



**P**acing, graded **A**ctivity and **C**ognitive behaviour  
therapy: a randomised **E**valuation

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Sharpe,  
And many others

# Aims

To describe results of the PACE trial,  
mechanisms of change and predictors  
of recovery

# Chronic Fatigue Syndrome

- Defined by physical and mental fatigue
- Associated with profound disability
- Co-morbid with anxiety and depression in up to 75% of patients in primary and secondary care
- Many patients do not believe they have anything psychologically wrong with them

# Why was a trial needed?

- Systematic reviews concluded that rehabilitative cognitive behaviour and graded exercise therapies were the most promising treatments for CFS in secondary care but also that more research was needed.
- Large surveys by patient charities concluded that CBT and GET often made patients worse rather than better. Pacing and specialist medical care were reported to be more helpful.

# The trial questions

Which of CBT, GET, pacing and SMC alone, are most effective?

Are any of the treatments more harmful than the others?

# Methods

# The Treatments

SMC

SMC + APT

SMC + CBT

SMC + GET

# Specialist Medical Care

- Diagnosis
- Advice and education
  - Sleep, activity, rest
- Medication
- Self-help



# Therapies

- Adaptive Pacing Therapy (APT)
- Cognitive Behaviour Therapy (CBT)
- Graded Exercise Therapy (GET)

# Differences between therapies

- One adaptive (APT)
- Two - behavioural activation / graded exposure (CBT & GET)
- One addresses thoughts and feelings (CBT)

# Design

- At least 3 sessions of SMC over 52 weeks
- 14 sessions of therapy over 23 weeks (+ booster session at 36 weeks)
- Outcome assessed at 12, 24 & 52 weeks

# Primary outcomes

**Fatigue** – Chalder Fatigue Scale

**Disability** - SF36 physical functioning subscale

# Results

# Recruitment of sample

- 3,158 clinic attenders clinically assessed
- 898 research screened
- 641 recruited
- Approximately 160 per treatment group

# Sample demographics

- Caucasian 93%
- Age (mean, SD) 38 (12)
- Female 78 %

# Sample clinical characteristics

- CDC criteria 67%
- ME criteria 51%
- Current depressive disorder 33%
- Median duration of illness 32 months
  
- Mean (SD) CFS score 28 (3.8)
- Mean (SD) SF36 PF score 38 (16)



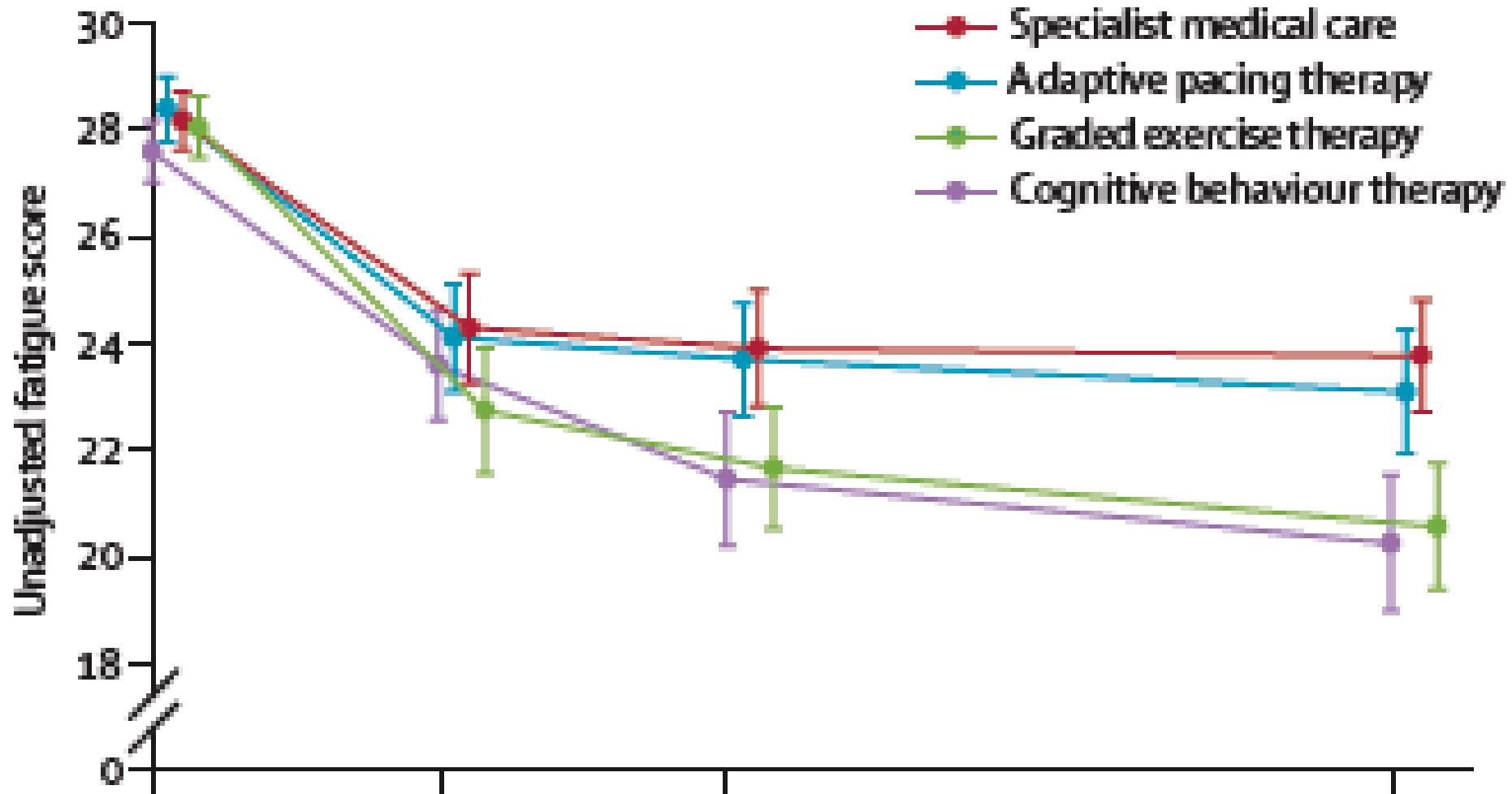
# Drop-outs: N (%)

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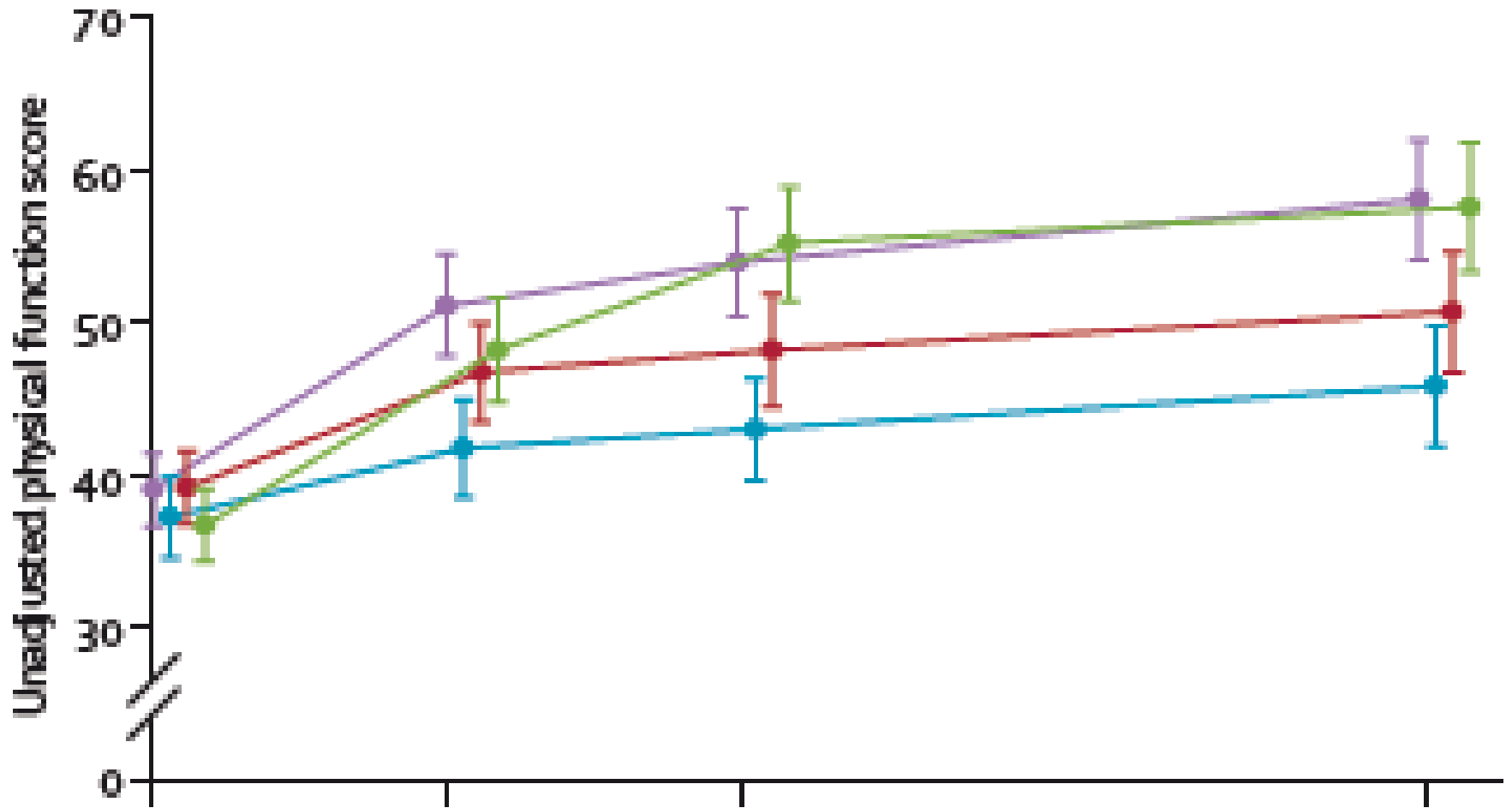
	<b>SMC</b>	<b>APT</b>	<b>CBT</b>	<b>GET</b>	<b>All</b>
No Rx received	1 (1)	1 (1)	3 (2)	0	5 (1)
Withdrawn from Rx	14 (9)	11 (7)	17 (11)	10 (6)	52 (8)
Lost to F.U.	8 (5)	6 (4)	13 (8)	6 (4)	33 (5)

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### A Fatigue: all participants



### E Physical function: all participants



# Primary outcomes models

- Baseline measures of outcome
- Time, time by intervention
- Stratification factors:
  - Centre
  - CDC criteria
  - London ME criteria
  - Depression diagnosis
- Cluster effects of therapist variation

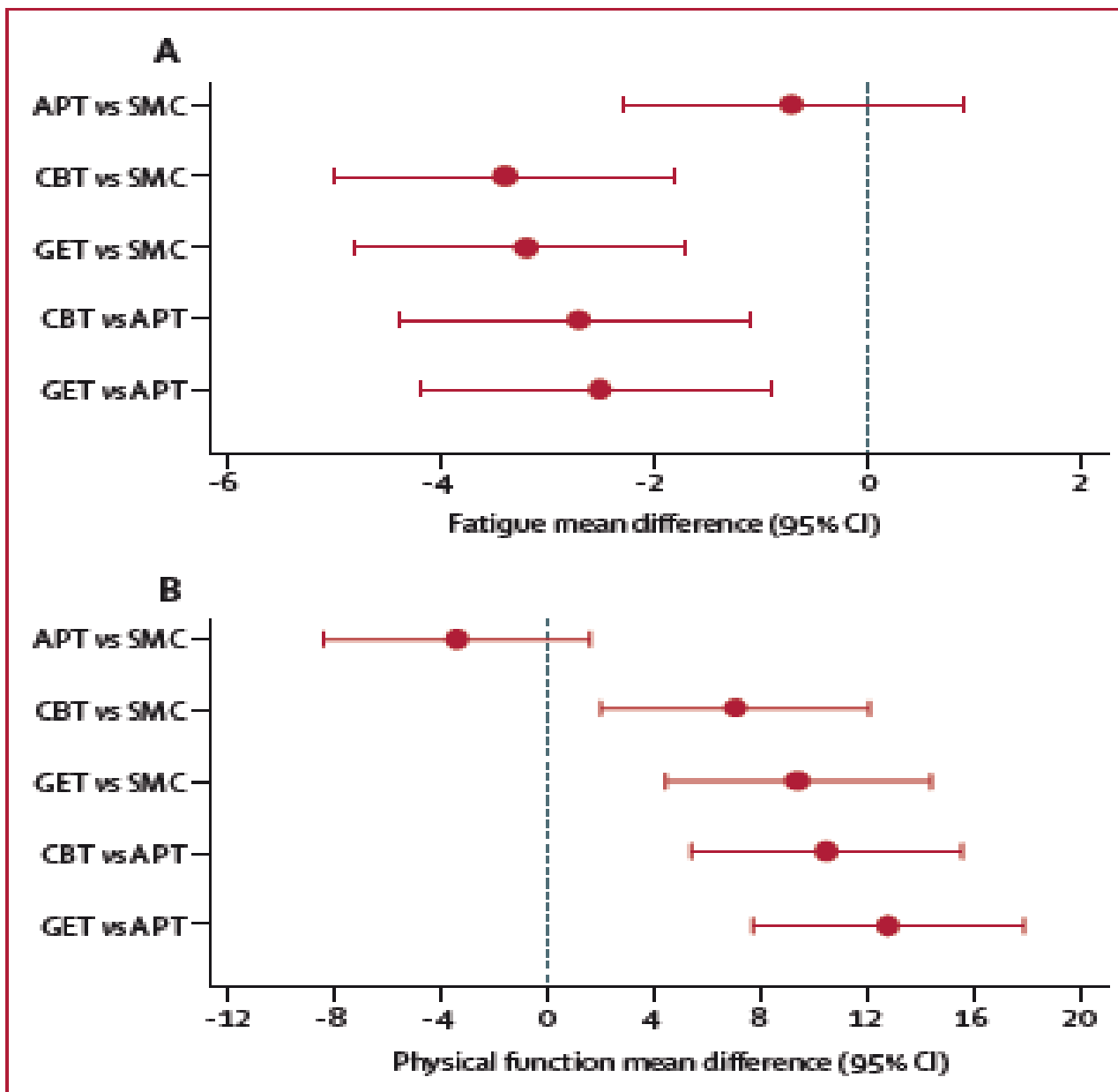


Figure 3: Primary outcome treatment differences for fatigue (A) and physical function (B) at 52 weeks

# Clinically significant difference

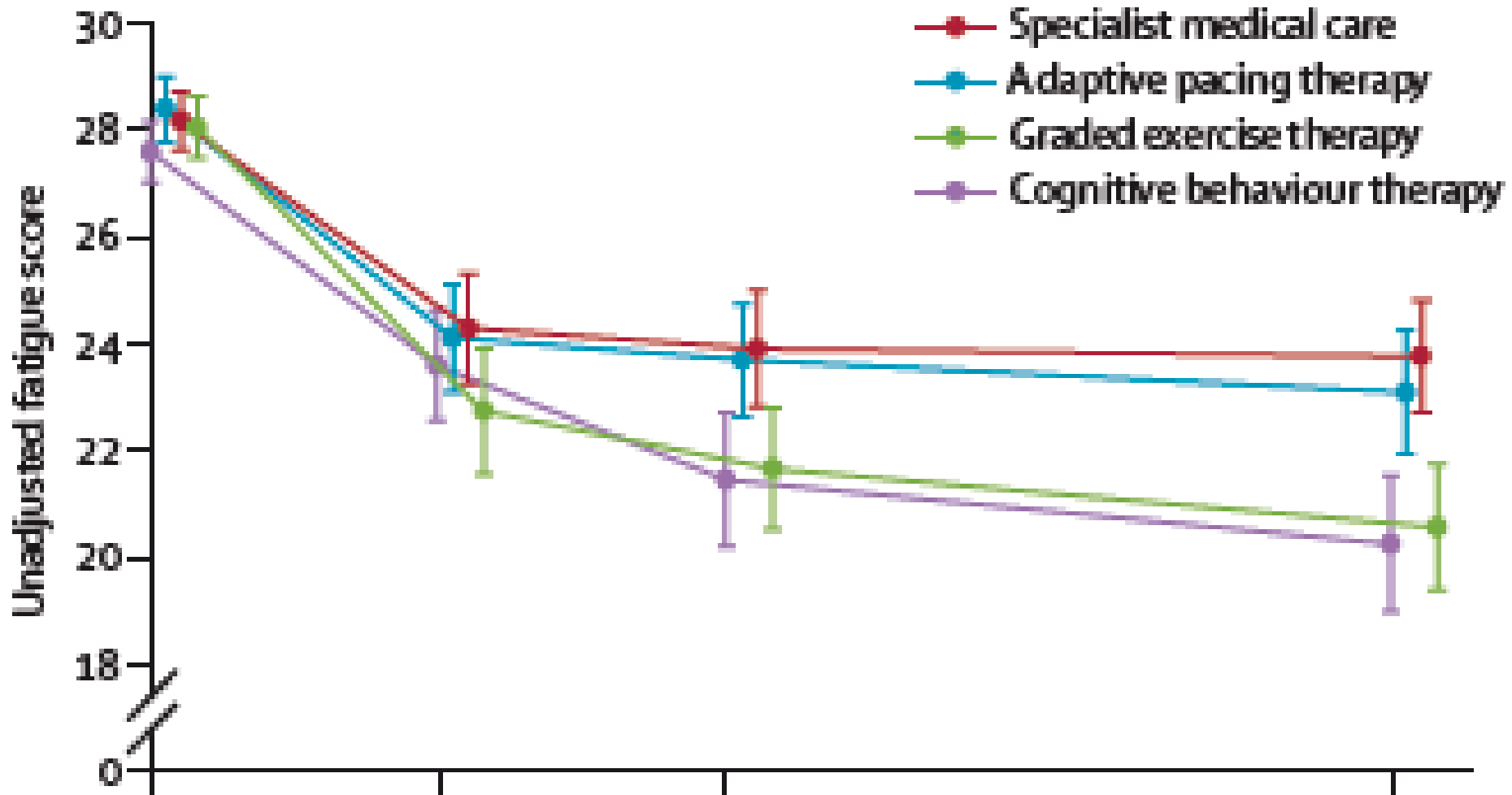
- Clinically significant difference (CUD) 0.5 SD of baseline scores
- Fatigue - 2 points
- Physical Function - 8 points

# How effective?

Percentage improved in both fatigue and function

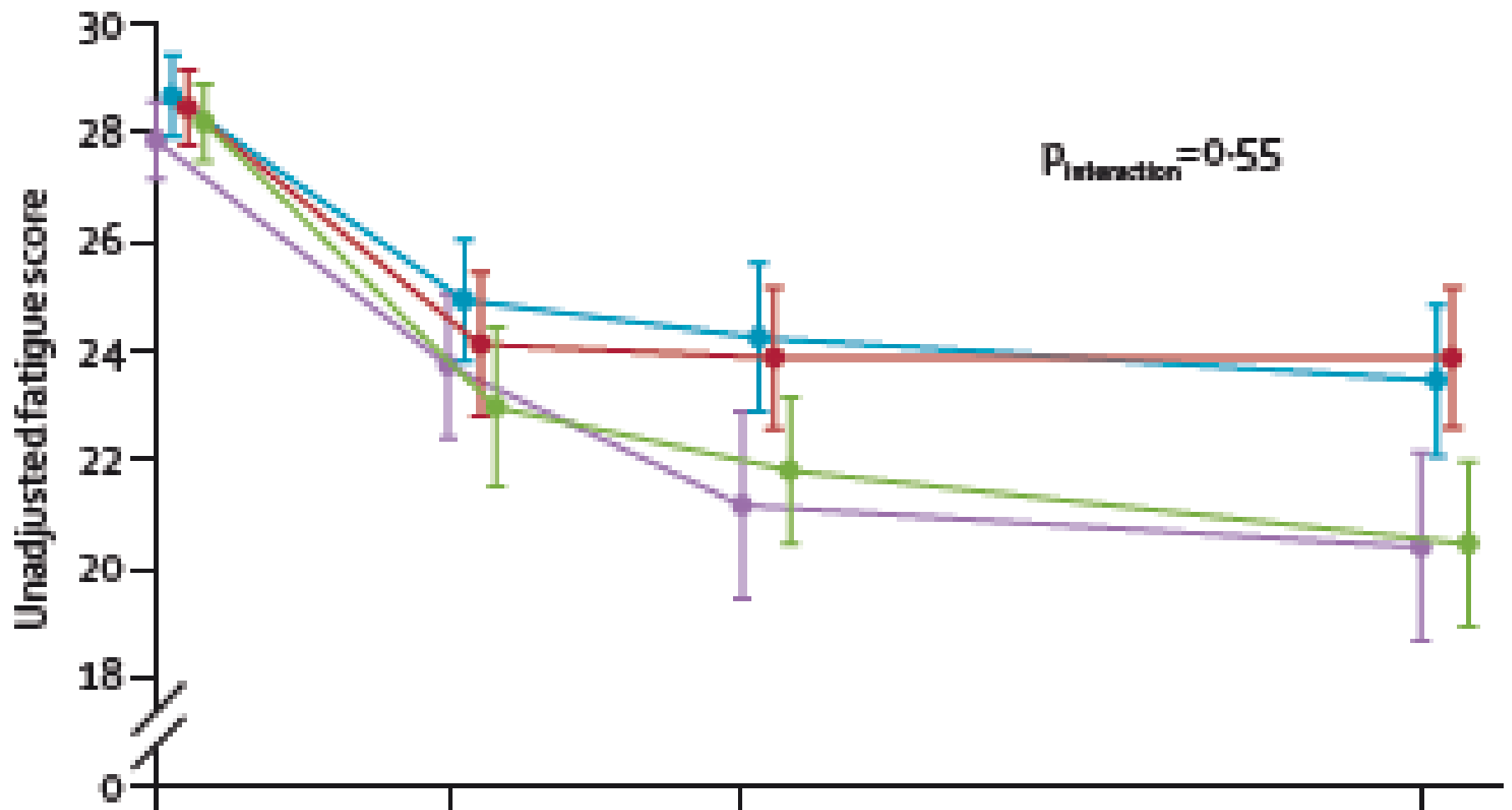
	<b>SMC</b>	<b>APT</b>	<b>CBT</b>	<b>GET</b>
% improved	45	42	59	61
% “normal” levels	15	16	30	28

# A Fatigue: all participants

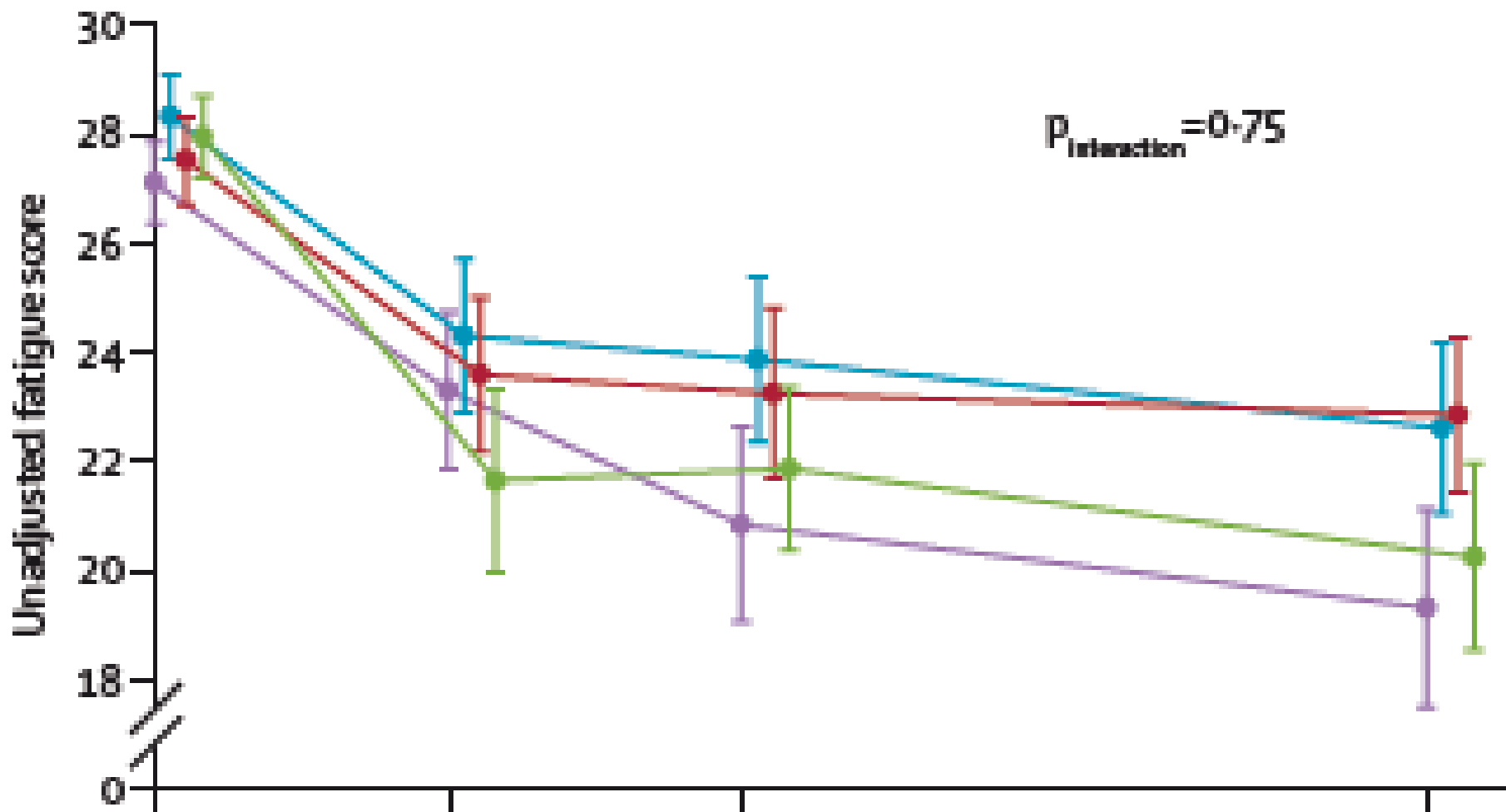




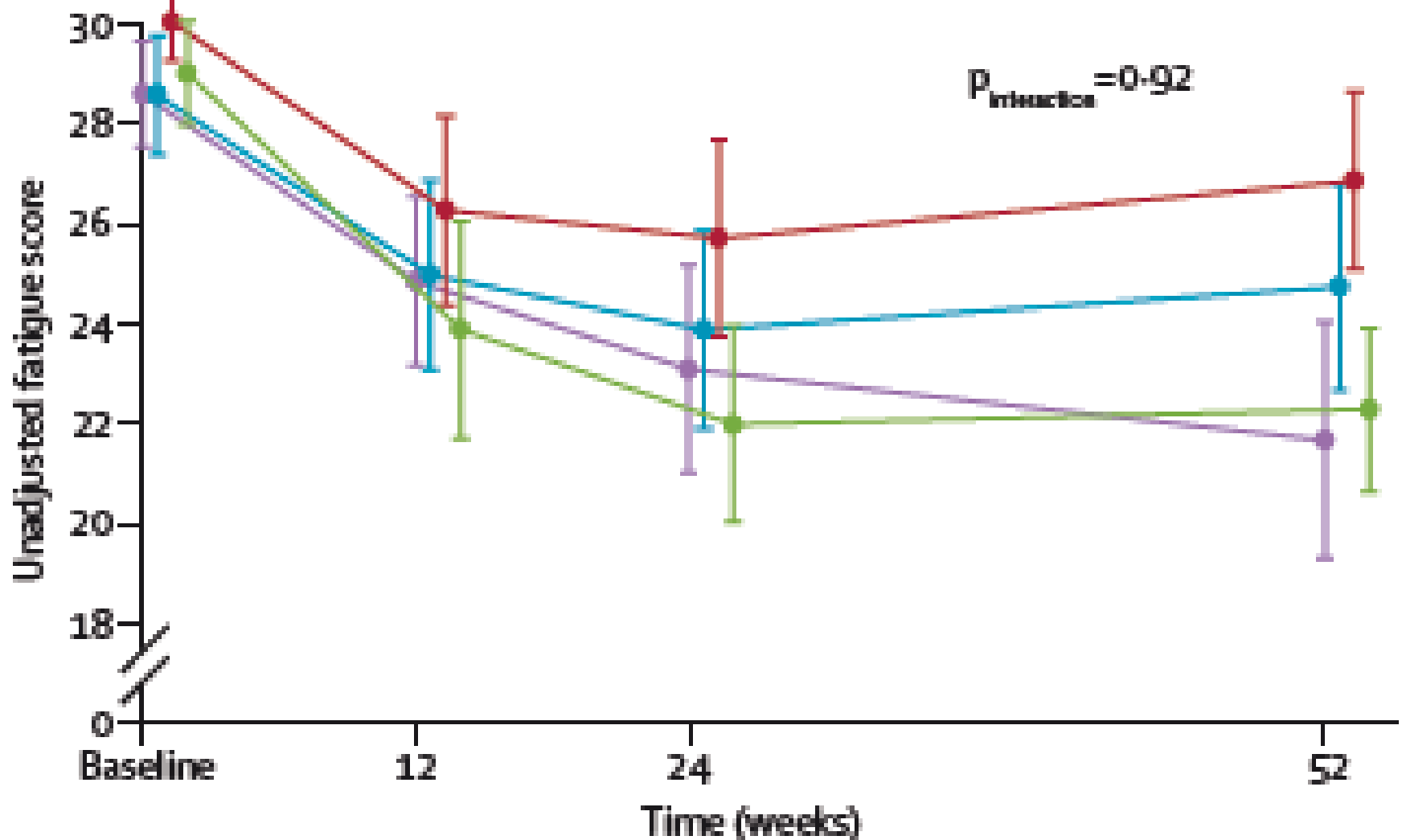
## B Fatigue: international CFS only



### C Fatigue: London ME only



### D Fatigue: depressive disorder only



# Clinical Global Impression

Overall, how much do you feel your health has changed since the start of the study? Please tick the one box below that most closely corresponds to how you feel now.

Very much better

Much better

A little better

No change

A little worse

Much Worse

Very much worse

# CGI (2 levels) %

	SMC	APT	CBT	GET
“Much”+ better	25	31	41	41
“Much”+ worse	9	7	6	7

# Other secondary outcomes

*CBT and GET best:*

Overall disability

Sleep disturbance

**Post-exertional malaise**

*GET best:*

Walking ability

*CBT best:*

Depression

*Mixed picture or no better:*

Anxiety, symptom count, poor concentration

# Recovery rates

- The percentages (number/total) meeting trial criteria for recovery were 22% (32/143) after CBT, 22% after GET, 8% after APT and 7% after SMC
- Similar proportions met criteria for clinical recovery. OR after CBT was 3.36 [95% (CI) 1.64–6.88] and for GET 3.38 (95% CI 1.65–6.93), when compared to APT

(White et al 2013 Psychological Medicine)

# Therapy quality

	<b>APT</b>	<b>CBT</b>	<b>GET</b>
N sessions	13	14	13
“Confident” before	72 %	57 %	70 %
“Satisfied” after	85 %	82 %	88 %
Alliance	6.5	6.5	6.5
Adherence	6	6	6.5



# Safety

Measured 5 ways

**% with events**

	SMC	APT	GET	CBT
Serious adverse reactions	1	1	1	2
Serious deterioration	9	8	6	9

# Conclusions

- CBT and GET are more effective than SMC alone and APT.
- APT is no different from SMC alone
- The effectiveness of CBT and GET is moderate
- The effect is similar however CFS/ME is defined and in those also depressed
- Treatments are safe, if given as described
- Pushing limits > staying within limits

# Funders



Its good to talk  
CBT style of course!

