

# Associations Between Depression and Coronary Heart Disease

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## Abstract

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Mental health, such as depression, and cardiovascular disease, such as coronary heart disease (CHD), are among two of the priority areas for health care and research in Australia and worldwide, and share many commonalities. First, depression and CHD are highly prevalent and frequently co-exist. Individually and together, they impose a significant burden of disease. Lastly, a reciprocal relationship exists, such that depressive symptoms are risk factors for the onset and progression of CHD (and vice versa), contributing to further morbidity, decreased quality of life (QoL) and mortality. The autonomic nervous system (ANS) has been implicated in the relationship between depression and CHD; and specifically, reduced heart variability (HRV; a marker of ANS activity) has been associated with both CHD and depression. Accordingly, psychological treatments with potential to enhance HRV (such as mindfulness-based cognitive therapy [MBCT]) may offer significant benefits to patients with either or both diagnoses.

This thesis utilised quantitative statistical analyses to investigate the mental health of Australians, focusing on some actual and potential relationships between CHD, HRV and depression. Three independent but related studies were undertaken. The three published manuscripts, and some additional unpublished results, are presented as chapters in the thesis.

Chapter One provides a context to this research, providing a comprehensive introduction to the literature on depression and its treatment MBCT, cardiac function and CHD, the relationships between depression and CHD, the ANS and HRV. Chapter Two outlines specific gaps identified in the literature leading to the thesis objectives. Chapter Three describes study measurement and types of psychometric questionnaires utilised. The three published manuscripts are then presented in Chapters Four to Six.

Pre-existing datasets were used to investigate the demographic, psychological and cardiac factors associated with depression (Study 1) and subsequent mortality (Study 2) in cardiac patient samples. A clinical pilot study (Study 3) was then designed and conducted to investigate changes in physiology among mental health outpatients undergoing MBCT.

A number of methods were employed to evaluate patient outcomes in the three studies. The major end points of this research focused upon patient-reported health and psychological measures (i.e., depression and QoL) and cardiac measures (i.e., HRV). Cross-sectional and longitudinal analyses were conducted using appropriate statistical analyses. Cross-sectional data were analysed using binary regression or Cox's proportional hazards model (Studies 1 and 2) whereas longitudinal data were analysed as panel data, utilising random effects model and logistic regression (Study 3).

A summary of findings, strengths and weaknesses of the three studies and their implications for future research and clinical practice form the discussion (Chapter Seven). Findings from the three studies have contributed to the epidemiological literature by providing empirical support for the relationships between depression and CHD, and between depression and mortality; and to evidence-based practice by reporting pilot data and methodological considerations concerning evaluation of the potential impact of MBCT on HRV. It is believed that results of this research will contribute to understanding the course and outcomes of depression in CHD and have implications for managing this comorbid condition.

## Declaration

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I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution 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. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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## List of Publications

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Publications are listed in order of appearance in this thesis.

Wheeler, A., Schrader, G., Tucker, G., Adams, R., Tavella, R., & Beltrame, J. F. (2013). Prevalence of depression in patients with chest pain and non-obstructive coronary artery disease. *American Journal of Cardiology*, *112*(5), 656-659. doi: 10.1016/j.amjcard.2013.04.042

Wheeler, A., Beltrame, J., Tucker, G., Air, T., Ling, L-H., & Schrader, G. (2012). Depression and 5-year mortality in patients with acute myocardial infarction: Analysis of the IDACC database. *Australian and New Zealand Journal of Psychiatry*, *46*(7), 669-675. doi: 10.1177/0004867412449875

Wheeler, A., Denson, L., Neil, C., Tucker, G., Kenny, M., Beltrame, J. F., Schrader, G., & Proeve, M. (2014). Investigating the effect of mindfulness training on heart rate variability in mental health outpatients: A pilot study. *Behaviour Change*, *31*(3), 175-188. doi: 10.1017/bec.2014.14

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## List of Abbreviations

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<b>ABS</b>	Australian Bureau of Statistics
<b>ACh</b>	acetylcholine
<b>ACS</b>	acute coronary syndrome
<b>ACTH</b>	adrenocorticotrophic hormone
<b>AIC</b>	Akaike's Information Criterion
<b>AIHW</b>	Australian Institute of Health and Welfare
<b>AMI</b>	acute myocardial infarction
<b>ANS</b>	autonomic nervous system
<b>APA</b>	American Psychiatric Association
<b>AV</b>	atrioventricular
<b>BDI</b>	Beck Depression Inventory
<b>BMI</b>	body mass index
<b>Ca<sup>++</sup></b>	calcium ion
<b>CAD</b>	coronary artery disease
<b>CBT</b>	cognitive behaviour therapy
<b>CES-D</b>	Center for Epidemiologic Studies Depression Scale
<b>CHD</b>	coronary heart disease
<b>CHF</b>	chronic heart failure
<b>CI</b>	confidence interval
<b>COPD</b>	chronic obstructive pulmonary disease
<b>CRH</b>	corticotrophin-releasing hormone
<b>CSA</b>	chronic stable angina
<b>CTAD</b>	Centre for Treatment of Anxiety and Depression
<b>CVC</b>	cardiac vagal control
<b>CVD</b>	cardiovascular disease
<b>DALYs</b>	disability adjusted life-years
<b>DHA</b>	docosahexaenoic acid
<b>DSM</b>	Diagnostic and Statistical Manual
<b>ECG</b>	electrocardiogram/electrocardiograph
<b>ECT</b>	electroconvulsive therapy
<b>EPA</b>	eicosapentaenoic acid
<b>HADS</b>	Hospital Anxiety and Depression Scale



<b>HF</b>	high frequency
<b>HPA</b>	hypothalamic-pituitary-adrenal
<b>HR<sup>1</sup></b>	heart rate
<b>HRQoL</b>	health-related quality of life
<b>HRV</b>	heart rate variability
<b>ICD</b>	International Classification of Diseases
<b>IDACC</b>	Identifying Depression as a Comorbid Condition
<b>IL</b>	interleukin
<b>IRSD</b>	Index of Relative Socioeconomic Disadvantage
<b>K<sup>+</sup></b>	potassium ion
<b>LAD</b>	left anterior descending
<b>LCA</b>	left coronary artery
<b>LDL</b>	low-density lipoprotein
<b>LF</b>	low frequency
<b>LF/HF</b>	low frequency to high frequency
<b>LOT</b>	Life Orientation Test
<b>LOT-R</b>	Life Orientation Test-Revised
<b>LVH</b>	left ventricular hypertrophy
<b>MAOI</b>	monoamine oxidase inhibitor
<b>MBCT</b>	mindfulness-based cognitive therapy
<b>MBSR</b>	mindfulness-based stress reduction
<b>MDD</b>	major depressive disorder
<b>MI</b>	myocardial infarction
<b>MSPSS</b>	Multidimensional Scale of Perceived Social Support
<b>MVD</b>	microvascular disease/microvascular dysfunction
<b>Na<sup>+</sup></b>	sodium ion
<b>NE</b>	norepinephrine
<b>NHFA</b>	National Heart Foundation of Australia
<b>NIMH</b>	National Institute of Mental Health
<b>NN</b>	normal to normal
<b>NoCAD</b>	non-obstructive coronary artery disease

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<sup>1</sup> In the published manuscript reporting Study 2 (see Chapter Five), hazard ratio was originally abbreviated to HR. However throughout this thesis, to prevent confusion, the abbreviation HR is used only for heart rate, and hazard ratio has not been abbreviated.

<b>NSTEMI</b>	non-ST elevation myocardial infarction
<b>nu</b>	normalised units
<b>NWAHS</b>	North West Adelaide Health Service
<b>OR</b>	odds ratio
<b>PhD</b>	Doctor of Philosophy
<b>PNS</b>	parasympathetic nervous system
<b>PSD</b>	power spectral density
<b>PSSS</b>	Perceived Social Support Scale
<b>PUFAs</b>	polyunsaturated fatty acids
<b>QoL</b>	quality of life
<b>QTc</b>	QT corrected
<b>RCA</b>	right coronary artery
<b>RMSSD</b>	root mean square of successive differences
<b>ROC</b>	receiver operator characteristic
<b>RSA</b>	respiratory sinus arrhythmia
<b>SA</b>	sinoatrial
<b>SAQ</b>	Seattle Angina Questionnaire
<b>SCWT</b>	Stroop Color and Word Test
<b>SDNN</b>	standard deviation of NN
<b>SF-36</b>	Short Form-36
<b>SNRI</b>	serotonin and norepinephrine reuptake inhibitor
<b>SNS</b>	sympathetic nervous system
<b>SPSS</b>	Statistical Package for the Social Sciences
<b>SSRI</b>	selective serotonin reuptake inhibitor
<b>STEMI</b>	ST-elevation myocardial infarction
<b>TAU</b>	treatment as usual
<b>TCA</b>	tricyclic antidepressant
<b>TM</b>	transcendental meditation
<b>TNF</b>	tumour necrosis factor
<b>TQEH</b>	The Queen Elizabeth Hospital
<b>UA</b>	unstable angina
<b>ULF</b>	ultra low frequency
<b>VLF</b>	very low frequency
<b>WHO</b>	World Health Organization