

# **Depression, Anxiety and Morbidity Outcomes After Cardiac Surgery**

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## SUMMARY

Depression and heart disease are among the top ten causes of an estimated 56 million deaths throughout the world (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006). Projections by the World Health Organisation indicate that depression and cardiac disorders will indeed remain among the top ten leading causes of disease burden by the year 2020 (Lopez et al., 2006; Murray & Lopez, 1997). The extant literature describes a prognostic association between depressive symptoms and adverse coronary artery disease (CAD) outcomes (Barth, Schumacher, & Herrmann-Lingen, 2004; Rugulies, 2002; Suls & Bunde, 2005; Van der Kooy et al., 2007). These findings extend to persons having undergone cardiac revascularisation surgery (Connerney, Shapiro, McLaughlin, Bagiella, & Sloan, 2001) and have prompted various consensus panels to call for routine depression assessment among heart disease patients (Ballenger et al., 2001; Davidson et al., 2006; Lichtman et al., 2008).

By comparison to depression, anxiety has attracted a smaller share of empirical investigation and consensus panel support with respect to heart disease morbidity outcomes. This is particularly the case with regard to heart disease patients who have undergone cardiac surgery. In fact, one unanswered question to date is whether or not anxiety is related to morbidity after cardiac surgery to the same degree as has been described for depression. Notwithstanding substantial interrelation, comorbidity, and diagnostic symptom overlap between affective states and diagnostic disorders (Clark & Watson, 1991), depression and anxiety have rarely been examined concurrently among heart disease patients (Kubzansky & Kawachi, 2000; Smith & Cundiff, in press; Suls & Bunde, 2005). Thus a second unanswered question to date is whether the associations between cardiac morbidity and anxiety and depression remain after controlling for symptom interrelation and shared variance. To sufficiently address these limitations cardiac research requires timely consideration of empirically validated and contemporary understandings of affect. Adoption of such theoretical frameworks would ensure examination of the unique and therefore discriminating symptomatology of depression (e.g. anhedonia/low positive affect) and anxiety (e.g. somatic tension/physiological hyperarousal) *per se* (for reviews see Clark & Watson, 1991; Craske et al., 2009). Likewise, investigation of general distress symptoms, those empirically demonstrated to underlie and account for shared variance between depression and anxiety, is essential.

The cardiac samples described herein were exclusively comprised of persons scheduled for cardiac surgery, most commonly, coronary artery bypass graft (CABG) surgery. The current body of work was designed to investigate the individual effects of

depression, anxiety and general distress on CABG patients' morbidity outcomes after cardiac surgery. Explicitly, throughout the research program attempts were made to measure general and non-specific distress along with unique depression and anxiety symptoms, that is, anhedonia/low positive affect and somatic tension/physiological hyperarousal respectively. Therefore, this dissertation describes perhaps the first attempt to concurrently examine core discriminating depressive and anxious symptoms, under an empirically validated framework, with respect to heart disease patients and also cardiac surgery outcomes. Eight separate but related studies are presented here; seven are published and one is submitted for publication.

Study One reports the association between preoperative depression, anxiety and general distress in relation to all-cause mortality after CABG surgery. The nearly twofold increased mortality risk attributable to anxiety, but not depression or distress, emphasises the requirement to expand psychosocial risk factor investigation beyond depression. Study Two investigates psychosocial risk factors for cardiac surgery related hospital readmission within six months of CABG surgery. A significant increased risk for readmission was found for preoperative anxiety and postoperative depression, even after adjustment for general distress. The findings highlight a differential pattern of association dependent on the timing of psychosocial risk factor assessment. Study Three followed up patients six months after CABG surgery and documents the association between perioperative depression and reduced quality of life, while no significant association was evident for anxiety and general distress at perioperative assessment. Study Four describes a serial assessment of neuropsychological function six months and five years after CABG surgery by comparison to a non-surgical community control group. The study shows no support for a consistent association between depression, anxiety and distress and the neuropsychological test scores that were, on average, significantly lower than those in a non surgical control group. Study Five describes a significant association between anxiety and increased odds for in hospital atrial fibrillation arrhythmias after CABG surgery.

Study Six, Study Seven and Study Eight describe the results of a prospective cohort of N = 158 CABG patients. Firstly, Study Six reports increased odds for developing delirium attributable to preoperative major depressive disorder, but not generalised anxiety/worry disorder or panic disorder. In Study Seven, the combined morbidity and mortality outcome described by the Society of Thoracic Surgeons (Shahian et al., 2009a) was investigated with respect to affective disorders, their characteristic symptoms, and personality traits. Findings suggested that increased odds for morbidity were associated with generalised anxiety disorder and trait NA.

To further explore depression and anxiety dimensions among cardiac patients, the final study investigated the receiver operating characteristics (ROC) of self-report measures of low positive affect, somatic tension/anxious arousal, and Type D personality in relation to diagnostically ascertained affective disorders. It was found that the affect dimension ROCs performed best in the prediction of affect concordant disorders (e.g. anxious arousal and panic disorder) supporting theoretical models of affect.

The present dissertation suggests that depression, anxiety and general distress exhibit discrete associations with cardiac surgery outcomes. The distinct pattern of results may in part be due to the theoretical conceptualisation of anhedonic depression, anxious arousal and general distress (i.e. NA); the latter is theorised to explain the interrelation between depression and anxiety emotions and disorders. Other factors that have potentially impacted upon the associations with cardiac outcomes include whether self-report measures capture trait or state distress, whether such measures were dichotomised or examined as continuous variables, and whether a diagnostic interview was performed. Also, the distress assessment timing would have influenced the pattern of results (e.g. preoperative, postoperative, six-months, five years). The findings presented herein have important implications for how researchers and clinicians conceptualise, investigate and measure distress among cardiac patients with respect to morbidity outcomes. One important methodological contribution of this body of work is that a series of studies were performed employing empirically validated theoretical models of depression and anxiety. In addition, various statistical methods were described in which the effects of depression and anxiety on cardiac outcome were analysed taking into consideration the shared variance of general distress.

## DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Phillip J. Tully and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968. The author acknowledges that copyright of published works contained within this thesis (as listed below) resides with the copyright holders of those works. I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library catalogue, the Australasian Digital Theses Program (ADTP) and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

### *Chapter III: Study One*

Tully, P. J., Baker, R. A., & Knight, J. L. (2008). Anxiety and depression as risk factors for mortality after coronary artery bypass surgery. *Journal of Psychosomatic Research*, 64(3), 285-290. DOI:10.1016/j.jpsychores.2007.09.007

### *Chapter IV: Study Two*

Tully, P. J., Baker, R. A., Turnbull, D., & Winefield, H. (2008). The role of depression and anxiety symptoms in hospital readmissions after cardiac surgery. *Journal of Behavioral Medicine*. 31(4), 281-290. DOI 10.1007/s10865-008-9153-8

### *Chapter V: Study Three*

Tully, P. J., Baker, R. A., Turnbull, D., Winefield, H.R., & Knight JL. (2009). Negative emotions and quality of life six months after cardiac surgery: the dominant role of depression not anxiety symptoms. *Journal of Behavioral Medicine*, 32(6), 510-522. DOI 10.1007/s10865-009-9225-4

### *Chapter VI: Study Four*

IV. Tully, P. J., Baker, R. A., Knight, J. L., Turnbull, D. A., & Winefield, H. R. (2009). Neuropsychological function five years after cardiac surgery and the effect of psychological distress. *Archives of Clinical Neuropsychology*, 24(8), 741-751. DOI:10.1093/arclin/acp082

### *Chapter VII: Study Five*

Tully, P. J., Bennetts, J.S., Baker, R.A., McGavican, A.D. Turnbull, D.A., Winefield, H.R. (2011). Anxiety, depression and stress as risk factors for atrial fibrillation after cardiac surgery. *Heart & Lung – The Journal of Acute and Critical Care*, 40(1), 4-11. DOI:10.1016/j.hrtlng.2009.12.010

### *Chapter VIII Study Six*

Tully P.J., Baker, R. A., Winefield, H. R. & Turnbull, D. A. (2010). Depression, anxiety disorders and Type D personality as risk factors for delirium after cardiac surgery. *Australian and New Zealand Journal of Psychiatry*, 44(11), 1005-1011.

*Chapter IX: Study Seven*

Tully, P. J., Pedersen, S. S., Winefield, H. R., Baker, R. A., Turnbull, D. A., Denollet, J. (in press). Morbidity and mortality after cardiac surgery and preoperative depression and anxiety: a disorder, symptom and trait analysis. *Psychology, Health & Medicine* (accepted 27/12/2010)

*Chapter X: Study Eight*

Tully, P. J. & Pennix, B. W. J. H. (Submitted). Depression and anxiety disorders, symptoms and traits among cardiac patients: a receiver operating characteristic study of the Mood and Anxiety Symptom Questionnaire.

*Appendix A*

Tully PJ. (2010) Theories of depression and anxiety and cardiovascular outcomes in psychosomatic medicine and behavioural cardiology. *Psychosomatic Medicine*, 72(2), 224-225. [Letter]

*Appendix B*

Tully PJ. (2010). Telephone-delivered collaborative care for post-CABG depression is more effective than usual care for improving mental-health-related quality of life. *Evidence Based Medicine*, 15(2), 57-58 [Invited Editorial Commentary]

*Appendix C*

Tully, P. J. (in press). On post traumatic stress disorder and neuropsychologic impairment among cardiac surgery patients, *Journal of Cardiac and Vascular Anesthesia* [Letter]

Phillip J. Tully

Signed: \_\_\_\_\_

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## DEDICATIONS

For Nanna and Poppy.

## LIST OF ABBREVIATIONS

AF, atrial fibrillation  
AUC, area under the curve  
CABG, coronary artery bypass graft  
CAD, coronary artery disease  
CHD, coronary heart disease  
CI, confidence interval  
DASS, depression anxiety and stress scales  
DS14, Type D distress scale  
Hb, haemoglobin  
HR, hazard ratio  
LVEF, left ventricular ejection fraction  
MASQ, Mood and Anxiety Symptom Questionnaire  
MINI, MINI International Neuropsychiatric Interview  
NA, negative affect  
OR, odds ratio  
PVD, peripheral vascular disease  
RCT, randomised control trial  
ROC, receiver operating characteristic  
SF-36, Medical Outcomes Study Short Form-36

## OVERVIEW

### Outline Of Candidature

The current dissertation was undertaken to fulfil the requirements of a combined Master of Clinical Psychology with Doctor of Philosophy at The University of Adelaide, South Australia, Australia. The program combines a Clinical Masters coursework load and 1,000 hours of clinical internship (equivalent two years fulltime) and a full research program for a Doctor of Philosophy (equivalent three years fulltime) within four years of candidature. The program rules stipulate that the research undertaken has to adopt a clinical psychology focus. All coursework and internship requirements of the Masters component of the program were completed successfully. The following thesis is submitted to fulfil the requirements of a Doctor of Philosophy.

### Outline Of Thesis

This thesis investigates the hypothesis that examination of interrelated negative emotions (i.e. anxiety, depression and a shared component of NA) will facilitate understanding of the individual differences that exist in health and morbidity outcomes after cardiac surgery. The present series of studies was designed to identify whether depression, anxiety or relatively non-specific distress (e.g. NA) were associated with cardiac surgery related morbidity that requires readmission to hospital, or cause neuropsychological deterioration, delirium, arrhythmia, poorer health related quality of life, or mortality. Eight separate but related studies are presented herein as chapters. Chapter I provides an overview of the literature concerning cardiac surgery and the psychogenic correlates of cardiac surgery morbidity. This chapter also argues, from a psychosomatic perspective, that cardiac outcome research must overcome the limitations of previous studies by adopting empirically validated dimensional or phenotypic measures of depression and anxiety through a theoretical framework. Chapter II provides a summary (exegesis) of the seven studies that comprise this thesis and describes each in context. Chapters III to X consist of the eight studies in manuscript format and a statement outlining each of the authors' contributions. Chapter XI provides a summary of the results and a concluding discussion based upon the entire research program.