are well described. I think that the article has improved significantly after revision. Well done!