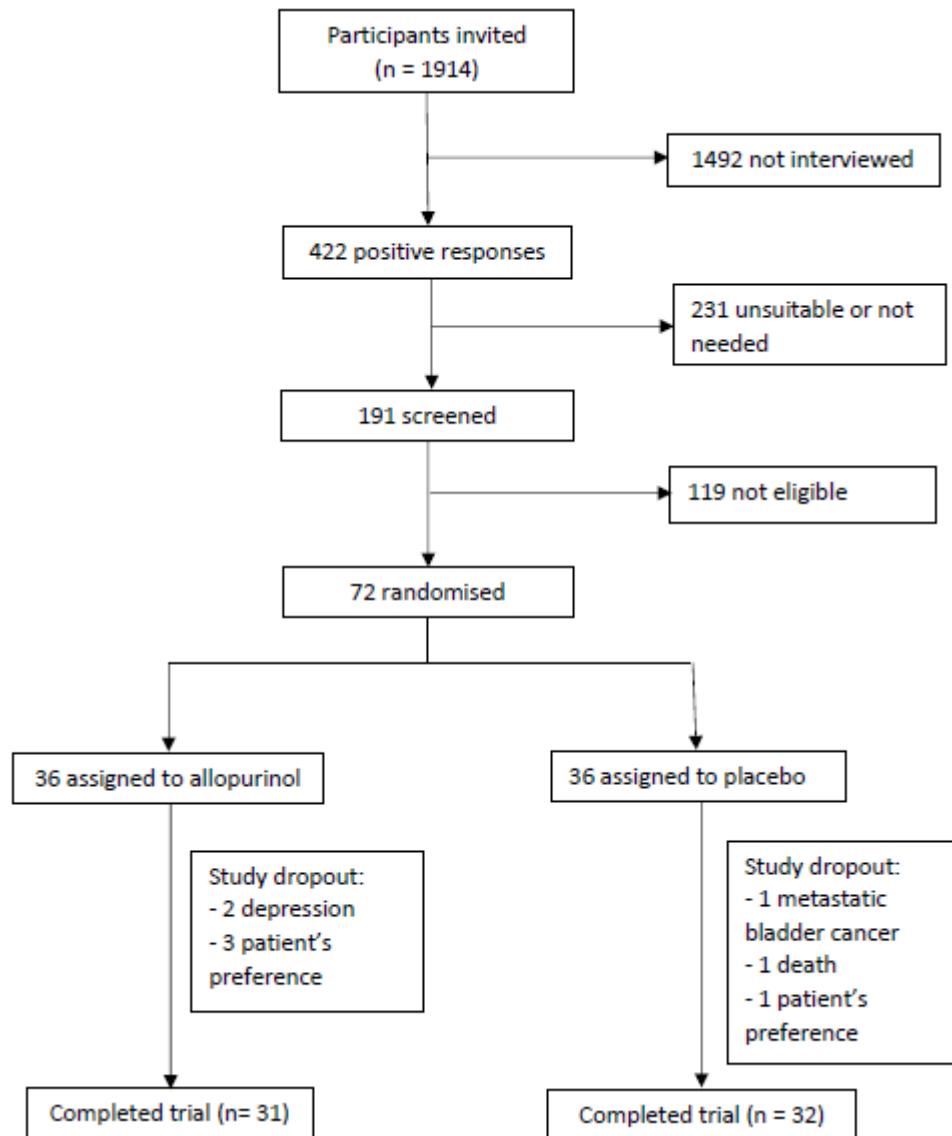


1. Participant Flow:



2. Baseline Characteristics:

| | Allopurinol (n = 36) | Placebo (n = 35) | p |
|--------------------------------|---------------------------------|-----------------------------|----------|
| Age (years) | 70 (5) | 71 (6) | 0.45 |
| Male sex (%) | 22 (61) | 22 (63) | |
| Height (m) | 1.65 (0.11) | 1.68 (0.09) | 0.29 |
| Weight (kg) | 80.2 (16.6) | 82.7 (17.0) | 0.54 |
| BMI (kg/m ²) | 29 (5) | 29 (5) | 0.98 |
| Heart rate (bpm) | 79 (14) | 78 (13) | 0.99 |
| Systolic BP (mm Hg) | 138 (16) | 140 (19) | 0.67 |
| Diastolic BP (mm Hg) | 76 (9) | 75 (14) | 0.93 |
| mMRC dyspnoea scale | 2.8 (1.3) | 2.7 (1.2) | 0.14 |
| WHO Functional class | 2.3 (0.8) | 2.4 (0.7) | 0.48 |
| Smoking status | | | |
| • Current smoker | 9 (25) | 8 (23) | |
| • Ex-/non-smoker | 27 (75) | 27 (77) | |
| Pack-year history | 46.9 (27.4) | 50.3 (28.6) | 0.61 |
| Long-term oxygen | 3 (8) | 2 (6) | |
| SaO ₂ (%) | 96 (3) | 96 (3) | 0.67 |
| PAT (ms) | 94.9 (9.6) | 97.1 (12.1) | 0.38 |
| FEV ₁ (L) | 1.51 (0.68) | 1.50 (0.67) | 0.99 |
| FEV ₁ (% predicted) | 62 (22) | 59 (20) | 0.53 |

3. Outcome Measures:

| | Allopurinol (n = 36) | Placebo (n = 35) | p |
|---------------------------------------|-----------------------------|-------------------------|----------|
| Right ventricle | | | |
| Change in RVM (g) | 1.85 (1.56) | 0.97 (1.20) | 0.66 |
| Change in RVMI (g/m ²) | 0.70 (0.75) | 0.50 (0.60) | 0.83 |
| Change in RVESV (ml) | 4.80 (2.49) | 3.79 (2.83) | 0.79 |
| Change in RVESVI (ml/m ²) | 1.91 (1.25) | 1.73 (1.42) | 0.92 |
| Change in RVEDV (ml) | 8.84 (4.23) | 5.61 (4.26) | 0.59 |
| Change in RVEDVI (ml/m ²) | 4.01 (2.16) | 3.05 (2.15) | 0.75 |
| Change in RVSV (ml) | 3.03 (3.15) | 1.57 (2.73) | 0.73 |
| Change in RVSVI (ml/m ²) | 1.42 (1.72) | 1.09 (1.33) | 0.88 |
| Change in RVEF (%) | 1.33 (2.42) | 1.67 (1.72) | 0.91 |
| Left ventricle | | | |
| Change in LVM (g) | 0.82 (3.16) | -1.95 (2.84) | 0.52 |
| Change in LVMI (g/m ²) | 0.09 (1.48) | -1.11 (1.22) | 0.53 |
| Change in LVESV (ml) | 1.26 (2.36) | 2.95 (2.62) | 0.63 |
| Change in LVESVI (ml/m ²) | 0.33 (1.18) | 1.61 (1.33) | 0.47 |
| Change in LVEDV (ml) | 7.24 (4.37) | 3.83 (4.15) | 0.57 |
| Change in LVEDVI (ml/m ²) | 3.36 (2.10) | 1.90 (2.14) | 0.63 |
| Change in LVSV (ml) | 5.83 (3.34) | 0.40 (2.59) | 0.20 |
| Change in LVSVI (ml/m ²) | 2.87 (1.73) | 0.34 (1.38) | 0.25 |
| Change in LVEF (%) | 2.96 (1.97) | -0.04 (1.27) | 0.20 |

Primary outcome is highlighted.

4. Adverse Events:

A total of 179 adverse events were recorded:

- 99 AE's in placebo group
 - 5 AE's possible causality from IMP, all recovered
- 80 AE's in allopurinol group
 - 3 AE's possible causality from IMP from same participant (malaise x2, lethargy). All three adverse events recovered when IMP dose reduced.

There were 7 serious adverse events (SAE) in the allopurinol group:

- Infective exacerbation of COPD
- Pneumonia
- Left leg cellulitis
- Prostate cancer
- Acute encephalopathy – unclear cause, probable opiate intoxication
- Transient oesophageal obstruction
- Community acquired pneumonia

There were 15 SAE's in the placebo group:

- Dehydration and chest infection
- Bladder tumour
- Metastatic cancer
- Drug-induced syncope
- Non-specific abdominal pain
- Diverticular disease
- Fracture left neck of femur
- Rectal bleed due to diverticular disease
- Urinary tract infection
- Postural hypotension
- Rectus sheath haematoma
- Atrial flutter
- Syncope
- Death due to atherosclerosis
- Urinary retention