Mental health and the heart

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Mental health and the heart

- Depression
- Anxiety
- Post-traumatic stress disorder

- Mental ill-health as a clinical condition
- Mental ill-health as a graded experience across the population
Mental health and the heart

• Mental ill-health is associated with an increased risk of heart disease
Observational Epidemiology

1. Baseline measures of health and standard risk factors in a large cohort

2. Measure of exposure to factor being tested (depression, anxiety, PTSD)

3. Tracking of sample prospectively for mortality and morbidity

4. Multivariate analysis of predictors
Depression and future coronary heart disease

Gan et al, 2014, BMC Psychiatry

<table>
<thead>
<tr>
<th>ID</th>
<th>RR (95% CI)</th>
<th>Weight</th>
</tr>
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<tbody>
<tr>
<td>Anda et al (1983 Fatal)</td>
<td>1.50 (1.00, 2.30)</td>
<td>1.88</td>
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<td>Anda et al (1993 Nonfatal)</td>
<td>1.60 (1.10, 2.40)</td>
<td>2.05</td>
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<td>Vogt et al (1994)</td>
<td>0.94 (0.70, 1.28)</td>
<td>2.80</td>
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<td>Patt et al (1995)</td>
<td>4.54 (1.65, 12.44)</td>
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<td>Barefoot and Schroll (1995)</td>
<td>1.72 (1.18, 2.51)</td>
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<td>Sesso et al (1988)</td>
<td>1.88 (0.77, 4.59)</td>
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<td>Sesso et al (1998)</td>
<td>1.75 (0.59, 5.15)</td>
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<td>Penninx et al (1998)</td>
<td>1.55 (0.94, 2.55)</td>
<td>1.44</td>
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<td>Perkesh et al (2000)</td>
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<td>2.04</td>
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<td>Cohen et al (2001)</td>
<td>2.13 (1.24, 3.68)</td>
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<td>Cohen et al (2001)</td>
<td>2.16 (1.07, 4.32)</td>
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<td>Penninx et al (2001)</td>
<td>5.20 (1.50, 17.0)</td>
<td>0.29</td>
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<td>Wasserthiel-Smoller et al (2004)</td>
<td>1.12 (0.89, 1.41)</td>
<td>3.02</td>
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<td>Marzani et al (2005 Men)</td>
<td>1.66 (1.06, 2.60)</td>
<td>1.99</td>
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<td>Gump et al (2005)</td>
<td>1.10 (0.91, 1.32)</td>
<td>4.22</td>
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<td>Gump et al (2005)</td>
<td>1.16 (0.86, 1.52)</td>
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<td>Wulson et al (2005)</td>
<td>0.64 (0.28, 1.49)</td>
<td>0.60</td>
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<td>Kamphuis et al (2005)</td>
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<td>Ahlo et al (2010)</td>
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<td>1.13 (0.90, 1.43)</td>
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<td>3.33</td>
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<td>Davidson et al (2009)</td>
<td>1.47 (1.08, 1.99)</td>
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<td>Nabi et al (2010)</td>
<td>1.21 (0.70, 1.54)</td>
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<td>1.03 (0.65, 1.60)</td>
<td>1.60</td>
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<td>1.48 (1.09, 2.02)</td>
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<td>1.29 (1.22, 1.37)</td>
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<td>Scherren et al (2011)</td>
<td>1.43 (1.10, 1.87)</td>
<td>3.19</td>
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<td>Majed et al (2012 0-5 y)</td>
<td>0.83 (0.61, 1.13)</td>
<td>2.73</td>
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<td>Majed et al (2012 5-10 y)</td>
<td>1.53 (1.34, 1.74)</td>
<td>5.01</td>
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<td>Mittag et al (2012)</td>
<td>2.21 (1.27, 3.87)</td>
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<tr>
<td>Pequinot et al (2013 Fatal)</td>
<td>0.94 (0.66, 1.33)</td>
<td>2.35</td>
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<td>Pequinot et al (2013 Nonfatal)</td>
<td>1.14 (0.77, 1.70)</td>
<td>2.01</td>
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<td>Sun et al (2013)</td>
<td>1.26 (0.79, 2.02)</td>
<td>1.58</td>
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<td>Rahnman et al (2013)</td>
<td>1.31 (1.03, 1.65)</td>
<td>3.51</td>
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<td>Gustad et al (2013)</td>
<td>1.38 (1.19, 1.60)</td>
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<td>Huang et al (2013)</td>
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<td>Hawkins et al (2014)</td>
<td>1.30 (1.22, 1.40)</td>
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</tbody>
</table>

NOTE: Weights are from random effects analysis
Posttraumatic stress disorder and heart disease

- Meta-analysis of 6 studies involving 402,274 participants
- Follow-up periods of 2-15 years
- PTSD from a variety of traumas: early life abuse, military combat
- Hazard ratio 1.55 (95% CI 1.34-1.79)
- Reduced to 1.27 (1.08-1.49) when depression taken into account

Edmondson et al, Am Heart J, 2013
Mental health and the heart

- Depression and distress associated with increased risk of heart disease
- Depression and distress are common among patients with acute heart disease
  - Major depressive disorder 19.8%
  - Elevated symptom levels 31.1%

Thombs et al, 2006
**Prevalence of Selected Psychological Disorders in the General Population and in the Coronary Heart Disease Population**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>12-month prevalence in general population</th>
<th>Prevalence in coronary heart disease population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>7.0</td>
<td>20</td>
</tr>
<tr>
<td>GAD</td>
<td>2.9</td>
<td>5.5</td>
</tr>
<tr>
<td>PTSD</td>
<td>3.0</td>
<td>32</td>
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<tr>
<td>Insomnia</td>
<td>10</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*Note. Data presented are percentages. GAD = generalized anxiety disorder; PTSD = posttraumatic stress disorder.*

**Davidson et al, 2018**
American Psychologist
Why does acute heart disease stimulate depression and distress

- Major life event
- Brush with death and fear of dying
- Major physiological disturbance
  - Increased inflammation
  - Neuroendocrine dysregulation
  - Autonomic imbalance
Acute distress and fear of dying

- I was frightened when my symptoms came on
- I thought I might be dying
- I found my cardiac event stressful

Rated from ‘not at all true’ to ‘extremely true’
Fear of dying and inflammation during MI

Adjusted for age, gender, ethnicity, marital status, social deprivation, statin use, Grace score, days in hospital and pain

Steptoe et al, Euro Heart J 2011
Fear of dying and depression

Adjusted for age, gender, deprivation, marital status, ethnicity, smoking, adverse cardiac events, GRACE score, and depression history.

Fear of dying intensity

BDI (12 m)

Low

Moderate

High
Persistent PTSD symptoms in cardiac patients

- Longitudinal study of 213 patients after myocardial infarction
- 12.2% severe PTSD symptoms at 12 months, and 12.8% at 36 months (PSS-SR measure)
- Not predicted by clinical cardiac measures
- Predicted by
  - Depressed mood in hospital
  - Recurrent cardiac symptoms

Wikman et al, 2008
Mental health and the heart

- Depression and distress are associated with increased risk of heart disease
- Depression and distress are common among patients with acute heart disease
- Depression and distress among cardiac patients predict adverse outcomes
Unplanned rehospitalisations after AMI

- 12,312 acute MI patients
- 1,326 (10.8%) unplanned rehospitalisations within 30 days
- Risk factors (odds ratios)
  - 1.41 Previous heart failure
  - 1.34 Atrial fibrillation
  - 1.31 Elevated depressive symptoms
  - 1.26 Low LVEF

Hess et al
Circulation, 2016
Depression and prognosis after MI

Lespérance et al, Circulation, 2002
Post-myocardial infarction depression and survival

- Meta-analysis of 29 studies involving 16,889 MI patients
- Follow-up periods average 16 months
- All-cause mortality – OR 2.25 (1.73-2.93)
- Cardiac mortality – OR 2.71 (1.68-4.36)
- Cardiac events – OR 1.59 (1.37-1.85)
- Most studies adjust for cardiac health

Meijer et al, 2011
Gen Hosp Psychiatry
Marital stress and recurrence of cardiac events in CHD patients

Adjusted for age, education, heart failure, blood pressure, cholesterol, diabetes, and smoking

Orth-Gomer et al, 2000, JAMA
Anxiety following MI and cardiac outcomes

Roest et al, 2010
Psychosomatic Med
Depression and distress

Behavioural factors:
- Smoking
- Physical inactivity
- Food choice
- Adherence to advice

Cardiac health

Steptoe, 2007
Depression and Physical Illness, Oxford University Press
Adherence to aspirin in CHD patients

Rieckmann et al 2006, JACC
Depression and distress

Biological factors:
- Immune
- Neuroendocrine
- Inflammatory
- Autonomic

Behavioural factors:
- Smoking
- Physical inactivity
- Food choice
- Adherence to advice

Cardiac health

Steptoe, 2007
Depression and Physical Illness,
Oxford University Press
Inflammation and depression

Interleukin 6

Study name

Cumulative std diff in means (95% CI)

Maes Met al., 1995a
Maes Met al., 1995b
Sluzewska A et al., 1996
Maes Met al., 1997
Kagaya A 2001
Mikova O et al., 2001
Bastide AO et al., 2005
Málhota SJ et al., 2005
Fitzgerald P et al., 2006
Leo R et al., 2006
Pavon L et al., 2006
Pike JL and Irwin MR 2006
O’Brien S et al., 2007
Yang K et al., 2007
Simon MMet al., 2008
Dhabhar FS et al., 2009
Weinstein AA et al., 2010
Yoshimura R et al., 2010
Euteneuer F et al., 2011
Fomaro, Met al., 2011
Hughes MMet al., 2012
Karlovic D et al., 2012
Voderholzer U et al., 2012
Canelho LA et al., 2013
Dunjic-Kostic B et al., 2013
Frodl T et al., 2013
Hennings, A et al., 2013
O’Donovan A et al., 2013
Dahl J et al., 2014
Kéri S et al., 2014
Rudolf S et al., 2014

-0.50
0.00
0.50
1.00
Controls
Depressed

C-reactive protein

Study name

Cumulative std diff in means (95% CI)

Joyce PR et al., 1992
Sluzewska A et al., 1996
Homig Met al., 1998
Lanquillon S et al., 2000
Rothermundt Met al., 2001
Tuglu C et al., 2003
Thomas AJ et al., 2005
Kling MA et al., 2006
Häfner S et al., 2008
Cizza, G et al., 2009
Dome P et al., 2009
Piletz JE et al., 2009
Weinstein, AA et al., 2010
Hughes MMet al., 2012
Karlovic D et al., 2012
Zahn D et al., 2012
Frodl T et al., 2013
O’Donovan A et al., 2013
Kéri S et al., 2014
Rudolf S et al., 2014

-1.00
-0.50
0.00
0.50
1.00
Controls
Depressed

Haapakoski et al
Brain Behav Immun, 2015
Coronary-Artery Bypass Grafting

Inflammation and depression in CHD

• Large increases in CRP, TNFα, IFN γ and other inflammatory markers during cardiac surgery
• Magnitude of inflammatory response during surgery and acute coronary syndrome predicts cardiac morbidity
Inflammation and depression after CABG

- Study of 145 patients undergoing CABG
- Depression measured 1 month before and 12 months after surgery
- Plasma IL-6 and IFNγ measured at baseline and 1-3 days after surgery
- Salivary cortisol measured at 2 months
- Multivariate analysis of predictors of 12 month depression
IFNγ concentration after surgery

Plasma IFNγ (pg/ml)

Response tertiles

Pre-surgery  Low  Medium  High
# Inflammation and depression after CABG

## Table 1: Interferon γ and Elevated Depressive Symptoms at 12 Months

<table>
<thead>
<tr>
<th></th>
<th>Depressed at 12 Months</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interferon γ</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>4/45 (8.9)</td>
<td>1 [ref]</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>9/52 (17.3)</td>
<td>2.11 (0.55–8.03)</td>
<td>0.28</td>
</tr>
<tr>
<td>High</td>
<td>16/48 (33.3)</td>
<td>4.32 (1.21–17.96)</td>
<td>0.024</td>
</tr>
<tr>
<td><strong>Pre-surgery depressive symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>11/107 (10.3)</td>
<td>1 [ref]</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>18/38 (47.4)</td>
<td>7.14 (2.84–17.96)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>EuroSCORE, %</strong></td>
<td></td>
<td>0.92 (0.77–1.09)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Values are n (%) unless otherwise indicated.

EuroSCORE = European System for Cardiac Operative Risk Evaluation; ref = reference.
Cortisol and depression after CABG

Adjusted for Euroscore, BMI baseline BDI, and smoking

Poole et al, 2016
Psychoneuroendocrinology
Challenges in patient management

- Identification of psychological issues
  - Brief screening questionnaires
- Spontaneous recovery
- Appropriate treatment
  - What treatment?
  - When?
Treatment of depression in CHD

• Pharmacotherapy
  ➢ Selective serotonin uptake inhibitors (SSRI)
    ➢ Sertraline, escitalopram, citalopram, paroxetine
  ➢ Safe, well tolerated, though some risk of bleeding
  ➢ Moderately effective in reducing depression
  ➢ No impact on cardiac morbidity yet established

Shapiro, 2015
Current Cardiology Reports
**CBT for depression in CVD patients**

Reavell et al, *Psychosom Med*, 2018
ENRICH'D - outline

• Multicentre, randomised controlled trial of cognitive-behavioural treatment for depression and low social support in post-myocardial infarction patients

• 34,043 screened within one month of MI
  2481 patients recruited (39% depression, 26% low support, 34% both)

• Up to 6 months of individual cognitive behavioural therapy, 12 weeks of group sessions

Berkman et al, JAMA, 2003
ENRICH-D study

Cumulative Proportion

Follow-up Time, mo

No. at Risk

Usual Care  1243  1099  1031  898  670  460  265  130
Intervention  1238  1083  1010  886  669  439  280  122
Is depression in CHD different?

• New onset depression appears more cardiotoxic than recurrent or pre-existing depression
• Somatic symptoms appear more cardiotoxic than cognitive/affective symptoms
• Should we focus on depression, or mental distress more generally?
Combining exercise rehabilitation with stress management

Blumenthal et al, 2016
Circulation
Combining exercise rehabilitation with stress management

Blumenthal et al, 2016
Circulation
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Dr Tara Kidd
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St. George’s, University of London

British Heart Foundation
Medical Research Council

University College London