

	Estimated mean difference	Lower CI of difference	Upper CI of difference
Body mass (kg)	0.24	-0.13	0.61
BMI (kg/m²)	0.08	-0.04	0.20
Abdominal SAT (kg)	0.08	0.02	0.15
f-FFA	0.04	-0.00	0.09
HbA1c (mmol/mol)	2.10	1.21	2.99
HbA1c (%)	2.3	2.2	2.4
M-value (μmol/kg/min)	-3.76	-6.42	-1.10
VO_{2peak} (ml/kg/min)	-1.09	-1.79	-0.39
	Estimated mean ratio	Lower CI of difference	Upper CI of difference
f-Glucose (mmol/L) *	0.98	0.95	1.01
f-Insulin (mmol/L) *	0.92	0.78	1.09
Cholesterol (mmol/L) *	1.11	1.06	1.15
HDL cholesterol (mmol/L)*	1.09	1.05	1.14
Triglycerides (mmol/L) *	1.13	1.01	1.30
Fat %*	1.04	1.02	1.06

Supplemental table 1. Differences of model-based means between pre and post training for each variable and their confidence interval in all male subjects (healthy and IR). For normally distributed parameters, the difference means the subtraction of pre-post and the difference and its confidence intervals are reported. For variables where logarithm transformation was used to achieve normality, difference is expressed as ratio (pre/post) after back-transformation. Logarithmic transformation has been done to the variables with *.

	Healthy vs IR men			IR SIT vs MICT			IR men vs IR women		
	Estimated mean ratio	Lower CI of difference	Upper CI of difference	Estimated mean ratio	Lower CI of difference	Upper CI of difference	Estimated mean ratio	Lower CI of difference	Upper CI of difference
Visceral GU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.89	0.81	0.97	0.86	0.77	0.97	0.88	0.77	1.00
Abdominal SAT GU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.83	0.64	1.08	0.91	0.73	1.14	0.97	0.78	1.20
Femoral SAT GU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.64	0.48	0.86	0.76	0.65	0.90	0.78	0.67	0.91
Visceral FAU ($\mu\text{mol}/100\text{g}/\text{min}$)*	1.23	1.06	1.42	1.18	1.04	1.34	1.20	1.01	1.42
Abdominal SAT FAU ($\mu\text{mol}/100\text{g}/\text{min}$)*	1.15	0.99	1.34	1.10	0.91	1.32	1.07	0.87	1.31
Femoral SAT FAU ($\mu\text{mol}/100\text{g}/\text{min}$)*	1.15	0.99	1.34	1.15	0.96	1.39	1.14	0.93	1.39

Supplemental Table 2. Differences of model-based means between pre and post training for each variable and their confidence interval in separate groups. Logarithmic transformation has been done to the variables with *. For variables where logarithm transformation was used to achieve normality, difference is expressed as ratio (pre/post) after back-transformation. SAT, subcutaneous adipose tissue; GU, glucose uptake; FAU, fasting free fatty acid uptake.

	IR SIT		IR MICT		Baseline	Time	Time* training
	Pre	Post	Pre	Post	p-value		
N (M/F)	13 (9/4)	11(7/4)	13 (7/6)	10 (6/4)	-	-	-
Age (y)	48 [46;49]	-	47 [44;49]	-	-	-	-
Body mass (kg)	91.6 [84.0;99.2]	91.2 [83.6;98.8]	92.0 [84.4;99.6]	91.5 [83.9;99.1]	0.9	0.09	0.96
BMI (kg/m²)	29.9 [28.3;31.5]	29.8 [28.2;31.4]	31.0 [29.4;32.6]	30.8 [29.2;32.4]	0.4	0.08	0.8
Whole body fat (%)*	32.2 [28.1;36.9]	31.2 [27.2;35.8]	33.0 [28.8;37.8]	32.0 [27.9;36.8]	0.8	0.01	0.9
Abdominal SAT (kg)*	7.1 [5.7;8.8]	6.9 [5.5;8.6]	7.1 [5.7;8.7]	6.9 [5.6;8.6]	0.97	0.046	0.9
Visceral fat (kg)*	3.1 [2.3;4.1]	3.0 [2.2;3.9]	3.6 [2.7;4.7]	3.4 [2.6;4.4]	0.4	0.01	0.4
Cholesterol (mmol/L)*	4.7 [4.2;5.2]	4.0 [3.6;4.5]	5.0 [4.4;5.6]	4.7 [4.2;5.3]	0.4	0.006	0.1
HDL (mmol/L)	1.3 [1.1;1.5]	1.2 [1.0;1.4]	1.3 [1.1;1.6]	1.3 [1.1;1.5]	0.8	0.01	0.8
LDL (mmol/L)	2.6 [2.2;3.0]	2.3 [1.8;2.7]	3.0 [2.5;3.5]	2.8 [2.2;3.2]	0.2	0.02	0.6
Triglycerides (mmol/L)*	1.5 [1.1;2.0]	1.3 [1.0;1.8]	1.5 [1.1;2.1]	1.5 [1.1;2.0]	0.9	0.4	0.7
f-FFA (mmol/L)	0.74 [0.61;0.85]	0.75 [0.62;0.88]	0.83 [0.72;0.95]	0.77 [0.65;0.89]	0.1	0.4	0.2
HbA1c (mmol/L)	39.6 [36.8;42.3]	37.8 [35.0;40.6]	39.5 [36.8;42.3]	37.5 [34.7;40.3]	0.99	0.001	0.8

HbA1c (%)	5.8 [5.5;6.0]	5.6 [5.4;5.9]	5.8 [5.5;6.0]	5.6 [5.3;5.8]	0.99	0.001	0.8
f-Glucose (mmol/L) [□]	6.9 [6.4;7.4]	6.9 [6.4;7.4]	6.5 [6.0;6.9]	6.3 [5.8;6.8]	0.09	0.4	0.4
f-Insulin (mmol/L) [□]	12.6 [8.4;18.8]	11.0 [7.3;16.5]	9.5 [6.6;13.7]	9.8 [6.7;14.2]	<0.001	0.4	0.2
M-value (μmol/kg/min)*	16.8 [11.9;23.9]	22.2 [15.4;32.0]	14.4 [10.4;19.8]	17.6 [12.5;24.8]	0.5	0.02	0.7
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VO_{2peak} (ml/kg/min)	27.0 [24.4;29.7]	28.4 [25.7;31.1]	27.4 [24.7;30.1]	27.2 [24.5;29.9]	0.9	0.1	0.048

Supplemental table 3. Descriptive statistics and results of two-way analysis of variance for characteristics of SIT and MICT training groups in insulin resistant (IR) subjects. The p-value for 'Baseline' describes the baseline differences between SIT (n=13) and MICT (n=13) groups. 'Time' shows all IR subjects after training. 'Time*training' demonstrates if there is an interaction between the change and the training mode. All the data are presented as model-based means [95% confidence interval, CI]. Logarithmic transformation has been done to the variables with * and square transformation to the variables with [□] to achieve the normal distribution. The values are LSmeans translated into the original unit. SAT, subcutaneous adipose tissue; HDL, high-density lipoprotein; LDL, low-density lipoprotein; FFA, free fatty acid; HbA1c, glycated hemoglobin; VO_{2peak}, aerobic capacity.

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	ALL SIT		ALL MICT		Time	Time* training
	Pre	Post	Pre	Post	P-value	
N (M/F)	27 (23/4)	24 (20/4)	27 (22/5)	23 (20/3)	-	-
Visceral GU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.93 [0.78;1.12]	0.94 [0.78;1.12]	1.08 [0.89;1.29]	0.98 [0.82;1.18]	0.01	0.21
Abdominal SAT GU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.73[0.61;0.88]	0.77 [0.64;0.92]	0.76 [0.63;0.91]	0.80 [0.66;0.96]	0.50	0.93
Femoral SAT GU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.72 [0.59;0.88]	0.64 [0.52;0.78]	0.92 [0.75;1.13]	0.72 [0.59;0.88]	<0.001	0.21
Visceral FFAU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.24 [0.19;0.29]	0.30 [0.25;0.36]	0.23 [0.18;0.28]	0.20 [0.16;0.24]	<0.001	0.001
Abdominal SAT FAU ($\mu\text{mol}/100\text{g}/\text{min}$)*	0.19 [0.15;0.23]	0.22 [0.18;0.26]	0.18 [0.15;0.23]	0.17 [0.14;0.21]	0.04	0.07
Femoral SAT FAU ($\mu\text{mol}/100\text{g}/\text{min}$)	0.20 [0.17;0.23]	0.22 [0.19;0.25]	0.16 [0.12;0.20]	0.19 [0.15;0.23]	0.005	0.76

Supplemental Table 4. Descriptive statistics and results linear mixed model with repeated measures for characteristics of SIT and MICT training groups in all healthy and insulin resistant (IR) subjects, including both men and women. 'Time' shows all healthy and IR subjects after training. 'Time*training' demonstrates if there is an interaction between the change and the training mode. All the data are presented as model-based means [95% confidence interval, CI]. Logarithmic transformation has been done to the variables with *. The values are model-based means translated into the original unit. SAT, subcutaneous adipose tissue; GU, glucose uptake; FAU, fasting free fatty acid uptake.

	IR Men ♂		IR Women ♀		Baseline	Time	Time* sex
	Pre	Post	Pre	Post	p-value		
N	16	13	10	8	-	-	-
Age (y)	47 [45;49]	-	52 [20;55]	-	0.002	-	-
Height (m)	1.8 [1.7;1.8]	-	1.7 [1.6;1.7]	-	<0.001	-	-
Body weight (kg)	96.4 [90.0;102.7]	96.2 [89.8;102.5]	84.0 [75.8;92.1]	83.0 [74.8;91.1]	0.02	0.04	0.1
BMI (kg/m ²)	30.5 [29.0;32.0]	30.4 [28.9;31.9]	30.4 [28.5;31.9]	30.1 [28.1;32.0]	0.97	0.03	0.09
Body fat (%)*	28.5 [26.3;30.8]	27.7 [25.5;30.0]	40.7 [36.7;45.2]	39.3 [35.4;43.6]	<0.001	0.02	0.8
Abdominal SAT (kg)*	6.0 [5.0;7.1]	5.9 [5.0;7.0]	9.1 [7.3;11.3]	8.8 [7.1;10.9]	0.003	0.03	0.2
Adj. SAT (TAT & height)	5.7 [5.1;6.5]	5.8 [5.1;6.6]	8.6 [7.2;10.4]	8.6 [7.3;10.3]	0.01	0.8	0.8
Visceral fat (kg)*	4.2 [3.4;5.1]	4.0 [3.2;4.9]	2.3 [1.8;3.0]	2.2 [1.7;2.8]	0.002	0.01	0.8
Adj. VAT (TAT & height)	4.5 [3.7;5.4]	4.4 [3.6;5.3]	1.8 [1.4;2.4]	1.8 [1.4;2.4]	<0.001	0.4	0.9
Cholesterol (mmol/L)*	4.7 [4.3;5.2]	4.3 [3.9;4.8]	5.0 [4.4;5.8]	4.4 [3.9;5.1]	0.3	0.01	0.5
HDL (mmol/L)	1.2 [1.1;1.4]	1.1 [0.9;1.3]	1.5 [1.3;1.7]	1.5 [1.2;1.7]	0.048	0.03	0.2
LDL (mmol/L)	2.7 [2.3;3.1]	2.6 [2.1;3.0]	2.9 [2.4;3.5]	2.4 [1.9;3.0]	0.4	0.01	0.1
Triglycerides (mmol/l)*	1.7 [1.3;2.2]	1.5 [1.1;2.0]	1.2 [0.9;1.8]	1.2 [0.8;1.7]	0.1	0.6	0.7

FFA_f (mmol/L)	0.69 [0.61;0.78]	0.68 [0.59;0.77]	0.96 [0.84;1.1]	0.90 [0.78;1.0]	<0.001	0.2	0.4
HbA1c (mmol/L)	39.6 [37.1;42.2]	37.7 [35.1;40.3]	39.7 [36.5;43.0]	37.9 [34.6;41.2]	0.99	0.003	0.9
HbA1c (%)	5.8 [5.5;6.0]	5.6 [5.4;5.8]	5.8 [5.5;6.1]	5.6 [5.3;5.9]	0.99	0.001	0.8
Glucose_f (mmol/L)	6.7 [6.2;7.2]	6.7 [6.2;7.2]	6.7 [6.1;7.2]	6.5 [5.9;7.1]	0.8	0.4	0.5
Insulin_f (mmol/L)*	13.1 [9.2;18.6]	12.1 [8.5;17.4]	8.3 [5.4;12.6]	8.2 [5.3;12.7]	0.1	0.6	0.6
M-value (μmol/kg/min)*	14.8 [10.8;20.3]	19.4 [14.0;27.0]	17.4 [11.8;25.5]	20.3 [13.4;30.6]	0.7	0.04	0.5

Supplemental table 5. Descriptive statistics and results of two-way analysis of variance for characteristics of women and men in insulin resistant (IR) subjects. The p-value for 'Baseline' describes the baseline differences between sexes. 'Time' shows all IR subjects after training. 'Time*sex' demonstrates if there is an interaction between the change and the sex. All the data are presented as model-based means [95% confidence interval, CI]. Logarithmic transformation has been done to the variables with * and square transformation to the variables with □ to achieve the normal distribution. The values are LSmeans translated into the original unit. SAT, subcutaneous adipose tissue; HDL, high-density lipoprotein; LDL, low-density lipoprotein; FFA, free fatty acid; HbA1c, glycated hemoglobin; VO₂peak, aerobic capacity.

	Model 1					Model 2				
	Training	DIA	Pre_post	Training* pre_post	DIA* Pre_post	Training	Sex	Pre_post	Sex* Pre_post	Training* pre_post
	p-value	p-value	p-value	p-value	p-value	p-value	p-value	p-value	p-value	p-value
VAT GU*	0.9	0.08	0.008	0.3	0.1	0.5	0.1	0.03	0.4	0.06
Abdominal SAT GU*	0.4	0.02	0.2	0.8	0.3	0.2	0.3	0.7	0.1	0.5
Femoral SAT GU	0.3	0.0003	0.003	0.1	0.8	0.4	0.4	0.004	0.04	0.7

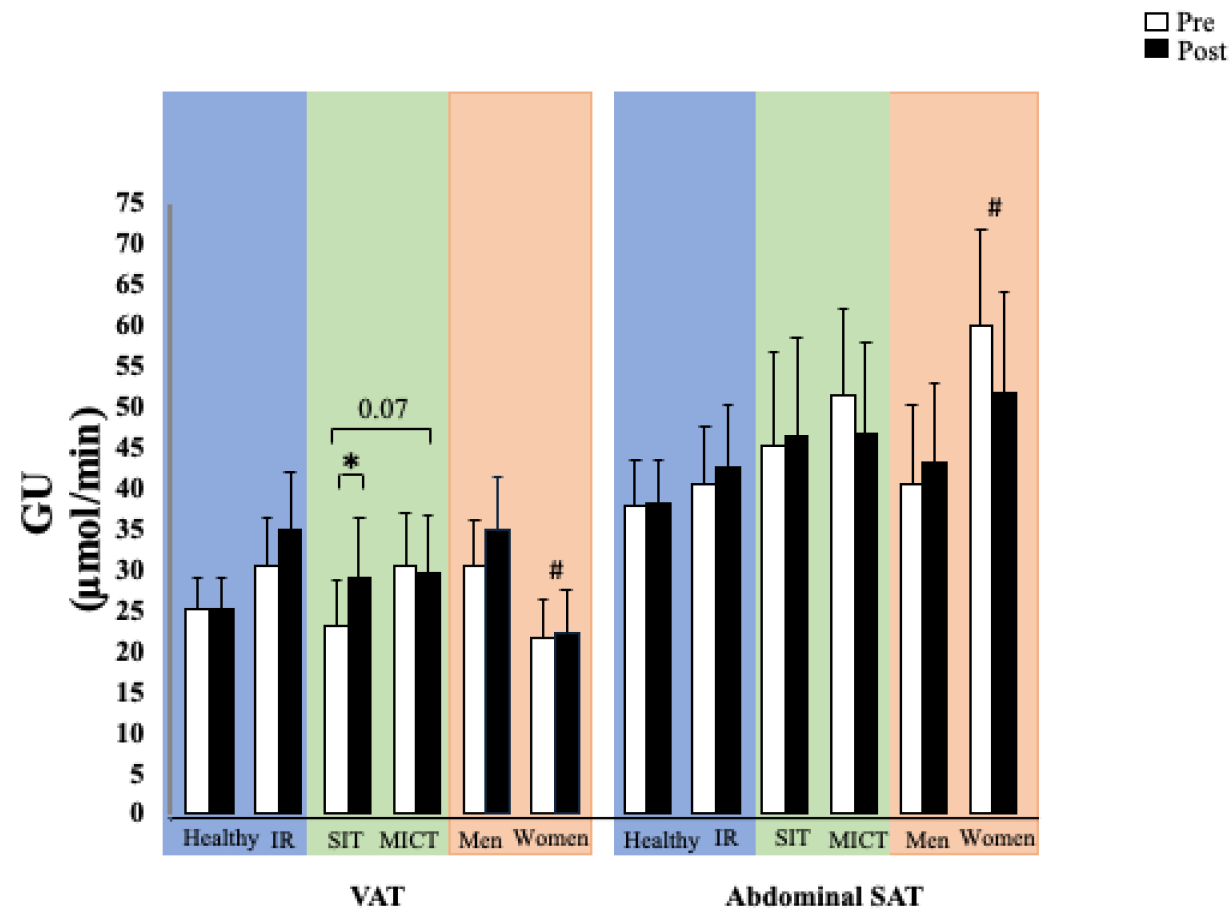
Supplemental table 6. Additional sensitivity analysis for the main findings.

Model 1: Effect of glucose tolerance state (DIA): 1. Training (whether the SIT and MICT groups differ at baseline), 2. DIA (whether healthy and IR differ at baseline), 3. Pre_post (overall training response), 4. Training*pre_post (whether the training response differs between training modes) and 5. DIA*pre_post (whether the training response differs between healthy and IR). The analysis includes only males, with adjustment for potential confounding effects of exercise regime.

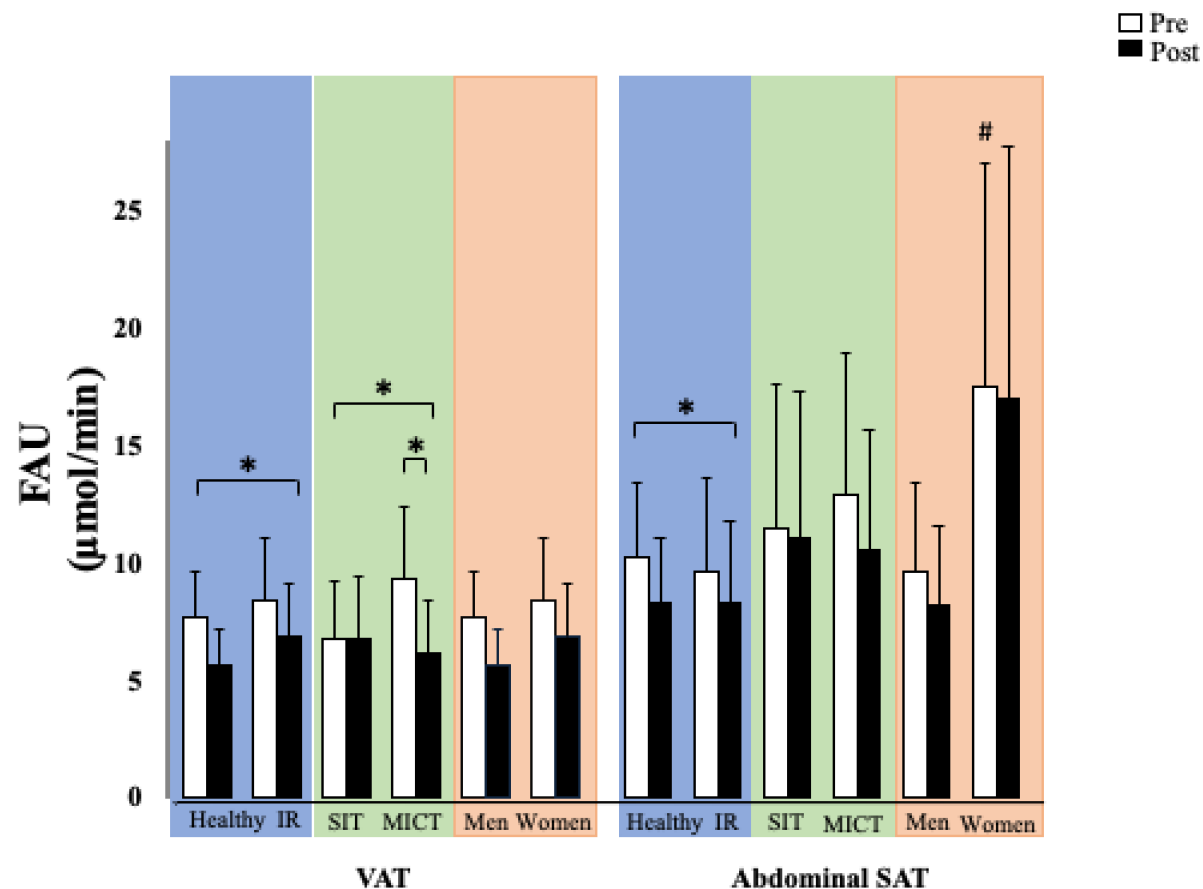
Model 2: Effect of the training regime and sex in IR subjects: 1. Training (whether the SIT and MICT groups differ at baseline), 2. Sex (whether men and woman differ at baseline), 3. Pre_post (overall training response), 4. Sex*pre_post (whether the training response differs between men and women) and 5. Training*pre_post (whether the training response differs between training modes). The analysis includes only in IR subjects, with adjustment for potential differential effects of sex.

Gene symbol	Forward primer (5'-3')	Reverse primer (5'-3')
PDK4	GAATTGCCTGTGAGACTCGC	TCTGGTCATCTGGGCTTTTCT
FASN	AACTCCAAGGACACAGTCACCAT	CAGCTGCTCCACGAACTCAA
CD36	AGCTTTCCAATGATTAGACG	GTTTCTACAAGCTCTGGTTC
CD68	GAGACTTTCATTTCCCTCCTTTC	TTTTGTGAGGACAGTCATTC
FABP4	CAAGAGCACCATAACCTTAG	CTCGTTTTCTCTTTATGGTGG
LPL	ACACAGAGGTAGATATTGGAG	CTTTTTCTGAGTCTCTCCTG
PPAR- γ	TGAATGTCGTGTCTGTGGAGA	GCAAGGCATTTCTGAAACCG
ANGPTL4	AGGCAGAGTGGACTATTTG	CCTCCATCTGAGGTCATC
YWHAZ	ACTTTTGGTACATTGTGGCTTCAA	CCGCCAGGACAAACCAGTAT
SLC2A4 (GLUT4)	TCCTTCCTCATTGGTATCATC	CCAAGGATGAGCATTTCATAG
36B4	CGACCTGGAAGTCCAACACTAC	ATCTGCTGCATCTGCTTG

Supplemental table 7: Human primer sequences for SYBR green real-time polymerase chain assay



Supplemental figure 1. Insulin stimulated glucose uptake (GU) per depot before (white bars) and after (black bars) the training intervention in visceral adipose tissue (VAT) and abdominal subcutaneous adipose tissue (SAT). GU is compared in three different comparisons: healthy vs IR men, sprint interval training (SIT) vs moderate intensity continuous training (MICT) in IR subjects and men vs women in IR subjects. All data is expressed as means and (95% CI). # $p < 0.05$; difference at baseline. * $p < 0.05$; the effect of exercise training over time in the whole group or a sub-group.



Supplemental figure 2. Fasting fatty acid uptake (FAU) per depot before (white bars) and after (black bars) the training intervention in visceral adipose tissue (VAT) and abdominal subcutaneous adipose tissue (SAT). FAU is visualized in three different comparisons: healthy vs IR men, sprint interval training (SIT) vs moderate intensity continuous training (MICT) in IR subjects and men vs women in IR subjects. All data is expressed as means and (95% CI). #p<0.05; difference at baseline. *p<0.05; the effect of exercise training over time in the whole group or a sub-group.

