Wolfson Research Institute for Health and Wellbeing
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Predictors of depression among people with long term conditions

Dr Leanne Trick
Assistant Professor (Research) in Psychology, Durham University
NIHR North East and North Cumbria Applied Research Collaboration Fellow

Durham University

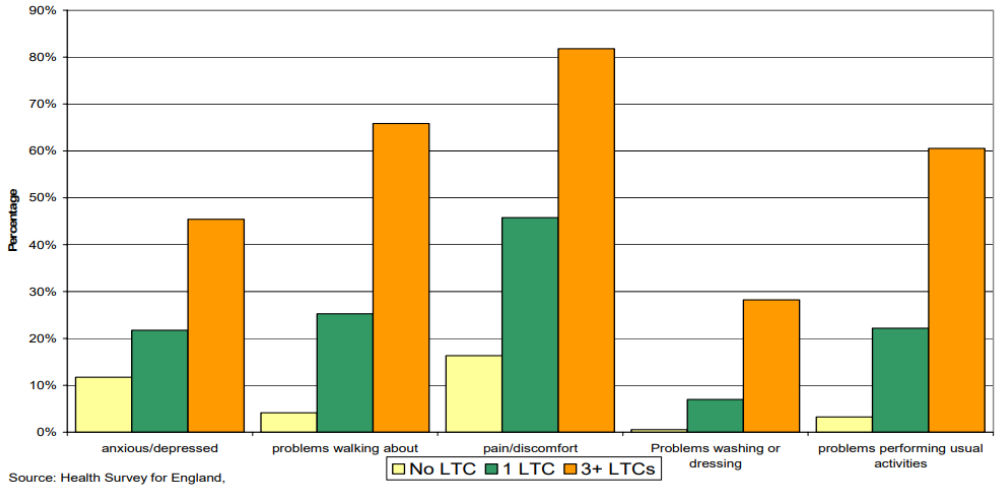
NIHR | Applied Research Collaboration North East and North Cumbria

Long term conditions (LTCs)

- Chronic conditions e.g. heart disease, diabetes, asthma
- ~26 million in UK living with at least 1 x LTC (~40%)

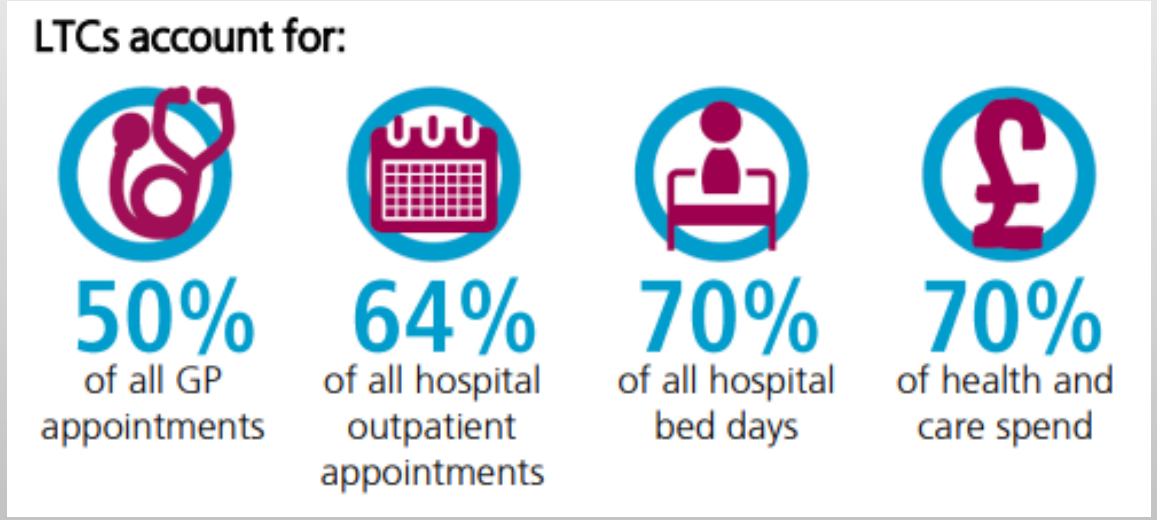
Health burden

% reporting difficulties with 5 dimensions of quality of life (no LTC, 1 x LTC or multiple LTCs)



Department of Health (2012)

Economic burden



NHS England (2018)

- **Major depressive disorder**
- Two key features
  - persistent sadness / low mood
  - anhedonia
- Other symptoms include:
  - changes in sleep or appetite
  - fatigue
  - problems concentrating
  - irritability
  - feeling guilty or worthless
  - suicidal thoughts
- Affects 5% population globally
- Second leading cause of disability

WHO (2021)

The problem of depression in LTCs

- Prevalence estimates vary from 10 – 50%
- Worse physical / medical outcomes
  - Reduced quality of life
  - Increased morbidity and mortality
  - Increased healthcare utilization and use of urgent care

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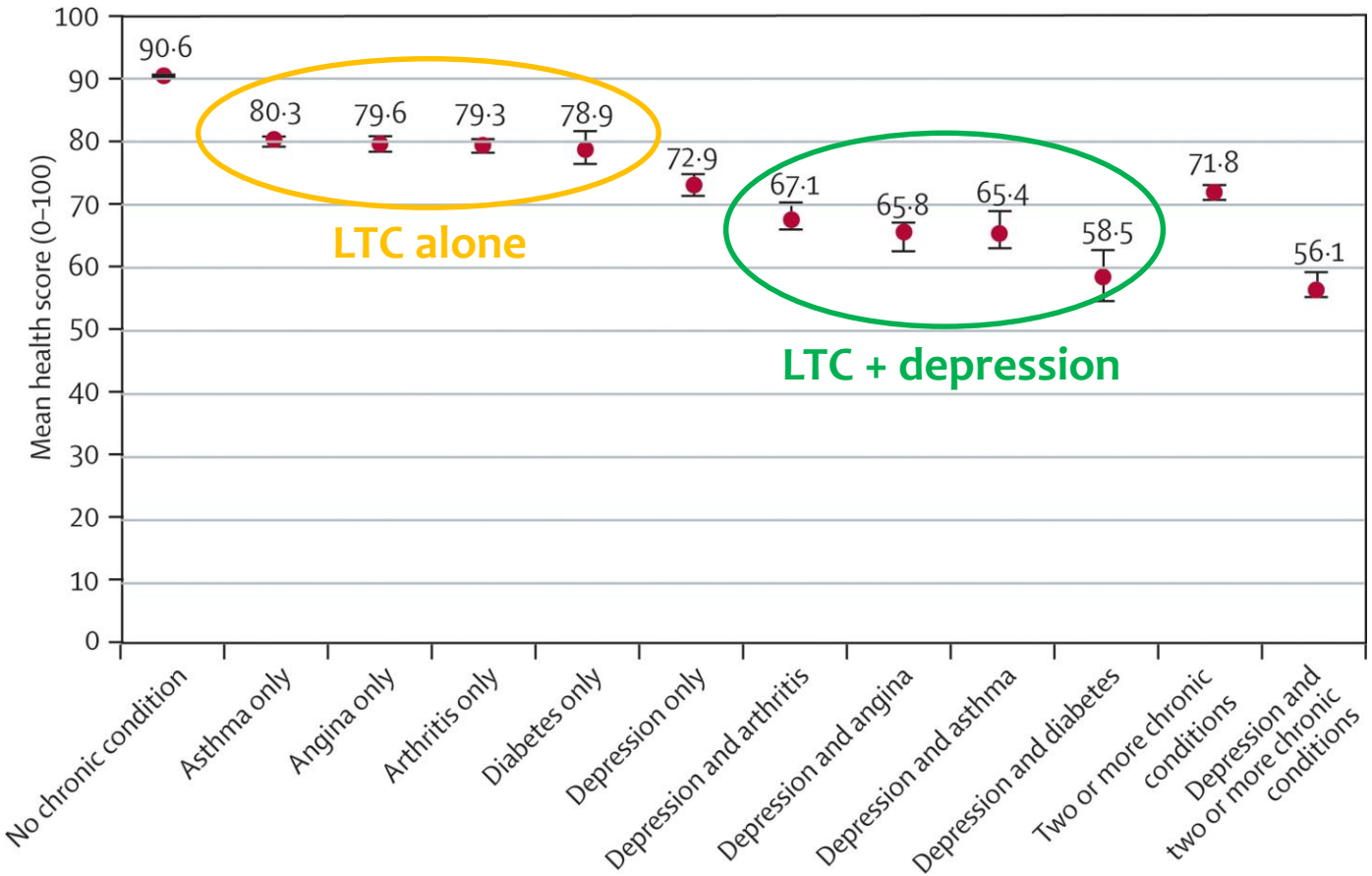

Moussavi et al. (2007) Lancet

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Treatment for depression

- **Under-recognized**
  - GP screening not routine (~27% post-MI) *Larsen et al. (2013)*
  - Inpatient healthcare providers recognize <15% cases *Huffman et al. (2006)*
  - Symptom overlap
  - Focus on physical symptoms during consultations *Coventry et al. (2011)*
  - "Normalization" of mental health symptoms
- **Under-treated**
  - ~15% access specialist psychological services *Diabetes UK (2008)*
  - Less likely to receive antidepressants or mental health referral from GP *Kendrick et al. (2009)*
- **Limited effectiveness** of pharmacological and psychological treatments
  - Small to moderate effect sizes e.g. SMD for CBT in CHD = 0.28 to 0.31 *Dickens et al. (2013)*

Nature of depression in LTCs?

- Nature and course of depression in LTCs complex
  - Can precede LTC (and may be risk factor for developing LTC)
  - Can arise as consequence of stressors related to LTC
  - Relationship could be bi-directional

- **Causes of depression in LTCs unclear**
  - Correlates of depression similar to general population?

- **Mechanism linking depression with worse physical outcomes unclear**
  - Physiological (e.g. changes in clotting, heart rate variability, inflammation, HPA-axis dysfunction)
  - Behavioural (e.g. poor adherence, worse health behaviours)

Better understanding the causes of depression in LTCs

- Identify subgroups ‘at risk’ for depression (and possibly worse physical outcomes)
- Identify novel targets for treatment
- Inform adaptations to existing treatments

→

Better treatments and improved patient outcomes

Potential to improve depression and physical outcomes

Exploring two possible mechanisms

1. Does **repetitive thought** (especially rumination) predict depression in coronary heart disease? And how?

2. Can **biases in emotional processing** explain the relationship between disease activity and depression in inflammatory bowel disease?

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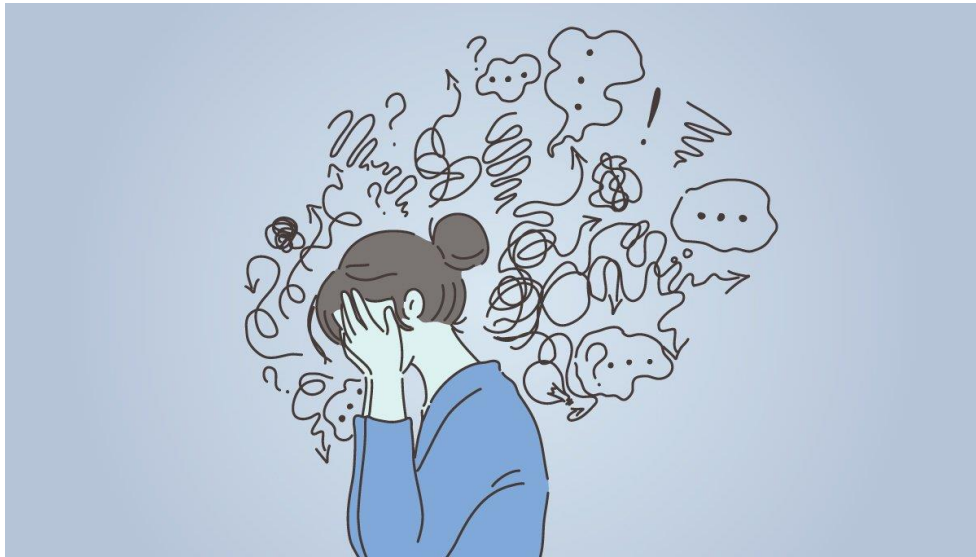
What is repetitive thought?

- Includes rumination and worry
- Repetitive, prolonged, recurrent thoughts
- Usually unconstructive and negative

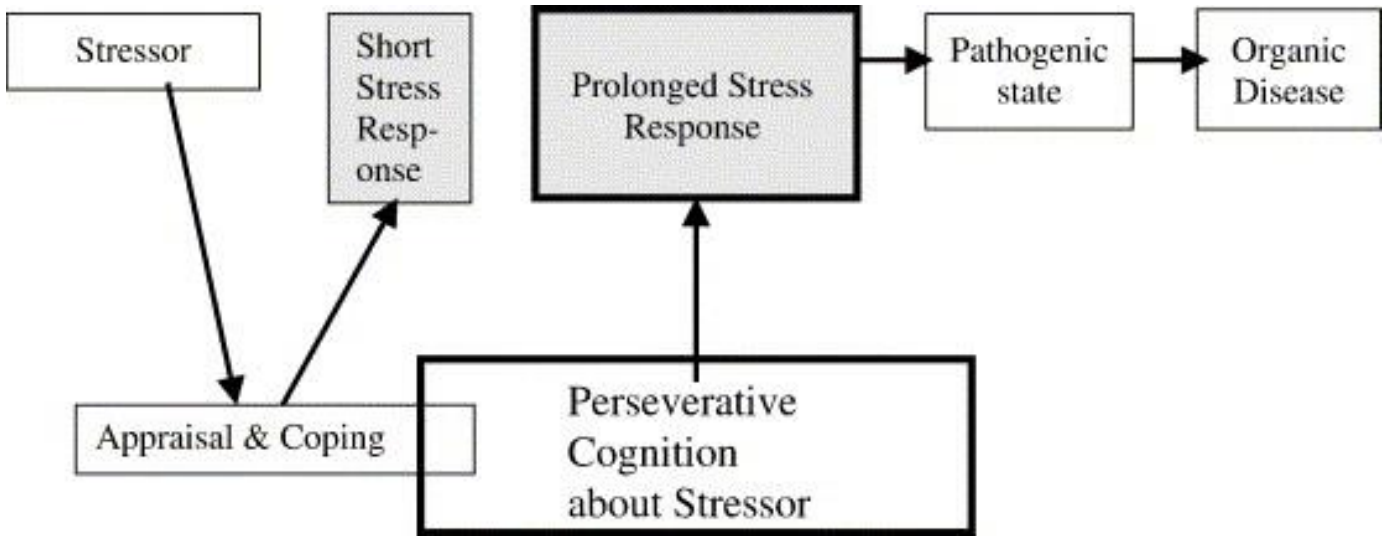
"passively and repetitively focusing on one's symptoms of distress"

Nolen-Hoeksema et al. (1997) J Pers Soc Psy



Consequences of repetitive thought

- Affective **and** physical consequences
- Vulnerability stress frameworks → amplifies effect of stressor
  - "Perseverative Cognition Hypothesis"



Brosschot et al. (2006) J Psychosom Res

- Increased health risk behaviours *Clancy et al. (2016)*

Association of repetitive thought and depression in LTCs

- Cross-sectional evidence – but causality unclear

- Systematic review of prospective studies in LTCs

✓ Association of repetitive thought with subsequent depression, anxiety and emotional distress

✗ Limitations - quality, no information on physical outcomes

Condition	Type of repetitive thought	Positive association (Repetitive thought → depression)
Cancer **Chronic pain** **Heart disease** Rheumatoid arthritis Infertility	**Catastrophizing** **Rumination** Anxious preoccupation Preoccupation with death	**14 / 25 controlled studies** Small effect sizes *(e.g. partial correlations r=0.23 to r=0.35)*

Trick et al. (2016) J Psychosom Res

Prospective cohort study in CHD

- Aims
  - Investigate prospective association of rumination with depression and health-related quality of life in people with CHD
  - Explore mechanisms by which rumination may impact on depression in people with CHD

- Main hypothesis
  - Higher rumination at baseline will predict greater depression and worse quality of life at 6 months

Potential mediators:

Social support

Problem solving

Pleasant activities

Negative cognitive bias

Method

- Design
  - Observational prospective cohort study

Baseline → 2 months → 6 months

Self-report assessments via postal survey

Depression
Health-related quality of life
Rumination
Social support
Problem solving
Pleasant activities

Diagnosis, severity of cardiac disease, functional limitations extracted from **medical records at baseline**

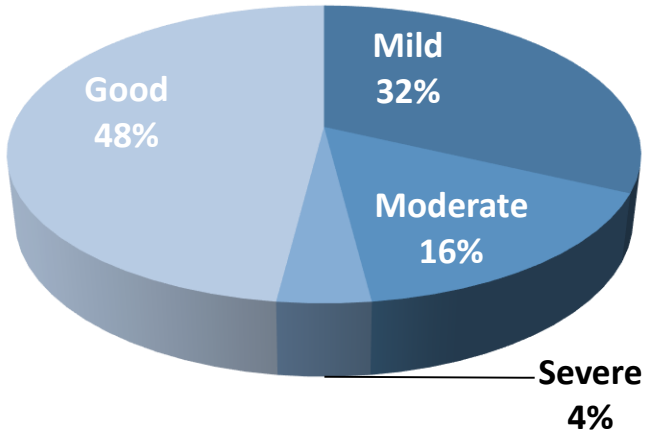
- Inclusion criteria/recruitment
  - Acute coronary syndrome
  - ≤ 6 months since hospitalisation
  - Adult inpatients and outpatients
- Measures
  - Socio-demographics (age, sex, SES, employment, education)
  - Psychiatric history
  - **Main outcome = depression score (PHQ-8)**

Results - baseline

Sample

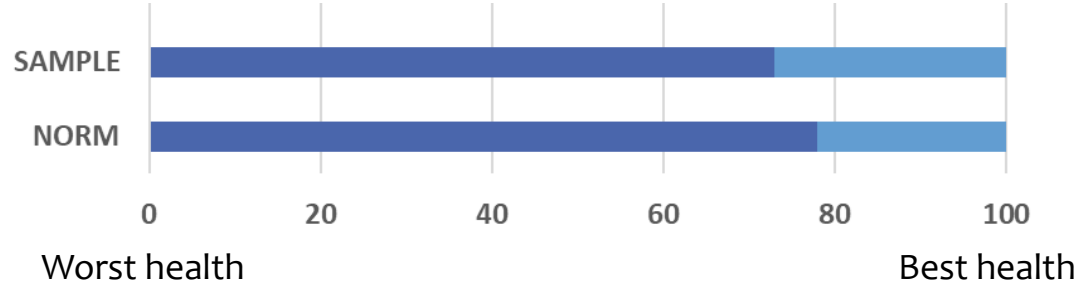
- N=169 (76% male)
- Mean age 66.8 years
- Diagnosis:
  - Angina 28%, NSTEMI 35%, STEMI 37%

Severity of heart disease
(Left ventricular function)



Depression and quality of life (QoL)

- 14.5% depressed (PHQ-≥10)
  - Younger, history of depression, lower socioeconomic status, lives alone, not in relationship, smoker, elevated CRP
- Low depression scores (PHQ = 4.3)
- QoL (EQ5D 'overall health') = 73



Results continued..

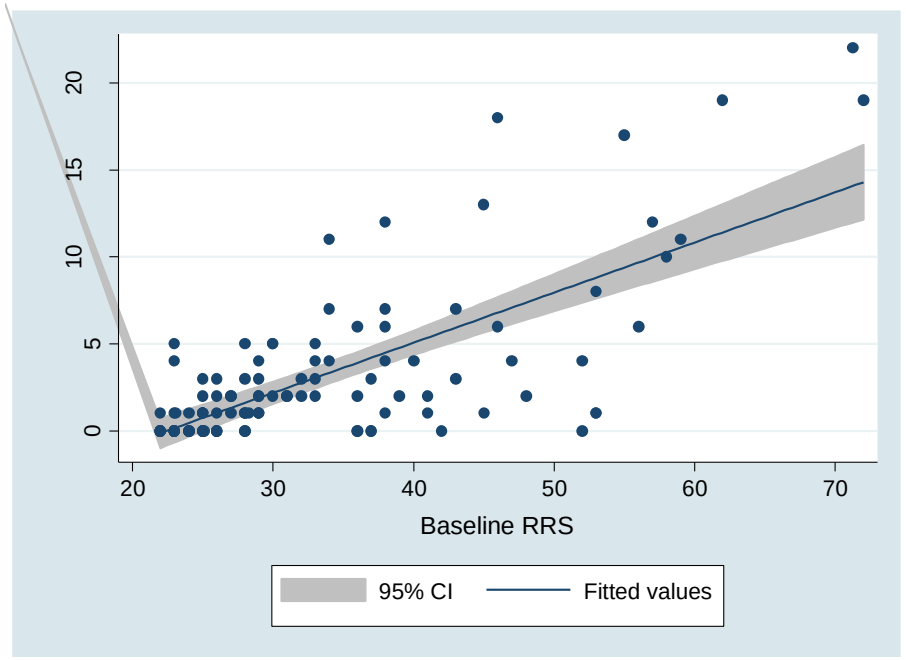
Repetitive thought associated with main outcomes at baseline

- Large correlation of rumination with depression (*r=0.55*)
- Moderate correlation of rumination with overall quality of life (*r=0.31*)

Follow-up data

- Attrition
  - N=125 at time 2 and N= 112 at time 3
  - Non-completers may have been more unwell
- No marked change over time in key variables

Baseline rumination predicts 6 month depression



RRS: β=0.20, t=2.36, p<0.05
Full model: adj R^2=0.64

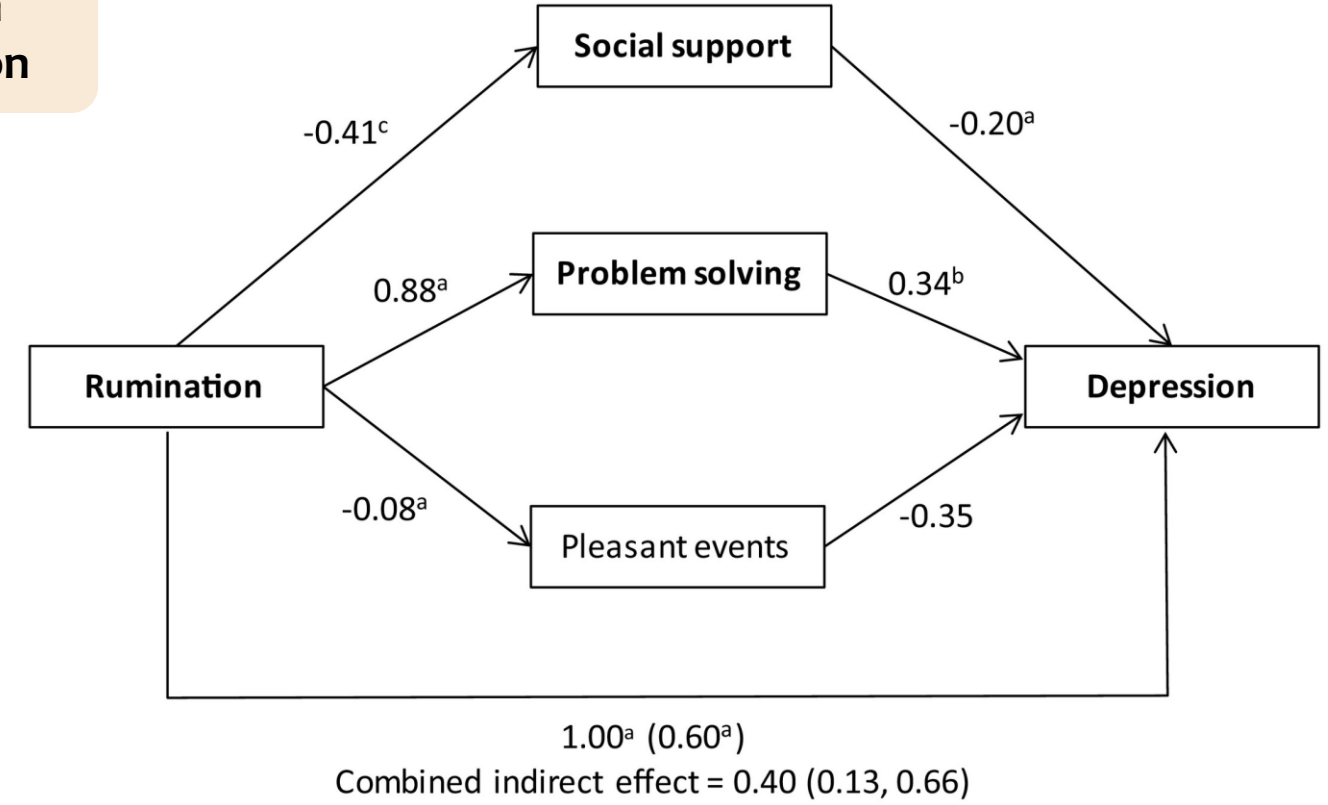
Rumination accounts for 2% of variance
After controlling for age, sex, SES, social support, severity of cardiac disease and history of depression, baseline depression

- Predictors of depression
  - Less social support
  - Greater depression at baseline
  - Rumination
- Rumination did not predict quality of life

Role of problem solving and social support

Baseline rumination → **2 month mediators** → **6 month depression**

- Potential mediating mechanisms
  - Low perceived availability of social support
  - Negative problem orientation
  - Low engagement in pleasant events



Trick et al. (2019) Gen Hosp Psych

Conclusions

- **Summary of findings**
  - Rumination is prospectively associated with depression in CHD
  - However, we did not observe any effect of rumination on quality of life
  - Problem solving may act as a partial mediator of the rumination → depression association

- **Clinical implications**
  - High ruminators could be at increased risk of depression
  - Rumination and problem solving may provide novel psychological targets for the development of evidence-based interventions to reduce depression among people with CHD

- **Future work**
  - Confirm if problem solving is a valuable target
  - Establish if problem solving training can improve depression

Exploring two possible mechanisms

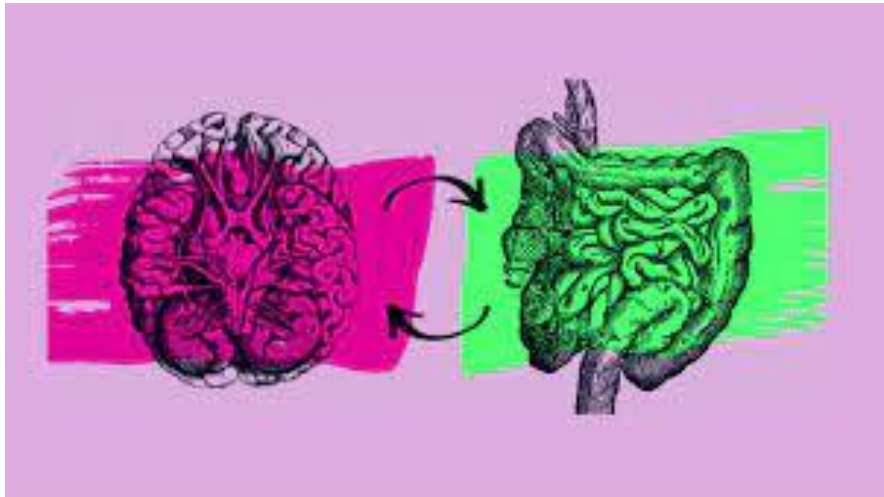
1. Does **repetitive thought** (especially rumination) predict depression in coronary heart disease? And how?

2. **Can biases in emotional processing explain the relationship between disease activity and depression in inflammatory bowel disease?**

Role of inflammation in depression

- Observational and experimental evidence
- In Crohn's disease anti-TNF-alpha drugs rapidly reduce depression ***independent of improvements in disease activity*** *Guloksuz et al. (2013)*

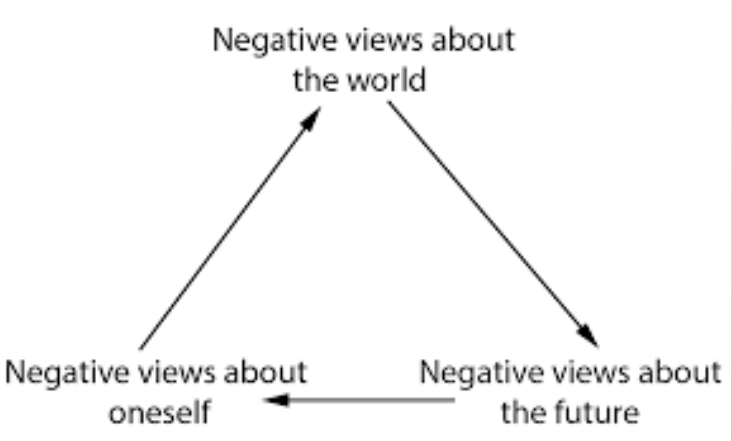
→ But, mechanism not known



Cognitive biases and depression

- Tendency to preferentially attend to and recall negative information, and to interpret events more negatively

- Negative biases in processing of emotionally salient information central to the development of depression
  - Increased biases in people with depression and ‘at risk’ of depression
  - Biases reduced with antidepressants



- *Acute experimentally induced inflammation also alters emotional processing* *Bollen et al. (2017)*

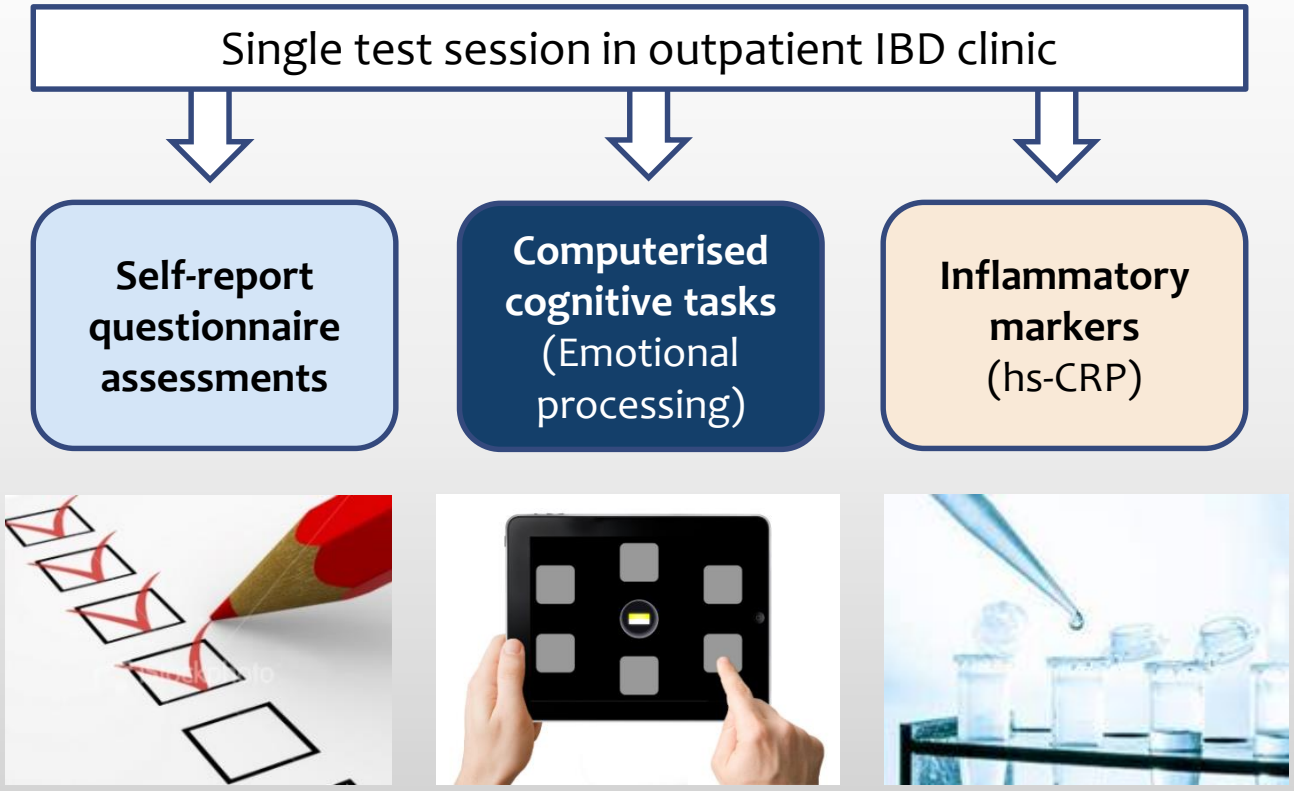
Cross-sectional pilot study in IBD

- Aims
  - Investigate factors associated with depression in IBD
  - Explore whether biases in emotional processing explain the relationship between disease activity and depression

- Hypotheses
  - ‘Traditional’ depression risk factors, disease activity, and negative biases in emotional processing will predict greater depression in people with IBD
  - The association between disease activity and depression will be mediated by negative biases in emotional recognition

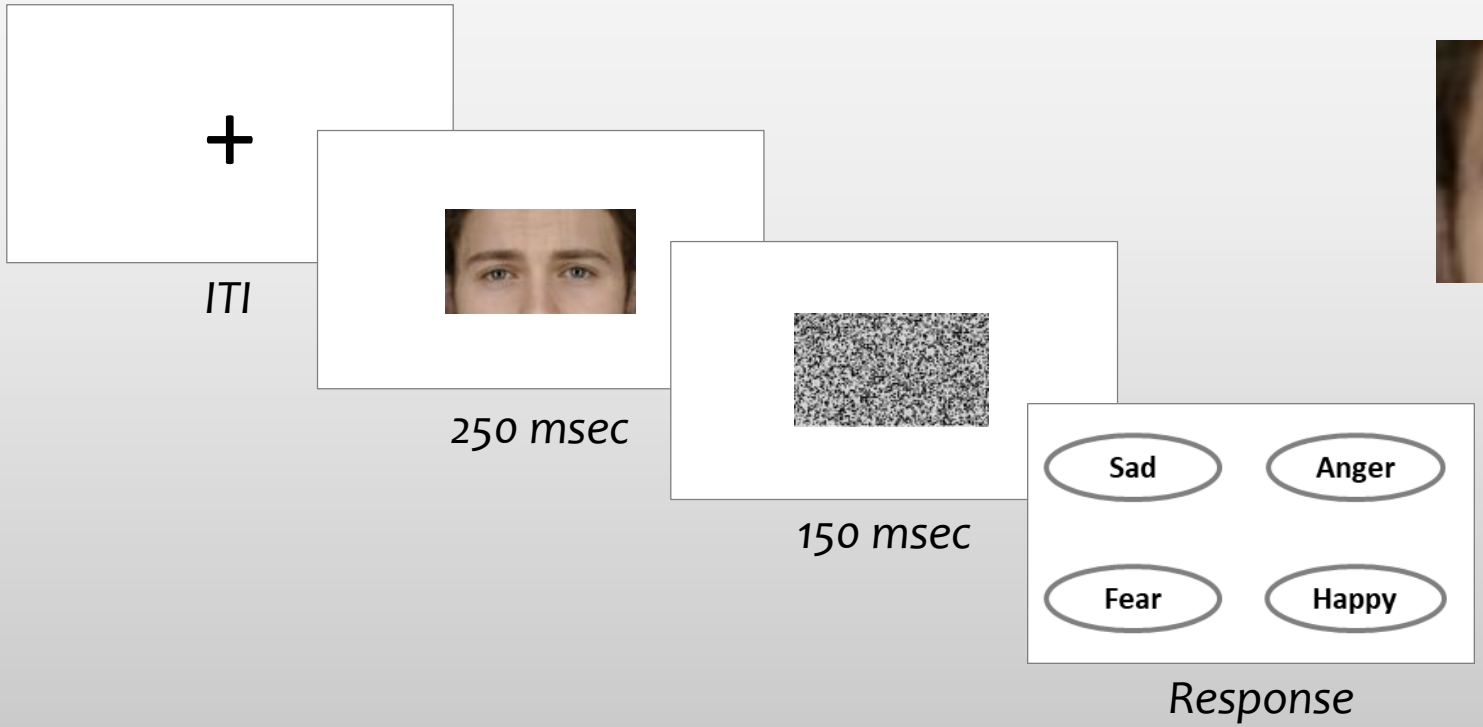
Method

- Design
  - Cross-sectional cohort study
- Inclusion criteria/recruitment
  - Crohn's disease or ulcerative colitis
  - Adult outpatients
- Measures
  - Socio-demographics (age, sex, SES, employment, education)
  - Psychiatric history
  - **Main outcome = depression score (PHQ-9)**



+ **Physician-ratings of disease activity, disease severity and current medications**

Emotional recognition task



Emotional recognition bias =
% accuracy for happy expressions minus % accuracy for sad expressions

Differences according to depression and disease status

Sample

- N=120 (68 Crohn's, 49 UC)
- Age 44 years, 52% male
- IBD duration 9 years
- Age at onset 30 years

Disease activity

- 29% had active (vs. remitted) IBD

Emotional recognition bias

- *Overall* a POSITIVE bias observed

Depression

- Low PHQ scores (mean = 5.5)
- 25% depressed (PHQ ≥10)
  - Female
  - Lack of social support
  - Active IBD
  - Worse quality of life
  - Not taking TNF inhibitors
  - Less positive emotion recognition bias

Factors associated with depression in IBD – multivariable analysis

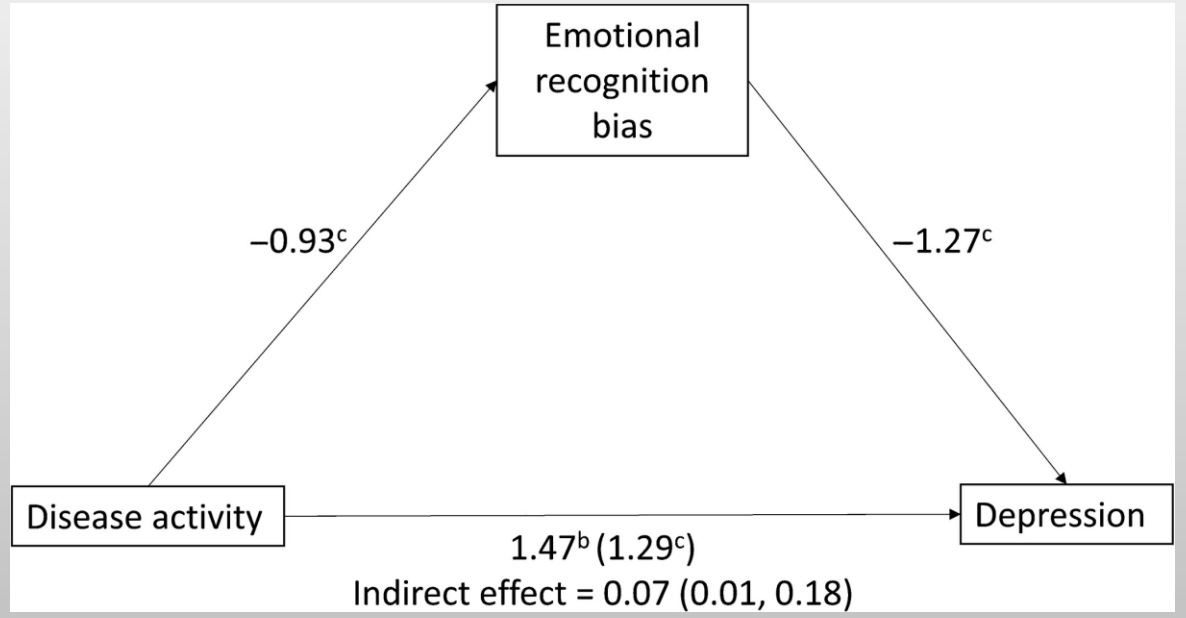
Predictors of depression status

	OR	95% CI	Sig.
1. Age	0.71	0.23-2.24	0.56
1. Sex	2.11	0.68-6.56	0.20
1. SES	0.82	0.27-2.51	0.72
1. Lack of social support	**0.25**	**0.08-0.76**	**0.02**
2. Type of IBD	1.44	0.54-3.88	0.47
2. Active disease	**3.64**	**1.14-11.60**	**0.03**
3. Less positive emotional recognition bias	0.39	0.12-1.27	0.12

Overall model fit: $\chi 2=24.9$, $p=0.001$, Cox & Snell $R^2=0.22$

NB. With disease activity removed from the model, social support and emotional recognition bias were the only significant predictors

Emotional recognition bias as a mediator of the association between disease activity and depression



Wilkinson et al. (2019) Neurogastroenterol Motil

Conclusions

- **Summary of findings**
  - Social support and disease activity predicted depression in people with IBD
  - Emotional recognition bias partially mediated the relationship between disease activity and depression

- **Clinical implications**
  - Higher than usual rates of depression in people with active IBD could be explained by biases in emotional processing
  - Emotional processing biases as a biomarker for risk of depression
  - Reducing inflammation in those with emotional processing biases could be helpful

- **Future work**
  - Findings to be confirmed prospectively....

Overall summary and conclusions

- Depression in LTCs problematic
  - Common
  - Linked with worse outcomes
  - Treatment not optimal

- Causes of depression in LTCs, and how it relates to worse physical outcomes, unclear

- Looking beyond traditional predictors of depression could help to identify:
  - Sub-groups 'at risk' of depression (and/or worse physical outcomes)
  - Novel targets for intervention
  - Opportunities for adaptations / personalised treatments

IMPROVED PATIENT OUTCOMES

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Thanks for listening!

Any questions?

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