Predicting Relapse of Depression and Anxiety after Cognitive Behavioural Therapy

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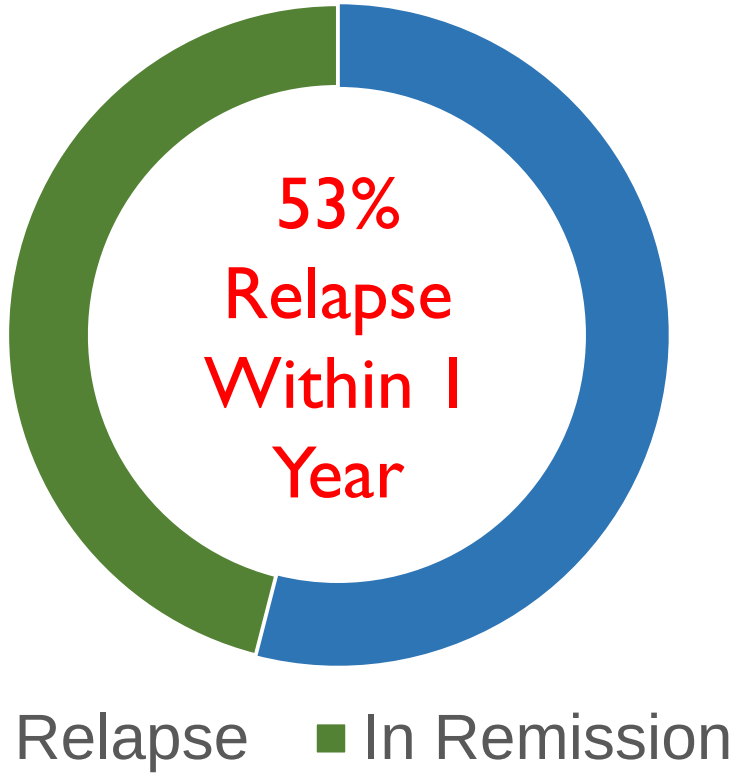
The University Of Sheffield.

Think Tank Seminar Series
University of Exeter
Friday 13th November 2020

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

Cognitive Behavioural Therapy (CBT)

- Lower rates of relapse than other interventions
- HOWEVER…
- Relapse remains common
  - (e.g. Ali et al., 2017)



Relapse - Knowledge Gap

- What causes it? Risk factors?

- Greater understanding needed
  1. More effective relapse prevention
  2. Stop the "revolving door" (Roscoe, 2019)

Two Systematic Reviews

- Review contemporary literature on predictors of relapse of …
  - Depression (Wojnarowski et al., 2019)
  - Anxiety-related disorders (Lorimer et al., 2020)

1. Estimate prevalence of relapse
2. Identify predictors

Results

	Depression (Wojnarowski et al., 2019)	**Anxiety** (Lorimer et al., 2020)
Eligible Studies		
Pooled Relapse Rate		
Meta-Analyses for Potential Predictors		

What does this tell us?

- Similar pooled relapse rates for depression and anxiety (33.4% vs 23.8%)
- Residual symptoms (*r*=0.34 vs *r*=0.35)
- Limited research in area of relapse after CBT

Limitations of Studies

- Underpowered samples
  - No depression studies sufficiently powered to detect medium effect sizes
  - Only one anxiety study powered to detect *large* effect sizes

- Heterogeneity of methods
  - Interventions
  - Relapse definition
  - Follow-up length
  - Therapy during follow-up

- No studies on PTSD, generalized anxiety disorder, specific phobia, separation anxiety disorder, or selective mutism

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Study 1

Exploring relapse using network analysis

Ben Lorimer, Dr Jaime Delgadillo, Dr Stephen Kellett - The University of Sheffield

Dr Gary Brown - Royal Holloway, University of London

Psychotherapy Research, 2020
Vol. 30, No. 5, 650–661, https://doi.org/10.1080/10503307.2019.1650980

Exploring relapse through a network analysis of residual depression and anxiety symptoms after cognitive behavioural therapy: A proof-of-concept study

BEN LORIMER [1], JAIME DELGADILLO [2], STEPHEN KELLETT [2], & GARY BROWN [3]

[1]*Sheffield Methods Institute, University of Sheffield, Sheffield, UK;* [2]*Clinical Psychology Unit, Department of Psychology, University of Sheffield, Sheffield, UK &* [3]*Department of Psychology, Royal Holloway, University of London, Egham, UK*

(Received 27 February 2019; revised 26 June 2019; accepted 29 June 2019)

What does this tell us?

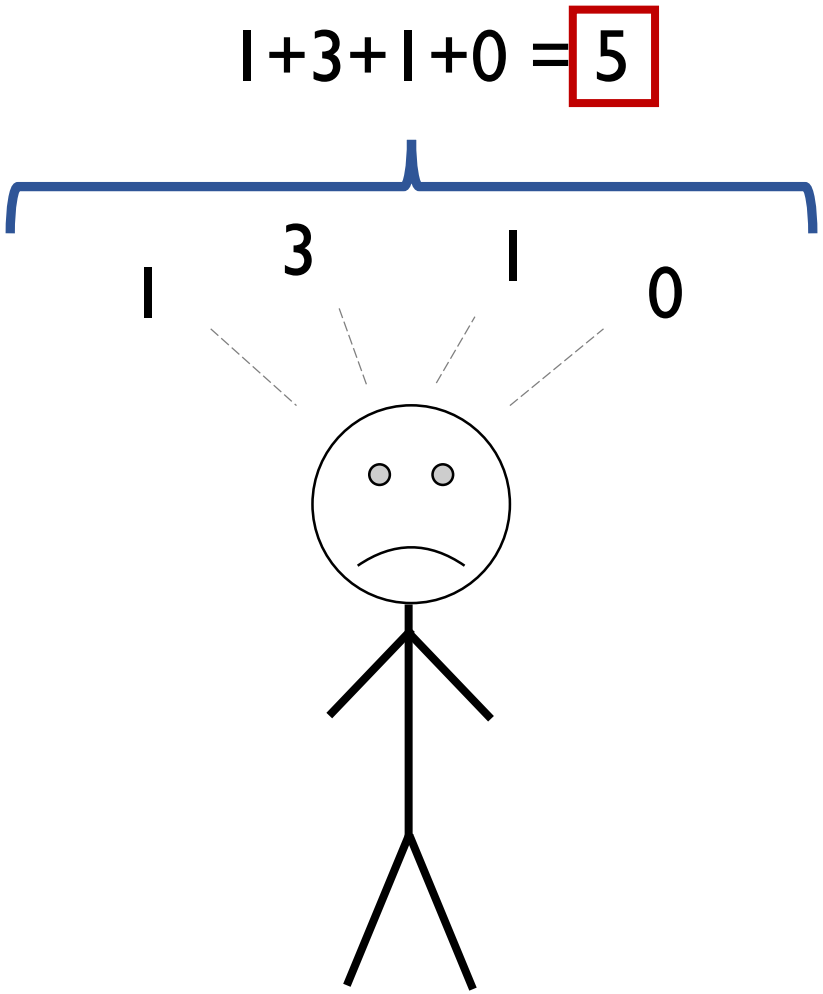
- Similar pooled relapse rates for depression and anxiety (33.4% vs 23.8%)
- **Residual symptoms (*r*=0.34 vs *r*=0.35)**
- Limited research in area of relapse after CBT

What are Residual Symptoms?

	PHQ-9	GAD-7
Clinical Threshold	10	8
Residual Symptoms	Score of 5-9	Score of 5-7

- Presence of residual symptoms at end of treatment significantly predicts relapse (Ali et al., 2017)

Residual Symptoms



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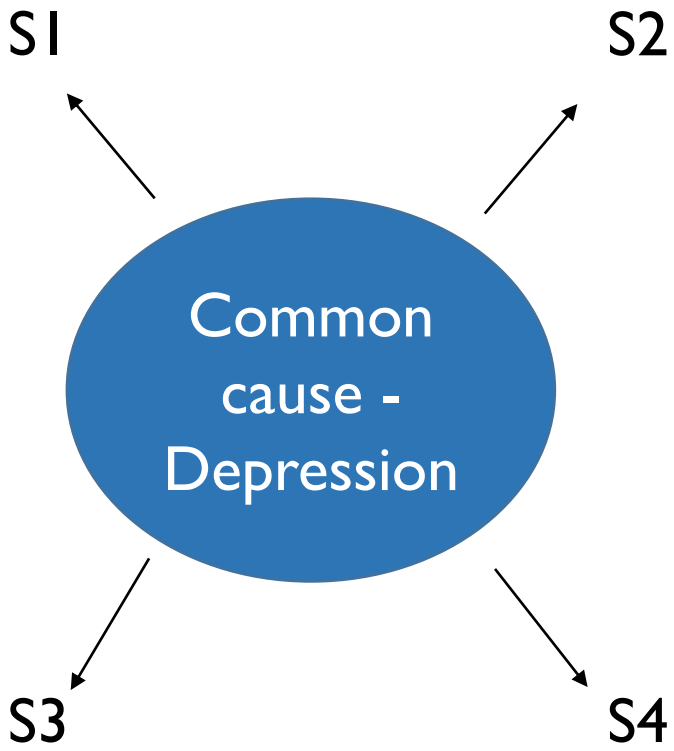


Rethinking the Sum-Score Approach

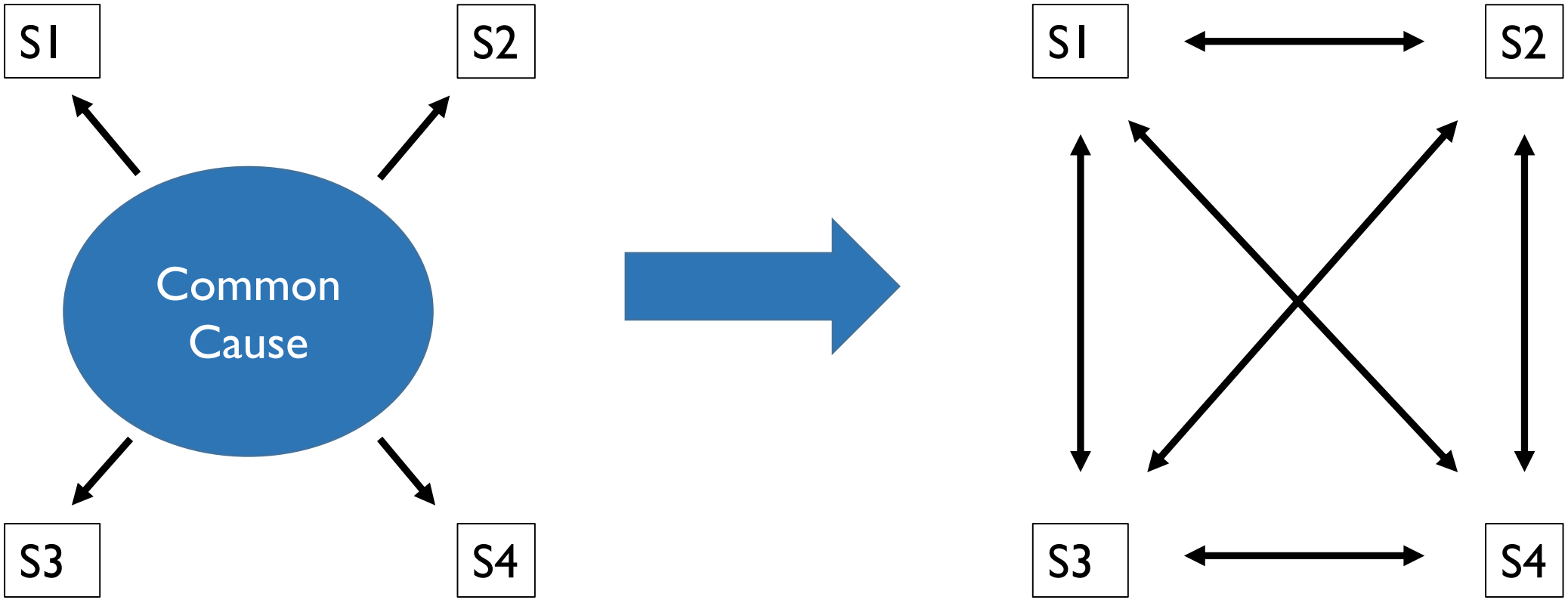
- Assumes symptoms develop from common cause and are interchangeable, equally important indicators of severity

- Heterogeneity of mental disorders
  - Approximately 1000 unique depression symptom profiles (Fried & Nesse, 2015)

- Symptoms are not independent from each other
  - Insomnia → Fatigue (Ferentinos et al., 2009)

The Network Approach

- Alternative to common cause approach
- Accommodates the possibility for local interactions between symptoms

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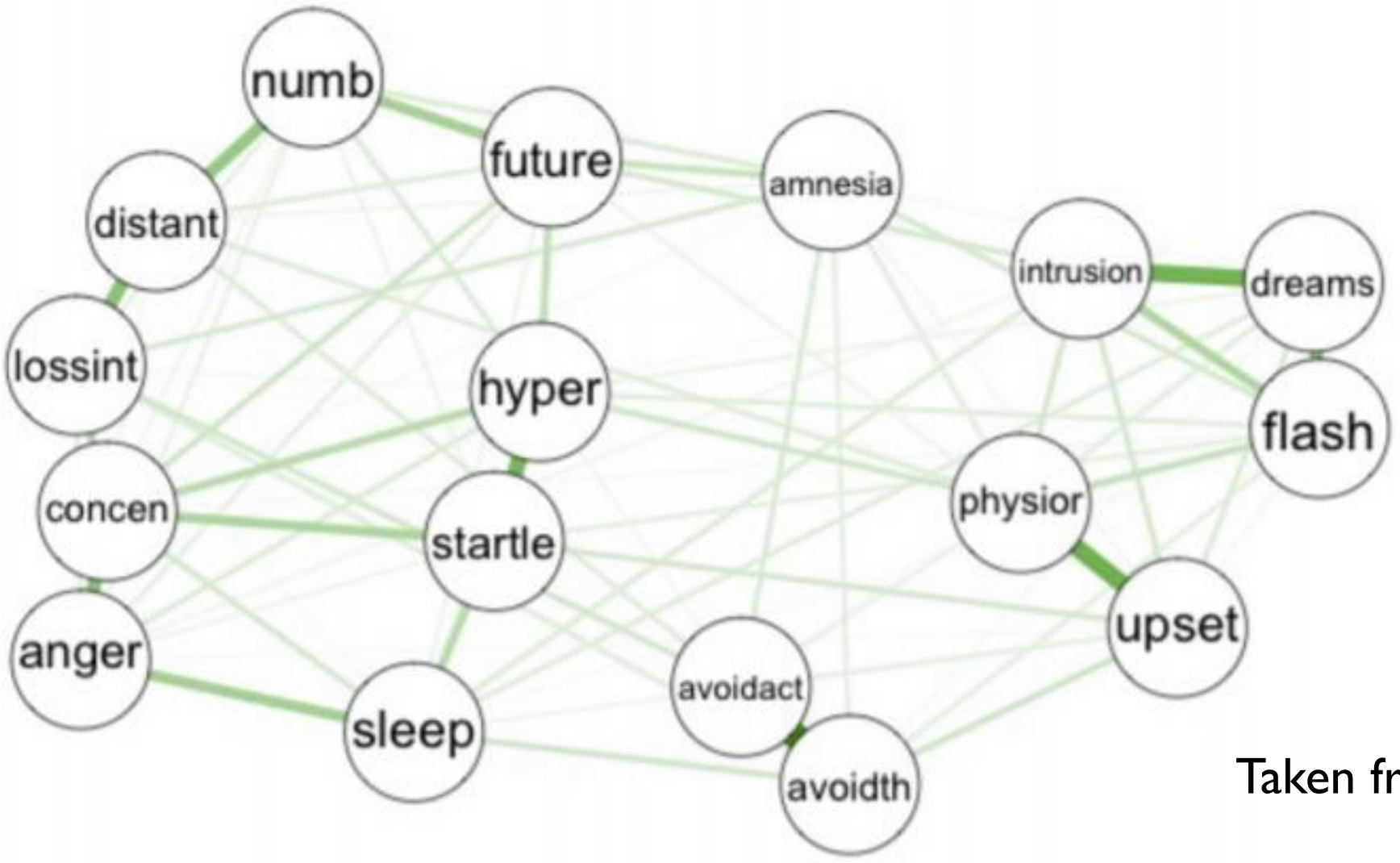
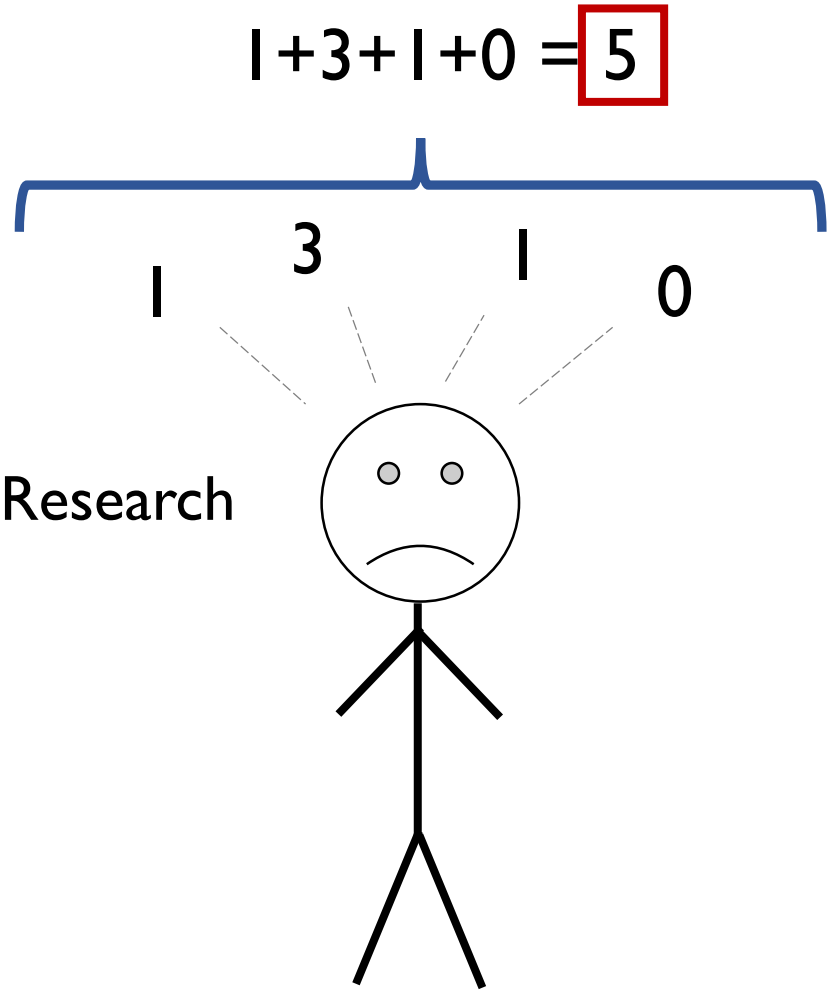
Network Example – PTSD



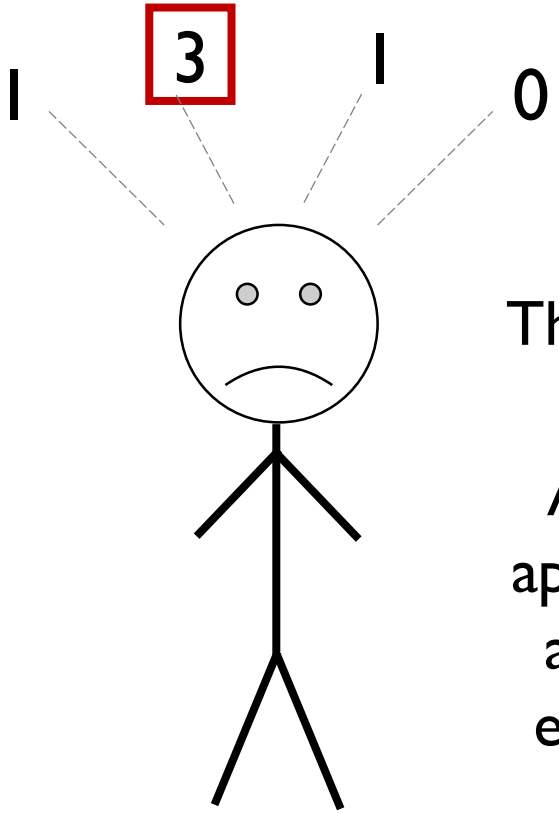
Taken from McNally (2016)

Research Aim

- To explore whether residual levels of **specific symptoms** of depression and anxiety predict relapse



Previous Research



This Research

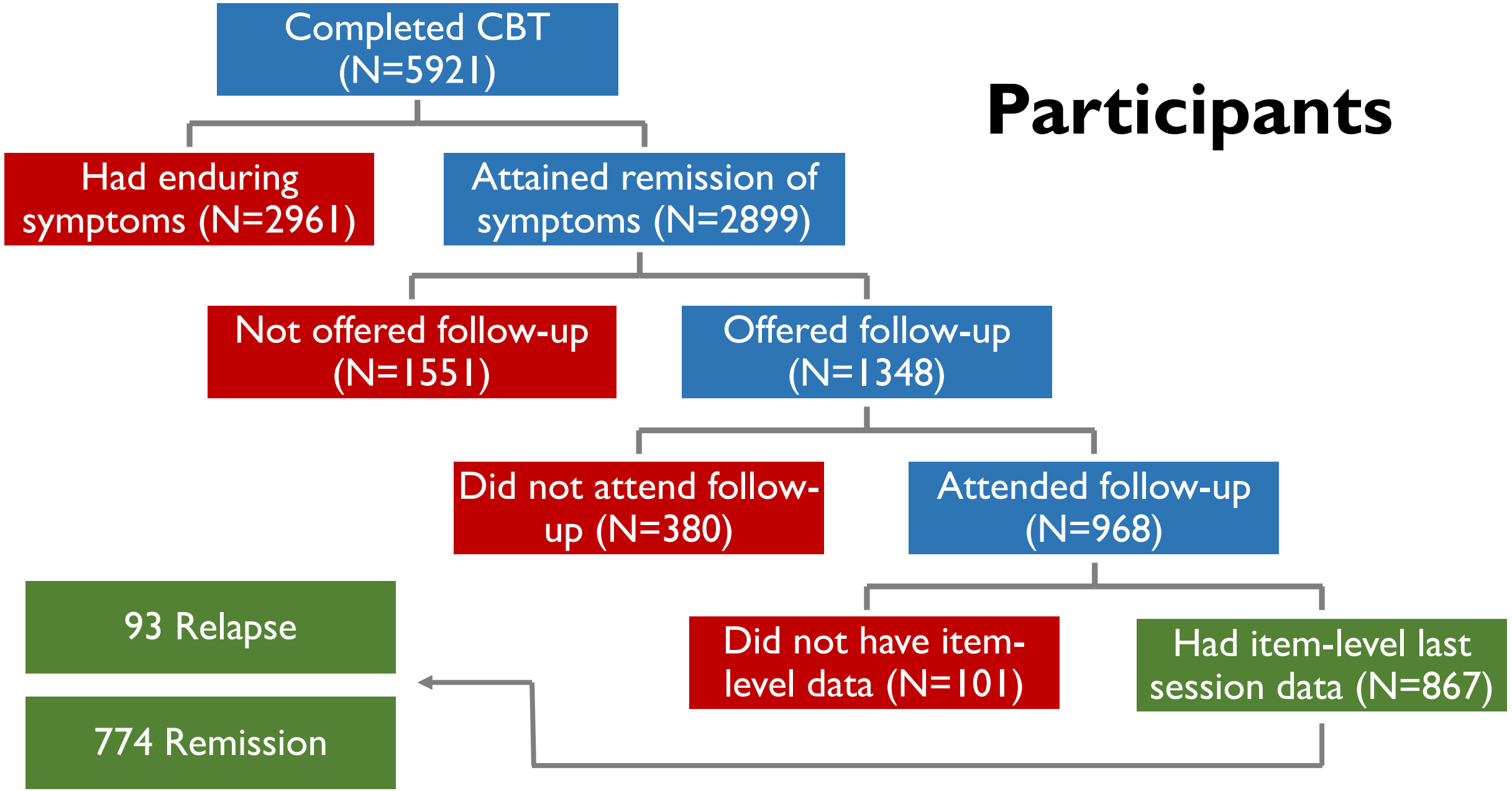
A network approach was adopted to explore this

Method

- Prospective cohort study based in an East Ryding IAPT service between 2013-2017
- Low-intensity and high-intensity CBT patients
- PHQ-9 (depression) and GAD-7 (anxiety) scores collected at final session and at follow-up appointment 3-6 months afterwards

- Relapse defined using reliable change indices:
  1. PHQ-9 and/or GAD-7 scores above threshold at follow-up
  2. Follow-up score above threshold was ≥5 points larger than score at final session

Participants



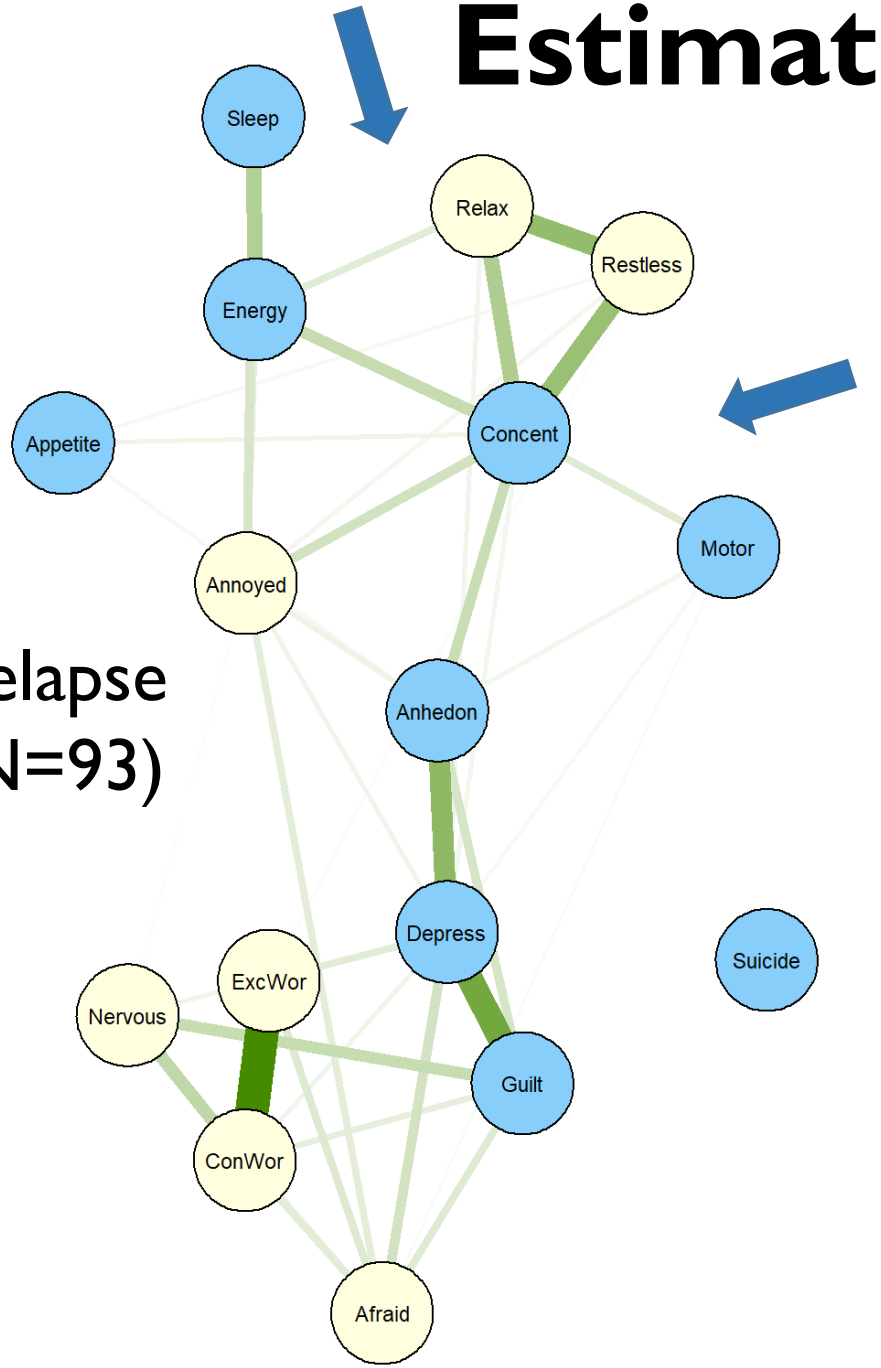
Analyses

- **Network analysis** of PHQ-9 and GAD-7 item scores at end of treatment and their relationship with relapse

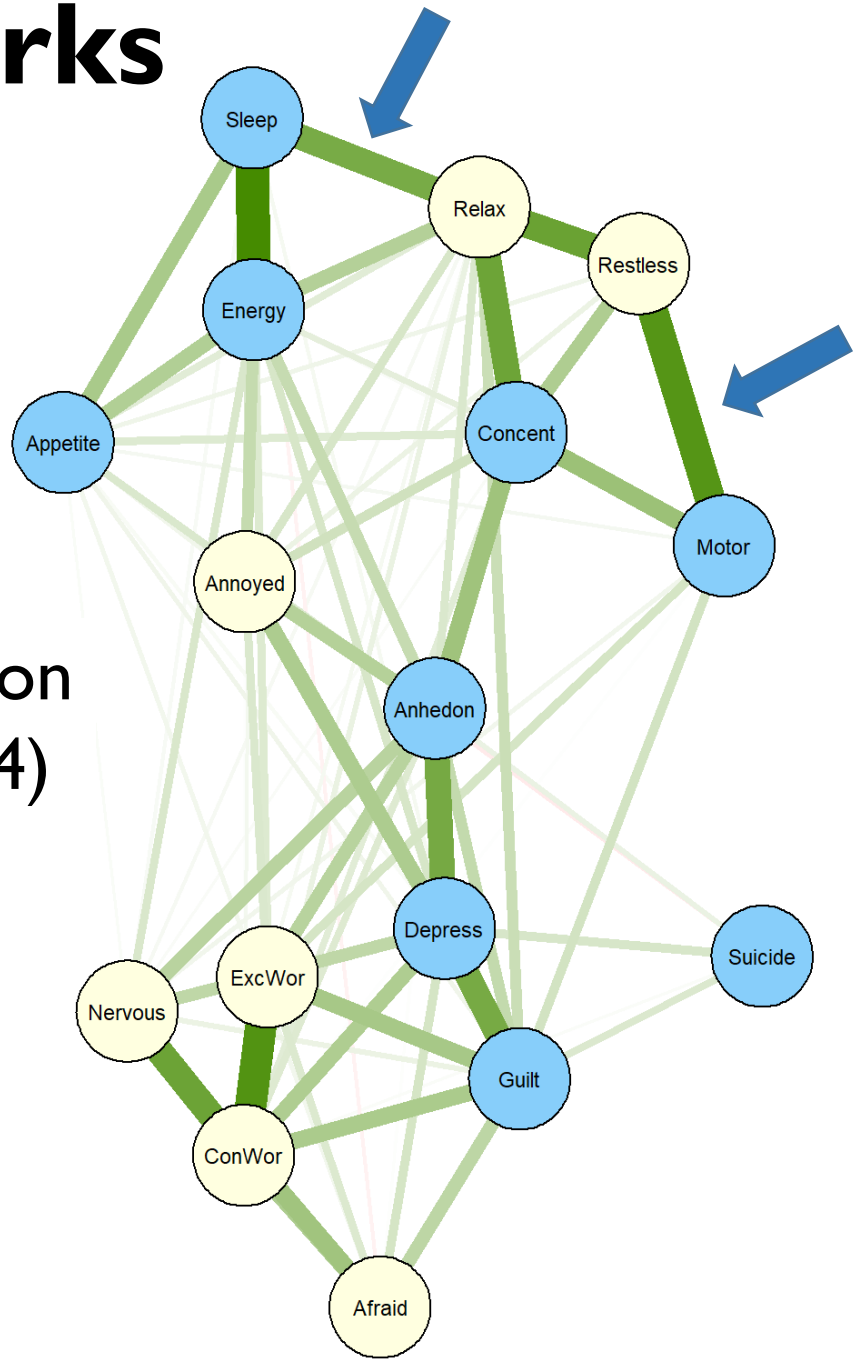
- Network for patients who relapse vs network for patients who remain in-remission
  - Qualitative comparison

Estimated Networks

Relapse
(N=93)



Remission
(N=774)



Centrality Analysis - Strength

	Relapse Network	Remission Network	
Symptom	Strength Rank (Strength Value)	Strength Rank (Strength Value)	Strength Rank Discrepancy
Relax	8 (0.540)	1 (1.048)	7
Concentrate	2 (0.937)	8 (0.837)	6
Anhedonia	6 (0.585)	2 (1.031)	4
Restless	7 (0.550)	11 (0.646)	4
		6 (0.8	
		15 (0	
		4 (0.9	
		12 (0	
		9 (0.7	
		10 (0	
		7 (0.8	
		5 (0.9	
Motor	14 (0.140)	13 (0.576)	1
Appetite	15 (0.081)	14 (0.537)	1
ConWor	3 (0.744)	3 (1.000)	0
Suicide	16 (0.000)	16 (0.175)	0

Relax
("Trouble relaxing")

Highly central in Remission Network
Average centrality in Relapse Network

Concentrate
("Trouble concentrating")

Highly central in Relapse Network
Average centrality in Remission Network

Discussion

- Networks appear mostly similar, but with some differences
  - Low connectivity in relapse = small sample size?

- "Trouble concentrating" highly central in relapse network, but not in remission network
  - Stronger exacerbating effects on other symptoms for relapsed patients?
  - Potential risk factor of relapse

- "Trouble relaxing" highly central in remission network, but not in relapse network

Limitations

- Small sample size – relapse
- Qualitative comparison
- Cross-sectional
- Replication needed with larger sample – this study is only the first step

Implications

- Clinical implications
  - Remitted patients having trouble concentrating? = potential worry
- Further research needed
  - More follow-up needed! = larger samples
- Focus on symptom interactions
- Identify predictive symptoms
  - ‘At-risk’ patients can be identified
  - Targeted with relapse prevention strategies

Study 2

Predicting relapse using machine learning

Ben Lorimer, Dr Jaime Delgadillo, Dr Stephen Kellett - The University of Sheffield

James Lawrence – Behavioural Insights Team, London

Psychotherapy Research, 2020
https://doi.org/10.1080/10503307.2020.1733127

EMPIRICAL PAPER

Dynamic prediction and identification of cases at risk of relapse following completion of low-intensity cognitive behavioural therapy

BEN LORIMER [1], JAIME DELGADILLO [2], STEPHEN KELLETT [2], & JAMES LAWRENCE [3]

[1] *Department of Psychology, University of Sheffield, Sheffield, UK;* [2] *Clinical Psychology Unit, Department of Psychology, University of Sheffield, Sheffield, UK &* [3] *The Behavioural Insights Team, London, UK*

(Received 26 December 2019; revised 14 February 2020; accepted 17 February 2020)

What is Machine Learning?

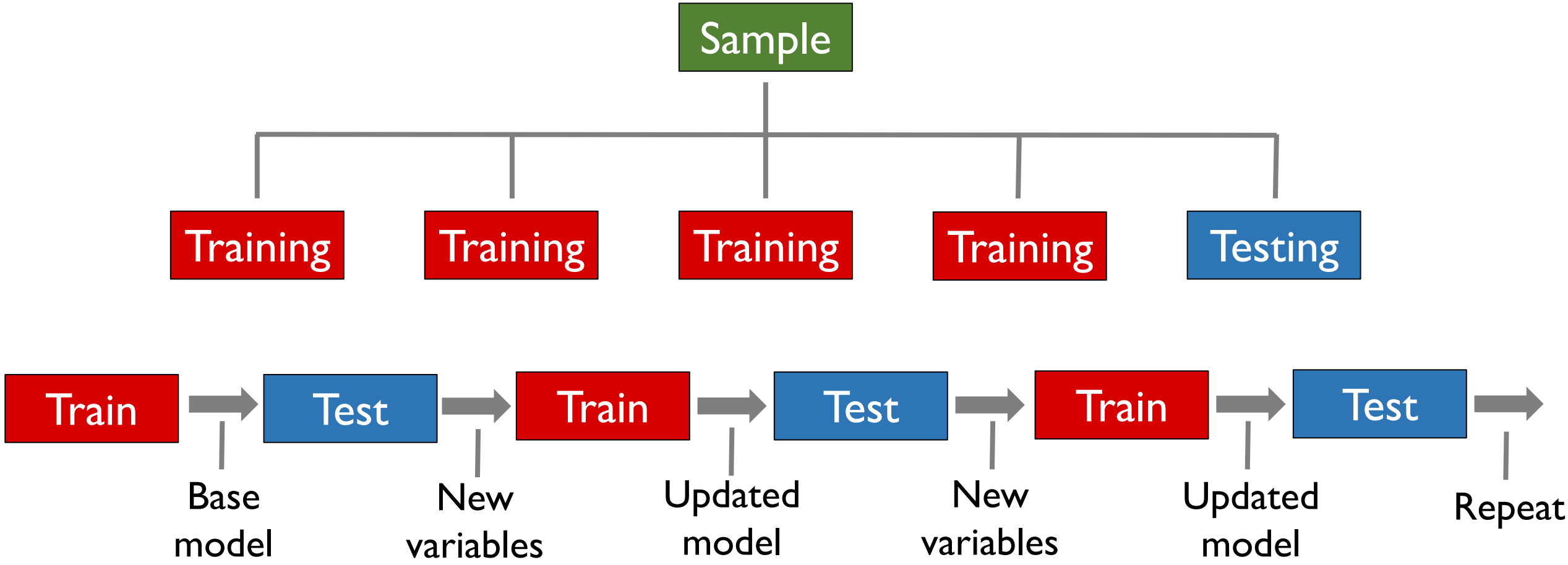
Why Machine Learning?

- Allows for more variables to be tested

- Commonly used statistical techniques are used to find a predictive model that fits a dataset best
  - Only applies to that dataset? = not generalizable?

- Machine learning helps produce **more robust and generalizable** results by training and then testing models

Machine Learning – Training and Testing



Repeat until the model becomes worse at prediction in the Testing subsample

Method

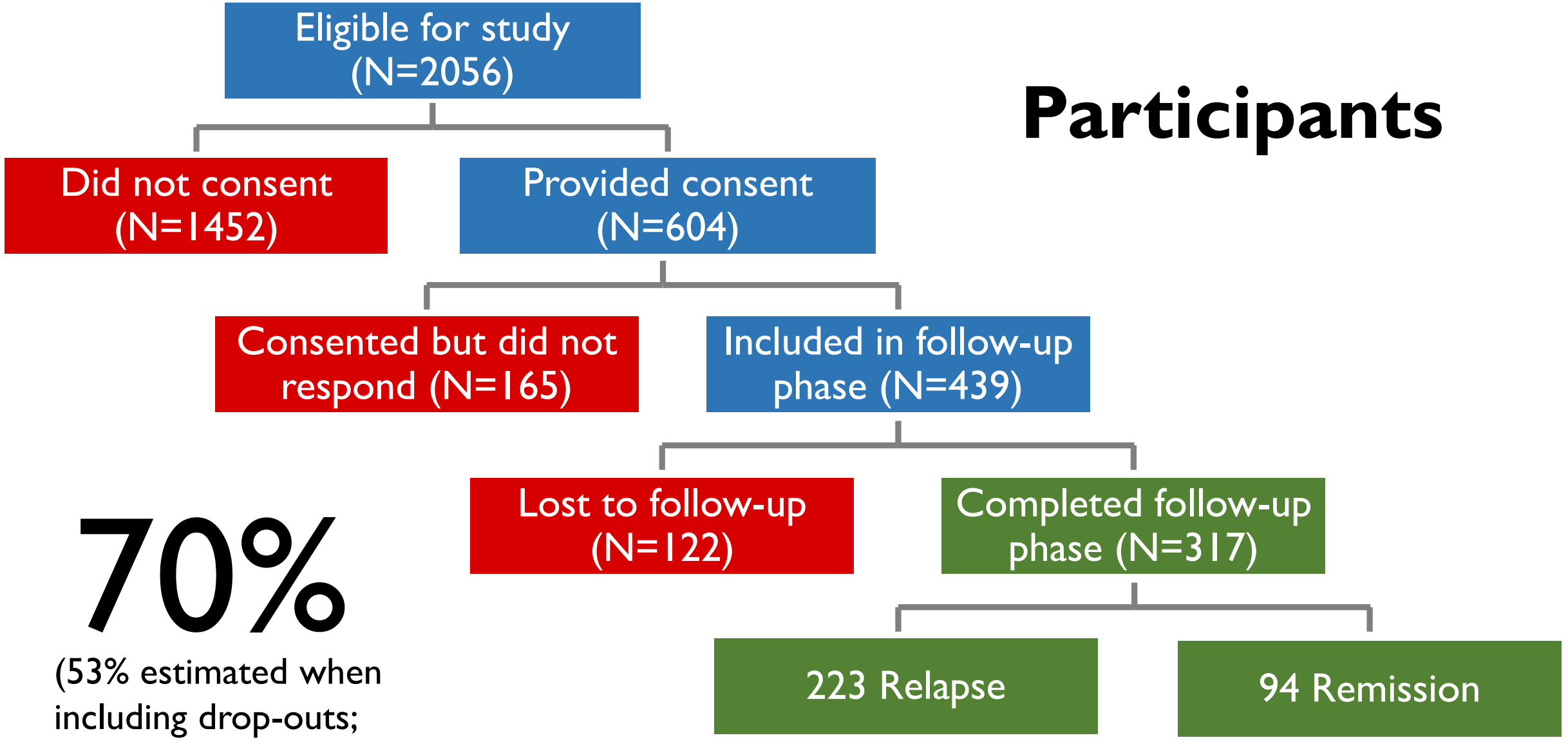
- Apply Machine Learning to predict relapse after ***low-intensity*** CBT

- Prospective cohort study based in West Yorkshire IAPT service between 2012-2016

- PHQ-9 and GAD-7 scores collected at final session and at 12 follow-up appointments (collection points) within the following year

- Relapse defined using reliable change indices:
  1. PHQ-9 and/or GAD-7 scores above threshold at follow-up
  2. Follow-up score above threshold was ≥5 points larger than score at final session

Participants



70%

(53% estimated when including drop-outs; Ali et al., 2017)

Predictive Models

I

Input: 17 Intake Variables

Age, Assessment WSAS, Unemployment Beginning, Disability, Family History, Taking Meds at First, Expectancy Q

AUC = 72.4%

Predictive Models

1	Baseline	AUC = 72.4%
2	Input: 17 + 15 Acute-Phase Treatment Variables (32 Total) Linear Change of WSAS, Age, Linear Change of GAD, Early PHQ Response, Last WSAS, Unemployment Beginning, Last PHQ, Assessment GAD, Unemployment End, Prev. Treatment, Taking Meds at First, Expectancy, Gender	AUC = 74.2%

Predictive Models

1	Baseline	AUC = 72.4%
2	End of Acute-Phase Treatment	AUC = 74.2%
3	Input: 17 + 15 + 7 Collection Point 1 Variables (39 Total) Age, CP1-WSAS, CP1-GAD, CP1-WSAS Change, CP1-PHQ Change, Unemployment Beginning, Taking Meds at First, Family History, Gender, Disability, Diagnosis	AUC = 77.2%

Predictive Models

1	Baseline	AUC = 72.4%
2	End of Acute-Phase Treatment	AUC = 74.2%
3	First Month of Follow-Up	AUC = 77.2%
4	Input: 17 + 15 + 7 + 14 Collection Point 3 Variables (53 Total) CP3-GAD, Linear Change of GAD, Linear Change of WSAS, CP2-PHQ Change, Age, CP1-WSAS Change, Chronicity, CP1-PHQ Change, CP3-WSAS Change, Early Response PHQ, Taking Meds at First	AUC = 83.9%

Predictive Models

1	Baseline	AUC = 72.4%
2	End of Acute-Phase Treatment	AUC = 74.2%
3	First Month of Follow-Up	AUC = 77.2%
4	Third Month of Follow-Up	AUC = 83.9%

- Predictive power increases the further you go along the patient journey
- Better predictions occur during follow-up

Three Important Predictors…

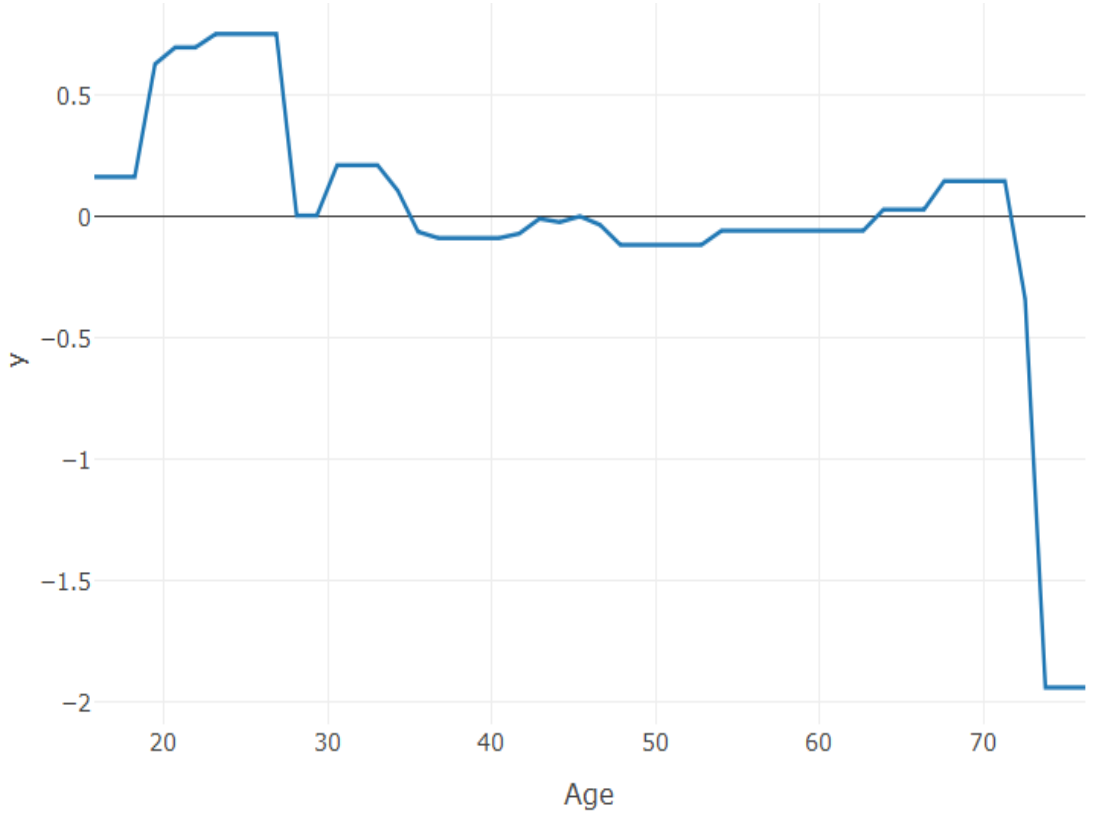
1	Age	Unemployment		AUC = 72.4%
2	Age	Unemployment	Residual Symptoms	AUC = 74.2%
3	Age	Unemployment	Residual Symptoms	AUC = 77.2%
4	Age		Residual Symptoms	AUC = 83.9%

- Residual symptoms already well established risk factor of relapse
- Let's explore Age and Unemployment further…

Age and Unemployment

Age

- Younger people at greater risk



Unemployment

- Employment is highly important

	Unemployed Beginning	Unemployed End
Relapse	31	37
Remission	0	2

- 56% relapsed within first month
- 77% relapsed within three months

Limitations

- Relatively small sample
- Lack of external validation
  - Needs tested on external dataset to assess generalizability
- Only low-intensity CBT
  - Same predictions for high-intensity?

Discussion

- Prediction of relapse improves further along patient journey
- Predictive models are complex
- Young age, unemployment and residual symptoms important risk factors of relapse
- Use models to identify ‘at-risk’ patients
  - Target with relapse prevention strategies

Take Home Message - Clinical

- Depression and anxiety are highly recurrent
- Relapse prevention needed
  - Tailored to patient
- Residual symptoms, young age, unemployment and other psychosocial factors important
- More follow-up needed

What next for research?

- Robust, standardized measure of relapse
- Bigger samples is a must
- Improved knowledge of relapse and risk factors can allow for ‘at-risk’ patients to be identified and targeted with relapse prevention interventions
- Help patients maintain their gains and stop the “revolving door”

Thank you!

Ben Lorimer, The University of Sheffield

Psychotherapy Evaluation and Research Lab @ Sheffield (PEARLS)

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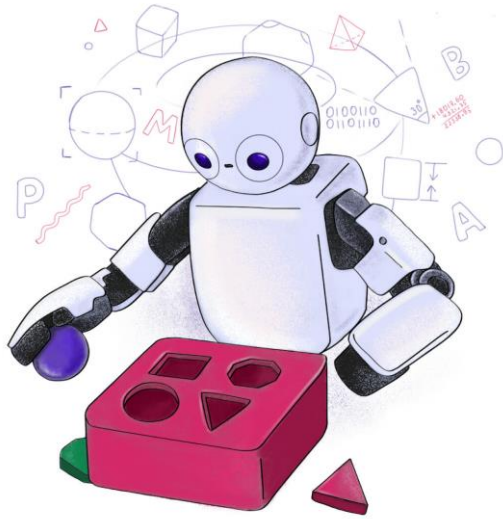
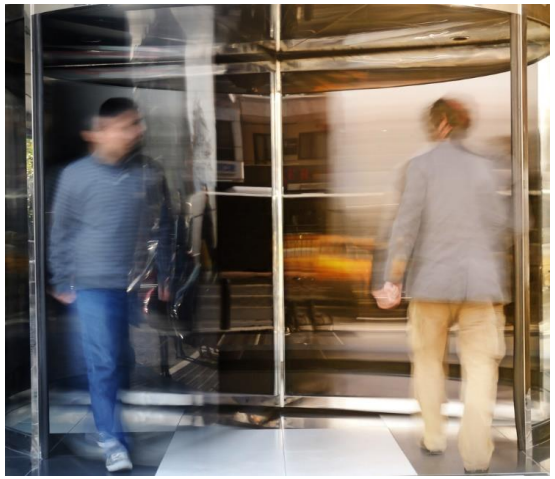
Funded by: Economic and Social Research Council - White Rose Social Sciences DTP

My Final Year

Develop ML models with bigger samples and HI-CBT patients





Investigate the extent of the "revolving door" phenomenon