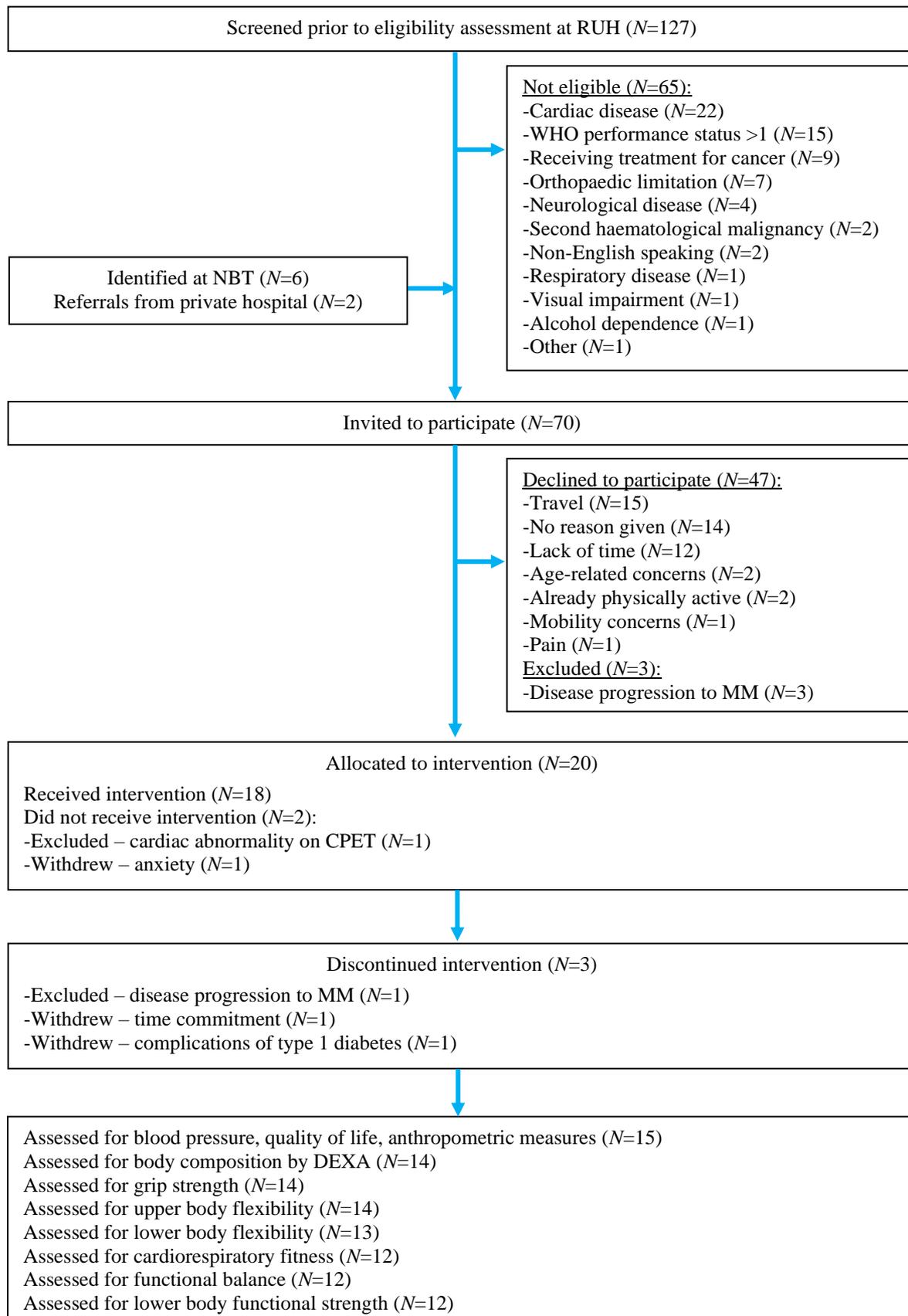


## Participant flow



RUH = Royal United Hospitals Bath, NBT = North Bristol NHS Trust, MM = Multiple myeloma, CPET = Cardiopulmonary exercise test, DEXA = Dual-energy x-ray absorptiometry.

## **Participant characteristics**

Age (years)	63 ± 8
Sex (N/15)	
Male	N=8
Female	N=7
MGUS diagnosis (N/3)	
IgG Kappa	N=1
IgG Lambda	N=1
Bi-clonal IgA Kappa	N=1
MGUS risk stratification (N/3) <sup>1</sup>	
High-intermediate risk	N=1
Low-intermediate risk	N=1
Low risk	N=1
SMM diagnosis (N/12)	
IgG Kappa	N=5
IgG Lambda	N=3
IgA Kappa	N=2
Bi-clonal IgA Lambda + IgG Lambda	N=1
Kappa light chain only	N=1
SMM risk stratification (N/12) <sup>2</sup>	
High risk	N=3
Intermediate risk	N=3
Low risk	N=6
Ethnicity (N/15)	
White	N=14
Mixed/multiple	N=1
Employment status (N/15)	
Employed	N=10
Retired	N=4
Unable to work	N=1
Smoking status (N/15)	
Non-smoker	N=10
Ex-smoker	N=5
BMI category (N/15)	
Healthy (<25 kg.m <sup>-2</sup> )	N=5
Overweight (25-29.9 kg.m <sup>-2</sup> )	N=5
Obese (>30 kg.m <sup>-2</sup> )	N=5
Physical activity level (N/15)	
Meeting guidelines (PAL ≥1.75)	N=8
Not meeting guidelines (PAL <1.75)	N=7

*MGUS = Monoclonal Gammopathy of Undetermined Significance; SMM = Smouldering Multiple Myeloma; BMI = Body mass index; PAL = Physical activity level (measured using BodyMedia Core device). IgG or IgA, and kappa or lambda indicate the involved, clonal immunoglobulin heavy chain and light chain, respectively, of the plasma cell neoplasia. <sup>1</sup>MGUS risk stratification (Rajkumar et al., 2005); <sup>2</sup>SMM risk stratification (Mateos et al., 2020).*

## Primary outcomes

### Safety

- No serious adverse events
- Grade 1 adverse events not related to the intervention resulted in  $N=20$  missed sessions (4% of 480 total sessions available): general infection/illness ( $N=12$ ); new foot pain ( $N=5$ ); exacerbation of pre-existing tendon pain ( $N=2$ ); exacerbation of psoriasis ( $N=1$ ).
- Grade 1 adverse events required dose modifications in  $N=30$  sessions (7% of 432 exercise sessions attended): pre-existing musculoskeletal pain ( $N=18$ ); new (not related to intervention) back pain ( $N=6$ ); pre-existing gastric pain ( $N=3$ ); new (related to intervention) muscle strain ( $N=3$ ).

### Feasibility

	Proportion (%)
Uptake	29
Retention	75
Adherence	
Supervised exercise	91 ± 6
Home-based exercise	88 ± 37
Compliance	
Supervised aerobic intensity	75 ± 23
Supervised aerobic duration	100 ± 3

*Uptake = proportion of clinically eligible patients invited to participate that enrolled; retention = the proportion of participants consented that completed the trial; adherence = the proportion of prescribed exercise sessions completed; compliance = the proportion of exercise sessions performed at the prescribed intensity or duration. Data are median ± interquartile range.*

## Secondary outcomes

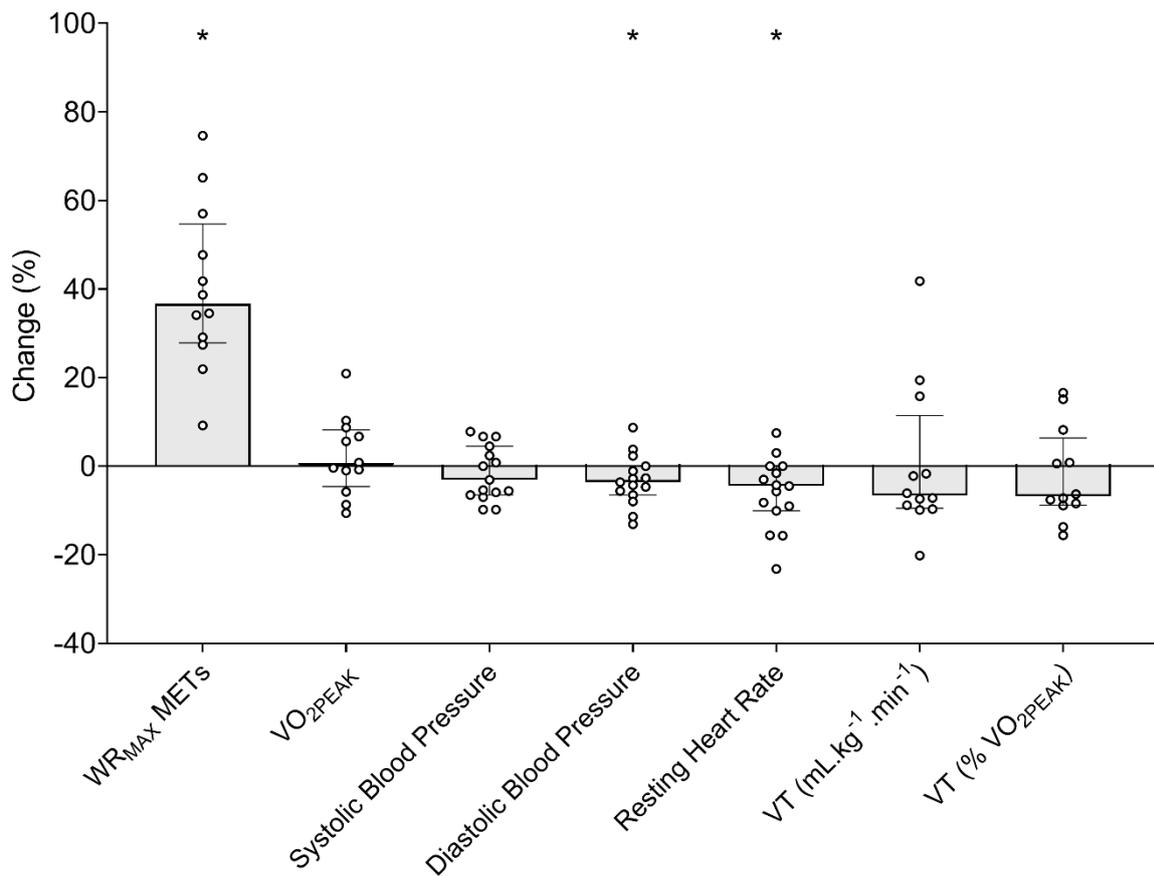


Figure 1. Percentage change to cardiorespiratory fitness and resting cardiovascular measurements from pre- to post-exercise training.

Block bars are median change, error bars are IQR. Open circles are individual responses. \* indicates statistically significant change  $P < .05$ . WR<sub>MAX</sub> METs = Work rate maximum [during maximal treadmill exercise test] expressed as metabolic equivalent of task;  $\dot{V}O_{2PEAK}$  = Peak oxygen uptake; VT = Ventilatory threshold.  $N=15$ , except WR<sub>MAX</sub> METs, VO<sub>2</sub>PEAK and VT ( $N=12$ ).

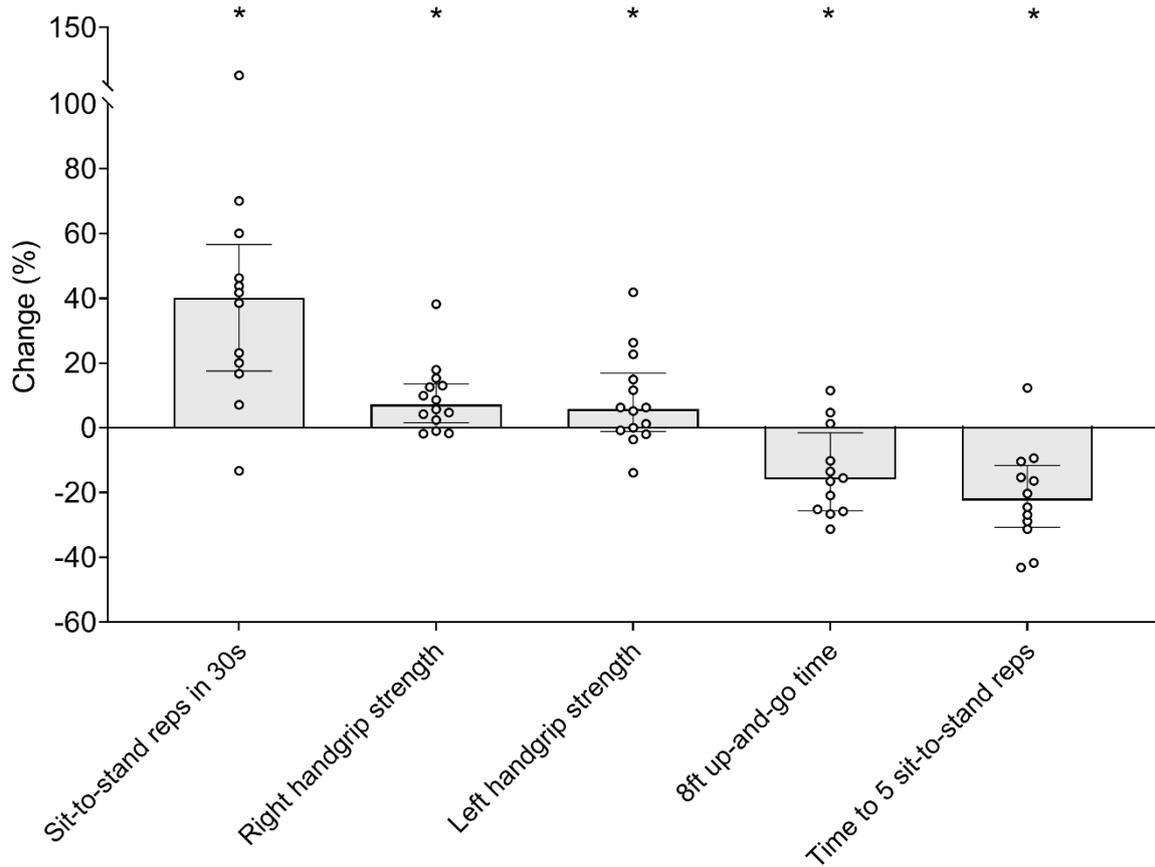


Figure 2. Percentage change to functional fitness pre- to post-exercise training.

Block bars are median and error bars are IQR. Open circles are individual responses. \* indicates statistically significant change  $P < .05$ .  $N=15$ , except right and left handgrip strength ( $N=14$ ) and sit-to-stand and 8ft up-and-go ( $N=12$ ).

Table 1. Change to flexibility and body composition from pre- to post-exercise training.

Variable	Pre-exercise training	Post-exercise training	Change (%)	<i>P</i> statistic	Effect size
<b>Flexibility</b>					
Back-scratch right (cm, <i>N</i> =14)	0.4 ± 13.3	-0.7 ± 13.6	-	.434	0.1
Back-scratch left (cm, <i>N</i> =14)	-7.2 ± 6.8	-6.7 ± 11.1	-	.506	0.1
Sit-and-reach right (cm, <i>N</i> =13)	4.3 ± 15.3	12.0 ± 9.9	-	<b>.016</b>	0.5
Sit-and-reach left (cm, <i>N</i> =13)	6.0 ± 13.9	11.0 ± 7.6	-	.114	0.4
<b>Body composition</b>					
Body mass index (kg.m <sup>-2</sup> )	27.3 ± 8.7	27.1 ± 9.0	-0.7 ± 3.0	.871	0.0
Waist circumference (cm)	98.2 ± 29.3	93.8 ± 20.9	-2.4 ± 4.7	<b>.014</b>	0.2
Hip circumference (cm)	103.9 ± 15.6	101.6 ± 16.6	-0.6 ± 2.5	.070	0.1
Total body fat (% , <i>N</i> =14)	30.35 ± 10.03	32.10 ± 10.60	0.5 ± 6.2	.924	0.0
Fat mass index (kg.m <sup>-2</sup> , <i>N</i> =14)	7.48 ± 3.18	7.56 ± 3.74	0.9 ± 8.7	.916	-
Android fat (kg, <i>N</i> =14)	2.1 ± 3.0	1.9 ± 2.6	-1.0 ± 15.4	.181	0.1
Gynoid fat (kg, <i>N</i> =14)	3.4 ± 2.2	3.8 ± 2.5	2.7 ± 10.9	.797	0.0
Lean soft-tissue mass (kg, <i>N</i> =14)	58.8 ± 17.9	58.6 ± 17.8	-0.2 ± 1.7	.818	0.0
Bone mineral density (g/cm <sup>2</sup> , <i>N</i> =14)	1.180 ± 0.215	1.198 ± 0.218	-0.2 ± 1.6	.866	0.0

*Data are median ± IQR. Percentage change scores are not reported where raw values or change scores span zero. N = 15 unless otherwise stated. Cohen's d effect sizes were calculated for normally distributed data only, as calculations for Cohen's d are based on mean as the measure of central tendency, which does not appropriately reflect non-normal data distribution.*

Table 2. Change to patient reported outcomes from pre- to post-exercise training.

Variable	Pre-exercise training	Post-exercise training	Change	<i>P</i> statistic	Effect size
<b>Quality of life</b>					
Satisfaction with life scale	24 ± 11	25 ± 9	1 ± 6	.202	0.3
FACIT-fatigue scale	5 ± 9	2 ± 11	0 ± 5	.640	0.1
PSQI	6 ± 5	5 ± 5	0 ± 4	.900	0.0
36-SF Physical function (%)	90 ± 30	95 ± 18	5 ± 10	<b>.022</b>	–
Physical role limitation (%)	100 ± 13	100 ± 0	0 ± 13	.594	–
Emotional role limitation (%)	100 ± 0	100 ± 0	0 ± 0	.999	–
Energy and fatigue (%)	65 ± 38	75 ± 23	10 ± 15	<b>.026</b>	0.5
Emotional wellbeing (%)	84 ± 22	84 ± 22	4 ± 12	.285	0.2
Social functioning (%)	88 ± 13	100 ± 19	0 ± 13	.364	0.2
Pain (%)	80 ± 23	90 ± 26	10 ± 15	.272	–
General health (%)	55 ± 15	55 ± 28	0 ± 8	.342	0.1

*Data are median ± IQR. N = 15 unless otherwise stated. FACIT = Functional assessment of chronic illness therapy; PSQI = Pittsburgh sleep quality index; 36-SF = 36-item short form. Cohen's d effect sizes were calculated for normally distributed data only, as calculations for Cohen's d are based on mean as the measure of central tendency, which does not appropriately reflect non-normal data distribution.*

Table 3. Change to device-measured and self-reported physical activity from pre- to post-exercise training.

Variable	Pre-exercise training	Post-exercise training	Change	<i>P</i> statistic	Effect size
<b>Device-measured</b>					
Total AEE (kcal/day, <i>N</i> =13)	1208 ± 456	1158 ± 587	-18 ± 484	.209	0.2
PAL ( <i>N</i> =13)	1.67 ± 0.40	1.79 ± 0.28	0.0 ± 0.4	.487	–
Sedentary wake-time (minutes/day, <i>N</i> =13)	750 ± 191	737 ± 155	-29 ± 139	.124	0.3
Sedentary wake-time (% , <i>N</i> =13)	66.1 ± 10.5	66.4 ± 19.0	-3.2 ± 13.6	.216	0.3
Light activity time (minutes/day, <i>N</i> =13)	118 ± 65	134 ± 70	14 ± 33	.252	–
Moderate activity time (minutes/day, <i>N</i> =13)	114 ± 123	127 ± 99	4 ± 83	.246	0.2
Vigorous activity time (min/day, <i>N</i> =13)	7 ± 16	11 ± 14	0 ± 15	.416	–
<b>Self-reported</b>					
Sitting time (minutes/day)	420 ± 240	330 ± 276	-60 ± 135	.348	0.3
Walking PA (MET-hours/week, <i>N</i> =13)	13.2 ± 16.5	23.1 ± 8.9	11.6 ± 23.1	.453	0.2
Moderate PA (MET-hours/week, <i>N</i> =13)	13.0 ± 26.3	10.7 ± 18.0	2.0 ± 24.2	.908	0.0
Vigorous PA (MET-hours/week, <i>N</i> =14)	0.0 ± 8.0	16.0 ± 40.0	16.0 ± 28.7	<b>.005</b>	–
Total PA (MET-hours/week, <i>N</i> =13)	44.4 ± 40.1	60.8 ± 50.0	37.0 ± 39.3	<b>.026</b>	0.6

*Data are median ± IQR. N = 15 unless otherwise stated. Device-measured physical activity measured using BodyMedia Core, analysed according to thresholds: sedentary <1.8 METs, light ≥1.8 to <3 METs, moderate ≥3 to <6 METs and vigorous ≥6 METs. Self-reported physical activity measured using IPAQ short form, analysed according to thresholds: walking 3.3 METs, moderate 4 METs and vigorous 8 METs. AEE = Active energy expenditure; PAL = Physical activity level; MVPA = Moderate-vigorous intensity physical activity; PA = Physical activity; MET = Metabolic equivalent of task. Cohen's *d* effect sizes were calculated for normally distributed data only, as calculations for Cohen's *d* are based on mean as the measure of central tendency, which does not appropriately reflect non-normal data distribution.*