

Can metformin prevent worsening of muscle weakness and frailty in older people who are showing early signs of frailty? (the MET-PREVENT trial)

Trial registration: ISRCTN29932357

CONSORT flow diagram (screening visit onwards):

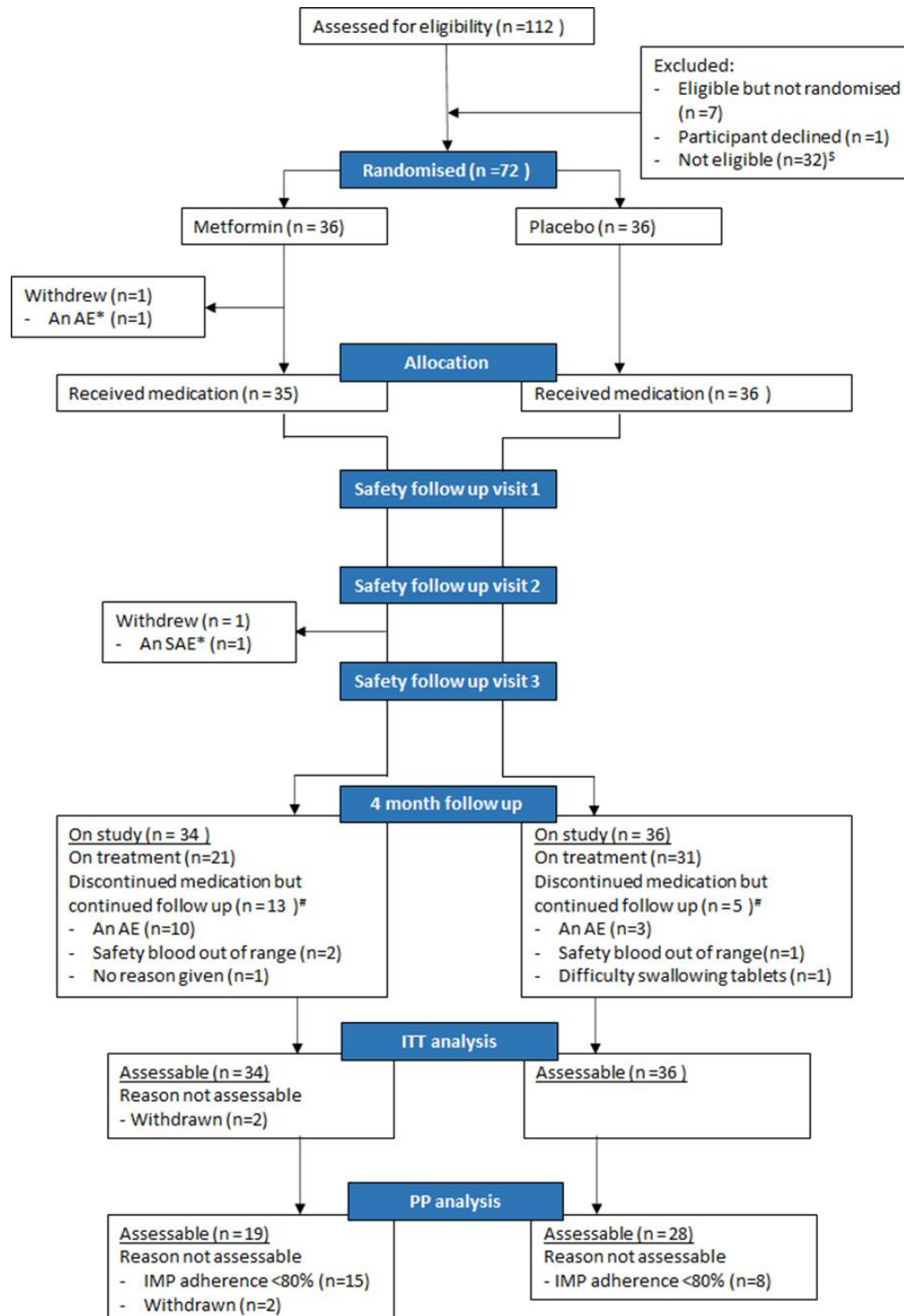


Table 1. Baseline participant details

	Metformin (n=36)	Placebo (n=36)
Mean age (yrs) (SD)	80.8 (6.0)	79.9 (5.5)
Female sex (%)	21 (58)	21 (58)
Lives in own home (%)	28 (78)	34 (94)
Walking aid (%)	19 (53)	20 (56)
<i>Comorbidity</i>		
Ischemic heart disease (%)	4 (11)	5 (14)
Stroke (%)	9 (25)	6 (17)
Hypertension (%)	17 (47)	21 (58)
Anxiety (%)	5 (14)	5 (14)
Depression (%)	10 (28)	9 (25)
Parkinsonism (%)	1 (3)	2 (6)
Asthma (%)	4 (11)	6 (17)
Other lung disease (%)	4 (11)	5 (14)
Osteoarthritis (%)	23 (64)	25 (69)
Max handgrip strength (men) (kg) (SD)	21.5 (7.2)	21.3 (8.1)
Max handgrip strength (women) (kg) (SD)	12.0 (5.0)	13.9 (4.8)
5x sit to stand completed (%)	27 (75)	26 (72)
Median 5x sit to stand time (s) (IQR)	19.5 (15.5 - 26.9)	16.6 (15.2 - 20.8)
4m walk speed (m/s) (SD)	0.59 (0.17)	0.60 (0.26)
Short Physical Performance Battery (SD)	5.6 (2.5)	6.1 (2.8)
Six min walk distance (m) (SD)*	181 (61)	192 (104)
BMI (kg/m ²) (SD)	27.1 (5.0)	27.4 (6.2)
Skeletal muscle mass index (men) (kg/m ²) (SD)	6.8 (0.9)	7.2 (1.2)
Skeletal muscle mass index (women) (kg/m ²) (SD)	6.1 (0.9)	6.3 (1.3)
EQ5D-5L (SD)	0.68 (0.22)	0.67 (0.30)
EQ5D thermometer (SD)	66 (16)	60 (23)
SF-36 Physical (SD)	37 (9)	36 (10)

SF-36 Mental (SD)	49 (12)	48 (13)
Nottingham EADL score (SD)	15 (5)	16 (5)
Random glucose (mmol/L) (SD)	5.3 (1.0)	5.2 (0.9)
HbA1c (mmol/mol) (SD)	39 (4)	39 (3)
AGE reader score (SD)	2.9 (0.6)	3.1 (1.3)

AGE: Advanced glycation end-products. BMI: Body mass index. EQ-5D: EuroQoL 5 dimension score.
HbA1c: Glycated haemoglobin. SF-36: Short-form 36 questionnaire

Table 2. Primary outcome results: 4 metre walk speed

		Metformin (n=34)	Placebo (n=36)	Unadjusted mean difference [95% CI]	p	Adjusted mean difference* [95% CI]	p
Baseline	<i>Mean (m/s) (sd)</i>	0.58 (0.17)	0.60 (0.26)	-0.02 (-0.12, 0.09)	0.76	0.00 (-0.06, 0.06)	0.96
4 months	<i>Mean (m/s) (sd)</i>	0.57 (0.19)	0.58 (0.24)				

*adjusted for baseline walk speed and sex

Table 3. Secondary outcomes

		Metformin (n=34)	Placebo (n=36)	Adjusted mean difference* [95% CI]	p
Mean grip strength (kg) (SD)	Baseline	15.9 (7.7)	17.0 (7.3)	-0.1 (-2.1, 1.9)	0.91
	4 months	16.5 (7.9)	17.4 (6.8)		
Mean SPPB (SD)	Baseline	5.5 (2.5)	6.1 (2.8)	0.3 (-0.5, 1.1)	0.47
	4 months	5.6 (2.6)	5.8 (2.9)		
Mean six min walk distance (m) (SD)	Baseline	192 (62)	216 (93)	11 (-19, 40)	0.46
	4 months	219 (86)	232 (89)		
Mean appendicular SMM (kg) (SD)	Baseline	17.8 (4.1)	18.2 (4.4)	-0.0 (-0.8, 0.8)	0.95
	4 months	17.3 (4.1)	17.7 (3.9)		
Mean Nottingham extended ADL score (SD)	Baseline	15.0 (4.6)	16.0 (5.3)	-0.4 (-1.1, 1.9)	0.64
	4 months	15.3 (4.8)	15.7 (5.2)		
Mean EQ5D-5L score (SD)	Baseline	0.67 (0.23)	0.66 (0.30)	-0.08 (-0.17, 0.01)	0.10
	4 months	0.56 (0.32)	0.65 (0.28)		
Mean EQ5D thermometer (SD)	Baseline	66 (16)	60 (23)	1 (-7, 8)	0.89
	4 months	63 (20)	59 (23)		
Mean SF-36 PCS (SD)	Baseline	36.1 (9.1)	35.5 (9.8)	-1.0 (-3.9, 1.9)	0.50
	4 months	37.2 (8.2)	37.9 (9.5)		
Mean SF-36 MCS (SD)	Baseline	48.9 (12.1)	48.3 (13.2)	0.7 (-2.9, 4.3)	0.69
	4 months	47.8 (13.0)	46.8 (13.1)		

SPPB: Short Physical Performance Battery. SMM: Skeletal Muscle Mass. ADL: Activities of Daily Living. EQ5D: EuroQoL 5 dimension score. SF-36: Short-Form 36 questionnaire. PCS: Physical component score. MCS: Mental component score

*adjusted for baseline variable under test, baseline walk speed and sex

Table 4. Summary of adverse events

		Metformin	Placebo
Number of participants with at least one AE (%)		36 (100)	33 (92)
Number of participants with at least one AR (%)		28 (78)	17 (47)
Number of participants with at least one SAE (%)		9 (25)	3 (8)
Number of participants with at least one SAR (%)		0 (0)	0 (0)
Number of participants with at least one SUSAR (%)		0 (0)	0 (0)
Total number of AEs		110	77
Median number of AEs per participant (IQR)		3 (2-4)	2 (1-3)
Most common AEs:	Diarrhoea	26	10
	Nausea	6	0
	Vomiting	4	0
	Elevated lactate	13	8
Hospital admissions		12	3
Deaths		1	0

AE: Adverse event. AR: Adverse reaction. SAE: Serious adverse event. SAR: Serious adverse reaction. SUSAR: Suspected unexpected serious adverse reaction. IRQ: Interquartile range