

CACE analysis in the Frailty Intervention Trial

Niki Fairhall

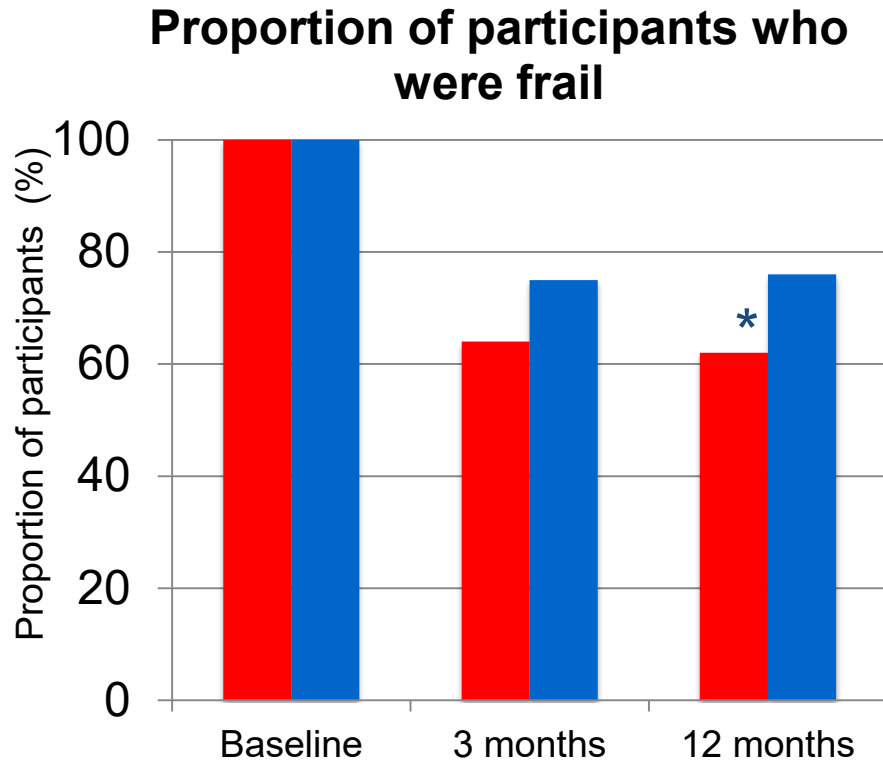
Frailty Intervention Trial

Aim	Determine whether a multifactorial, interdisciplinary intervention reduces frailty and improves mobility
Method	RCT
Participants	241 frail community-dwelling people, aged \geq 70 years
Intervention	<p>12-month interdisciplinary intervention targeting frailty</p> <ul style="list-style-type: none">• Home exercise programme<ul style="list-style-type: none">• 'Weight Bearing Exercise for Better Balance Programme'• 10 physiotherapy home visits + home exercise prog 3x/week• Dietician input• Referral for follow-up of medical conditions• Geriatrician review, home medicines review, psychologist assessment if indicated, case co-ordination by physiotherapist• Referral to services
Control	Usual care

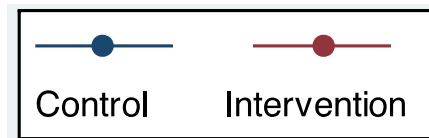
Frailty Intervention Trial – ITT, results

Outcome (0, 3 and 12 months)
Frailty <ul style="list-style-type: none">• Frailty phenotype• range 0-5
Mobility <ul style="list-style-type: none">• Short Physical Performance Battery• range 0-12
Fall rate

Frailty Intervention Trial – ITT, results

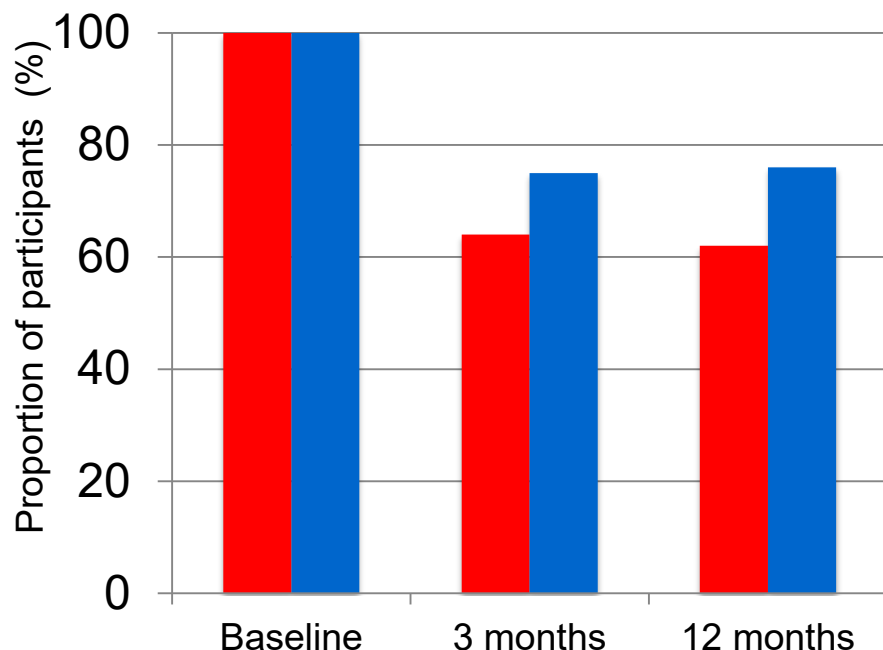


*Between group
difference = 0.41,
(95% CI 0.1 to 0.7)
 $p < 0.01$

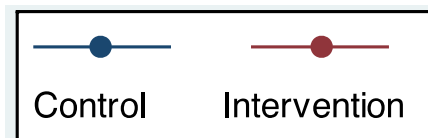


Frailty Intervention Trial – ITT, results

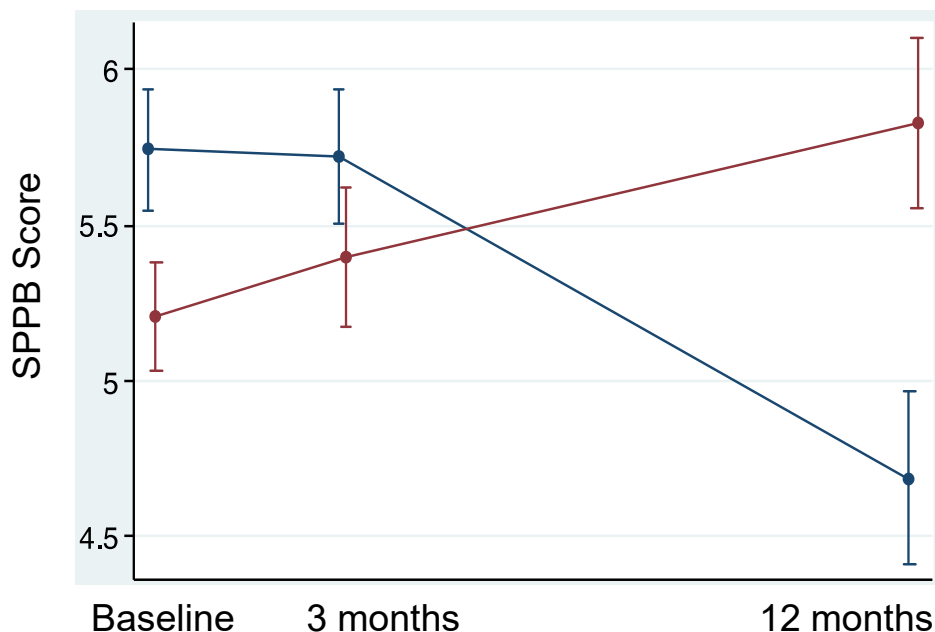
Proportion of participants who were frail



Between group
difference = 0.41,
(95% CI 0.1 to 0.7)
 $p < 0.01$



SPPB score



Mean between group
difference = 1.44 points
(95%CI 0.80 to 2.07)
 $p < 0.001$

Frailty Intervention Trial – ITT, results

Intention to treat analysis

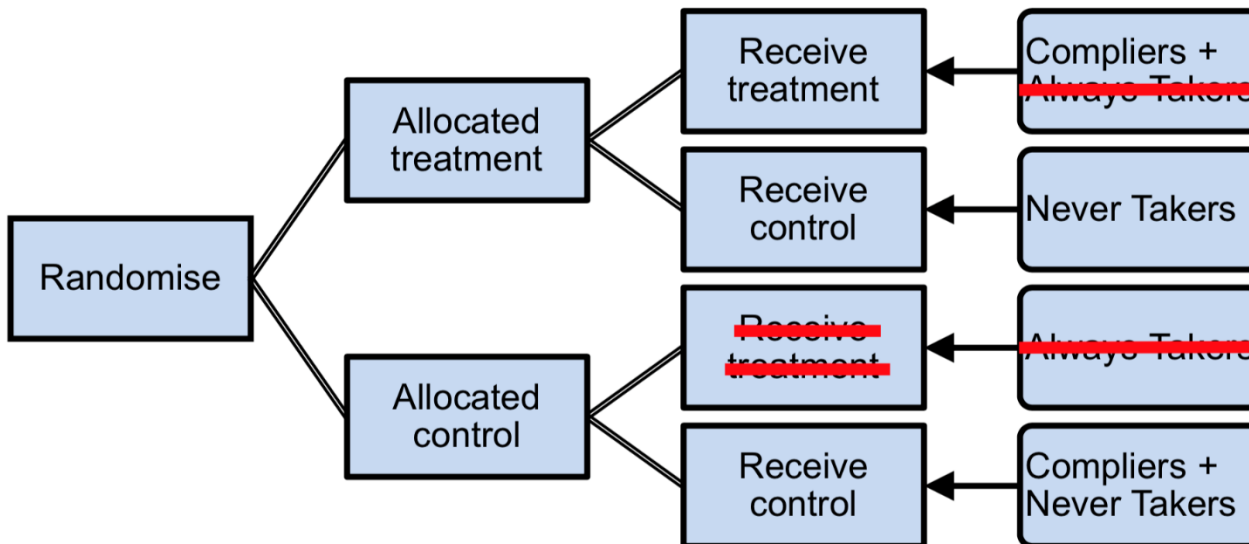
Outcome (12 months)	Mean treatment effect (95% CI)	p-value
Frailty <ul style="list-style-type: none">• Frailty phenotype• range 0-5	-0.4 (-0.1 to -0.7)	0.004
Mobility <ul style="list-style-type: none">• Short Physical Performance Battery• range 0-12	1.4 (0.8 to 2.1)	<0.001
Fall rate	Incidence rate ratio 1.12 (0.78–1.63)	0.53

Frailty Intervention Trial – CACE

Aim

Find the average effect of treatment in people who comply with allocation

i.e. find the complier average causal effect (CACE)



Frailty Intervention Trial – CACE, methods

Methods

1. Quantify amount of treatment received

$$\frac{\text{amount of treatment received}}{\text{amount of treatment prescribed}}$$

Frailty Intervention Trial – CACE, methods

Methods

1. Quantify amount of treatment received

$$\frac{\text{amount of treatment received}}{\text{amount of treatment prescribed}}$$

0%

1-25%

26-50%

51-75%

76-100%

Frailty Intervention Trial – CACE, methods

Methods

1. Quantify amount of treatment received

$$\frac{\text{amount of treatment received}}{\text{amount of treatment prescribed}}$$

0%

1-25%

26-50%

51-75%

76-100%

2. Instrumental variable regression

ivregress 2sls SPPB_12 SPPB_0 (amt oftreatment = group), first

estimator:
two-stage
least
squares

dependent
variable

baseline
covariate

endogenous
variable:
amount of
treatment

Instrumental
variable:
allocated
group

Frailty Intervention Trial – CACE, methods

Methods

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$$\frac{\text{amount of treatment received}}{\text{amount of treatment prescribed}}$$

0%

1-25%

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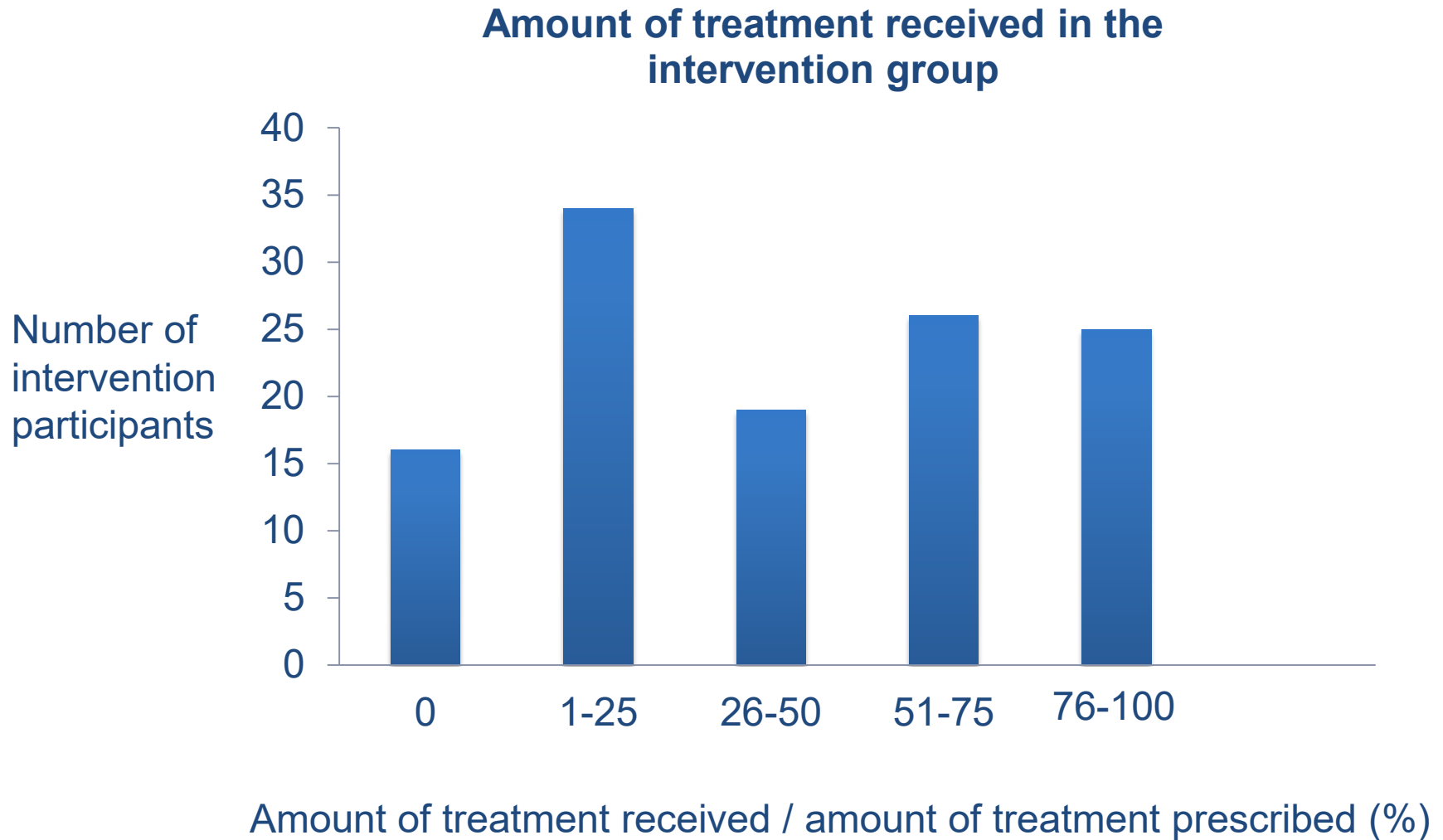
76-100%

2. Instrumental variable regression

`ivregress 2sls SPPB_12 SPPB_0 (amtsoftreatment = group), first`

`ivregress 2sls SPPB12 SPPB0 age walk_aid MMSE mood EQ5D
(amtsoftreatment = SPPB0 group age walk_aid MMSE mood EQ5D), first`

Frailty Intervention Trial – CACE, results



Frailty Intervention Trial - CACE, results

Outcome	Mean treatment effect (95% CI)	p-value
Frailty	-1.0 (-0.4 to -1.5)	0.002
Mobility	3.2 (1.9 to 4.7)	<0.001

One point reduction in frailty
(95% CI 0.4 to 1.15 point reduction)

3.2 point improvement in mobility
(95% 1.9 to 4.7 point improvement)

CACE

Frailty Intervention Trial - CACE, results

Outcome	CACE		Intention to treat	
	Mean treatment effect (95% CI)	p-value	Mean treatment effect (95% CI)	p-value
Frailty	-1.0 (-0.4 to -1.5)	0.002	-0.4 (-0.1 to -0.7)	0.004
Mobility	3.2 (1.9 to 4.7)	<0.001	1.4 (0.8 to 2.1)	<0.001

CACE

Intention to treat

Frailty Intervention Trial - CACE, results

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CACE

Mean treatment effect (95% CI)	p-value
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Intention to treat

2.5 x
greater
reduction
in frailty

Frailty Intervention Trial - CACE, results

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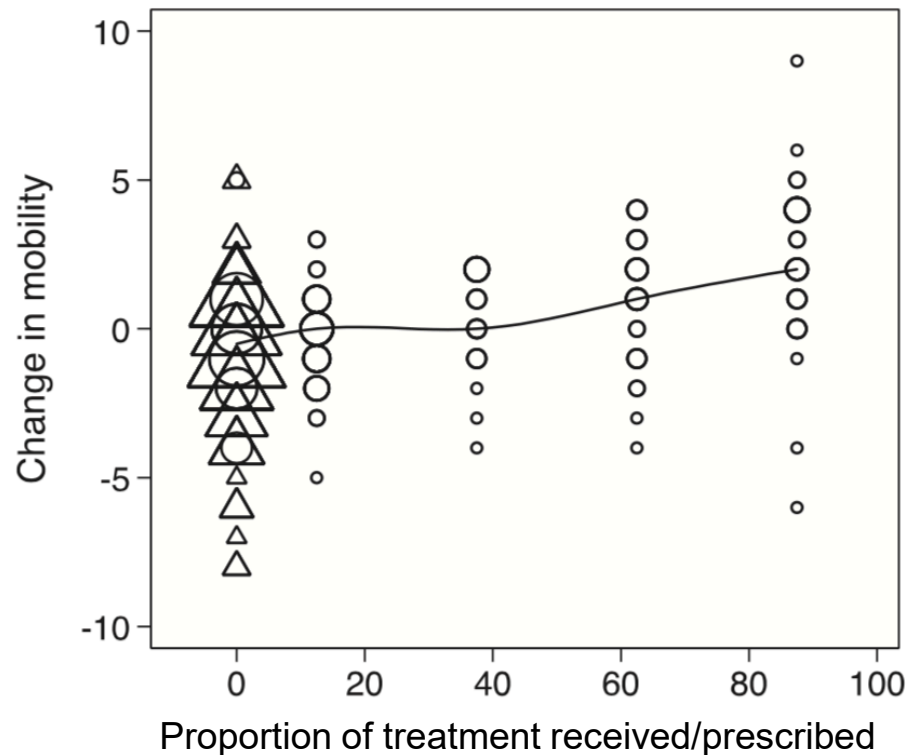
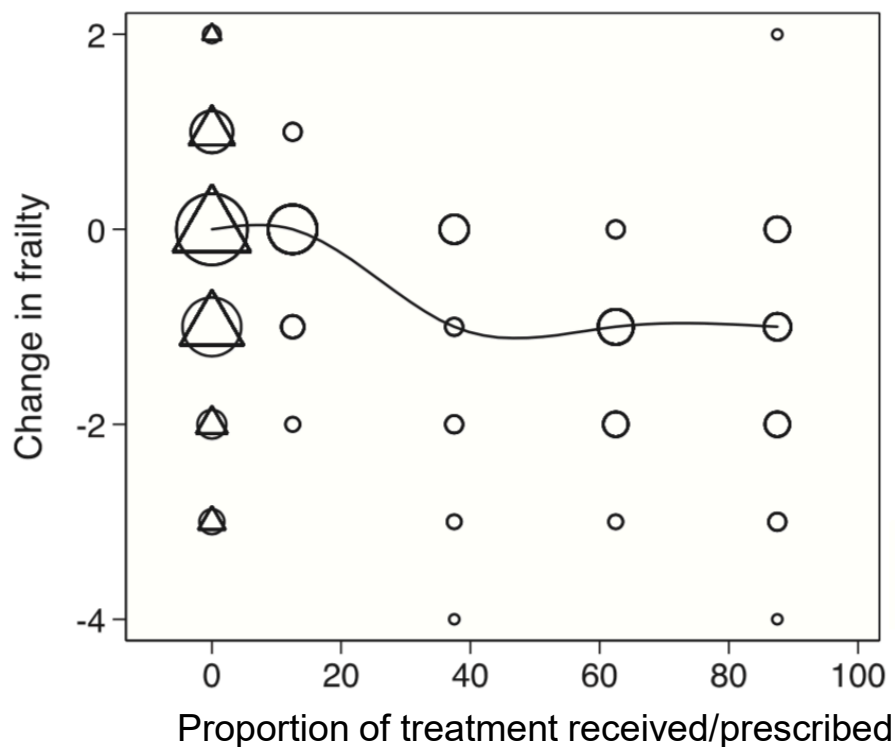
CACE

Mean treatment effect (95% CI)	p-value
-0.4 (-0.1 to -0.7)	0.004
1.4 (0.8 to 2.1)	<0.001

Intention to treat

2.25 x
greater
improvement
in mobility

Relationship between amount of treatment received and the change in frailty and mobility outcomes over 12 months in intervention and control groups



▲ Control
○ intervention

Symbol area = proportional to the number of participants.

What does this mean?

Consideration of both the intention-to-treat and CACE analyses provides a more complete understanding of the effects of the intervention.

Future studies:

- accurately record and evaluate the amount of treatment received
- estimate effects of intervention in compliant participants

But beware of limitations

Limitations

- The CACE is the average effect of treatment in compliers. It tells us nothing about the effect of compliance.
- How to measure compliers and non-compliers?
- Control participants may undertake intervention.
- Assumption of CACE = Exclusion restriction.
 - *The offer of treatment affords no additional benefit to non-compliers randomised to the intervention group compared with non-compliers randomised to the control group*

Conclusions

CACE seems useful approach.

A rigorous method for evaluating whether there are greater effects in compliers than in the whole population.

Useful for fall prevention studies.

RESEARCH ARTICLE

Open Access

A multifactorial interdisciplinary intervention reduces frailty in older people: randomized trial

Ian D Cameron^{1*}, Nicola Fairhall^{1,2}, Colleen Langron³, Keri Lockwood¹, Noeline Monaghan¹, Christina Aggar⁴, Catherine Sherrington², Stephen R Lord⁵ and Susan E Kurrle³

RESEARCH ARTICLE

Open Access

Effect of a multifactorial interdisciplinary intervention on mobility-related disability in frail older people: randomised controlled trial

Nicola Fairhall^{1,2*}, Catherine Sherrington², Susan E Kurrle³, Stephen R Lord⁴, Keri Lockwood³ and Ian D Cameron¹



Journal of **PHYSIOTHERAPY**

journal homepage: www.elsevier.com/locate/jphys

Research

A multifactorial intervention for frail older people is more than twice as effective among those who are compliant: complier average causal effect analysis of a randomised trial

Nicola Fairhall^a, Catherine Sherrington^a, Ian D Cameron^b, Susan E Kurrle^c,
Stephen R Lord^d, Keri Lockwood^c, Robert D Herbert^d