



University of
Sheffield

Multiple Symptoms Study 3 - developing and testing a complex intervention.

Chris Burton

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NIHR

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Health and Care Research

Overview

- The problem of persistent physical symptoms / medically unexplained symptoms ...
... and a possible approach
- Intervention development
- Trial design and its challenges
- Headline results
- Process evaluations

The Context

Medically Unexplained Symptoms

Symptoms in absence of disease

(Pain, fatigue, dizziness, IBS,)

Associated with distress

Assumed or implied psychological cause

Somatisation / mind-body dualism

Persistent Physical Symptoms

Symptoms OR syndromes

(Pain, fatigue, dizziness, IBS,)

Associated with distress

Psychological and biomedical factors

EPIC (embodied predictive interoceptive coding)

~2% adults have **multiple symptoms** with impaired QoL

~30% GP Consultations

30-50% Specialist referrals

10% NHS Spend on working age adults

No effective GP-based interventions!

What's the problem with Medically Unexplained Symptoms?

I'm glad you came to see me about this

I'm glad you came to see me about this

Your [insert symptoms] are clearly causing you a lot of difficulty.

Your [insert symptoms] are clearly causing you a lot of difficulty.

From what you say, and the tests I've done it's clear that you've got

From what you say and the negative tests I've done, I'm confident you don't have [insert non-diagnosis]

Epistemic Incongruence

What this means is [treatment]

What this means is [non-treatment]

And I'm here to support you

But I'm here to believe you

Relational congruence

Could explanation be a solution?

I'm glad you came to see me about this

I'm glad you came to see me about this

Your [insert symptoms] are clearly causing you a lot of difficulty.

Your [insert symptoms] are clearly causing you a lot of difficulty.

From what you say, and the tests I've done it's clear that you've got [insert diagnosis]

From what you say, and the tests I've done we can explain this in terms of [insert explanation]

Epistemic congruence

What this means is [treatment]

What this means is [treatment]

And I'm here to support you

And I'm here to support you

Relational congruence

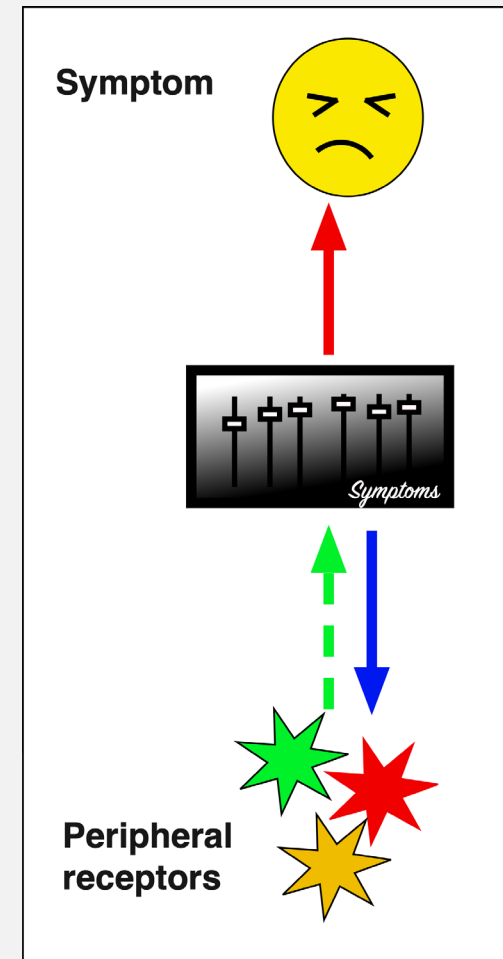
Explanations and current models of persistent physical symptoms

What is a symptom?

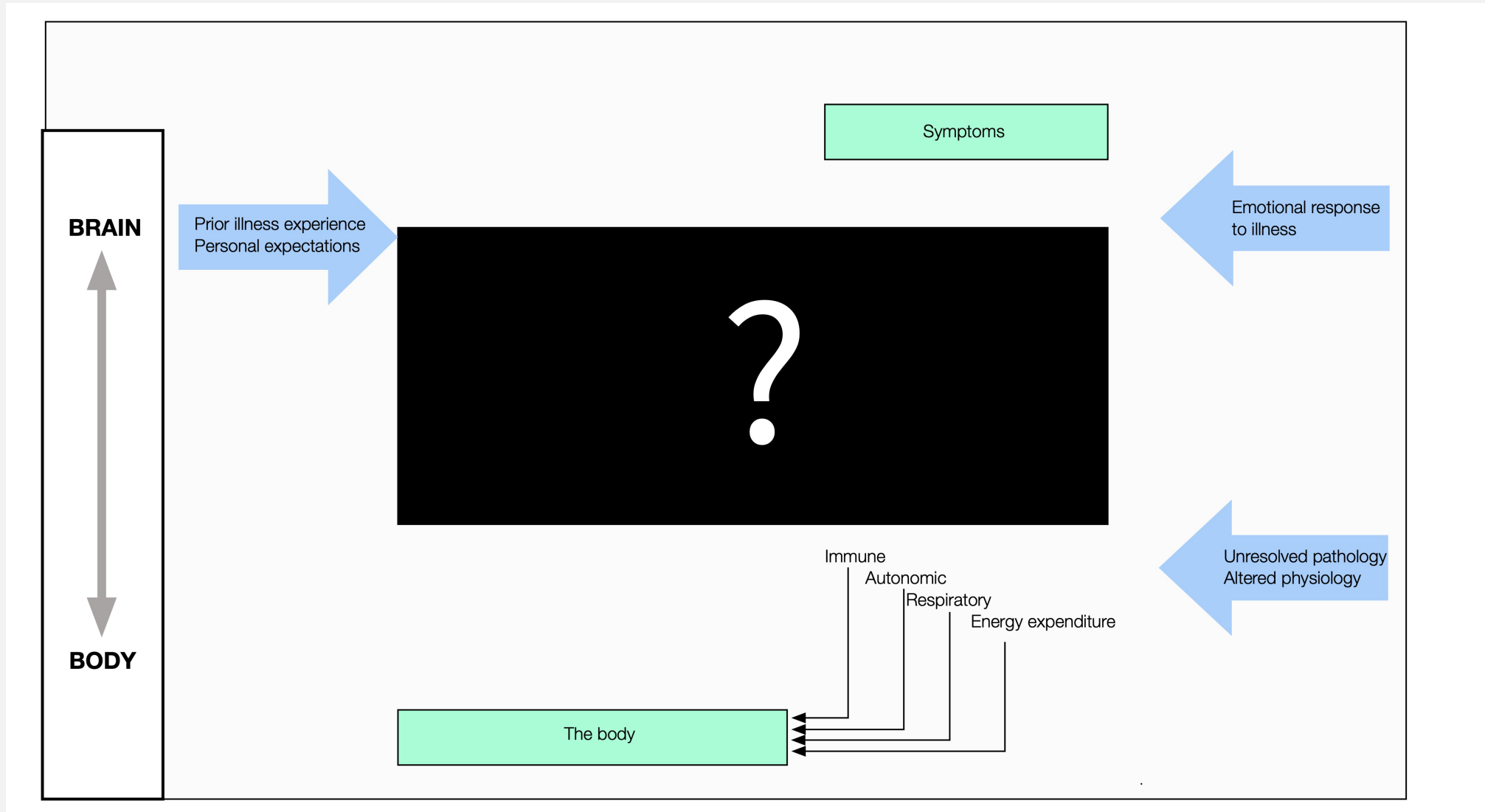
A physical sensation indicating actual or threatened disease



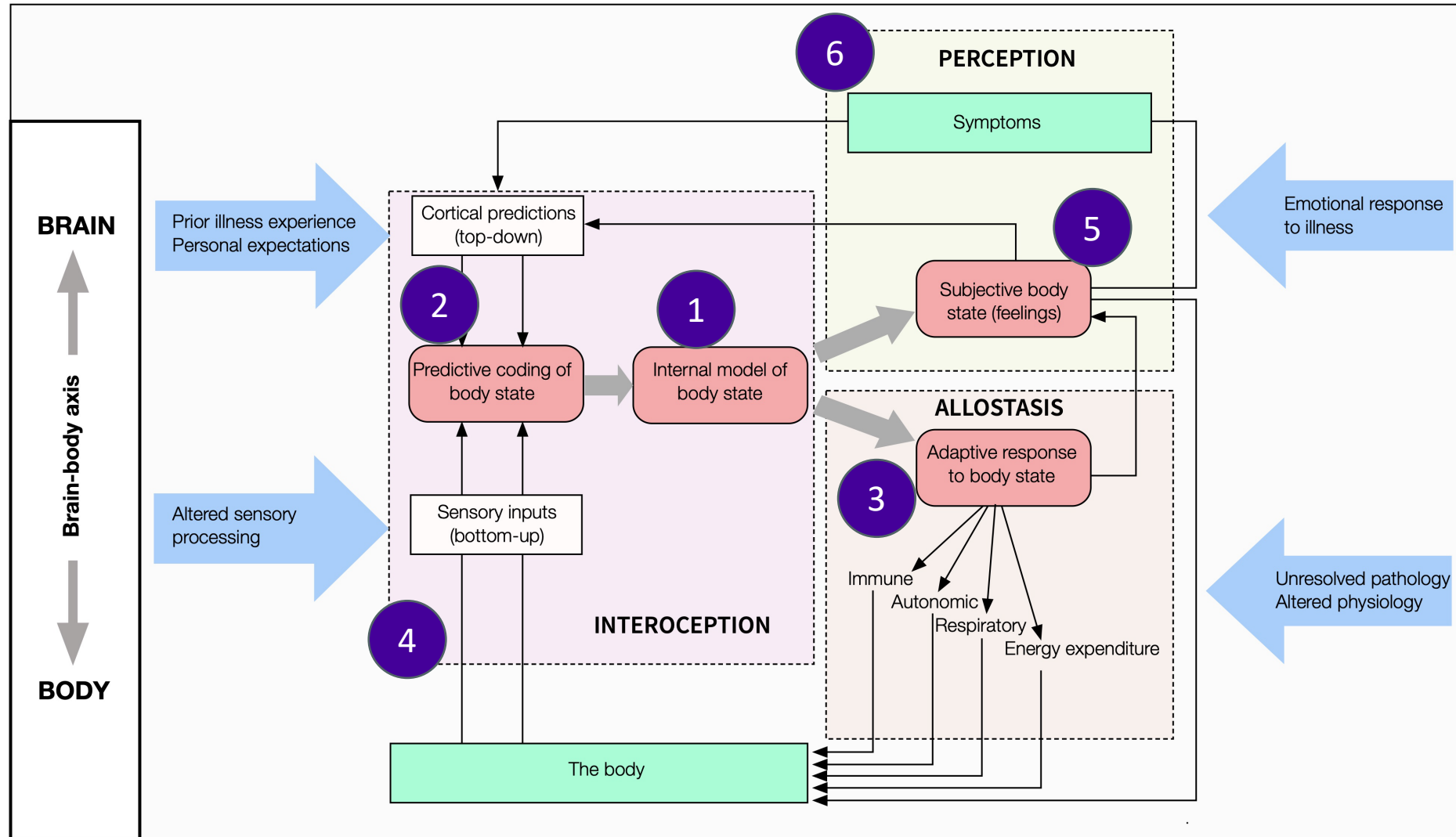
When persistent may become an **entity** rather than a **signifier**



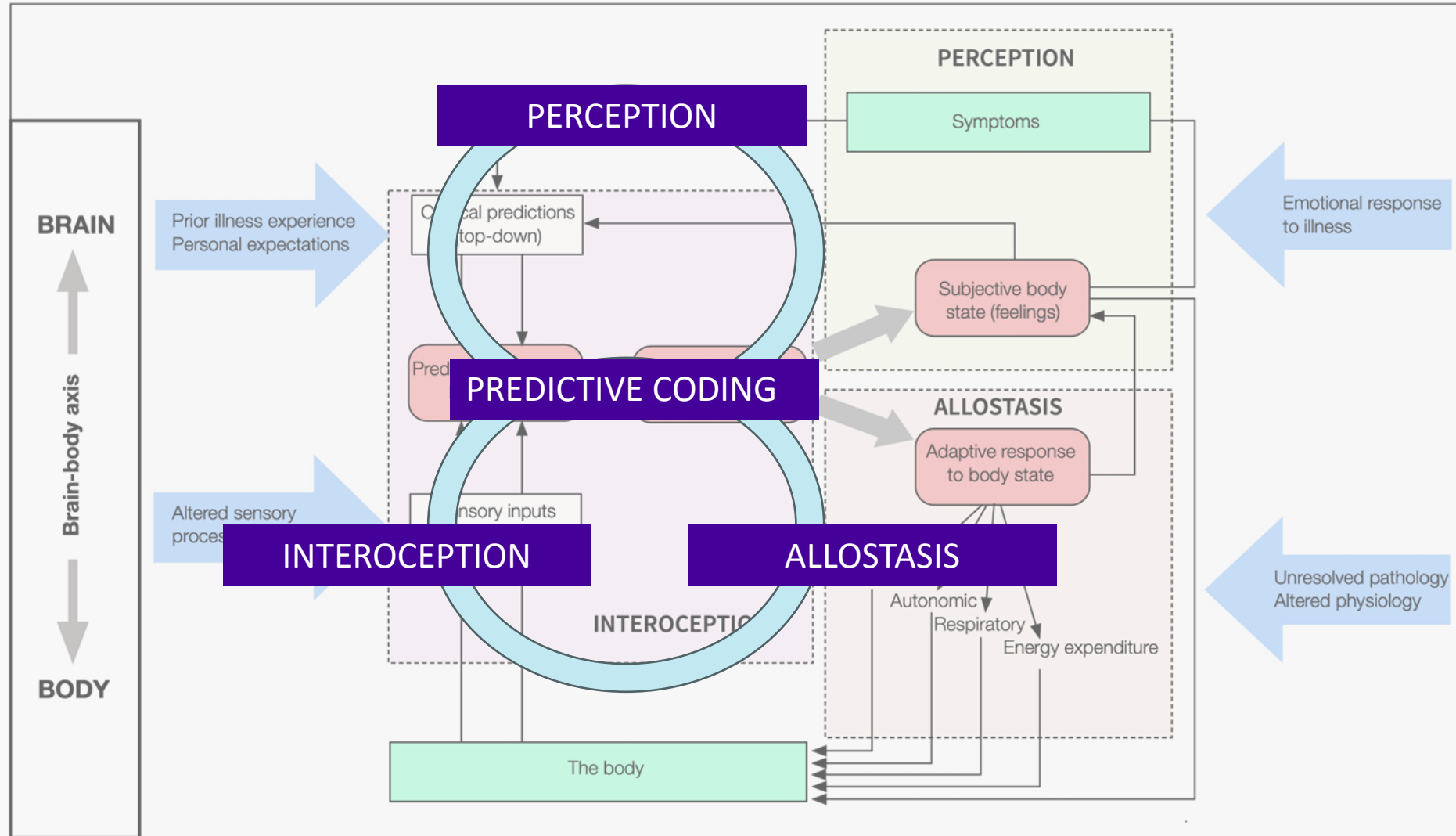
What processes are we explaining here



Symptoms Science 2024



Symptoms Science 2024



Translating science into explanation



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Patient Education and Counseling

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Research Paper

A taxonomy of explanations in a general practitioner clinic for patients with persistent “medically unexplained” physical symptoms



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ABSTRACT

Objective: To develop a taxonomy of explanations for patients with persistent physical symptoms.

Methods: We analysed doctors' explanations from two studies of a moderately-intensive consultation intervention for patients with multiple, often “medically-unexplained,” physical symptoms. We used a constant comparative method to develop a taxonomy which was then applied to all verbatim explanations.

Results: We analysed 138 explanations provided by five general practitioners to 38 patients. The taxonomy comprised explanation types and explanation components. Three explanation types described the overall structure of the explanations: Rational Adaptive, Automatic Adaptive, and Complex. These differed in terms of who or what was given agency within the explanation. Three explanation components described the content of the explanation: Facts – generic statements about normal or dysfunctional processes; Causes – person-specific statements about proximal or distal causes for symptoms; Mechanisms – processes by which symptoms arise or persist in the individual. Most explanations conformed to one type and contained several components.

Conclusions: This novel taxonomy for classifying clinical explanations permits detailed classification of explanation types and content. Explanation types appear to carry different implications of agency.

Practice implications: The taxonomy is suitable for examining explanations and developing prototype explanatory scripts in both training and research settings.

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Intervention Development – Symptoms Clinic / REAL

Development stages (not a linear process)

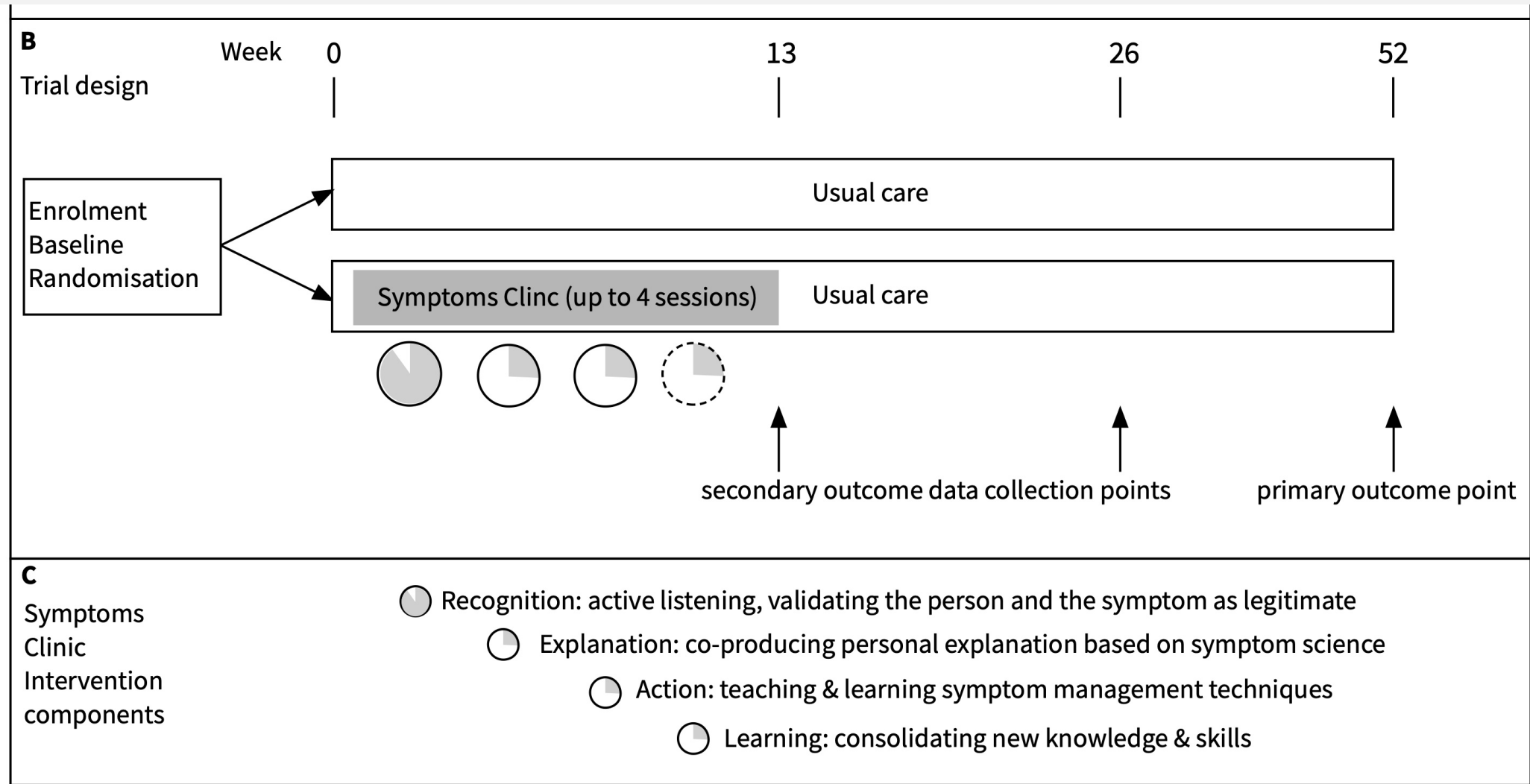
- 2 Literature reviews (one home-made, one borrowed)
- Multi-perspective analyses of descriptive study (multi-method)
- Trial and error constructing explanations in practice and for a book
- 2 funded pilot studies (Multiple Symptom Studies 1 & 2)
- Serial PPI work (formal and informal)
- Construction and testing of a taxonomy of explanation and analysis of acceptance / negotiation of explanations.
- Formulation of Recognition, Explanation, Action, Learning (REAL) model
- Reflection on teaching of GPs in order to understand how practitioners accept / use explanations

Intervention Development – Symptoms Clinic / REAL model

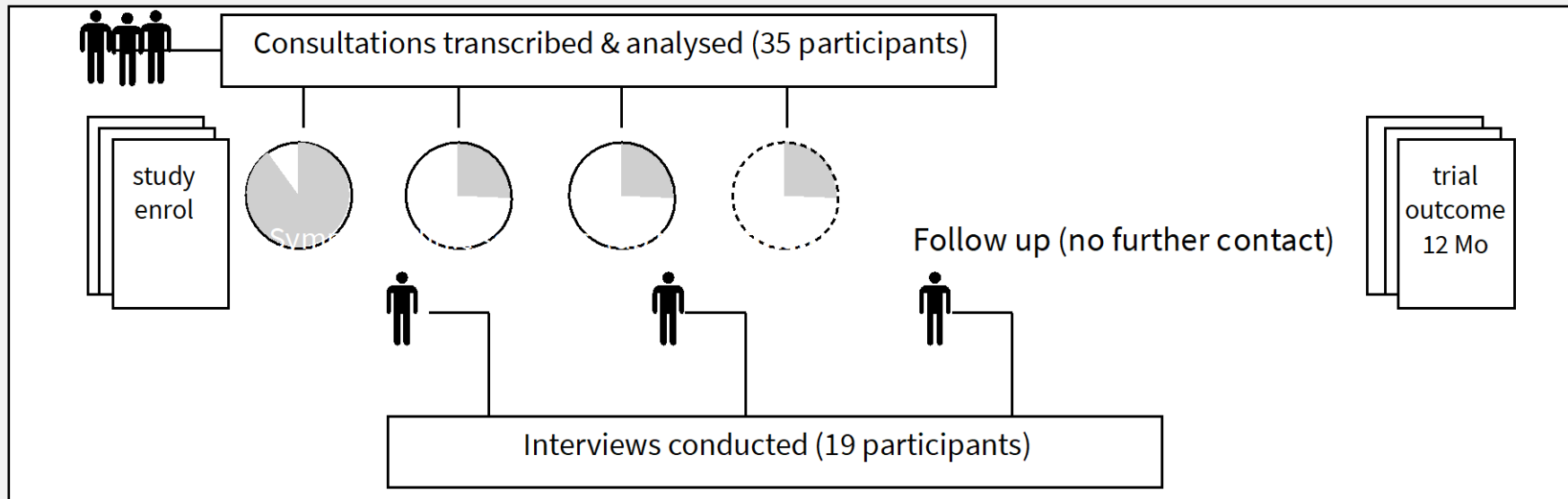
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- Reflection on teaching of GPs in order to understand how practitioners accept / use explanations
- 10 years!

Multiple Symptoms Study 3: Trial Design



MSS3 process evaluation



Challenges in trial design

Inclusion	High heterogeneity to maximise face validity (strong confidence in common processes)
Structure	Mild flexibility to maximise reproducibility (while minimising explainable non-adherence)
Content	High flexibility driven by aim to personalise formulation and plan
Fidelity	Need for structure but adaptability – flexible fidelity

The trial: Multiple Symptoms Study 3

Delivery:

- GPwExtended Role (10 sessions training)
- 4 Centres (6 GPs)
- In person (to March 2020) then video-consults

Eligibility:

- one or more functional syndromes
- Repeated referrals to specialists
- PHQ15 in range 10-20

Outcome

- Primary outcome: PHQ15 at 12 month
- Clinically important 3 point change in PHQ15
- 1 point within group + 2 points between group

Process evaluation (fidelity and mechanisms of change)

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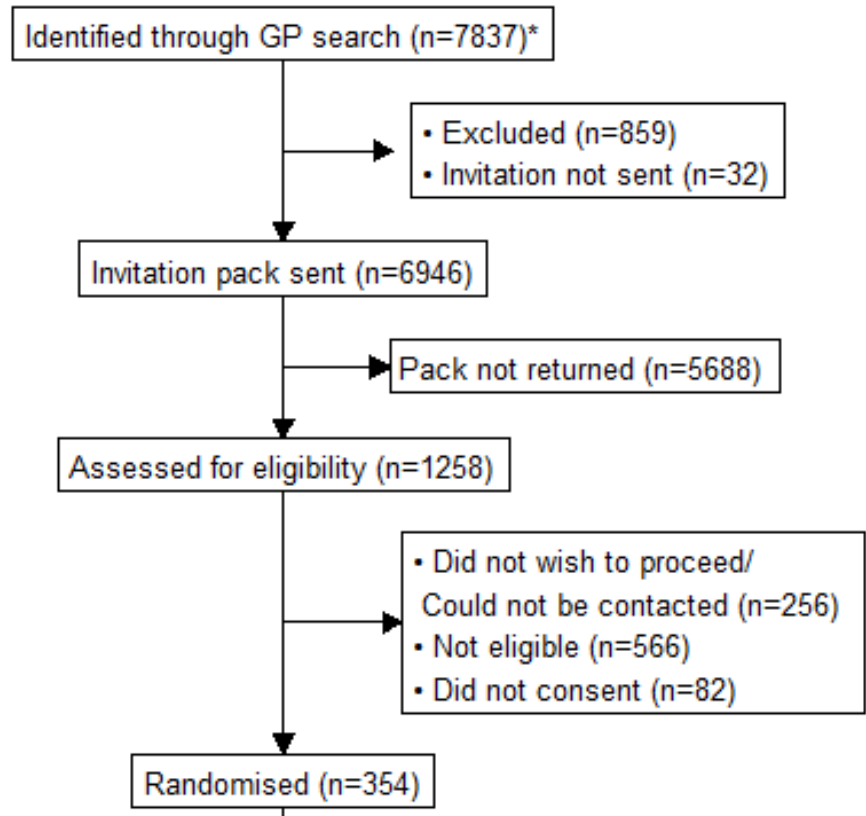


Burton et al Lancet 2024

Process evaluation 1: Fidelity

GP		1	1	1	2	2	2	3	3	3	4	4	4	5	5	5
Consultations checked		1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4	1,2,3,4	1,2	1,2,3,4	1,2,3	1	1,2,3,4	1,2,3	1,2,4	1
Recognition	Active listening	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	Picking up on cues	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	Impact	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	What it feels like	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	Patient concerns	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	Validating patient	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Explanation	Transition to explanation	2	1	1	1	1	1	1	1	1	1	1	1	1	2	
	Type / content	2	1	1	1	1	1	2	2	2	1		1	2	2	
	Delivery / negotiation	2	1	2	1	1	1	1	2	2	1		2	2	2	
	Linkage to explanation	2	2	2	1	1	1	2	2	2	1		1	2	2	
Action	Action type / content	2	2	2	2	1	1	2	2	2	1		1	2		
	Teaching	2	2	2	2	1	2	2	2	2	1		1	2		
	Deployment / activation	2	2	2	2	1	1	2	1	2	1	1	1	2		
Learning	Ask about learning	3	3	3	2	4	2	4		3	3		2	2	4	
	Consolidating	3	4	3	2	4	3	4		3	3		2		4	
	Wrapping up	3	4	4	2	4	3	4		4	3		4		4	

Results: CONSORT

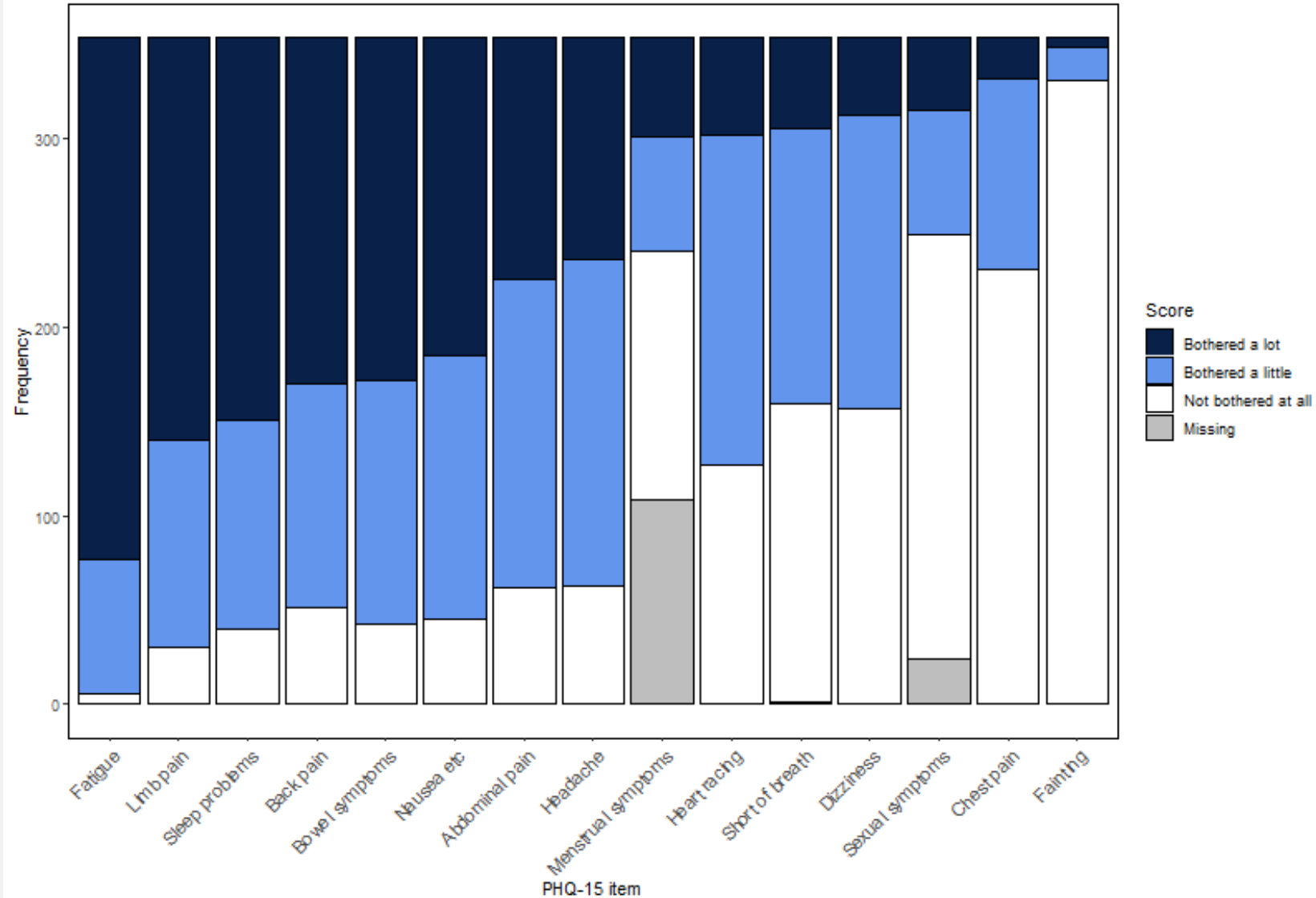


Baseline characteristics

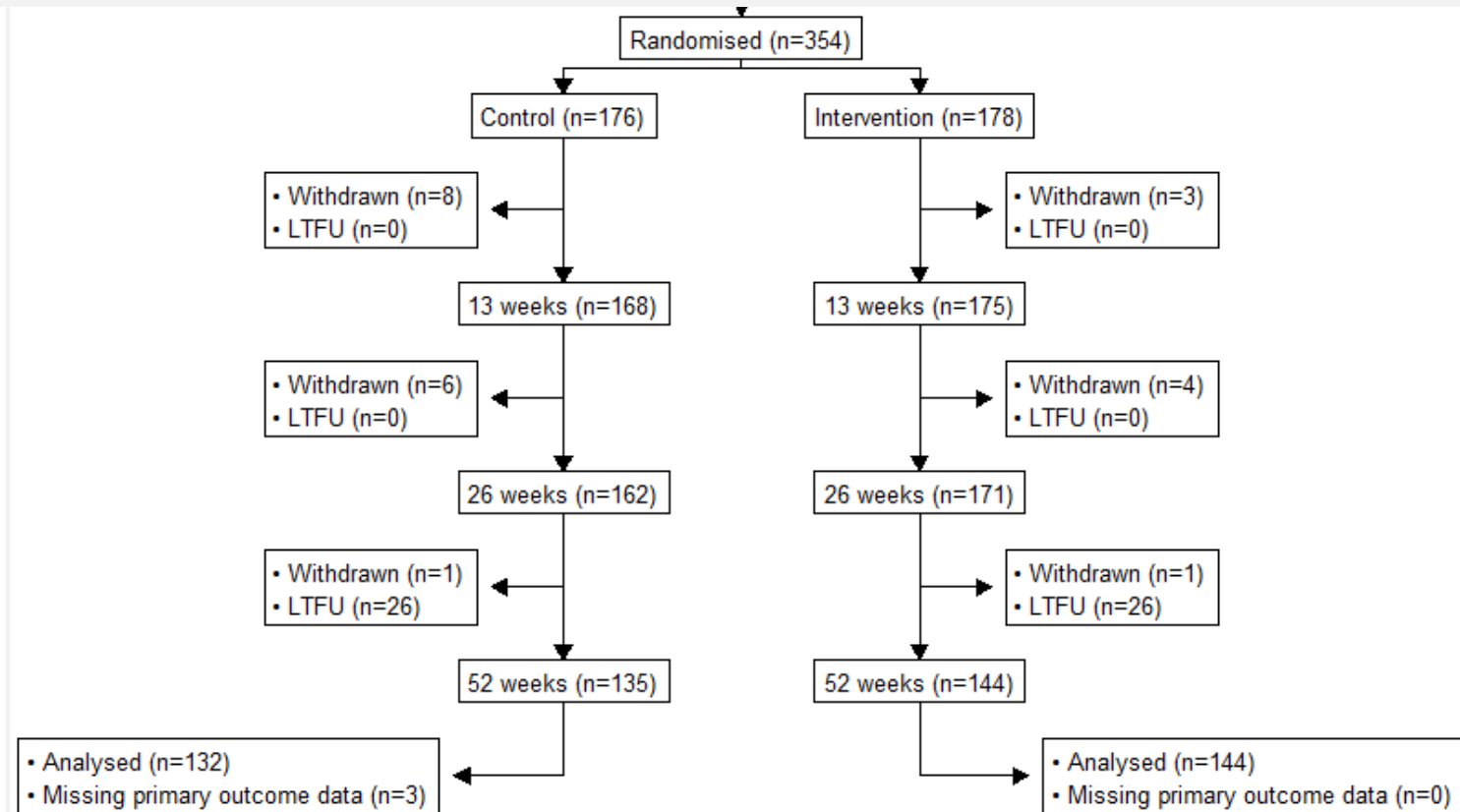
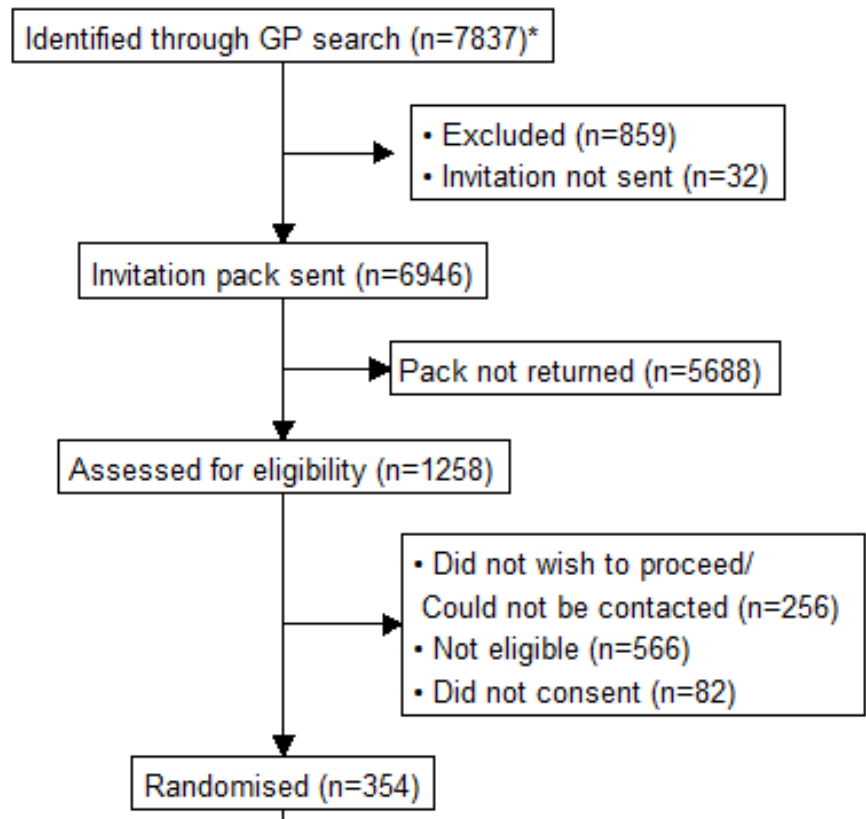
	Usual care (N=176)	Intervention (N=178)
Age (years)		
Mean (SD)	46.1 (12.9)	45.2 (12.7)
Median (IQR)	48.0 (36.8, 56.0)	47.0 (35.2, 56.0)
Range	20.0 - 69.0	18.0 - 70.0
Sex		
Male	32 (18.2%)	31 (17.4%)
Female	144 (81.8%)	147 (82.6%)
Ethnicity		
Asian	7 (4.0%)	7 (3.9%)
Mixed/Other	6 (3.4%)	5 (2.8%)
White	163 (92.6%)	166 (93.3%)
First language		
English language	163 (92.6%)	167 (93.8%)
Other European	3 (1.7%)	4 (2.2%)
Asian language	5 (2.8%)	1 (0.6%)
Other language	5 (2.8%)	6 (3.4%)
Level of education		
Missing	3	5
GSCE or equivalent	61 (35.3%)	59 (34.1%)
A-level or equivalent	48 (27.7%)	43 (24.9%)
Bachelor's degree	40 (23.1%)	49 (28.3%)
Higher degree	15 (8.7%)	15 (8.7%)
No formal qualifications	9 (5.2%)	7 (4.0%)
PHQ-15		
Mean (SD)	14.9 (3.0)	15.0 (2.9)
Median (IQR)	15.0 (12.9, 17.0)	15.0 (12.2, 17.0)
Range	10.0 - 21.9	10.0 - 23.1

	Usual care (N=176)	Intervention (N=178)
PHQ-15		
Mean (SD)	14.9 (3.0)	15.0 (2.9)
Median (IQR)	15.0 (12.9, 17.0)	15.0 (12.2, 17.0)
Range	10.0 - 21.9	10.0 - 23.1
GAD-7		
Mean (SD)	9.1 (5.5)	8.9 (5.4)
Median (IQR)	8.0 (5.0, 13.0)	8.0 (5.0, 12.0)
Range	0.0 - 21.0	0.0 - 21.0
PHQ-9		
Mean (SD)	11.6 (5.4)	10.8 (5.8)
Median (IQR)	11.0 (7.0, 15.0)	10.0 (6.0, 15.0)
Range	1.0 - 26.0	0.0 - 24.0
Health Literacy		
Missing	8	7
Inadequate	23 (13.7%)	27 (15.8%)
Problematic	82 (48.8%)	85 (49.7%)
Sufficient	63 (37.5%)	59 (34.5%)

Baseline symptoms on PHQ15

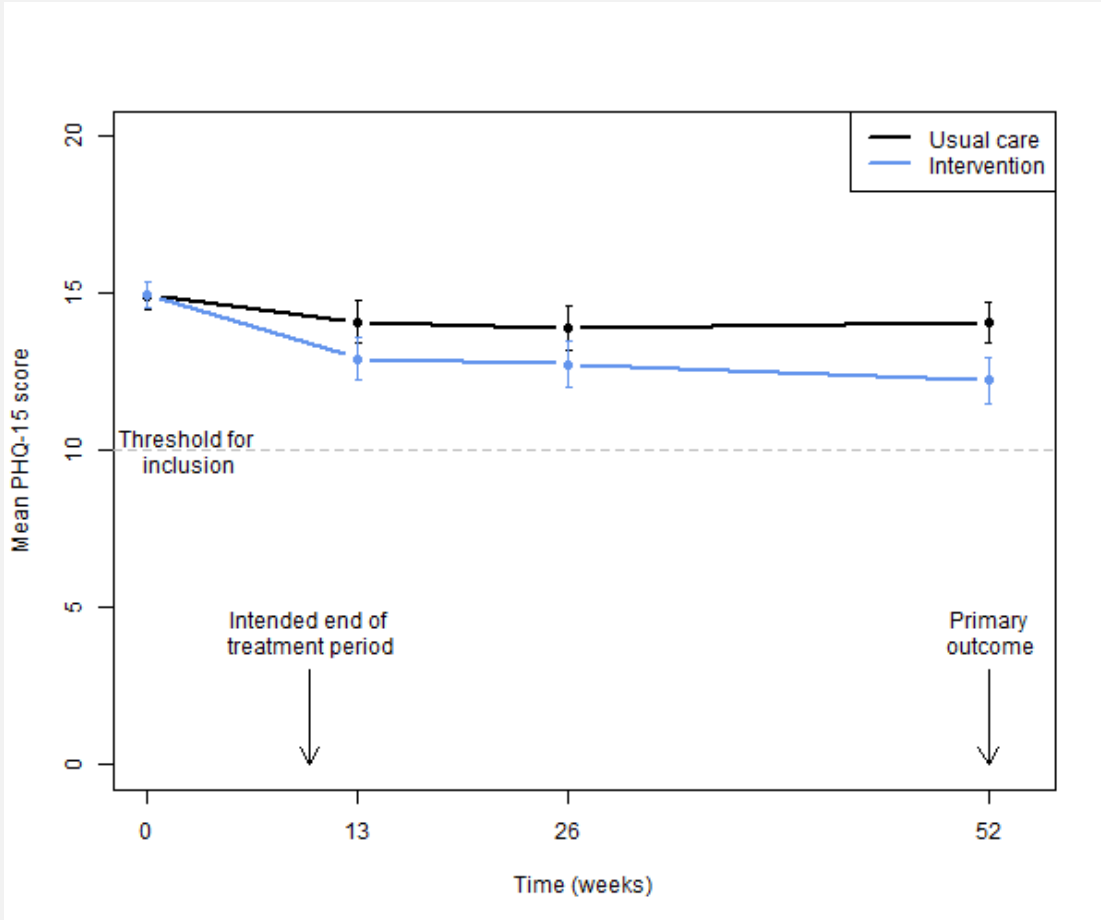


Results: CONSORT



Primary outcome obtained for $276/354 = 77.9\%$

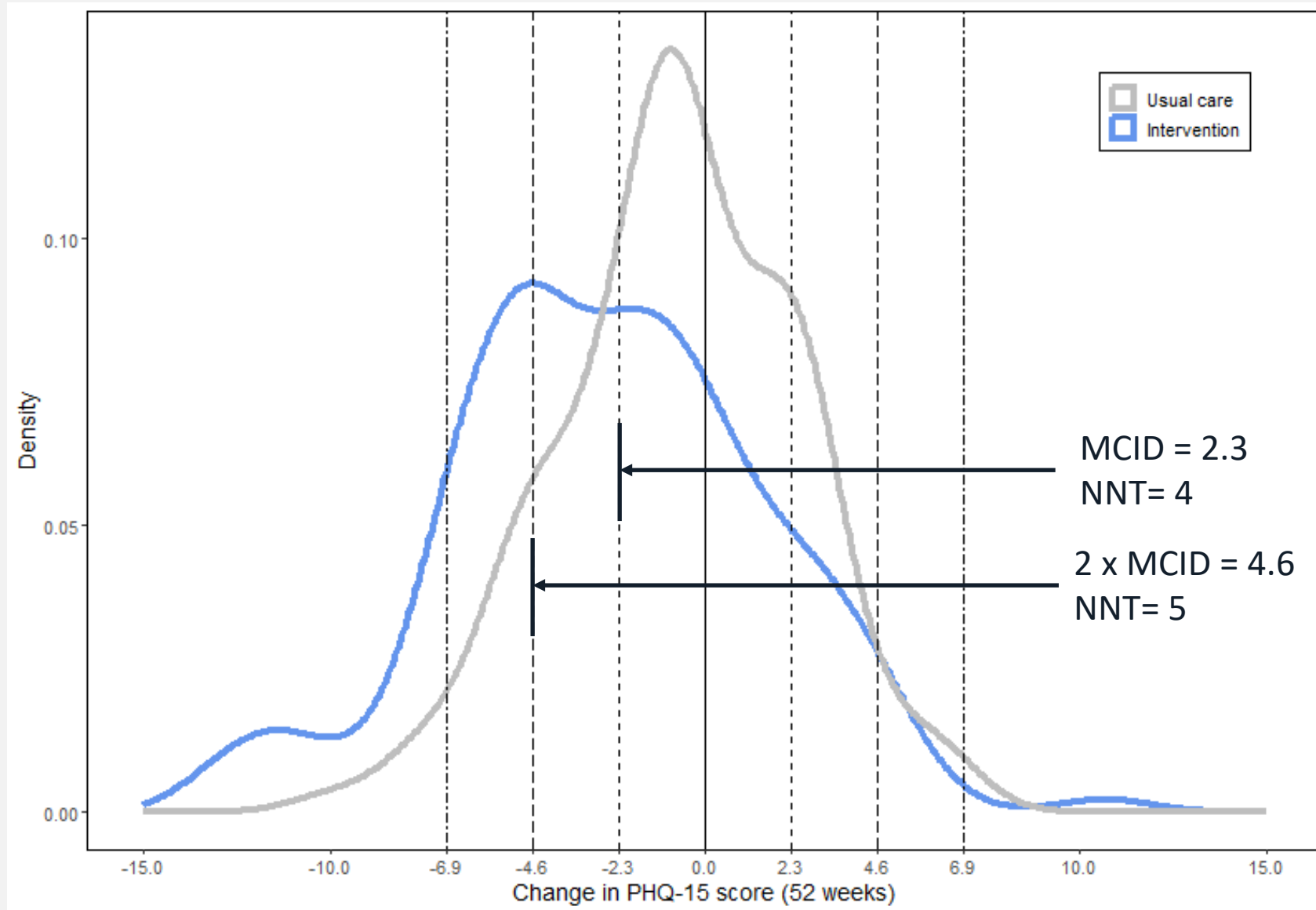
Results: Outcomes at 52 weeks



		Control	Intervention	Adjusted model*		
	N	Mean (SD)	N	Mean (SD)	Effect (95% CI)	p-val
PHQ-15	132	14.1 (3.7)	144	12.2 (4.5)	-1.8 (-2.7, -1)	<0.001
EQ-5D	128	0.5 (0.30)	130	0.57 (0.27)	0.07 (0, 0.15)	0.054
PHQ-9	133	10.9 (6)	142	8.8 (6.1)	-1.6 (-5.3, 2)	0.15

*adjusted for age, sex, baseline PROM value and interventionist effects

Results: in relation to minimum clinically important difference (MCID)



Process evaluation 2 – perceptions of intervention delivery and mechanisms

RECOGNITION	Well, basically, he's the first person who's actually listened to me, I says, as a person, and not just said oh its wear and tear, there's nothing you can do...I says I came out of there and I felt as if something is actually gonna help us now
EXPLANATION	If I'd gone in for like a normal ten-minute appointment and my GP had said try mindfulness, I would've said yeah OK, just refill my prescription please...the way that you'd explained it with medical evidence as well, cos I'm a sciencey person, has been really helpful, so it's made me want to commit to it
ACTION	It wasn't all together new, what it was, was just casting a different light on it, so instead of seeing them as a problem it was trying to explain what I could do with the symptoms
LEARNING	For me it's been useful to learn about the nerves and things as well. But I just feel like I need, not let it kind of control my life really. It's hard because sometimes when you're in that much pain. But I think it's been helpful, just you explaining not to do too much and trying to build it up gradually

Process evaluation 3 – analysis in light of theory: biographical repair

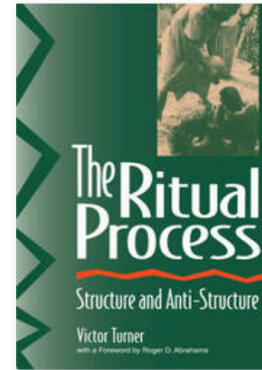
PERSISTENT SYMPTOMS AS DISRUPTION	Pervasive state of disrupted biography, work to maintain moral identity, difference from normal in the body by which they define themselves. Ongoing search for meaning a trapped state with no resolution in sight.
EXPLANATIONS IN THE CLINIC	Explanations informed by biomedical / neuro- science acting to explicitly relocate the origin of the symptoms within the (lived) body. Working collaboratively to “retrain the brain” to adapt to the body
BIOGRAPHICAL REPAIR	Renewed sense of being the same as before but different. With new skills Not in all, some achieved biographical continuity
RELATION TO FRANK’S NARRATIVES	“Honouring the chaos”, while moving towards a quest.



Sanders, Fryer et al
SocSciMed-QR 2024

Process evaluation 4 – in progress

Additional examination of transcripts etc through the lens of Turner's work on ritual and liminal spaces



Book

The Ritual Process

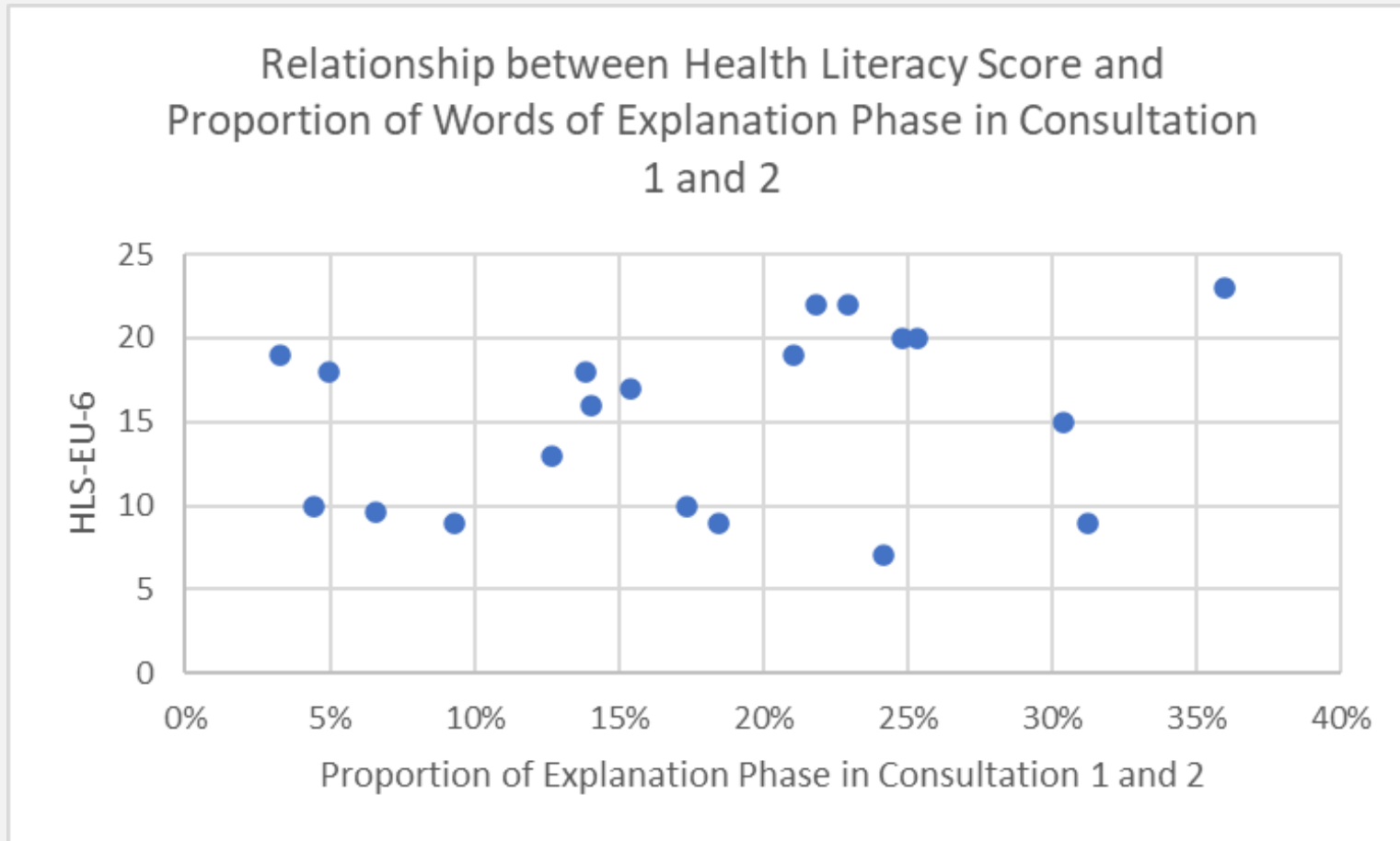
Structure and Anti-Structure

By *Victor Turner, Roger Abrahams, Alfred Harris*

Edition	1st Edition
First Published	1969
eBook Published	31 December 1995
Pub. Location	New York
Imprint	Routledge
DOI	https://doi.org/10.4324/9781315134666
Pages	232
eBook ISBN	9781315134666
Subjects	Social Sciences

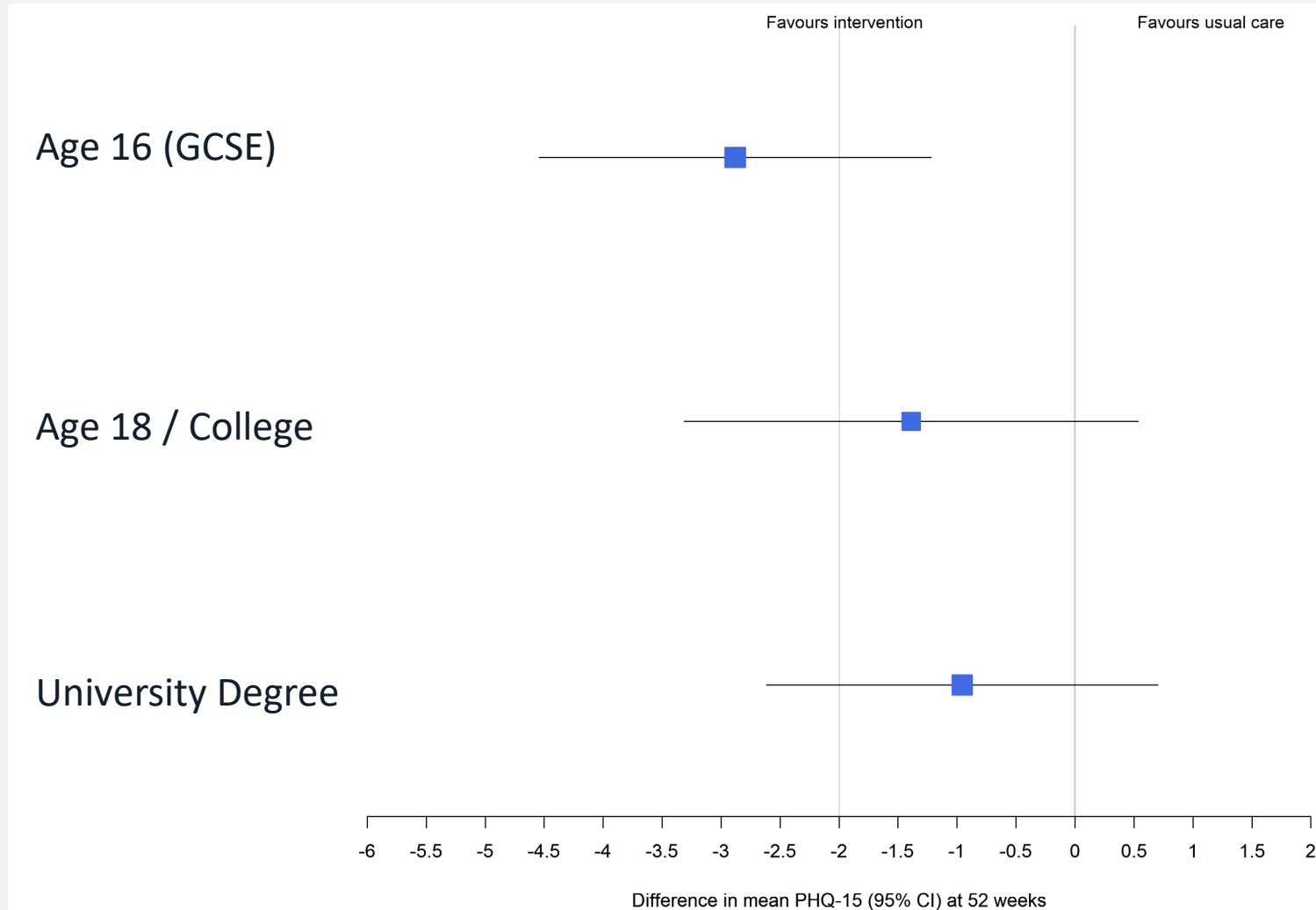
Process evaluation 5: Health literacy / education

1. Did people with low HL spend as much time in explanation phase?



But what about health inequalities: (health literacy, education)

2. Did people with less education do better or worse in terms of primary outcome?



Summary

- Complex intervention development and evaluation takes many years from idea to completion.
- Pragmatic trials address questions about what works in the real world (compared to what would happen otherwise)
- This opens up unavoidable questions about efficacy and whether observed effectiveness is specific or non-specific
- Process evaluation – theory driven – can be used to test dosing, measure, “internal” processes, examine mechanisms

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Sanders, Monica Greco, Vincent Deary

The Symptom Clinic GPs!

Phoebe McArthur, Bethany Oaten

Trial Steering Committee and Data
Monitoring Committee

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