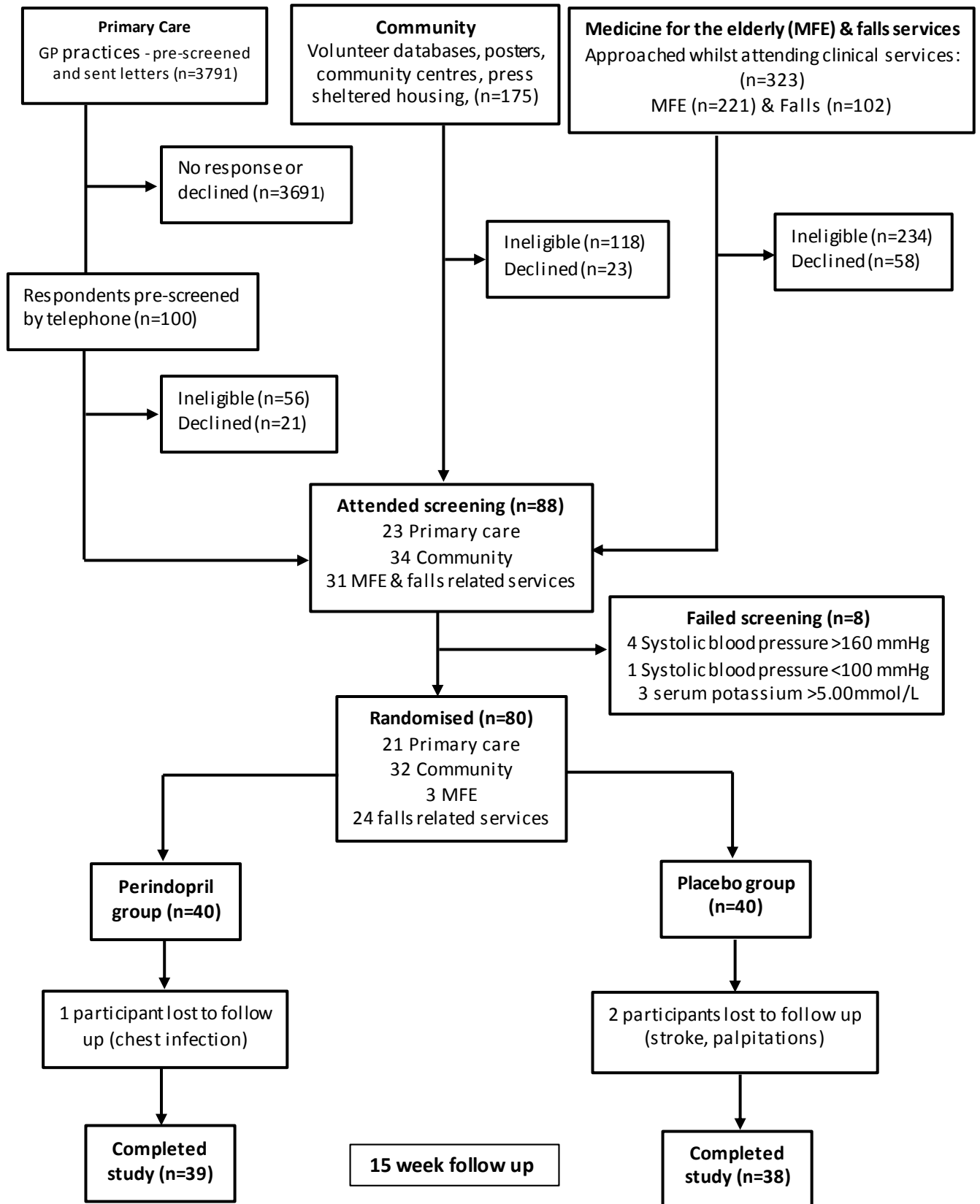


# Participant Flow



## Baseline Characteristics

|                                 | Perindopril (n=40) | Placebo (n=40) |
|---------------------------------|--------------------|----------------|
| Mean age (years) (SD)           | 78.1 (7.3)         | 78.0 (7.6)     |
| Male sex (%)                    | 10 (25)            | 10 (25)        |
| Smoking pack years (SD)         | 10.4 (18.4)        | 13.0 (27.5)    |
| Alcohol units/week (SD)         | 2.6 (3.3)          | 2.2 (4.1)      |
| SIMD decile 1-5 (%)             | 10 (25)            | 10 (25)        |
|                                 |                    |                |
| <b>Home circumstances</b>       |                    |                |
| Home alone (%)                  | 20 (50)            | 17 (42)        |
| Home with family/friends (%)    | 17 (43)            | 16 (40)        |
| Sheltered Housing (alone) (%)   | 3 (7)              | 7 (18)         |
|                                 |                    |                |
| <b>Walking aid</b>              |                    |                |
| None (%)                        | 20 (50)            | 19 (47)        |
| Walking stick (%)               | 16 (40)            | 14 (35)        |
| Other (%)                       | 4 (10)             | 7 (18)         |
|                                 |                    |                |
| <b>Co-morbidities</b>           |                    |                |
| Hypertension (%)                | 16 (40)            | 16 (40)        |
| Ischaemic heart disease (%)     | 5 (13)             | 3 (7)          |
| Previous stroke/TIA (%)         | 3 (7)              | 3 (7)          |
| Peripheral vascular disease (%) | 0                  | 1 (2)          |
| Diabetes (%)                    | 2 (5)              | 2 (5)          |
| COPD (%)                        | 4 (10)             | 5 (13)         |
| Anaemia (%)                     | 3 (7)              | 2 (5)          |
| Peripheral neuropathy (%)       | 2 (5)              | 7 (18)         |
| Vertigo (%)                     | 3 (7)              | 4 (10)         |
| Tinnitus (%)                    | 6 (15)             | 9 (23)         |
| Registered blind (%)            | 1 (2)              | 0 (0)          |
|                                 |                    |                |

|                                       |             |             |
|---------------------------------------|-------------|-------------|
| <b>Anthropometry</b>                  |             |             |
| Mean height (m) (SD)                  | 1.58 (0.10) | 1.59 (0.08) |
| Mean weight (kg) (SD)                 | 72.5 (14.0) | 71.9 (14.3) |
| Mean BMI (kg/m <sup>2</sup> ) (SD)    | 29.0 (4.3)  | 28.5 (5.2)  |
| Height-adjusted Muscle mass kg/m (SD) | 13.9 (2.9)  | 13.7 (3.0)  |
| Height-adjusted Fat mass kg/m (SD)    | 18.9 (4.9)  | 18.2 (5.8)  |
| eGFR >60ml/min/1.73m <sup>2</sup> (%) | 35 (87)     | 37 (93)     |
| 30-60ml/min/1.73m <sup>2</sup> (%)    | 5 (13)      | 3 (7)       |
|                                       |             |             |
| <b>Concomitant medications</b>        |             |             |
| Beta blockers (%)                     | 11 (28)     | 8 (20)      |
| Thiazides (%)                         | 6 (15)      | 4 (10)      |
| Other diuretics (%)                   | 2 (5)       | 4 (10)      |
| Calcium channel blockers (%)          | 5 (13)      | 10 (25)     |
| Nitrates (%)                          | 5 (13)      | 3 (7)       |
| Sedatives and antipsychotics (%)      | 2 (5)       | 2 (5)       |
| Opioid based analgesia (%)            | 10 (25)     | 5 (13)      |

SIMD: Scottish Index of Multiple Deprivation; 1-5 = more deprived; 6-10 = less deprived. BMI: Body Mass Index. COPD: Chronic obstructive pulmonary disease. eGFR: estimated glomerular filtration rate

## Outcome Measures

|  |           | Perindopril |            | Placebo |            | Treatment effect* (95% CI) | P    |
|--|-----------|-------------|------------|---------|------------|----------------------------|------|
| <b>Primary outcome</b>                           |           |             |            |         |            |                            |      |
| A-P Sway range (mm)<br>(eyes closed)             | Baseline  | N=36        | 63 (33)    | N=39    | 64 (35)    | 2 (-7 to 12)               | 0.59 |
|  | Follow up | N=34        | 59 (31)    | N=37    | 57 (31)    |                            |      |
| A-P Sway range (mm)<br>(eyes open)               | Baseline  | N=40        | 53 (27)    | N=40    | 53 (30)    | 0 (-8 to 7)                | 0.91 |
|  | Follow up | N=39        | 45 (19)    | N=38    | 45 (28)    |                            |      |
| <b>Secondary outcomes</b>                        |           |             |            |         |            |                            |      |
| Maximal voluntary quadriceps<br>contraction (kg) | Baseline  | N=39        | 18.6 (9.0) | N=39    | 19.2 (7.5) | -1.4 (-3.0 to 0.3)         | 0.11 |
|  | Follow up | N=36        | 16.8 (6.7) | N=35    | 18.5 (7.4) |                            |      |
| Quadriceps twitch tension at rest (kg)           | Baseline  | N=31        | 2.7 (1.1)  | N=33    | 2.8 (1.6)  | 0.2 (0.0 to 0.4)           | 0.08 |
|  | Follow up | N=29        | 2.9 (1.3)  | N=30    | 2.6 (1.2)  |                            |      |
| Quadriceps twitch tension after<br>fatigue (kg)  | Baseline  | N=32        | 3.1 (1.5)  | N=32    | 3.6 (2.0)  | 0.8 (-0.1 to 1.7)          | 0.08 |
|  | Follow up | N=32        | 3.5 (2.5)  | N=30    | 2.9 (1.6)  |                            |      |
| Six minute walk distance (m)                     | Baseline  | N=40        | 336 (94)   | N=40    | 330 (113)  | -9 (-29 to 12)             | 0.41 |
|  | Follow up | N=38        | 338 (104)  | N=38    | 351 (111)  |                            |      |
| Postural change in systolic BP**<br>(mmHg)       | Baseline  | N=40        | -11 (12)   | N=40    | -15 (16)   | -1 (-6 to 4)               | 0.79 |
|  | Follow up | N=38        | -18 (11)   | N=38    | -18 (14)   |                            |      |
| Postural change in diastolic BP*<br>(mmHg)       | Baseline  | N=40        | -3 (9)     | N=40    | -4 (6)     | -1 (-4 to 2)               | 0.48 |
|  | Follow up | N=38        | -4 (9)     | N=38    | -4 (7)     |                            |      |

|                                    |           |      |                |      |                |                   |      |
|------------------------------------|-----------|------|----------------|------|----------------|-------------------|------|
| M-L sway range (mm)                | Baseline  | N=36 | 37 (40)        |      | 44 (55)        | -4 (-13 to 5)     | 0.38 |
|                                    | Follow up | N=34 | 34 (27)        |      | 41 (50)        |                   |      |
| Sway velocity (mm/s)               | Baseline  | N=36 | 83 (19)        | N=39 | 86 (22)        | -3 (-9 to 3)      | 0.31 |
|                                    | Follow up | N=34 | 81 (16)        | N=37 | 85 (28)        |                   |      |
| Total sway area (mm <sup>2</sup> ) | Baseline  | N=36 | 2389<br>(6100) | N=39 | 2071<br>(3753) | -53 (-604 to 499) | 0.85 |
|                                    | Follow up | N=34 | 1666<br>(3095) | N=37 | 1647<br>(2184) |                   |      |
| Forward reach A-P sway (mm)        | Baseline  | N=36 | 48 (23)        | N=39 | 47 (21)        | 3 (-9 to 14)      | 0.66 |
|                                    | Follow up | N=34 | 48 (30)        | N=37 | 45 (28)        |                   |      |
| Left reach M-L sway (mm)           | Baseline  | N=36 | 53 (44)        | N=39 | 49 (40)        | 9 (-1 to 20)      | 0.07 |
|                                    | Follow up | N=34 | 45 (27)        | N=37 | 36 (24)        |                   |      |
| Right reach M-L sway (mm)          | Baseline  | N=36 | 49 (35)        | N=39 | 48 (42)        | 5 (-8 to 18)      | 0.45 |
|                                    | Follow up | N=34 | 46 (44)        | N=37 | 42 (25)        |                   |      |

\*Adjusted for baseline values of variable under test \*\*Negative values denote a fall in blood pressure on standing

A-P: Antero-posterior. M-L: Medio-lateral

## Adverse Events

Excluding falls:

|  | Perindopril | Placebo |
|--|-------------|---------|
| Participants with at least one adverse event (%)                           | 33 (83)     | 31 (78) |
| Adverse events excluding falls   | 84          | 82      |
| Severity: Mild (%)   | 61 (73)     | 56 (68) |
| Moderate (%)   | 20 (23)     | 21 (26) |
| Severe (%)   | 3 (5)       | 5 (6)   |
| Participants with $\geq 1$ serious adverse event (%)                       | 1 (2)       | 3 (7)   |
| Hospitalisations   | 2           | 3       |
|  |             |         |
| <i>Frequent AE's (occurring in &gt;10%) or AE's of particular interest</i> |             |         |
| Cough  | 11          | 4       |
| Respiratory infections - upper   | 10          | 9       |
| lower  | 5           | 3       |
| Gastrointestinal problems  | 9           | 10      |
| Dizziness  | 2           | 3       |
| Collapse   | 0           | 1       |
| Headache   | 4           | 4       |

Falls (during study, from falls diary):

|                                | Perindopril<br>n=40 | Placebo<br>n=40 |
|--------------------------------|---------------------|-----------------|
| Participants with no falls (%) | 17 (44)             | 13 (33)         |
| 1-2 falls (%)                  | 10 (26)             | 18 (45)         |
| 3-5 falls (%)                  | 5 (13)              | 6 (15)          |
| 6-10 falls (%)                 | 1 (3)               | 1 (3)           |
| >10 falls (%)                  | 6 (15)              | 2 (5)           |
| Median falls (IQR)             | 1 (0,4)             | 1(0,2)          |
|                                |                     |                 |
| Total falls                    | 156                 | 95              |
|                                |                     |                 |
| Contusion from fall            | 4                   | 4               |

|                             |    |    |
|-----------------------------|----|----|
| Skin laceration/excoriation | 0  | 4  |
| Musculoskeletal injury      | 6  | 2  |
| Fracture                    | 0  | 2  |
| Total                       | 10 | 12 |