Supplementary Materials

The effect of high-intensity interval training on mitochondrial function in overweight and obese adults: A Systematic Review and Meta-analysis

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Table of contents

Key word algorithms

PubMed

#**1**: (((((((High Intensity Interval Training[Title/Abstract]) OR (High Intensity Exercise[Title/Abstract])) OR (HIIT[Title/Abstract])) OR (Sprint Interval Training[Title/Abstract])) OR (intense intermittent exercise[Title/Abstract])) OR (SIT[Title/Abstract])) OR (anaerobic training[Title/Abstract])) OR (anaerobic exercise[Title/Abstract]) **AND** ((((((Obese[Title/Abstract]) OR (overweight[Title/Abstract])) OR (bmi[Title/Abstract])) OR (corpulence[Title/Abstract])) OR (Obesity[Title/Abstract])) OR (body mass index[Title/Abstract])) OR (sedentary[Title/Abstract]) **AND** (((Peroxisome proliferator-activated receptor gamma coactivator 1-alpha[Title/Abstract]) OR (PGC-1α[Title/Abstract])) OR (PGC-1a[Title/Abstract])) OR (PGC 1α[Title/Abstract])) OR (PGC 1a[Title/Abstract])) OR (PGC1a[Title/Abstract])) OR (PGC1 alpha[Title/Abstract])) OR (PGC 1alpha[Title/Abstract])) OR (PGC1alpha[Title/Abstract])) OR (PPARGC1A[Title/Abstract])) OR (Mitochondrial respiratory complex[Title/Abstract])) OR (NADH dehydrogenase[Title/Abstract])) OR (complex I[Title/Abstract])) OR (complex 1[Title/Abstract])) OR (COXI[Title/Abstract])) OR (COX-I[Title/Abstract])) OR (COX 1[Title/Abstract])) OR (Succinate dehydrogenase[Title/Abstract])) OR (complex II[Title/Abstract])) OR (complex 2[Title/Abstract])) OR (COXII[Title/Abstract])) OR (COX-II[Title/Abstract])) OR (COX II[Title/Abstract])) OR (COX 2[Title/Abstract])) OR (coenzyme Q[Title/Abstract])) OR (cytochrome bc1[Title/Abstract])) OR (complex III[Title/Abstract])) OR (complex 3[Title/Abstract])) OR (COXIII[Title/Abstract])) OR (COX III[Title/Abstract])) OR (COX-III[Title/Abstract])) OR (COX 3[Title/Abstract])) OR (cytochrome c[Title/Abstract])) OR (Complex IV[Title/Abstract])) OR (Complex 4[Title/Abstract])) OR (COXIV[Title/Abstract])) OR (COX IV[Title/Abstract])) OR (COX-IV[Title/Abstract])) OR (COX4[Title/Abstract])) OR (COX-4[Title/Abstract])) OR (COX 4[Title/Abstract])) OR (Complex V[Title/Abstract])) OR (Complex 5[Title/Abstract])) OR (COXV[Title/Abstract])) OR (COX V[Title/Abstract])) OR (COX-V[Title/Abstract])) OR (COX5[Title/Abstract])) OR (COX-5[Title/Abstract])) OR (COX 5[Title/Abstract])) OR (β-hydroxyacyl-CoA dehydrogenase[Title/Abstract])) OR (β-HAD[Title/Abstract])) OR (β HAD[Title/Abstract])) OR (b-HAD[Title/Abstract])) OR (b HAD[Title/Abstract])) OR (beta-HAD[Title/Abstract])) OR (CS[Title/Abstract])) OR (Citric Synthase[Title/Abstract])) OR (Mitofusin 1[Title/Abstract])) OR (Mitofusin 2[Title/Abstract])) OR (MFN1[Title/Abstract])) OR (MFN2[Title/Abstract])) OR (MFN-1[Title/Abstract])) OR (MFN-2[Title/Abstract])) OR (Sirtuin 1[Title/Abstract])) OR (Sirtuin-1[Title/Abstract])) OR (SIRT1[Title/Abstract])) OR (SIRT-1[Title/Abstract])) OR (SIRT 1[Title/Abstract])) OR (Mitochondrial density[Title/Abstract])) OR (Mitochondrial morphology[Title/Abstract])) OR (Mitochondrial volume[Title/Abstract])) OR (Mitochondrial content[Title/Abstract])) OR (VO2max[Title/Abstract])) OR (Mitochondrial size[Title/Abstract])) OR (VO2 max[Title/Abstract])) OR (VO2peak[Title/Abstract])) OR (VO2 peak[Title/Abstract])

#**2**: MeSH Humans

#**3**: MeSH Animals

#**4**: #3 NOT #2#**5**: #1 NOT #4

SCOPUS

(TITLE-ABS-KEY ("hiit") OR TITLE-ABS-KEY ("high intensity interval training") OR TITLE-ABS-KEY ("high intensity exercise") OR TITLE-ABS-KEY ("SIT") OR TITLE-ABS-KEY ("sprint interval training") OR TITLE-ABS-KEY ("anaerobic training") OR TITLE-ABS-KEY ("anaerobic exercise") OR TITLE-ABS-KEY ("intense intermittent exercise")) **AND** (TITLE-ABS-KEY ("obese") OR TITLE-ABS-KEY ("obesity") OR TITLE-ABS-KEY ("overweight") OR TITLE-ABS-KEY ("corpulence") OR TITLE-ABS-KEY ("bmi") OR TITLE-ABS-KEY ("body mass index") OR TITLE-ABS-KEY ("sedentary")) **AND** (TITLE-ABS-KEY ("PGC-1α") OR TITLE-ABS-KEY ("PGC-1a") OR TITLE-ABS-KEY ("PGC 1α") OR TITLE-ABS-KEY ("PGC 1a") OR TITLE-ABS-KEY ("PGC1α") OR TITLE-ABS-KEY ("PGC1a") OR TITLE-ABS-KEY ("PGC1 alpha") OR TITLE-ABS-KEY ("PGC 1alpha") OR TITLE-ABS-KEY ("COX 1") OR TITLE-ABS-KEY ("COX-I") OR TITLE-ABS-KEY ("COX I") OR TITLE-ABS-KEY ("COXI") OR TITLE-ABS-KEY ("NADH dehydrogenase") OR TITLE-ABS-KEY ("COX 2") OR TITLE-ABS-KEY ("COX-II") OR TITLE-ABS-KEY ("COX II") OR TITLE-ABS-KEY ("COXII") OR TITLE-ABS-KEY ("succinate ubiquinone oxidoreductase") OR TITLE-ABS-KEY ("coenzyme Q") OR TITLE-ABS-KEY ("cytochrome bc1") OR TITLE-ABS-KEY ("cytochrome c") OR TITLE-ABS-KEY ("COXIII") OR TITLE-ABS-KEY ("COX III") OR TITLE-ABS-KEY ("COX-III") OR TITLE-ABS-KEY ("COX 3") OR TITLE-ABS-KEY ("cytochrome c") OR TITLE-ABS-KEY ("Complex IV") OR TITLE-ABS-KEY ("COMPLEX 4") OR TITLE-ABS-KEY ("COXIV") OR TITLE-ABS-KEY ("COX IV") OR TITLE-ABS-KEY ("COX-IV") OR TITLE-ABS-KEY ("COX4") OR TITLE-ABS-KEY ("COX 4") OR TITLE-ABS-KEY ("COX-4") OR TITLE-ABS-KEY ("Complex V") OR TITLE-ABS-KEY ("COMPLEX 5") OR TITLE-ABS-KEY ("COXV") OR TITLE-ABS-KEY ("COX -V") OR TITLE-ABS-KEY ("COX5") OR TITLE-ABS-KEY ("COX-5") OR TITLE-ABS-KEY ("β-hydroxyacyl-CoA dehydrogenase") OR TITLE-ABS-KEY ("β-HAD") OR TITLE-ABS-KEY ("β HAD") OR TITLE-ABS-KEY ("b-HAD") OR TITLE-ABS-KEY ("beta-HAD") OR TITLE-ABS-KEY ("beta HAD") OR TITLE-ABS-KEY ("b HAD") OR TITLE-ABS-KEY ("Mitochondrial respiratory complex") OR TITLE-ABS-KEY ("Peroxisome proliferator-activated receptor gamma coactivator 1-alpha") OR TITLE-ABS-KEY ("citrate synthase") OR TITLE-ABS-KEY ("CS") OR TITLE-ABS-KEY ("MFN1") OR TITLE-ABS-KEY ("Mitofusin 1") OR TITLE-ABS-KEY ("Mitofusin 2") OR TITLE-ABS-KEY ("MFN2") OR TITLE-ABS-KEY ("Mfn-1") OR TITLE-ABS-KEY ("Mfn-2") OR TITLE-ABS-KEY ("Sirtuin 1") OR TITLE-ABS-KEY ("Sirtuin-1") OR TITLE-ABS-KEY ("SIRT1") OR TITLE-ABS-KEY ("SIRT 1") OR TITLE-ABS-KEY ("SIRT-1") OR TITLE-ABS-KEY ("Mitochondrial density") OR TITLE-ABS-KEY ("Mitochondrial morphology") OR TITLE-ABS-KEY ("Mitochondrial volume") OR TITLE-ABS-KEY ("Mitochondrial content") OR TITLE-ABS-KEY ("Mitochondrial size") OR TITLE-ABS-KEY ("VO2max") OR TITLE-ABS-KEY ("VO2peak") OR TITLE-ABS-KEY ("VO2 max") OR TITLE-ABS-KEY ("VO2 peak"))

WEB OF SCIENCE

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AB=(High Intensity Interval Training) OR AB=(High Intensity Exercise) OR AB=(HIIT) OR AB=(SIT) OR AB=(Sprint Interval Training) OR AB=(anaerobic training) OR AB=(anaerobic exercise) OR AB=(interval training) OR AB=(intense intermittent exercise)

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(KeyWord Plus) (#4)

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#1 OR #2 OR #3 OR #4 (#5)

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#6 OR #7 OR #8 OR #9 (#10)

(Abstract) (#11)

AB=(Peroxisome proliferator-activated receptor gamma coactivator 1-alpha) OR AB=(PGC-1α) OR AB=(PGC-1a) OR AB=(PGC 1α) OR AB=(PGC 1a) OR AB=(PGC1a) OR AB=(PGC1 alpha) OR AB=(PGC 1alpha) OR AB=(PGC1alpha) OR AB=(PPARGC1A) OR AB=(Mitochondrial respiratory complex) OR AB=(NADH dehydrogenase) OR AB=(complex I) OR AB=(COMPLEX 1) OR AB=(COXI) OR AB=(COX-I) OR AB=(COX 1) OR AB=(Succinate dehydrogenase) OR AB=(complex II) OR AB=(COMPLEX 2) OR AB=(COXII) OR AB=(COX-II) OR AB=(COX II) OR AB=(COX 2) OR AB=(coenzyme Q) OR AB=(cytochrome bc1) OR AB=(complex III) OR AB=(COMPLEX 3) OR AB=(COXIII) OR AB=(COX III) OR AB=(COX-III) OR AB=(COX 3) OR AB=(cytochrome c) OR AB=(Complex IV) OR AB=(Complex 4) OR AB=(COXIV) OR AB=(COX IV) OR AB=(COX-IV) OR AB=(COX4) OR AB=(COX 4) OR AB=(COX-4) OR AB=(Complex V) OR AB=(Complex 5) OR AB=(COXV) OR AB=(COX V) OR AB=(COX-V) OR AB=(COX5) OR AB=(COX 5) OR AB=(COX-5) OR AB=(β-hydroxyacyl-CoA dehydrogenase) OR AB=(β-HAD) OR AB=(β HAD) OR AB=(b-HAD) OR AB=(b HAD) OR AB=(beta-HAD) OR AB=(CS) OR AB=(Citric Synthase) OR AB=(Mitofusin 1) OR AB=(Mitofusin 2) OR AB=(MFN1) OR AB=(MFN2) OR AB=(MFN-1) OR AB=(MFN-2) OR AB=(Sirtuin 1) OR AB=(Sirtuin-1) OR AB=(SIRT1) OR AB=(SIRT-1) OR AB=(SIRT 1) OR AB=(Mitochondrial density) OR AB=(Mitochondrial morphology) OR AB=(Mitochondrial volume) OR AB=(Mitochondrial content) OR AB=(Mitochondrial size) OR AB=(VO2max) OR AB=(VO2 max) OR AB=(VO2peak) OR AB=(VO2 peak)

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(Author KeyWords) (#13)

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(KeyWords Plus) (#14)

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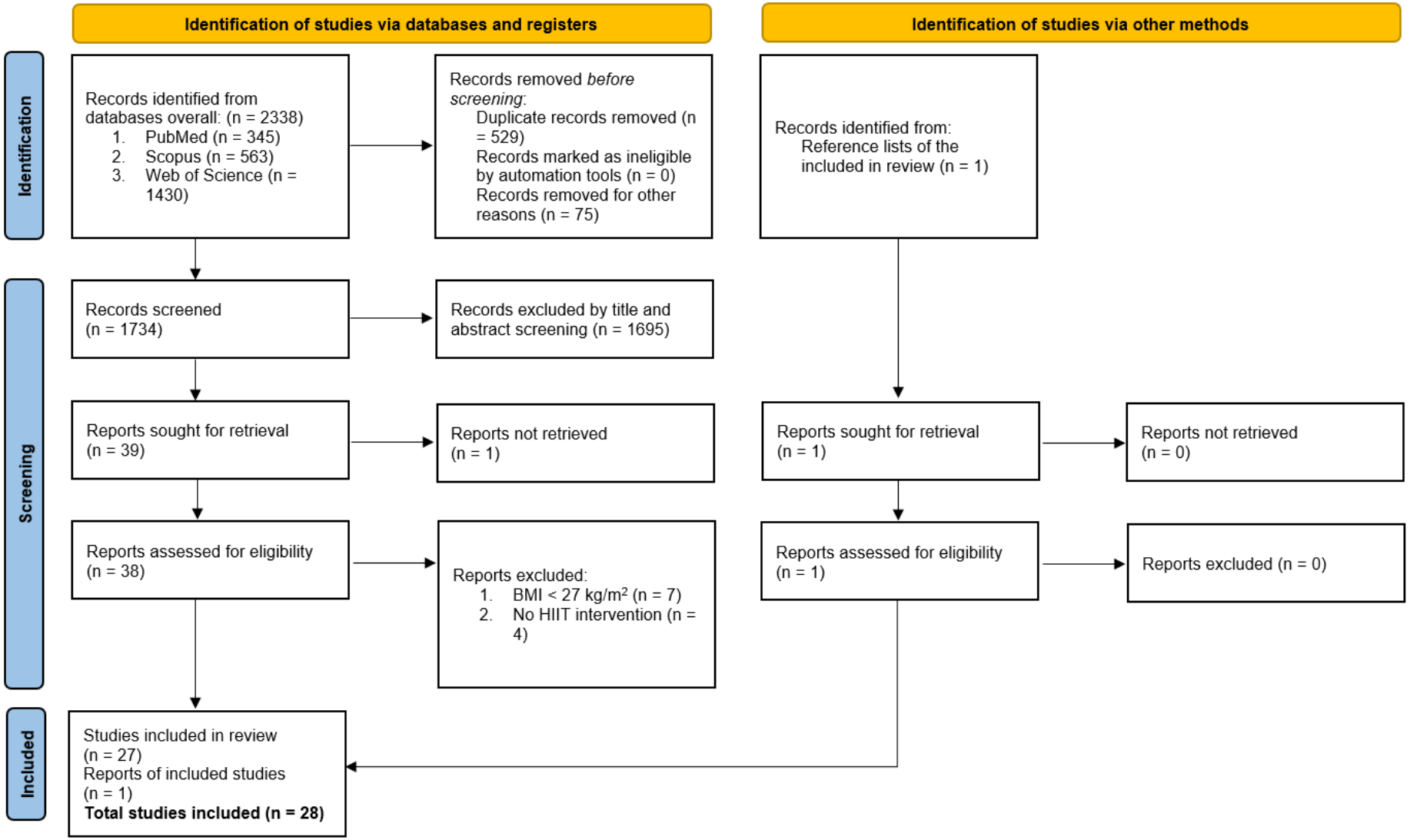
#11 OR #12 OR #13 OR #14 (#15)

#5 AND #10 AND #15 (#16)

Supplementary Fig. 1: PRISMA flow diagram [1]



Supplementary Table 1: Characteristics of the eligible studies

Study ID	Design	Participants (number, age, health status)	BMI (kg/m²)	Train Period (Weeks)/(Sessions/Week)	Training (sets/intensity)	Main outcome
1.Flensted-Jensen et al. 2021 [2]	Single Arm (Pre Vs Post)	n=12 (6 females) Age=37.2±2.4 years (Sedentary participants)	34.0±1.4	6 weeks, 3 sessions/week	five 1-min sets of high-intensity cycling (125% of VO2peak), with 90 s recovery in between sets	**VO2max:** PRE: 2.9±0.2 (n=12) POST: 3.1±0.2 (n=12) L/min, mean±SD, p<0.05 **Complex I:** PRE: 47.91±9.2 (n=8) POST: 55.65±13.8 (n=8) pmol·s−1·mg ww−1 means±95% confidence intervals, P = 0.001 **Complex I+II** PRE: 63.6±5.65 (n=8) POST: 75.72±18.62 (n=8) pmol·s−1·mg ww−1 means±95% confidence intervals, P = 0.001
2.Gillen et al. 2016 [3]	Single arm (Pre Vs Post)	n=9 Age=27 ± 7 (sedentary participants)	27 ± 5	12 weeks, 3 sessions/week	3x20-second 'all-out' cycle sprints (~500W) interspersed with 2 minutes of cycling at 50W	**VO2peak:** PRE: 2.6±0.8 (n=9) POST: 3.0±0.7 (n=9) L/min, mean±SD, p<0.05 **Complex I:** POST: 1.57±1.05 (n=9) vs. same group at PRE,

						mean±SD, p<0.05 **<u>Complex II:</u>** POST: 1.52±0.38 (n=9) vs. same group at PRE, mean±SD, p<0.05 **<u>Complex III:</u>** POST: 1.76±0.56 (n=9) vs. same group at PRE, mean±SD, p<0.05 **<u>Complex IV:</u>** POST: 1.56±0.38 (n=9) vs. same group at PRE, mean±SD, p<0.05 **<u>CS:</u>** PRE: 3.03±0.81 (n=9) POST: 4.49±0.87 (n=9) mmol/kg protein/hr, mean±SD, p<0.05
3.Gillen et al. 2013 [4]	Single arm (Pre Vs Post)	FED: n=8 (8 females) Age=27 ± 7) FASTED: n=8 (8 females) Age=27 ± 9 (Sedentary participants)	FED: 29 ± 3 FASTED: 29 ± 4	18 training sessions over 6 week	10× 60-s cycling efforts at ~90% maximal heart rate, 60-s recovery	**<u>VO2peak:</u>** FED: PRE: 28.2±6.1 (n=8) POST: 34.3±5.2 (n=8) FASTED: PRE: 27.4±6.4 (n=8) POST: 31.3±5.7 (n=8) ml/kg/min, mean±SD, p<0.001 **<u>CS:</u>** FED: PRE: 5±1.2 (n=8) POST: 6.2±1.2 (n=8) FASTED: PRE: 4.6±0.5 (n=6)

						POST: 5.7±0.96 (n=6) mmol/kg protein/hr, means±SD, p<0.05 **β-HAD:** FED: PRE: 1.96±0.94 (n=8) POST: 2.18±0.37 (n=8) FASTED: PRE: 2.15±0.47 (n=6) POST: 2.57±0.71 (n=6) mmol/kg protein/hr, means±SD, p<0.05
4.Gillen et al. 2014 [5]	Single arm (Pre Vs Post)	MEN: n=7 Age=29 ± 9 WOMEN: n=7 Age=30 ± 10 (Sedentary participants)	MEN: 31 ± 2 WOMEN: 29 ± 2	18 training sessions over 6 week	Each session began with a 2 min warm-up at 50 W, followed by 3×20 s "all-out" sprints against 5.0% body mass (mean power output: ~450–500 W) interspersed with 2 min of recovery at 50 W, followed by a 3 min cool-down at 50 W	**VO2peak:** MEN: PRE: 31±4 (n=7) WOMEN: PRE: 28±4 (n=7) L/min, means±SD **COX-IV**: MEN: PRE: 1.0 (n=7) POST: 1.8±0.8 (n=7) WOMEN: PRE: 1.0 (n=7) POST: 1.5±0.9 (n=7) fold change vs. PRE, means±SD, p<0.05 **CS**: MEN: PRE: 3.96±0.61 (n=7) POST: 5.48±1.38 (n=7) WOMEN: PRE: 3.58±0.45 (n=7) POST: 5±1.09 (n=7)

						mmol/kg protein/hr, means±SD, p<0.05 **β-HAD**: MEN: PRE: 1.73±0.4 (n=7) POST: 2.2±0.54 (n=7) WOMEN: PRE: 2.31±0.55 (n=7) POST: 2.25±0.64 (n=7) mmol/kg protein/hr, means±SD, p<0.05
5.Hood et al. 2011 [6]	Single arm (Pre Vs Post)	n=7 (3 females) Age=45 ± 5 (Sedentary - healthy participants)	27 ± 5	2 weeks, 3 sessions/week	10 x 1-min cycling at ~60% of peak power achieved during a ramp VO2peak test (eliciting ~80%-95% of HR reserve)	**COX-IV:** PRE: 0.56±0.13 (n=7) POST: 0.65±0.19 (n=7) protein content (A.U.), means±SD, p<0.05 **CS:** PRE: 0.41±0.13 (n=7) POST: 0.54±0.14 (n=7) protein content (A.U.), means±SD, p<0.05 **PGC-1a:** PRE: 0.05±0.016 (n=7) POST: 0.065±0.009 (n=7) protein content (A.U.), means±SD, p<0.05
6. Afzalpour et al. 2017 [7]	RCT	HIIT + tea: n=10 (10 females) Age: 22.47 ± 3.32 HIIT + Placebo: n=10 (10 females) Age: 23.58 ±	HIIT + tea: 27.15 ± 1.47 HIIT + Placebo: 27.32 ± 1.27 Placebo: 28.03 ± 1.04	HIIT + tea: 10 weeks, 3 sessions/week HIIT + Placebo: 10 weeks, 3 sessions/week	HIIT + tea: 4 X 30s all-out cycling HIIT + Placebo: 4 X 30s all-out cycling Placebo: -	**VO2max**: HIIT + tea: PRE: 24.5±2.32 (n=10) POST: 28.42±2.23 (n=10) HIIT + Placebo: PRE: 23.65±3.31 (n=10) POST: 25.47±2.91 (n=10) Placebo: PRE: 24.05±3.16 (n=10)

		2.23 Placebo: n=10 (10 females) Age: 21.85 ± 1.34 (sedentary participants)		Placebo: -		POST: 25.8±3.38 (n=10) mL·kg·min, mean±SD, p=0.69 **PGC-1a:** HIIT + tea: PRE: 18.81±3.57 (n=10) POST: 40.68±7.74 (n=10) HIIT + Placebo: PRE: 21.05±5.68 (n=10) POST: 33.62±6.38 (n=10) Placebo: PRE: 20.7±3.76 (n=10) POST: 30.88±4.24 (n=10) pg/mL, mean±SD, p<0.0001 **SIRT1:** HIIT + tea: PRE: 0.23±0.09 (n=10) POST: 0.46±0.14 (n=10) HIIT + Placebo: PRE: 0.16±0.04 (n=10) POST: 0.27±0.04 (n=10) Placebo: PRE: 0.19±0.04 (n=10) POST: 0.25±0.03 (n=10) ng/mL, mean±SD, p<0.0001
7.Ryan et al. 2020 [8]	RCT (parallel)	n=16 (9 females) Age: 32 ± 7 (Sedentary - healthy participants)	32.4 ± 2.5	12 weeks, 4 sessions/week	10 x 1-minute intervals at 90% HRmax	**VO2max:** PRE: 2.5±0.6 (n=16) POST: 2.8±0.6 (n=16) L/min, mean±SD, p<0.001 **COX-IV:** PRE: 1.2±0.08 (n=16) 1day PostEX: 1.45±0.08 (n=16)

						4days PostEX: 1.42±0.08 (n=16) protein content (A.U.), mean±SEM, p<0.01 **<u>Complex I:</u>** PRE: 1.41±0.13 (n=16) 1day PostEX: 2.04±0.08 (n=16) 4days PostEX: 2.10±0.21 (n=16) protein content (A.U.), mean±SEM, p<0.01 **<u>Complex II:</u>** PRE: 1.47±0.1 (n=16) 1day PostEX: 1.68±0.1 (n=16) 4days PostEX: 1.73±0.09 (n=16) protein content (A.U.), mean±SEM, p<0.01 **<u>Complex III:</u>** PRE: 1.27±0.12 (n=16) 1day PostEX: 1.96±0.21 (n=16) 4days PostEX: 1.94±0.13 (n=16) protein content (A.U.), mean±SEM, p<0.01 **<u>Complex IV:</u>** PRE: 1.42±0.08 (n=16) 1day PostEX: 1.91±0.12 (n=16) 4days PostEX: 1.85±0.11 (n=16) protein content (A.U.), mean±SEM, p<0.01 **<u>Complex V:</u>** PRE: 1.22±0.05 (n=16) 1day PostEX: 1.38±0.06 (n=16) 4days PostEX: 1.37±0.05 (n=16) protein content (A.U.), mean±SEM, p<0.01
8.Sanayei et al. 2022 [9]	RCT	<u>HIIT+CV</u> n=12 (12 females)	<u>HIIT+CV:</u> 31.1	8 weeks, 3 sessions/week	20 × 40 s protocol (intensity of 50–60 % max HR) at	**<u>VO2max:</u>** HIIT+CV: PRE: 33.74±9.01 (n=12)

		Age: 18 to 35 <u>HIIT+Placebo</u> n=11 (11 females) Age: 18 to 35 <u>Placebo</u> n=11 (11 females) Age: 18 to 35 (Sedentary - healthy participants)	<u>HIIT+Placebo</u>: 29.9 <u>Placebo:</u> 28.6		the first week; this was followed by 20 × 35 s (intensity of 60–70 % max HR) in the second week, 16 × 30 s (intensity of 70–80 % max HR) in the third week, 16 × 25 s (intensity of 80–90 % max HR) in the fourth week and 12 × 20 s (intensity of 90–100 % max HR) in the last month	POST: 40.51±8.26 (n=12) HIIT+Placebo: PRE: 37.4±4.77 (n=11) POST: 42.59±4.51 (n=11) Placebo: PRE: 38.81±3.85 (n=11) POST: 37.96±3.13 (n=11) ml O2/kg, mean±SD, p<0.05 **<u>PGC-1a:</u>** HIIT+CV: PRE: 11.56±10.38 (n=12) POST: 19.99±12.80 (n=12) HIIT+Placebo: PRE: 12.51±11.24 (n=11) POST: 19.33±10.05 (n=11) Placebo: PRE: 10.91±11.56 (n=11) POST: 11.25±11.46 (n=11) ng/ml, mean±SD, p<0.05 **<u>SIRT1:</u>** HIIT+CV: PRE: 24.98±21.06 (n=12) POST: 35.18±30.82 (n=12) HIIT+Placebo: PRE: 26.97±31.72 (n=11) POST: 30.62±34.09 (n=11) Placebo: PRE: 32.10±47.00 (n=11) POST: 31.57±43.68 (n=11) pg/ml, mean±SD, p<0.05

9.Scott et al. 2019 [10]	Non-randomised, parallel CT	Home-HIT - type **I+II** fibers: n=9 (5 females) Age: 32 ± 8 Lab-HIT - type **I+II** fibers: n=10 (5 females) Age: 37 ± 13 (sedentary obese with at least two further cardiovascular disease factors participants)	Home-HIT - type **I+II** fibers: 35.9 ± 4.1 Lab-HIT - type I+**II** fibers: 34.2 ± 4.2	12 weeks 3 sessions/week	8 X 60s >80% HRmax	**VO2max:** Home-HIT: PRE: 23.8±2.5 (n=9) POST: 27.6±4.7 (n=9) Lab-HIT: PRE: 24.8±6.4 (n=10) POST: 29.8±8.2 (n=10) mL·kg·min, mean±SD, p<0.05 **COX-IV:** Home-HIT - type **I** fibers: PRE: 34.19±13.72 (n=8) POST: 39.07±17.91 (n=8) Home-HIT - type **II** fibers: PRE: 29.07±20 (n=8) POST: 36.05±22.09 (n=8) Lab-HIT - type **I** fibers: PRE: 32.33±13.25 (n=8) POST: 43.26±23.72 (n=8) Lab-HIT - type **II** fibers: PRE: 28.60±14.42 (n=8) POST: 38.14±20.93 (n=8) COX-IV expression-fluorescence intensity, mean±SD, p<0.05
10.Shepherd et al. 2017 [11]	Parallel group (Pre Vs Post)	SIT-type I+II fibers: n=8 Age: 24 ± 2 (Sedentary - healthy participants)	35.8 ± 0.8	4 weeks 3 sessions/week	4-7 X 30s sprints	**VO2max:** PRE: 33.9±1.2 (n=8) POST: 36.3±1.6 (n=8) ml.kg-1.min-1, mean±SEM, p<0.05) **COX-IV:** SIT-type I fibers: PRE: 37.44±4.19 (n=8) POST: 48.03±5.91 (n=8)

						SIT-type II fibers: PRE: 22.66±4.19 (n=8) POST: 33.74±5.91 (n=8) COX-IV expression-fluorescence intensity, mean±SEM, p<0.01 **Mitochondrial Volume Density:** PRE: 3.71±0.48 (n=8) POST: 5.49±0.44 (n=8) %area of muscle occupied by mitochondria or LDs, mean±SEM, p<0.01 **Mitochondrial Number:** PRE: 0.28±0.02 (n=8) POST: 0.37±0.02 (n=8) #$\mu m^2 tissue^{-1}$, mean±SEM, p<0.01 **Mitochondrial Size:** PRE: 0.085±0.007 (n=8) POST: 1.08±0.004 (n=8) μm^2, mean±SEM, p<0.01
11.Søgaard et al. 2019 [12]	Single arm (Pre Vs Post)	Young: n=14 (5 females) Age: 32 ± 2 Old: n=22 (11 females) Age: 63 ± 1 (Sedentary - healthy participants)	Young: 34.8 ± 1.0 Old: 30.7 ± 0.7	6 weeks 3 sessions/week	Up to 9 intervals where the load was increased with 10% at each interval starting at 85% of their maximal load measured at the VO2max test	**VO2max:** Young: PRE:28.3±1.2 (n=14) POST:29.7±1.5 (n=14) ml·kg-1·min-1, mean±SEM, p=0.007 Old: PRE:25.2±1.0 (n=22) POST:26.7±1.1 (n=22) ml·kg-1·min-1, mean±SEM, NS **CS:** Young: PRE:132±7 (n=14) POST: 165±8 (n=14)

						μmol/g-1/min-1, mean±SEM, NS Old: PRE:122±10 (n=22) POST: 169±10 (n=22) μmol/g-1/min-1, mean±SEM, p<0.001 **β-HAD**: Young: PRE:116±7 (n=14) POST:130±7 (n=14) (μmol/g-1/min-1), mean±SEM, NS Old: PRE:112±10 (n=22) POST:141±5 (n=22) (μmol/g-1/min-1), mean±SEM, p<0.001
12.Tan et al. 2018 [13]	Single arm (Pre Vs Post)	type **I+II** fibers: n=13 (13 females) Age): 26 ± 7 (sedentary participants)	30 ± 4	6 weeks 3 sessions/week	10 X 60s cycling ~90% HRmax - 60s active recovery	**VO2max:** PRE: 27±6.5 (n=13) POST:32±5.6 (n=13) (ml·kg-1·min-1), mean±SD, p<0.05 **COX-IV**: type I fibers: PRE:3500±858 (n=13) POST:4442±1377 (n=13) type II fibers: PRE:2632±629 (n=13) POST:3863±1307 (n=13) AU, mean±SD, p<0.05
13.Vaccari et al. 2020 [14]	Single arm (Pre Vs Post)	n=16 (NA females) Age: NA	35.1 ± 0.9	12 weeks 3 sessions / week	3-7 X 3min ~100% VO2max	**VO2max:** PRE:44.26±0.45 (n=16) POST:51.51±0.40 (n=16)

		(Sedentary - healthy participants)				ml·kg-1·min-1FFM, mean±SEM, p<0.001 **Complex I:** PRE: 1.01±0.14 (n=6) POST: 1.61±0.27 (n=8) pmol O2 s−1 mU−1, mean±SEM, p>0.05 **Complex II:** PRE: 0.48±0.23 (n=6) POST: 0.77±0.17 (n=8) pmol O2 s−1 mU−1, mean±SEM, p>0.05 **Complex I+II:** PRE: 1.48±0.37 (n=6) POST: 2.38±0.38 (n=8) pmol O2 s−1 mU−1, mean±SEM, p<0.05 **CS:** PRE: 308±34 (n=6) POST: 268±21 (n=8) μU/mg, mean±SEM, p>0.05
14.Bækkerud et al. 2016 [15]	Single arm (Pre Vs Post)	4 HIIT: n=12 (7 females) Age: 39 ± 10 1 HIIT: n=9 (6 females) Age: 45 ± 8 (Sedentary - healthy participants)	4 HIIT: 31.4 ± 5.3 1 HIIT: 30.8 ± 4.8	6 weeks 3 sessions / week	4 HIIT: 4 X 4min ~85-95% HRmax interspaced by 3 min of treadmill walking at 70% HRmax. 1 HIIT: 10 X 1min ~90% HRmax interspaced by 3 min of treadmill	**VO2max:** 4 HIIT: PRE: 31.9±6.9 (n=8) POST: 34.7±8.7 (n=8) 1 HIIT: PRE: 33.6±6.8 (n=9) POST: 34.5±7.8 (n=9) ml·kg-1·min-1, mean±SD, p<0.05 **CS:** 4 HIIT: PRE: 8.05±2.88 (n=5) POST: 10.92±2.82 (n=5) 1 HIIT: PRE: 6.64±0.71 (n=5)

					walking at 70% HRmax.	POST: 8.96±1.65 (n=5) μmol/kg-1/hr-1, mean±SEM, p>0.05
15.Bartlett et al. 2020 [16]	Single arm (Pre Vs Post)	n=10 (6 females) Age: 71 ± 5 sedentary adults with prediabetes (HbA1c: 6.1 ± 0.3%)	29.4 ± 3	10 weeks 3 sessions / week	10 X 60s ~80%-90% HRR	**<u>VO2max:</u>** PRE: 19.35±3.09 (n=10) POST: 22.44±04.06 (n=10) (ml·kg-1·min-1), mean±SD, p=0.002 **<u>Mitochondrial Membrane potential of isolated neutrophils:</u>** PRE: 0.91±0.17 (n=5) POST: 01.05±0.1(n=5) JC-1 ΔΨ, mean±SD , p=0.011
16.Boyd et al. 2013 [17]	Single arm (Pre Vs Post)	n=9 Age: 22.7 ± 3.8 (Sedentary participants)	32.3 ± 2.1	3 weeks 3 sessions / week	8-9-10 X 60s ~ 100% - 60s cycling	**<u>VO2max:</u>** PRE: 35.4±5.7 (n=9) POST: 44.7±4.9 (n=9) (ml/kg/min), mean±SD, p<0.05 **<u>COX-IV:</u>** PRE: 1±0.07 (n=9) POST: 1.18±0.10 (n=9) fold change vs pre-test (A.U.), mean±SD, p<0.05 **<u>Complex I:</u>** PRE: 1±0.06 (n=9) POST: 1.19±0.10 (n=9) fold change vs pre-test (A.U.), mean±SD, p<0.05 **<u>CS:</u>** PRE: 43.6±4.5 (n=9) POST: 49.9±8.8 (n=9) fold change vs pre-test (A.U.), mean±SD, p<0.05 **<u>β-HAD:</u>** PRE: 2.7±0.7 (n=9)

						POST: 3.1±0.4 (n=9) fold change vs pre-test (A.U.), mean±SD, p=0.07 **PGC-1a:** PRE: 1±0.08 (n=9) POST: 1.22±0.09 (n=9) fold change vs pre-test (A.U.), mean±SD, p<0.05 **SIRT1:** PRE: 1±0.06 (n=9) POST: 1.43±0.15 (n=9) fold change vs pre-test (A.U.), mean±SD, p<0.05
17.Chrøis et al. 2020 [18]	Single arm (Pre Vs Post)	Male n=11 (0 females) Age: 63 ± 2 Female n=11 (11 females) Age: 63 ± 1 (sedentary participants)	Male: 31 ± 1 Female: 31 ± 1	6 weeks 3 sessions/week	5 X 1min HIIT	**VO2max:** Male: PRE:27±2 (n=11) POST: 30±2 (n=11) female: PRE: 23±1 (n=11) POST: 24±1 (n=11) ml·kg-1·min-1, mean ± SEM, p=0.024 **Complex I:** Male: PRE:0.88±0.1 (n=11) POST: 1.11±0.1 (n=10) Female: PRE: 1.05±0.2 (n=10) POST: 1.57±0.3 (n=10) Protein content A.U., mean ± SEM. p < 0.05 **Complex II:** Male: PRE:0.96 ±0.1 (n=11) POST: 1.15±0.1 (n=10) Female:

						PRE: 0.95±0.06 (n=10) POST: 1.32±0.29 (n=10) Protein content A.U., mean ± SEM. $p < 0.05$ **Complex III:** Male: PRE:0.87 ±0.1 (n=11) POST: 1.25±0.09 (n=10) Female: PRE: 0.80±0.09 (n=10) POST: 1.12±0.09 (n=10) Protein content A.U., mean ± SEM. $p < 0.05$ **Complex IV:** Male: PRE:0.66 ±0.1 (n=11) POST: 1.07±0.19 (n=10) Female: PRE: 0.81±0.1 (n=10) POST: 1.67±0.39 (n=10) Protein content A.U., mean ± SEM. $p < 0.05$ **Complex V:** Male: PRE:0.99 ±0.1 (n=11) POST: 1.16±0.19 (n=10) Female: PRE: 0.9±0.09 (n=10) POST: 1.16±0.1 (n=10) Protein content A.U., mean ± SEM. $p < 0.05$ **Complex I+II:** Male Coupled CI+II: PRE:61.23 ±4.08 (n=11) POST: 89.8±5.44 (n=10)

						Male Uncoupled CI+II: PRE:70.75 ±3.40 (n=11) POST: 98.64±6.12 (n=10) Female Coupled CI+II : PRE: 59.86±2.72 (n=10) POST: 65.99±4.76 (n=10) Female Uncoupled CI+II : PRE: 72.11±2.72 (n=10) POST:76..19±4.08 (n=10) O2 flux pmol/mg/s, mean ± SEM, p<0.001
18.Dela et al. 2018 [19]	RCT	Type 2 Diabetes-trained leg n=10 Age: 57±2 Healthy control-trained leg n=10 Age: 53±2 (participants with type 2 Diabetes Mellitus)	Type 2 Diabetes-trained leg 31 ± 1 Healthy control-trained leg 31 ± 1		one legged training (10X60s at>80%, ergometer bicycle)	**VO2max:** Type 2 Diabetes- trained leg: PRE: 2.3±0.1 (n=10) POST: 2.4±0.1 (n=10) Healthy control-trained leg: PRE: 2.4±0.2 (n=10) POST: 2.4±0.2 (n=10) L/min, mean±SEM, p< 0.05 **Complex I:** Type 2 Diabetes- trained leg: POST: 1.28±0.26 (n=10) Healthy control-trained leg: POST: 1.8±0.29 (n=10) **Complex II:** Type 2 Diabetes- trained leg: POST: 1.17±0.12 (n=10) Healthy control-trained leg: POST: 1.46±0.17 (n=10) **Complex III:** Type 2 Diabetes- trained leg: POST: 1.2±0.12 (n=10)

						Healthy control-trained leg: POST: 1.3±0.15 (n=10) **Complex IV:** Type 2 Diabetes- trained leg: POST:1.24±0.19 (n=10) Healthy control-trained leg: POST: 1.62±0.19 (n=10) **Complex V:** Type 2 Diabetes- trained leg: POST: 1.13±0.12 (n=10) Healthy control-trained leg: POST:1.2±0.1 (n=10) **CS:** Type 2 Diabetes- trained leg: POST: 127.32±6.58 (n=10) Healthy control-trained leg: POST: 138.29±4.39 (n=10) μmol/min/kg, mean±SE, $p < 0.05$ **β-HAD:** Type 2 Diabetes- trained leg: POST: 108±6 (n=10) Healthy control-trained leg: POST: 116±8 (n=10) μmol/min/kg, mean±SE, $p < 0.05$ **PGC-1*α*:** Type 2 Diabetes- trained leg: POST: 0.9±0.17 (n=10) Healthy control-trained leg: POST: 0.97±0.17 (n=10) AU, geometric mean +- SE*T>UT, $p < 0.05$

19.Matos et al. 2018 [20]	Single arm (Pre Vs Post)	Obese non-insulin OB n=9 (6 females) Age: 32±10 Obese insulin resistant OBR n=8 (5 females) Age: 30±11 (sedentary - healthy participants)	Obese non-insulin OB: 35.1±3.8 Obese insulin resistant OBR: 37.8±4.6	8 weeks, 3 sessions/ week	8-12 X60s, 80-110% intensity of the peak power, (8-12 cycling exercise bouts)	**VO2max:** Obese non-insulin OB: PRE: 27.2±6.8 (n=9) POST: 30.5±3.4 (n=9) Obese insulin resistant OBR: PRE: 24.8±5.9 (n=8) POST: 27.4±6.1 (n=8) (ml·kg-1·min-1), mean±SD, p<0.0001 **COX-IV:** Obese non-insulin OB: PRE: 121.42±57.15 (n=9) POST: 200±78.57 (n=9) Obese insulin resistant OBR: PRE: 107.14±42.86 (n=8) POST: 178.57±42.85 (n=8) %control pre-training, mean±SD, p=0.006 **β-HAD:** Obese non-insulin OB: PRE:146.87±9.38 (n=9) POST:203.12±46.88 (n=9) Obese insulin resistant OBR: PRE:118.75±46.87 (n=8) POST:203.12±84.38 (n=8) %control pre-training, mean±SD, p=0.046 **PGC-1a:** Obese non-insulin OB: PRE:187.09±12.91 (n=9) POST:135.48±64.52 (n=9) Obese insulin resistant OBR: PRE:193.54±77.42 (n=8) POST:187.09±77.42 (n=8)

						%control pre-training, mean±SD, p>0.05
20.Dohlmann et al. 2018 [21]	Single arm (Pre Vs Post)	n=12 (7 females) Age: 40±2 (sedentary - healthy participants)	32±2	6 weeks, 3 sessions/week	7X60s, at app. 100% VO2max	**<u>VO2max:</u>** PRE:27±2 (ml·kg-1·min-1) (n=12) POST: 29±2 (ml·kg-1·min-1) (n=12) (ml·kg-1·min-1), mean±SEM, p=0.010 **<u>Complex I:</u>** CI, CI+II subgroup: PRE: 0.49±0.13 (n=8) POST: 0.4±0.08 (n=8) CI, CI+II (mtDNA) subgroup: PRE: 0.04±0.02 (n=6) POST: 0.07±0.04 (n=6) (pmolO2/s/mg), mean±SEM, p<0.05 **<u>Complex I+II:</u>** CI, CI+II subgroup: PRE: 1.3±0.38 (n=8) POST: 1.05±0.25 (n=8) CI, CI+II (mtDNA) subgroup: PRE: 0.12±0.05 (n=6) POST: 0.20±0.11 (n=6) (pmolO2/s/mg), mean±SEM, p<0.05 **<u>CS:</u>** PRE:119±9 (n=11) POST:136±1 (n=11) (μmolXmin^-1XmgXdw^-1),mean±SEM, p=0.027 **<u>β-HAD:</u>** PRE:103±7 (n=11) POST:111±11 (n=11) (μmolXmin^-1XmgXdw^-1),mean±SEM, p=0.236
21.Koh et al.	Single arm	n=8	27.6±2.7	11 weeks	10X60s cycle	**<u>VO2max:</u>**

2018 [22]	(Pre Vs Post)	(3 females) Age: 56±5 (sedentary - healthy participants)		3 sessions/ week	intervals at 95% of Wpeak, 82±0.4 HR	PRE:45.4±7.0 (n=8) POST: 54.8±7.8 (n=8) (ml min-1 kg-1 fat free mass), mean±SD, p<0.001 **Complex I:** PRE: 0.48±0.30 (n=8) POST: 0.36±0.06 (n=8) protein content (A.U.), mean±SD, p>0.05 **Complex II:** PRE: 0.44±0.12 (n=8) POST:0.41±0.17 (n=8) protein content (A.U.), mean±SD, p>0.05 **Complex III:** PRE: 0.32±0.09 (n=8) POST:0.36±0.01 (n=8) protein content (A.U.), mean±SD, p>0.05 **Complex IV:** PRE: 0.56±0.11 (n=8) POST:0.47±0.07 (n=8) protein content (A.U.), mean±SD, p>0.05 **Complex V:** PRE: 0.32±0.14 (n=8) POST:0.31±0.02 (n=8) protein content (A.U.), mean±SD, p>0.05
22.Larsen et al. 2014 [23]	Single arm (Pre Vs Post)	n=10 (2 females) Age: 38±3 (sedentary - healthy participants)	32.53±4.25	6 weeks 3 sessions/week	5X60s bouts	**VO2max:** PRE: 29±2 (n=10) POST: 31±2 (n=10) (ml·kg-1·min-1), mean±SEM, p=0.006 **COX-IV:** PRE: 1.22±0.17 (n=10) POST: 1.4±0.19 (n=10) (pmol/s/mg), mean±SEM, p=0.026

						<u>CS:</u> PRE: 107±8 (n=10) POST:145±7 (n=8) (μmol/g/min),mean±SEM, p=0.012 **<u>β-HAD:</u>** PRE:100±7 (n=10) POST:117±5 (n=10) (μmol/g/min),mean±SEM, p=0.236
23. Little JP et al. 2011 [24]	Single arm (Pre Vs Post)	n=8 Age: 62.5±7.6 (participants are Type 2 Diabetes patients)	31.7±5.8	2 weeks 3 sessions/ week	10X60s at 90%HRmax,cycling intervals	**<u>Complex I:</u>** PRE: 0.99±0.28 (n=7) POST: 1.76±0.75 (n=7) (AU), mean±SD, p<0.05 **<u>Complex II:</u>** PRE: 0.99±0.33 (n=7) POST: 1.38±0.5 (n=7) (AU), mean±SD, p<0.05 **<u>Complex III:</u>** PRE: 0.99±0.25 (n=7) POST: 1.52±0.5 (n=7) (AU), mean±SD, p<0.05 **<u>Complex IV:</u>** PRE: 0.99±0.14 (n=7) POST: 1.69±0.33 (n=7) (AU), mean±SD, p<0.05 **<u>CS:</u>** PRE: 0.295±0.036 (n=7) POST: 0.353±0.084 (n=7) (mmolXkg protein^-1Xhr^-1), mean±SD, p<0.05

24.Mora-Rodriguez R et al. 2014 [25]	Single arm (Pre Vs Post)	n=48 (26 females) Age: 52.0±8.8 years (participants were patients with metabolic syndrome)	32.8±0.6	measurement 1 : 4 weeks 3 sessions/ week measurement 2: 8 weeks 3 sessions/ week measurement 3: 12 weeks 3 sessions/ week measurement 4: 16 weeks 3 sessions/ week measurement 5: 1 month after measurement 4, without any exercise	4X4min intervals at 90% HRpeak with 3 min recovery at 70%HRpeak (for all measurements and durations)	**VO2max:** PRE: 21.5±0.7 (n=48) POST - measurement 1: 23.4±0.8 (n=48) POST - measurement 2: 24.4±0.7 (n=48) POST - measurement 3: 25.7±0.8 (n=48) POST - measurement 4: 26.1±0.9 (n=48) POST - measurement 5: 23.7±0.7 (n=48) (ml*kg-1*min-1), mean±SEM, $p<0.05$ **CS:** PRE: 12±4.3 (n=7) POST: 19.3±5 (n=7) (μmol/g wet weight/min), mean±SEM, $p<0.05$

25.Morales-Palomo F et al. 2020 [26]	Non-randomised - control CT	Non Statin Group (Control Group) n=60 (28 females) Age: 53±8 Statin Group n=46 (21 females) Age: 55±8 (participants were patients with metabolic syndrome)	Non Statin Group: 32.6±4.2 Statin Group: 31.3±3.8	16 weeks, 3 sessions/ week (for all groups)	4X4min intervals at 90% HRpeak with 3min recovery at 70%HRpeak (for all groups)	**VO2max:** Non Statin Group: PRE: 1.91±0.57 (n=60) POST: 2.29±0.69 (n=60) Statin Group: PRE: 1.9±0.68 (n=46) POST: 2.16±0.69 (n=46) (LXmin^-1), mean±SD, p<0.001 **CS:** Non Statin Group: PRE: 63.75±21.75 (n=60) POST: 87.75±23.25 (n=60) Statin Group: PRE: 51.59±15 (n=46) POST: 85.68±23.18 (n=46) (μmolXg^-1Xmin^-1), mean±SD, p<0.001 **β-HAD:** Non Statin Group: PRE: 144.76±22.85 (n=60) POST: 149.52±12.38 (n=60) Statin Group: PRE: 111.74±20.87 (n=46) POST: 147.39±13.91 (n=46) (μmol/g/min), mean±SD, p>0.05
26.Guadalupe-Grau, A et al. 2018 [27]	Single arm (Pre Vs Post)	n=11 (3 females) Age: 54.5±0.7 (participants were patients with metabolic	32.8±0.3	24 weeks, 3 sessions/ week	4X4min intervals at 90%HRmax	**VO2max:** PRE: 25.6±7.2 (n=11) POST: 27.9±8.0 (n=11) (mL/Kg/min), mean±SD, p=0.1 **CS:** PRE: 139.99±40 (n=11) POST: 171.99±32 (n=11)

		syndrome)				(μmol/g/min), mean±SD, p<0.05 **β-HAD:** PRE: 125±46.87 (n=11) POST: 143.75±21.87 (n=11) (μmol/g/min), mean±SD, p>0.05
27.Skleryk et al. 2013 [28]	(Pre Vs Post) Parallel group	n=8 Age: 40.2±2.3 (sedentary participants)	32.2 ± 2.1	2 weeks, 3 sessions/ week	8-12X10sec sprints "all out" cycling efforts (8-12 repeated 10 s 'all out' cycling efforts against a resistance equivalent to 0.05 kg body mass-1)	**VO2max:** PRE: 29.7±1.3 (n=8) POST: 29.3±1.9 (n=8) (ml·kg-1·min-1), mean±SEM, p>0.05 **COX-IV:** PRE: 1±0.12 (n=8) POST: 1.01±0.16 (n=8) total protein expression normalised to α-tubulin (A.U.), mean±SEM, p=0.478 **Complex II:** PRE: 1±0.12 (n=8) POST: 1.01±0.16 (n=8) total protein expression normalised to α-tubulin (A.U.), mean±SEM, p=0.701 **SIRT 1:** PRE: 1±0.06 (n=8) POST: 0.88±0.1 (n=8) (A.U.), mean±SEM, p=0.204
28. Nordsborg et al. 2015 [29]	RCT	HIIT: n=21 (21 females) Age: 44 ± 5 Control: n=20	HIIT: 28.4 Control: 28.1	HIIT: 3 weeks, 15 sessions/ week	6 X 30s all-out cycling - 2min passive recovery	**Complex I:** Post HIIT - m. deltoideus: 142±111% (n=12), p<0.05 Post HIIT - m. vastus lateralis: 32±73% (n=13), NS Post Control - m. deltoideus: 132±138% (n=10), NS Post Control - m. vastus lateralis: 9±53% (n=11), NS mean±SD

		(20 females) Age: 45 ± 4 (sedentary, premenopausal participants)		<u>Control:</u> No exercise		**<u>Complex II:</u>** Post HIIT - m. deltoideus: 162±120% (n=16), p<0.01 Post HIIT - m. vastus lateralis: 39±50% (n=18), NS Post Control - m. deltoideus: 53±9% (n=15), p=0.08 Post Control - m. vastus lateralis: 16±20% (n=15), NS mean±SD **<u>Complex III:</u>** Post HIIT - m. deltoideus: 172±161% (n=16), p<0.01 Post HIIT - m. vastus lateralis: 122±43% (n=18), p<0.001 Post Control - m. deltoideus: 89±47% (n=15), NS Post Control - m. vastus lateralis: 12±74% (n=15), NS mean±SD **<u>Complex IV:</u>** Post HIIT - m. deltoideus: 213±168% (n=16), p<0.001 Post HIIT - m. vastus lateralis: 41±76% (n=17), p=0.06 Post Control - m. deltoideus: 18±69% (n=13), NS Post Control - m. vastus lateralis: 20±89% (n=14), NS mean±SD **<u>Complex V:</u>** Post HIIT - m. deltoideus: 81±3% (n=16), p<0.001 Post HIIT - m. vastus lateralis: 28±11% (n=18), p=0.06 Post Control - m. deltoideus: 12±58% (n=15), NS

						Post Control - m. vastus lateralis: 2±34% (n=15), NS mean±SD **<u>CS:</u>** PRE: HIIT - m. deltoideus: 11.32±4.12 (n=12) HIIT - m. vastus lateralis: 16.73±5.4 (n=16) Control - m. deltoideus: 12.22±6.31 (n=7) Control - m. vastus lateralis: 16.6±4.63 (n=15) POST: HIIT - m. deltoideus: 19.3±4.25 (n=12) HIIT - m. vastus lateralis: 22±4.25 (n=16) Control - m. deltoideus: 13.25±4.25 (n=7) Control - m. vastus lateralis: 16.73±21.62 (n=15) (μmol x g^{-1} x min^{-1}), mean±SD, p<0.001 **<u>β-HAD:</u>** PRE: HIIT - m. deltoideus: 16.88±3.6 (n=12) HIIT - m. vastus lateralis: 21.03±3.87 (n=16) Control - m. deltoideus: 16.46±4.71 (n=7) Control - m. vastus lateralis: 21.86±3.32 (n=15) POST: HIIT - m. deltoideus: 21.58±4.29 (n=12) HIIT - m. vastus lateralis: 24.07±4.01 (n=16) Control - m. deltoideus: 18.68±4.84 (n=7) Control - m. vastus lateralis: 20.47±5.12 (n=15) (μmol x g^{-1} x min^{-1}), mean±SD, p<0.01 for m. vastus lateralis, p<0.001 for m. deltoideus

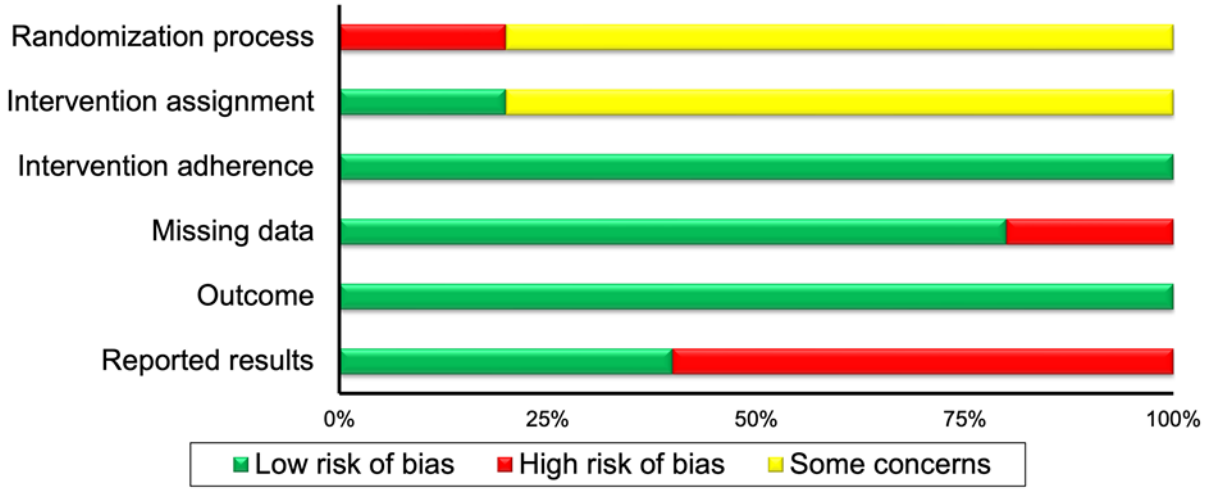
Supplementary Table 2: Risk of bias assessment outcomes

Key: +: low, ?: some concerns, -: high, N: not applicable [30,31].

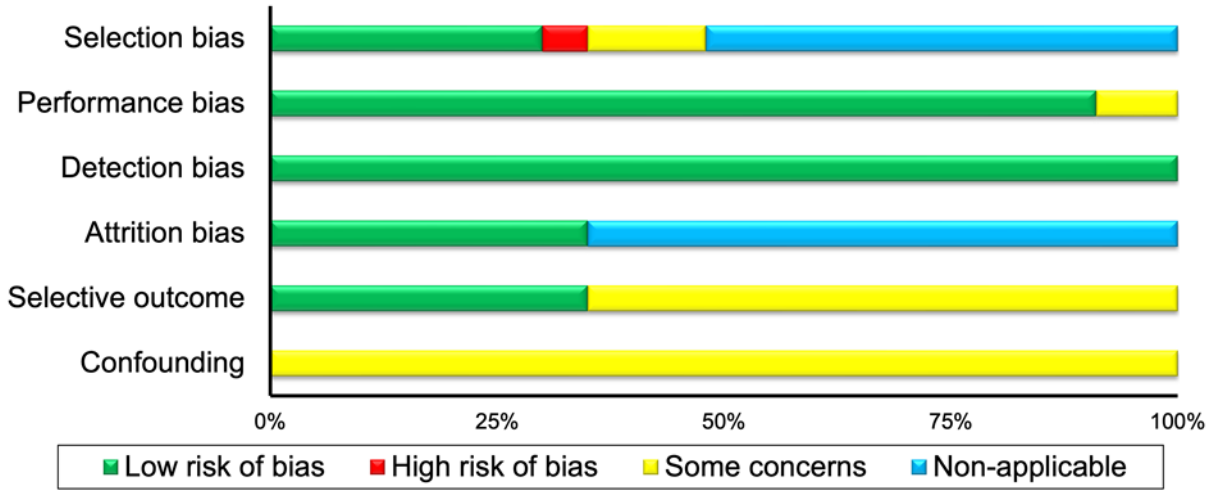
Randomized controlled trials						
First author	Randomization process	Intervention assignment	Intervention adherence	Missing data	Outcome	Reported results
Afzalpour 2017	?	?	+	-	+	+
Ryan 2020	?	?	+	+	+	?
Sanayei 2021	?	+	+	+	+	+
Dela 2018	-	?	+	+	+	?
Nordsborg 2015	?	?	+	+	+	?
Controlled trials & single arm design studies						
First author	Selection	Performance	Detection	Attrition	Selective Outcome	Confounding
Flensted-Jensen, 2021	NA	?	+	NA	+	?
Hood, 2011	NA	?	+	NA	+	?
Søgaard, 2019	?	+	+	+	+	?
Vaccari, 2020	NA	+	+	NA	+	?
Gillen, 2016	+	+	+	NA	+	?
Gillen, 2013	+	+	+	NA	+	?
Gillen, 2014	+	+	+	NA	+	?
Scott, 2019	-	+	+	+	+	?
Shepherd, 2017	+	+	+	+	?	?
Tan, 2018	NA	+	+	NA	?	?
Baekerrud, 2016	+	+	+	+	?	?
Bartlett, 2020	NA	+	+	NA	?	?
Boyd, 2013	NA	+	+	NA	?	?
Chrois, 2020	NA	+	+	NA	?	?
Matos, 2018	?	+	+	+	?	?
Dohlmann, 2018	NA	+	+	NA	?	?
Koh, 2018	+	+	+	+	?	?
Larsen, 2014	NA	+	+	NA	?	?
Little, 2011	NA	+	+	NA	?	?
Mora-Rodriguez, 2014	NA	+	+	NA	?	?
Morales-Palomo, 2020	?	+	+	+	?	?
Guadalupe-Grau, 2017	NA	+	+	NA	?	?
Skleryk, 2013	+	+	+	+	?	?

Supplementary Fig. 2: Summary of risk of bias [30,31]

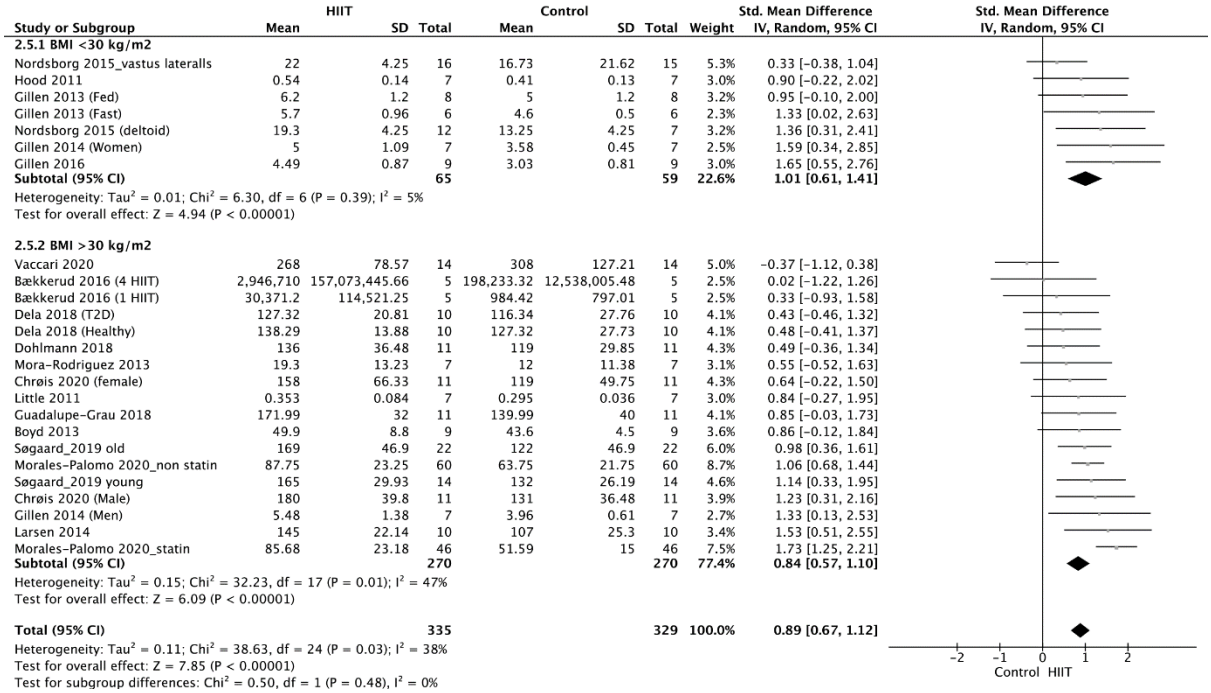
A. Randomized controlled trials



B. Controlled trials & single arm design studies

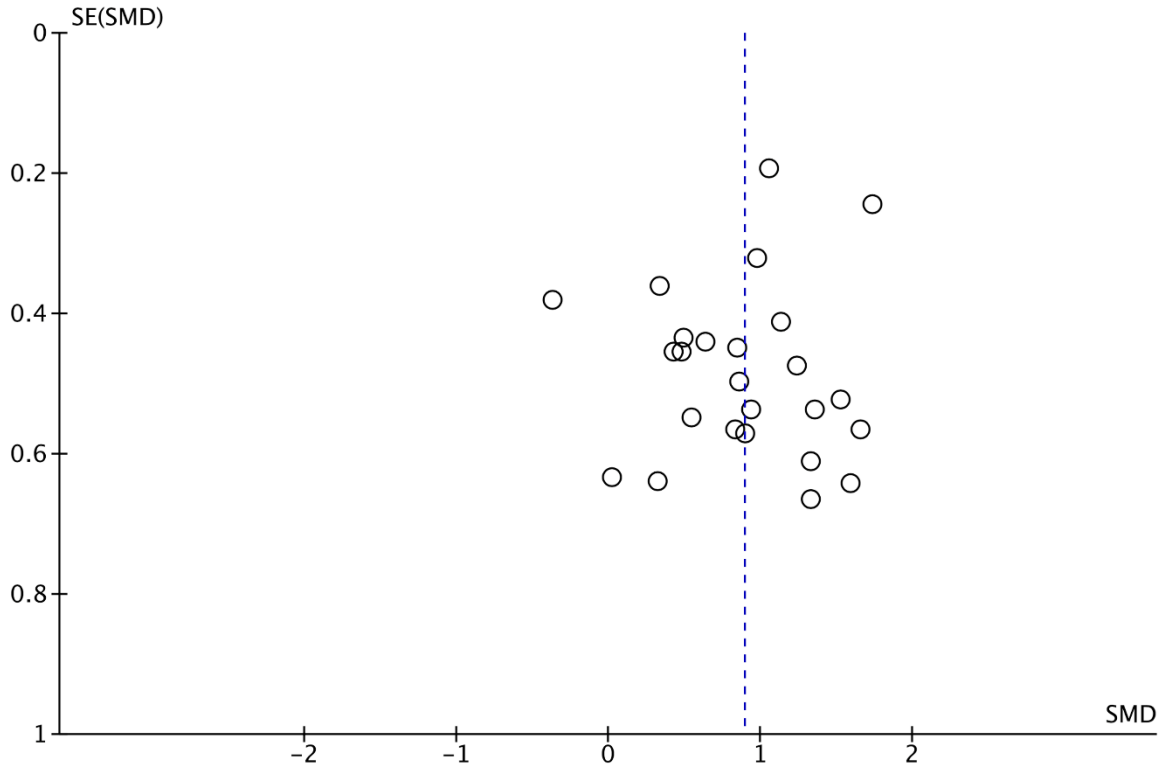


Supplementary Fig. 3: Forest plot of the effect of HIIT on CS (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval

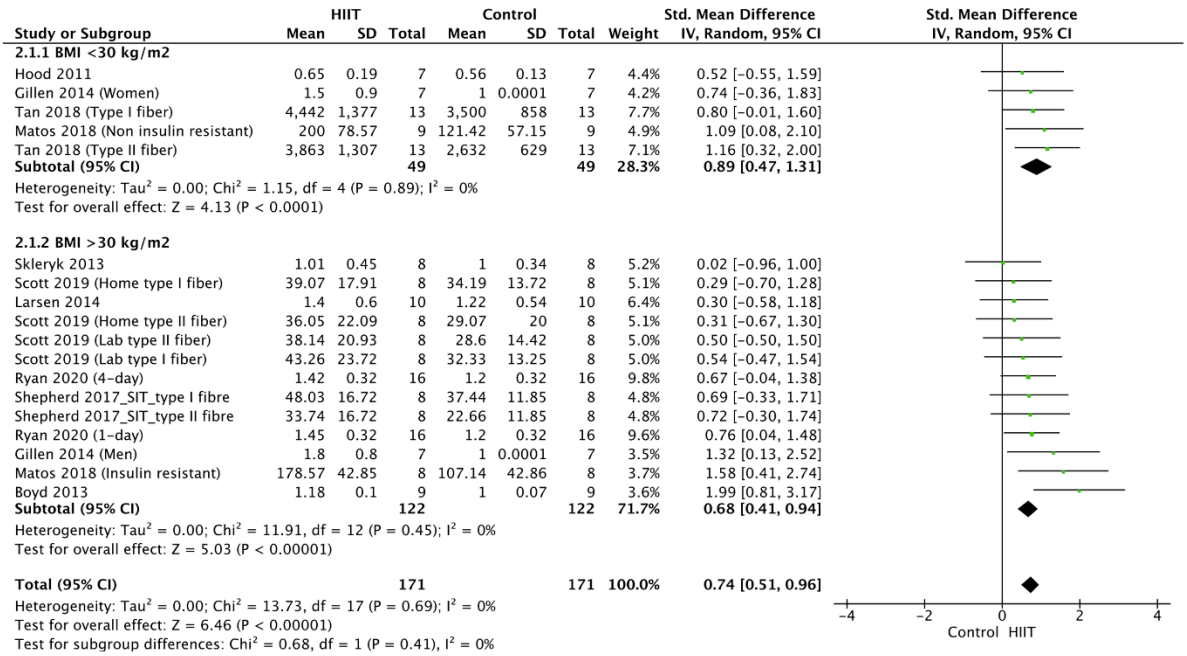


Study or Subgroup	HIIT Mean	HIIT SD	HIIT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.5.1 BMI <30 kg/m2								
Nordsborg 2015_vastus lateralls	22	4.25	16	16.73	21.62	15	5.3%	0.33 [−0.38, 1.04]
Hood 2011	0.54	0.14	7	0.41	0.13	7	3.0%	0.90 [−0.22, 2.02]
Gillen 2013 (Fed)	6.2	1.2	8	5	1.2	8	3.2%	0.95 [−0.10, 2.00]
Gillen 2013 (Fast)	5.7	0.96	6	4.6	0.5	6	2.3%	1.33 [0.02, 2.63]
Nordsborg 2015 (deltoid)	19.3	4.25	12	13.25	4.25	7	3.2%	1.36 [0.31, 2.41]
Gillen 2014 (Women)	5	1.09	7	3.58	0.45	7	2.5%	1.59 [0.34, 2.85]
Gillen 2016	4.49	0.87	9	3.03	0.81	9	3.0%	1.65 [0.55, 2.76]
Subtotal (95% CI)			**65**			**59**	**22.6%**	**1.01 [0.61, 1.41]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.30$, df = 6 (P = 0.39); $I^2 = 5\%$								
Test for overall effect: Z = 4.94 (P < 0.00001)								
2.5.2 BMI >30 kg/m2								
Vaccari 2020	268	78.57	14	308	127.21	14	5.0%	−0.37 [−1.12, 0.38]
Bækkerud 2016 (4 HIIT)	2,946,710	157,073,445.66	5	198,233.32	12,538,005.48	5	2.5%	0.02 [−1.22, 1.26]
Bækkerud 2016 (1 HIIT)	30,371.2	114,521.25	5	984.42	797.01	5	2.5%	0.33 [−0.93, 1.58]
Dela 2018 (T2D)	127.32	20.81	10	116.34	27.76	10	4.1%	0.43 [−0.46, 1.32]
Dela 2018 (Healthy)	138.29	13.88	10	127.32	27.73	10	4.1%	0.48 [−0.41, 1.37]
Dohlmann 2018	136	36.48	11	119	29.85	11	4.3%	0.49 [−0.36, 1.34]
Mora-Rodriguez 2013	19.3	13.23	7	12	11.38	7	3.1%	0.55 [−0.52, 1.63]
Chrøis 2020 (female)	158	66.33	11	119	49.75	11	4.3%	0.64 [−0.22, 1.50]
Little 2011	0.353	0.084	7	0.295	0.036	7	3.0%	0.84 [−0.27, 1.95]
Guadalupe-Grau 2018	171.99	32	11	139.99	40	11	4.1%	0.85 [−0.03, 1.73]
Boyd 2013	49.9	8.8	9	43.6	4.5	9	3.6%	0.86 [−0.12, 1.84]
Søgaard_2019 old	169	46.9	22	122	46.9	22	6.0%	0.98 [0.36, 1.61]
Morales-Palomo 2020_non statin	87.75	23.25	60	63.75	21.75	60	8.7%	1.06 [0.68, 1.44]
Søgaard_2019 young	165	29.93	14	132	26.19	14	4.6%	1.14 [0.33, 1.95]
Chrøis 2020 (Male)	180	39.8	11	131	36.48	11	3.9%	1.23 [0.31, 2.16]
Gillen 2014 (Men)	5.48	1.38	7	3.96	0.61	7	2.7%	1.33 [0.13, 2.53]
Larsen 2014	145	22.14	10	107	25.3	10	3.4%	1.53 [0.51, 2.55]
Morales-Palomo 2020_statin	85.68	23.18	46	51.59	15	46	7.5%	1.73 [1.25, 2.21]
Subtotal (95% CI)			**270**			**270**	**77.4%**	**0.84 [0.57, 1.10]**
Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 32.23$, df = 17 (P = 0.01); $I^2 = 47\%$								
Test for overall effect: Z = 6.09 (P < 0.00001)								
Total (95% CI)			**335**			**329**	**100.0%**	**0.89 [0.67, 1.12]**
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 38.63$, df = 24 (P = 0.03); $I^2 = 38\%$								
Test for overall effect: Z = 7.85 (P < 0.00001)								
Test for subgroup differences: $Chi^2 = 0.50$, df = 1 (P = 0.48), $I^2 = 0\%$								

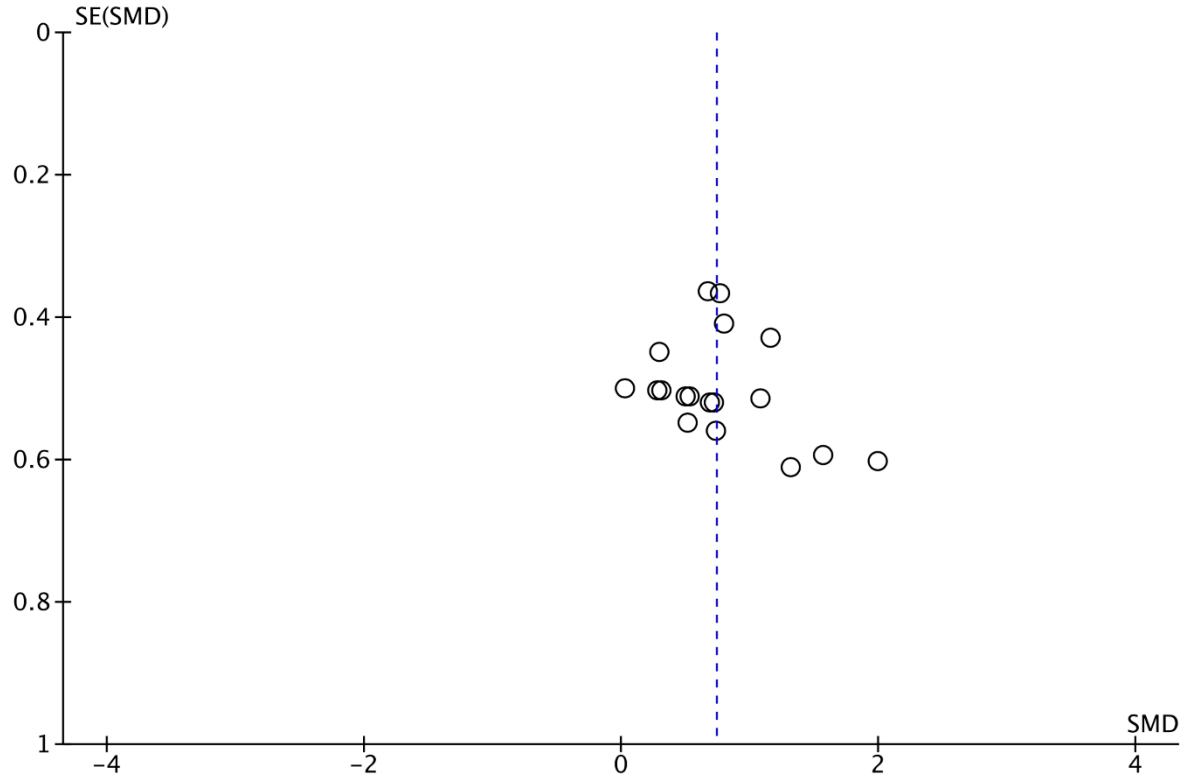
Supplementary Fig. 4: Funnel plot of the effects of HIIT on Citrate Synthase of overweight and obese people. SMD: standardized mean difference; SE: standard error



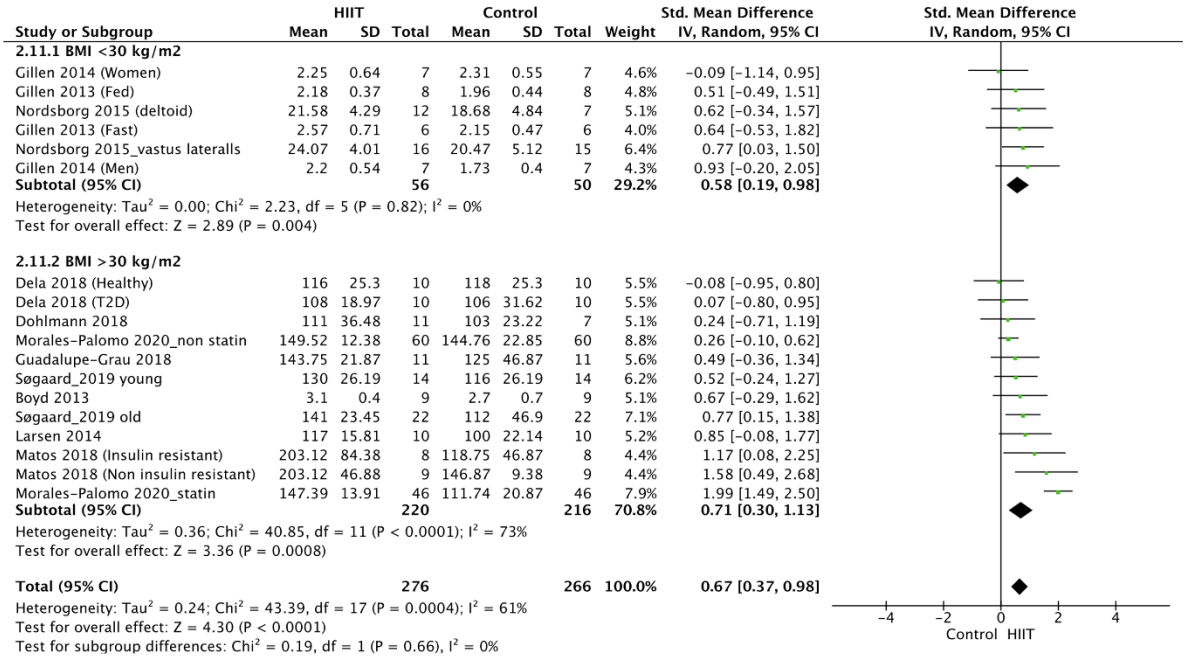
Supplementary Fig. 5: Forest plot of the effect of HIIT on COX-IV (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



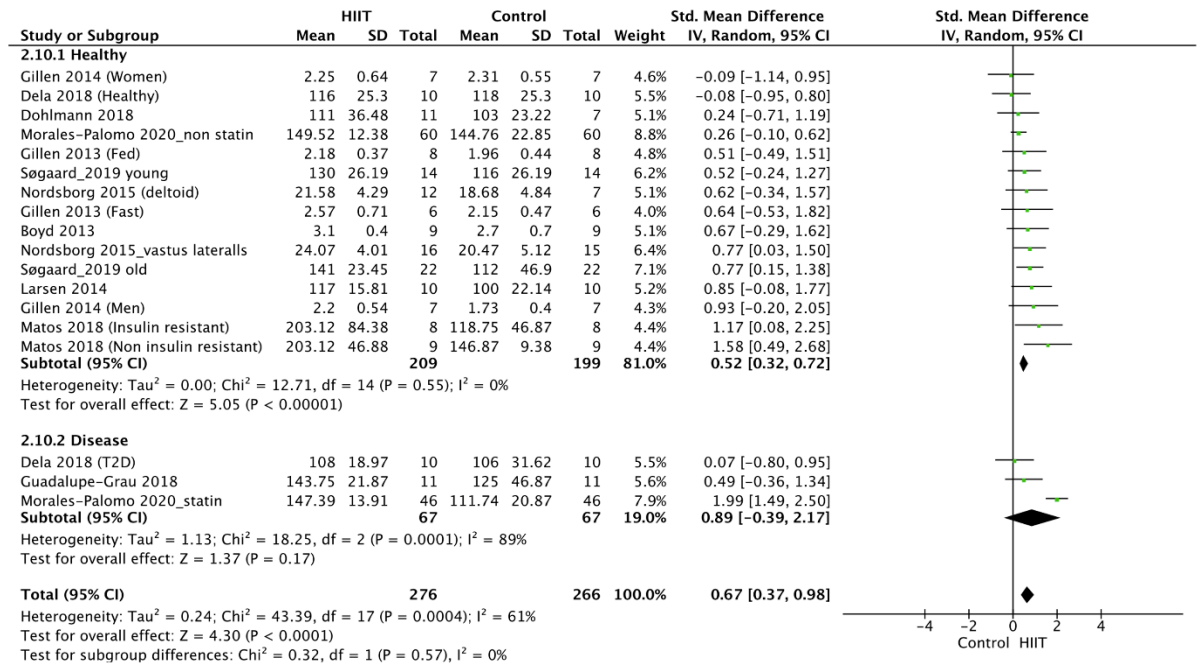
Supplementary Fig. 6: Funnel plot of the effects of HIIT on COX-IV of overweight and obese people. SMD: standardized mean difference; SE: standard error



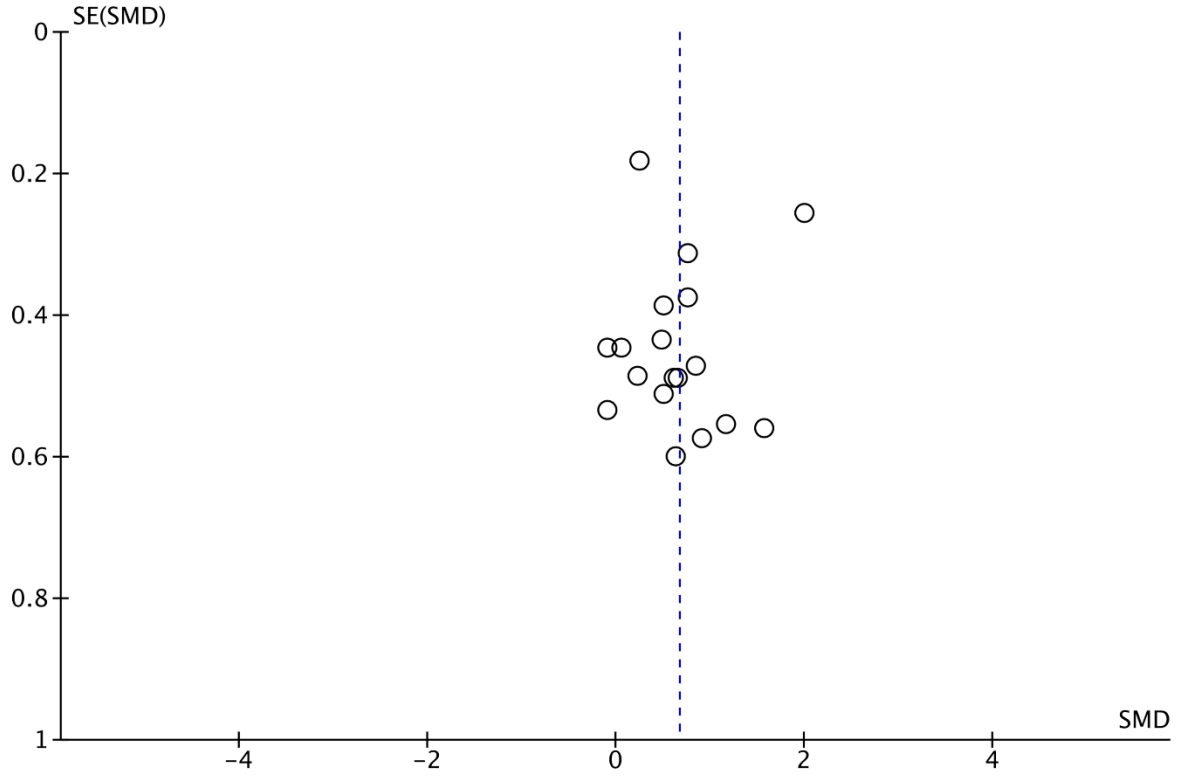
Supplementary Fig. 7: Forest plot of the effect of HIIT on β-HAD (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



Supplementary Fig. 8: Forest plot of the effect of HIIT on β-HAD (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval

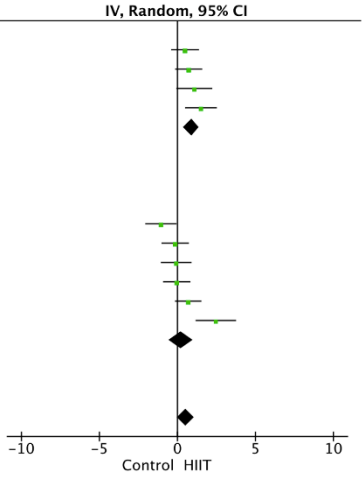


Supplementary Fig. 9: Funnel plot of the effects of HIIT on β-HAD of overweight and obese people. SMD: standardized mean difference; SE: standard error

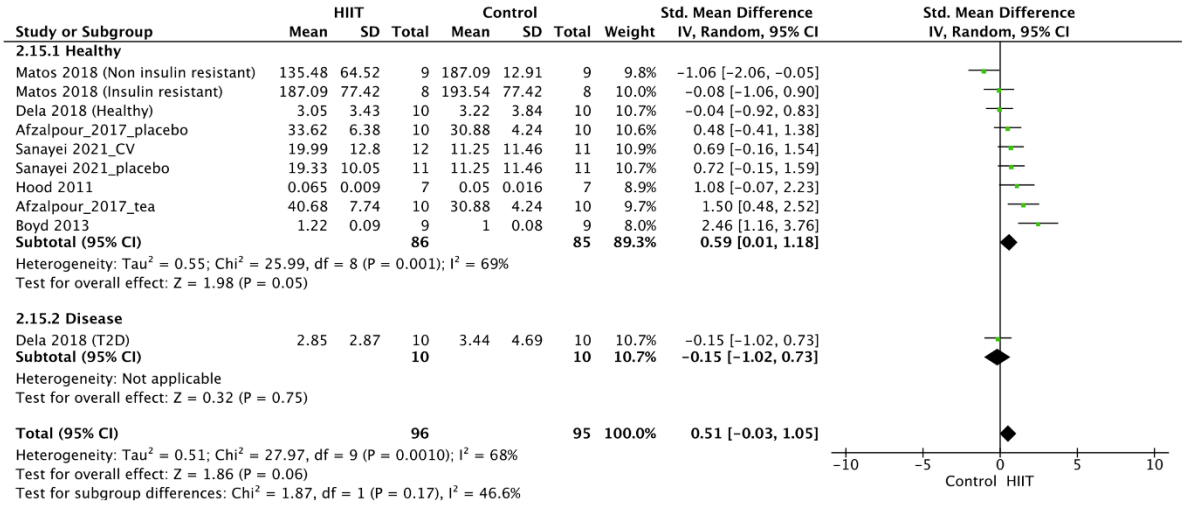


Supplementary Fig. 10: Forest plot of the effect of HIIT on PGC-1a (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval

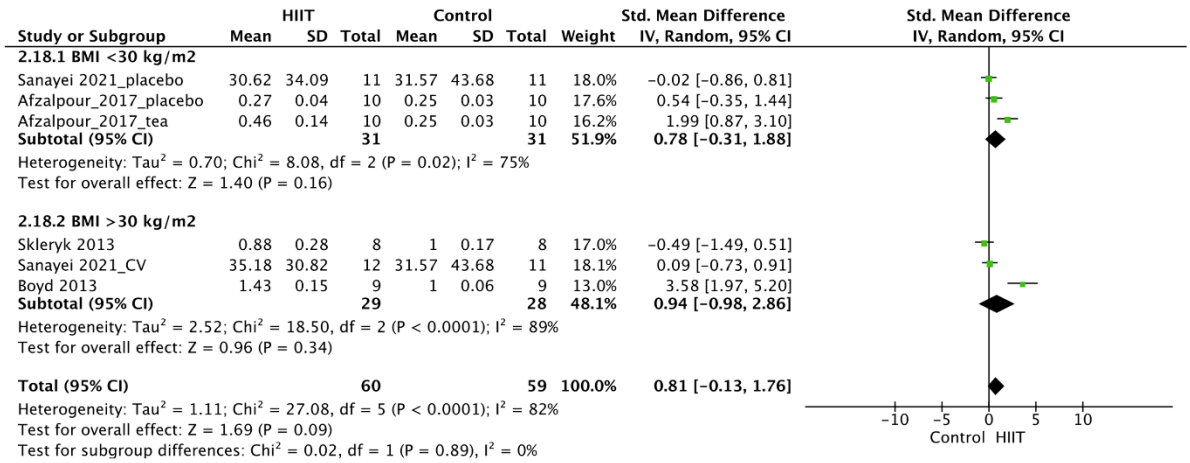
Study or Subgroup	HIIT Mean	HIIT SD	HIIT Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.14.1 BMI <30 kg/m2								
Afzalpour_2017_placebo	33.62	6.38	10	30.88	4.24	10	10.6%	0.48 [−0.41, 1.38]
Sanayei 2021_placebo	19.33	10.05	11	11.25	11.46	11	10.7%	0.72 [−0.15, 1.59]
Hood 2011	0.065	0.009	7	0.05	0.016	7	8.9%	1.08 [−0.07, 2.23]
Afzalpour_2017_tea	40.68	7.74	10	30.88	4.24	10	9.7%	1.50 [0.48, 2.52]
Subtotal (95% CI)			**38**			**38**	**39.9%**	**0.89 [0.41, 1.37]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.44$, df = 3 (P = 0.49); $I^2 = 0\%$								
Test for overall effect: Z = 3.62 (P = 0.0003)								
2.14.2 BMI >30 kg/m2								
Matos 2018 (Non insulin resistant)	135.48	64.52	9	187.09	12.91	9	9.8%	−1.06 [−2.06, −0.05]
Dela 2018 (T2D)	2.85	2.87	10	3.44	4.69	10	10.7%	−0.15 [−1.02, 0.73]
Matos 2018 (Insulin resistant)	187.09	77.42	8	193.54	77.42	8	10.0%	−0.08 [−1.06, 0.90]
Dela 2018 (Healthy)	3.05	3.43	10	3.22	3.84	10	10.7%	−0.04 [−0.92, 0.83]
Sanayei 2021_CV	19.99	12.8	12	11.25	11.46	11	10.9%	0.69 [−0.16, 1.54]
Boyd 2013	1.22	0.09	9	1	0.08	9	8.0%	2.46 [1.16, 3.76]
Subtotal (95% CI)			**58**			**57**	**60.1%**	**0.25 [−0.54, 1.04]**
Heterogeneity: $Tau^2 = 0.72$; $Chi^2 = 20.16$, df = 5 (P = 0.001); $I^2 = 75\%$								
Test for overall effect: Z = 0.61 (P = 0.54)								
Total (95% CI)			**96**			**95**	**100.0%**	**0.51 [−0.03, 1.05]**
Heterogeneity: $Tau^2 = 0.51$; $Chi^2 = 27.97$, df = 9 (P = 0.0010); $I^2 = 68\%$								
Test for overall effect: Z = 1.86 (P = 0.06)								
Test for subgroup differences: $Chi^2 = 1.86$, df = 1 (P = 0.17), $I^2 = 46.3\%$								



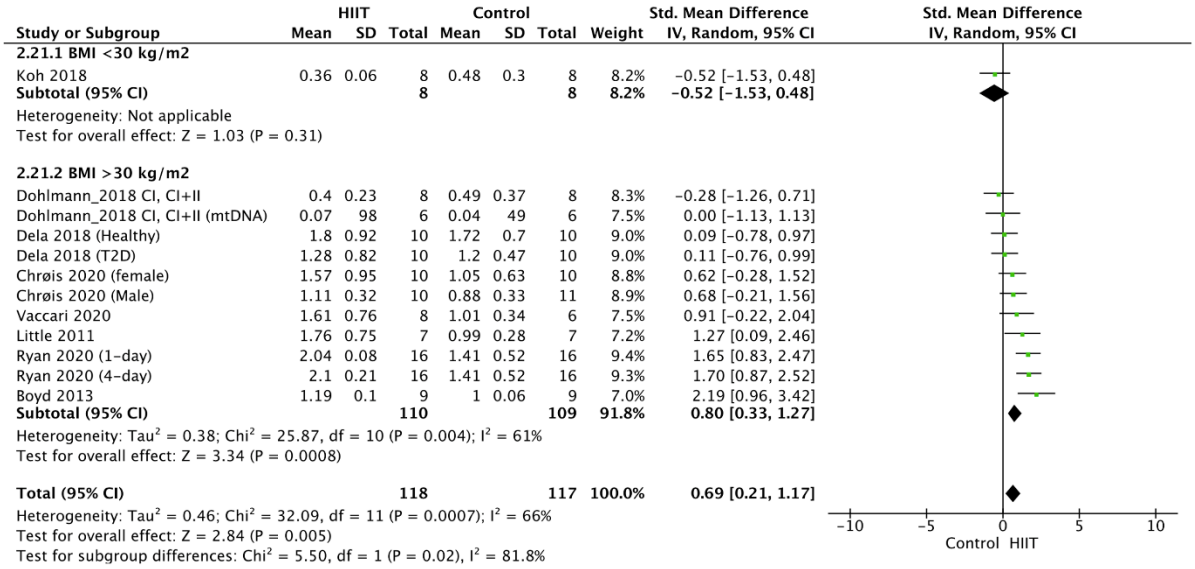
Supplementary Fig. 11: Forest plot of the effect of HIIT on PGC-1a (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval



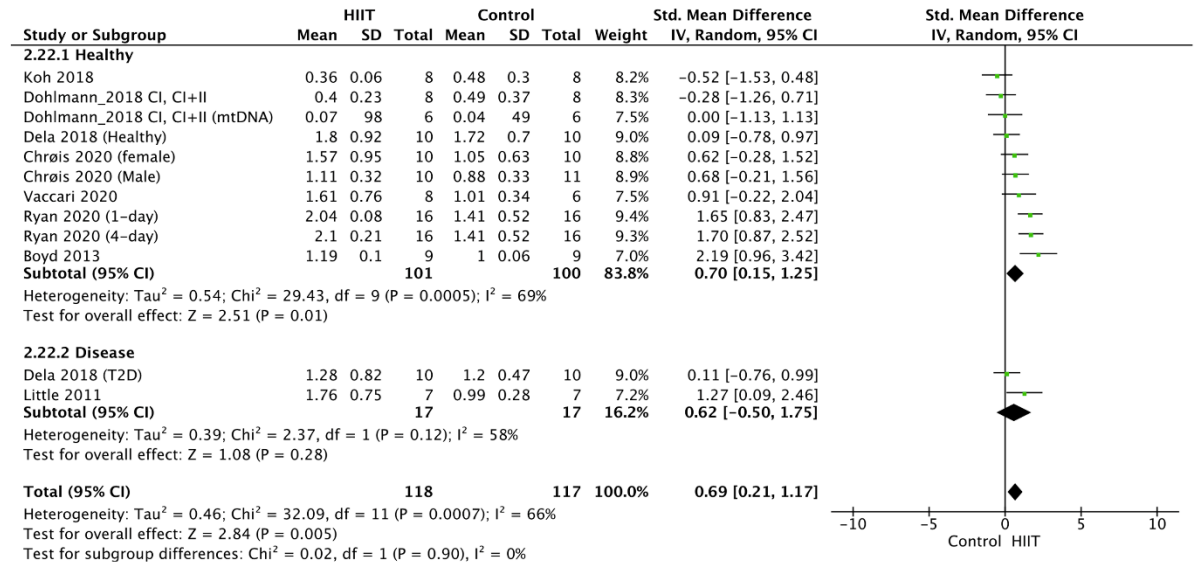
Supplementary Fig. 12: Forest plot of the effect of HIIT on SIRT1 (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



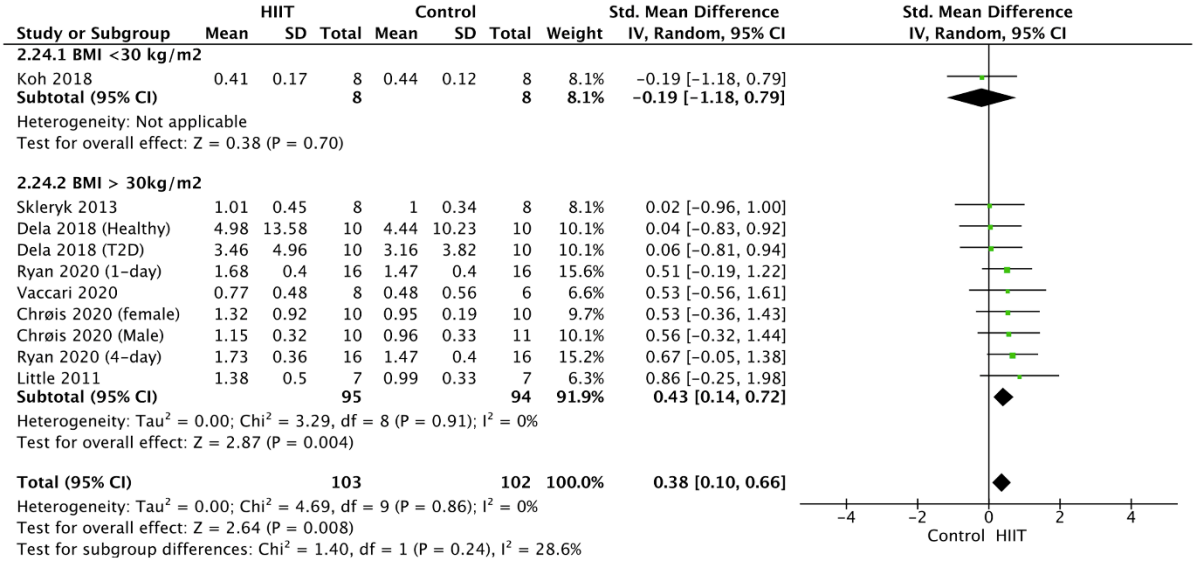
Supplementary Fig. 13: Forest plot of the effect of HIIT on Complex I (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



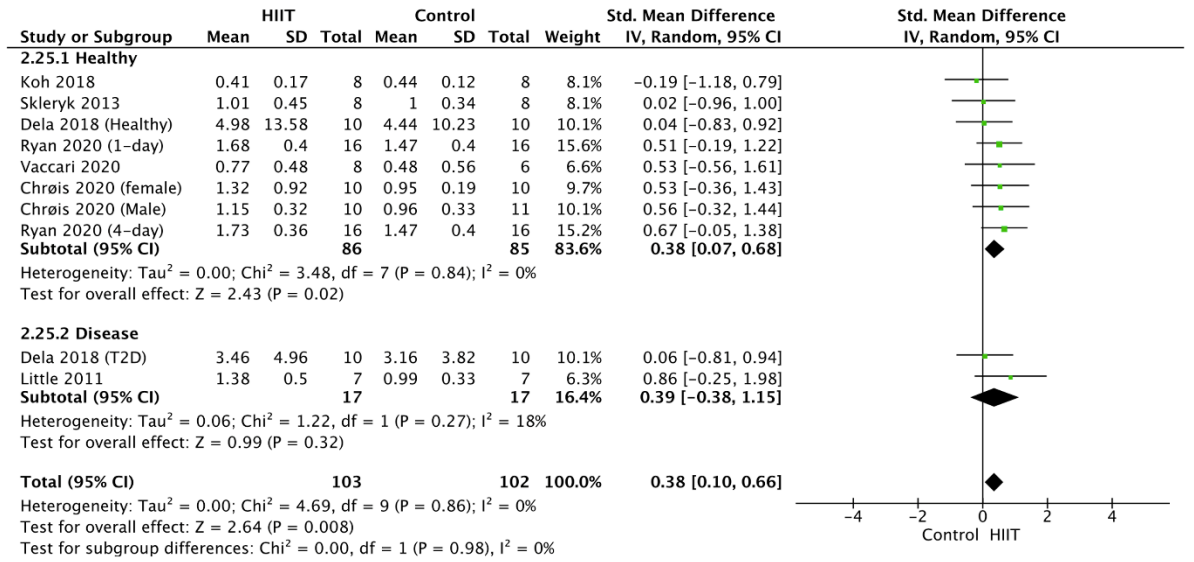
Supplementary Fig. 14: Forest plot of the effect of HIIT on Complex I (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval



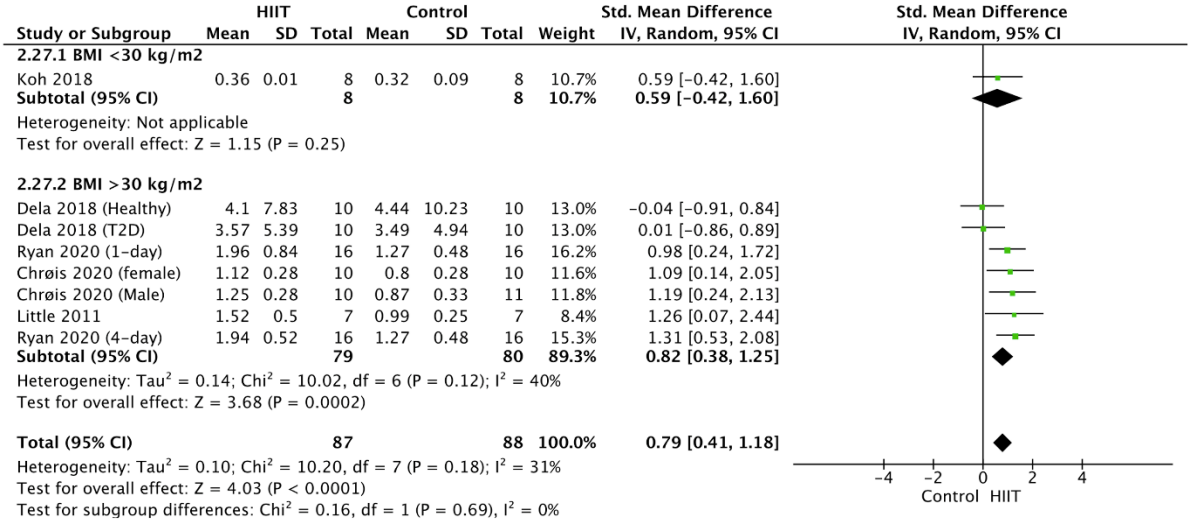
Supplementary Fig. 15: Forest plot of the effect of HIIT on Complex II (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



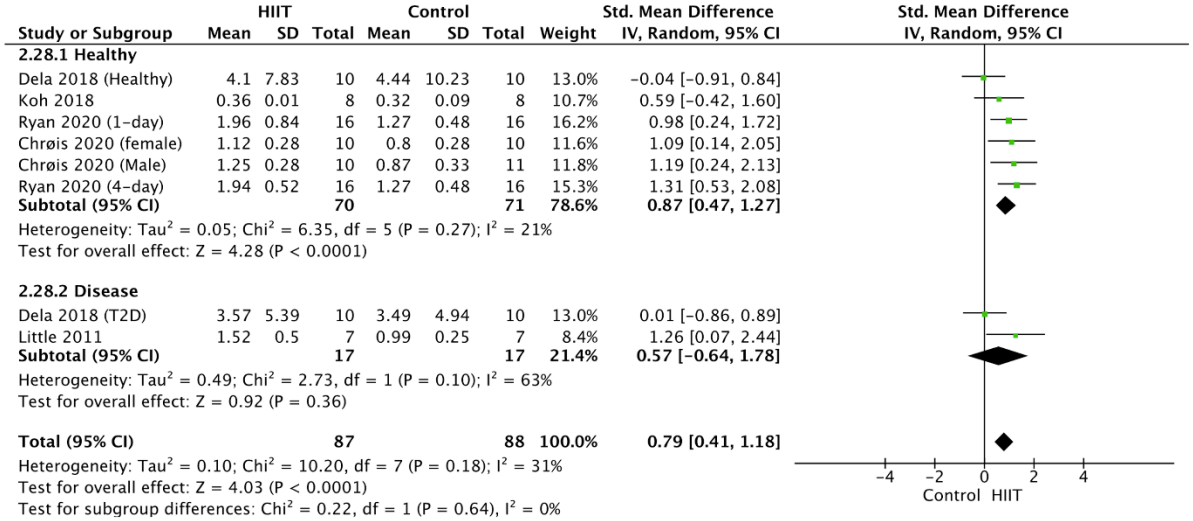
Supplementary Fig. 16: Forest plot of the effect of HIIT on Complex II (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval



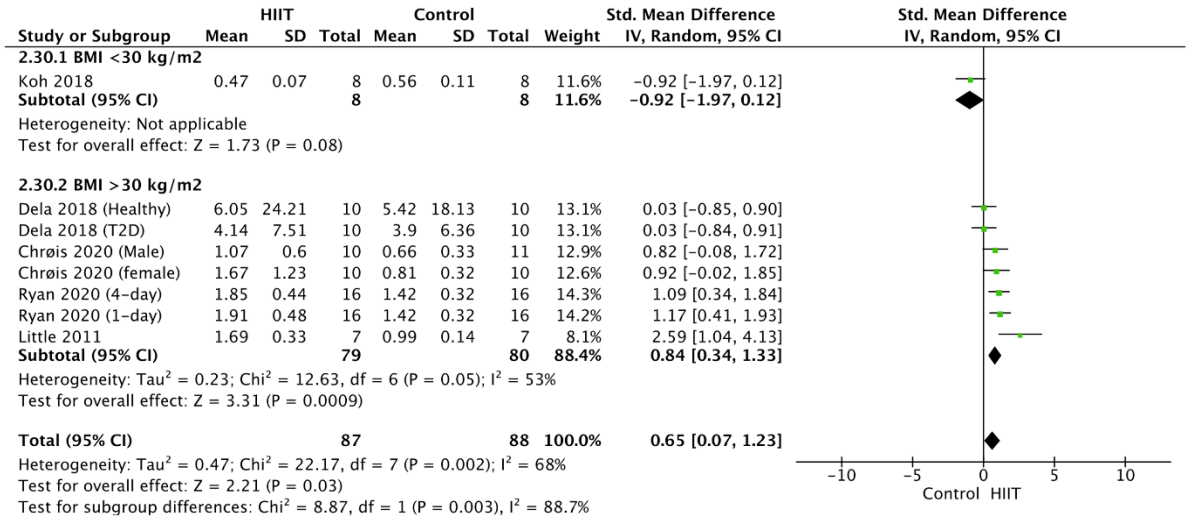
Supplementary Fig. 17: Forest plot of the effect of HIIT on Complex III (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



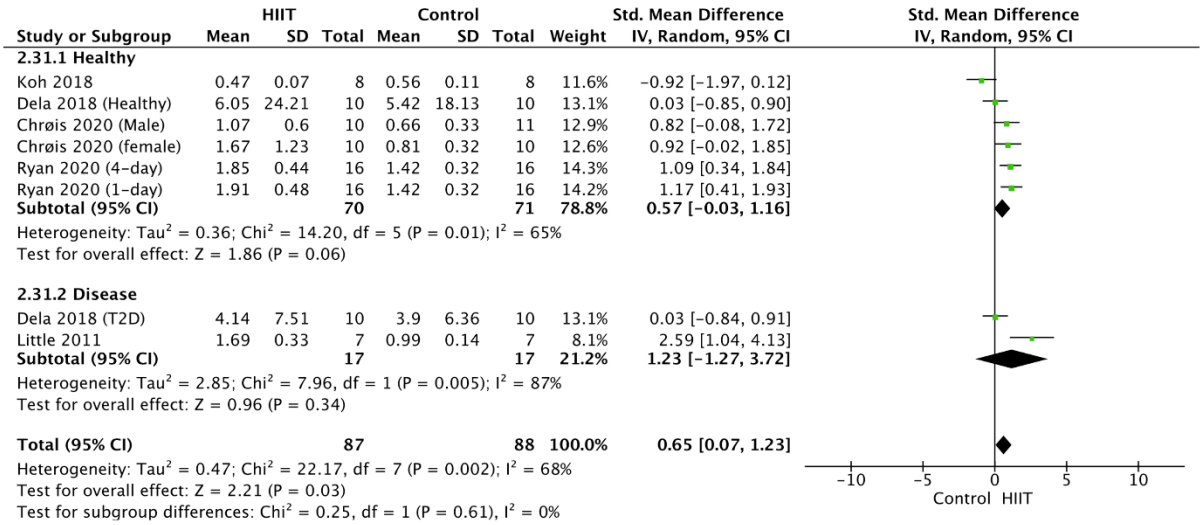
Supplementary Fig. 18: Forest plot of the effect of HIIT on Complex III (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval



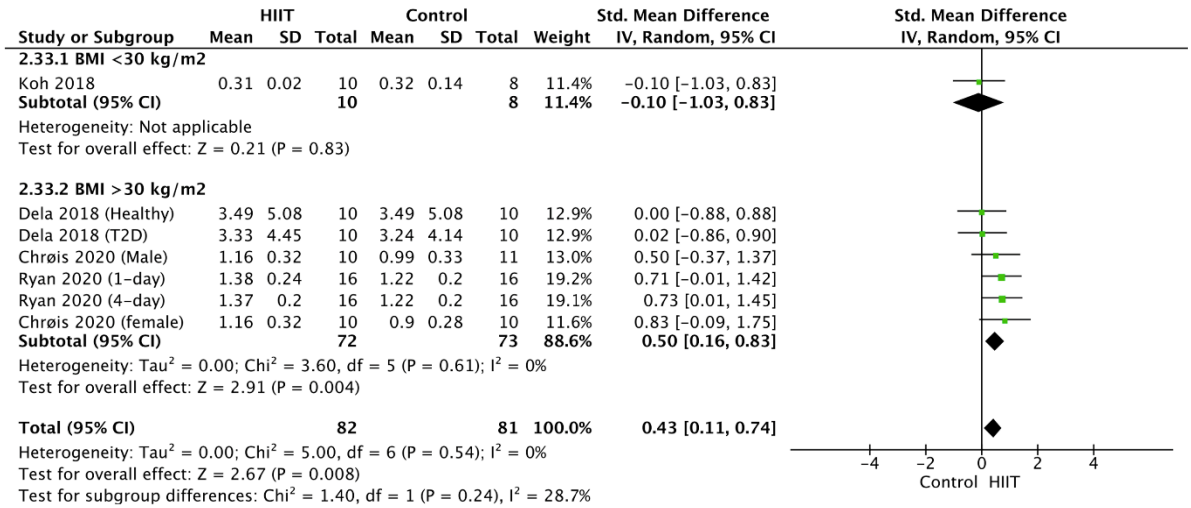
Supplementary Fig. 19: Forest plot of the effect of HIIT on Complex IV (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



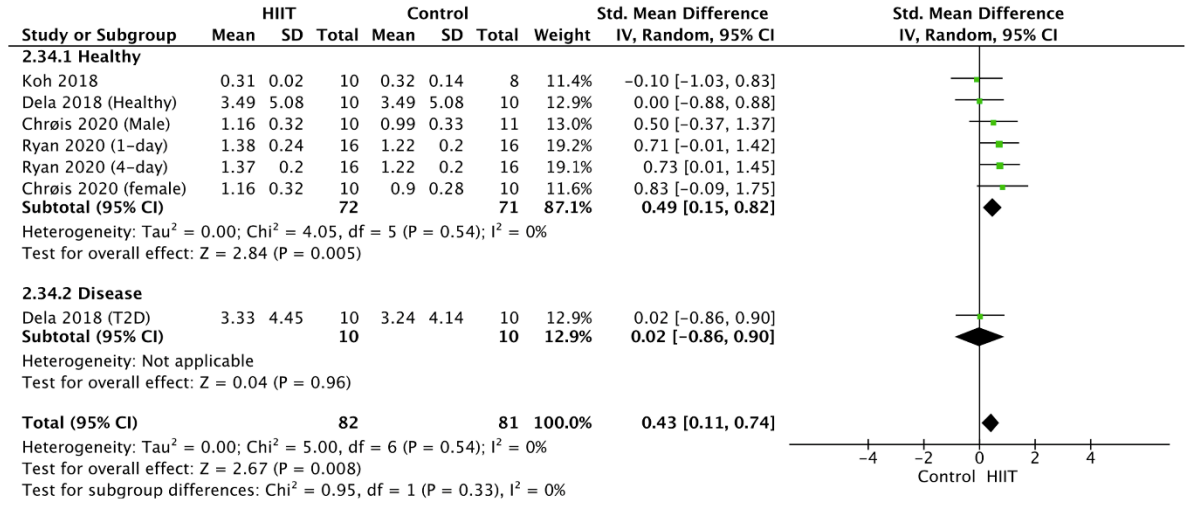
Supplementary Fig. 20: Forest plot of the effect of HIIT on Complex IV (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval



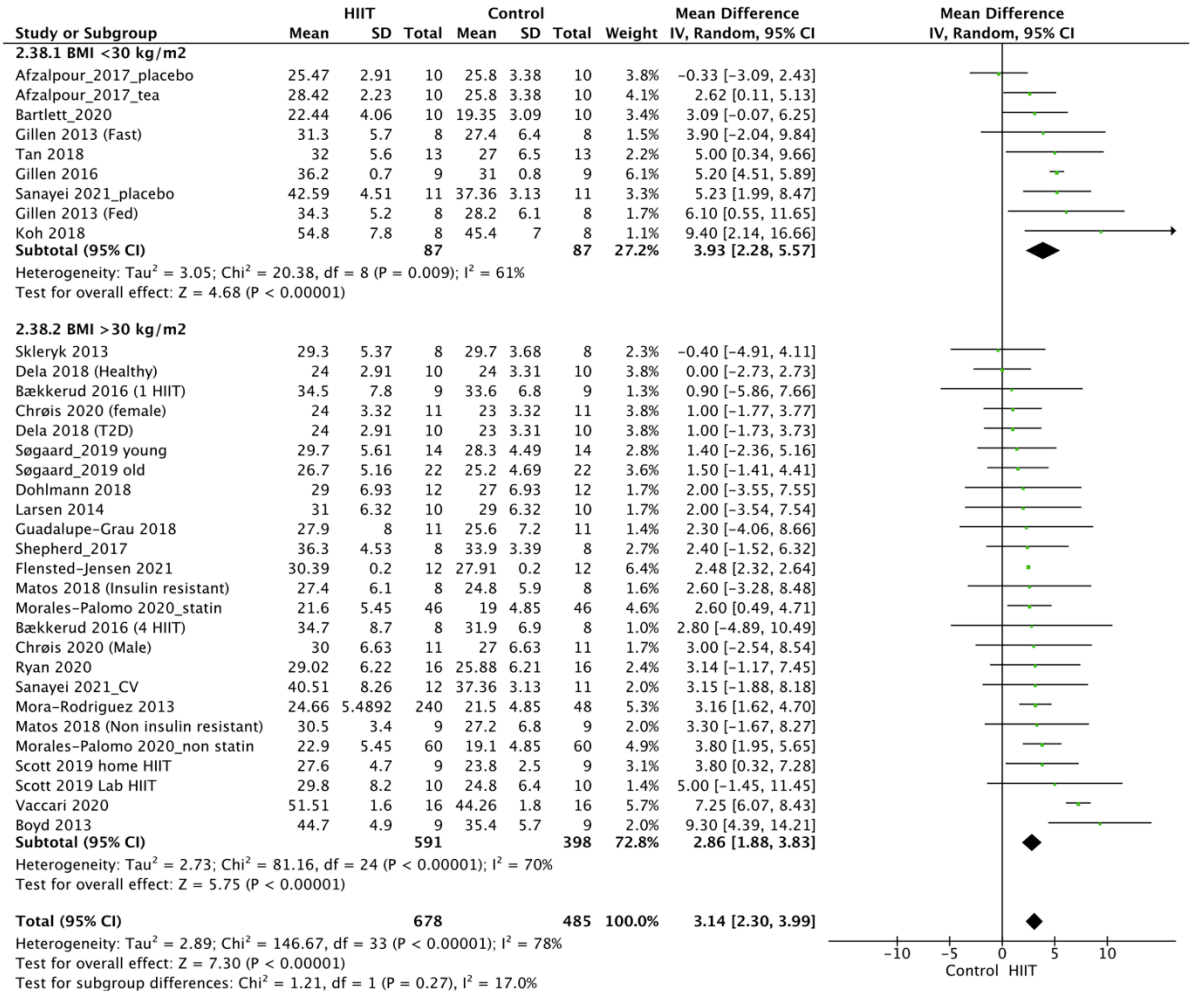
Supplementary Fig. 21: Forest plot of the effect of HIIT on Complex V (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



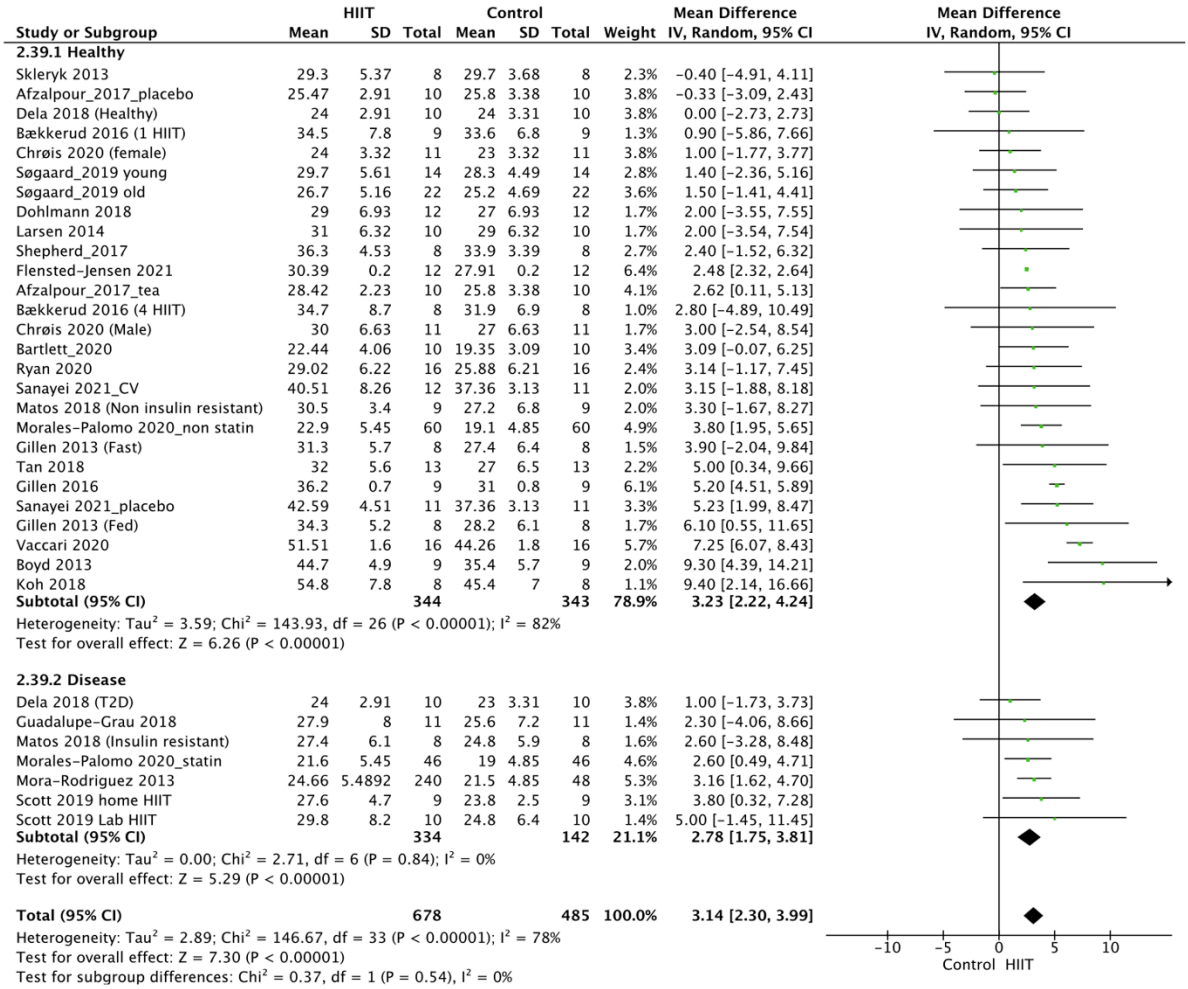
Supplementary Fig. 22: Forest plot of the effect of HIIT on Complex V (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval



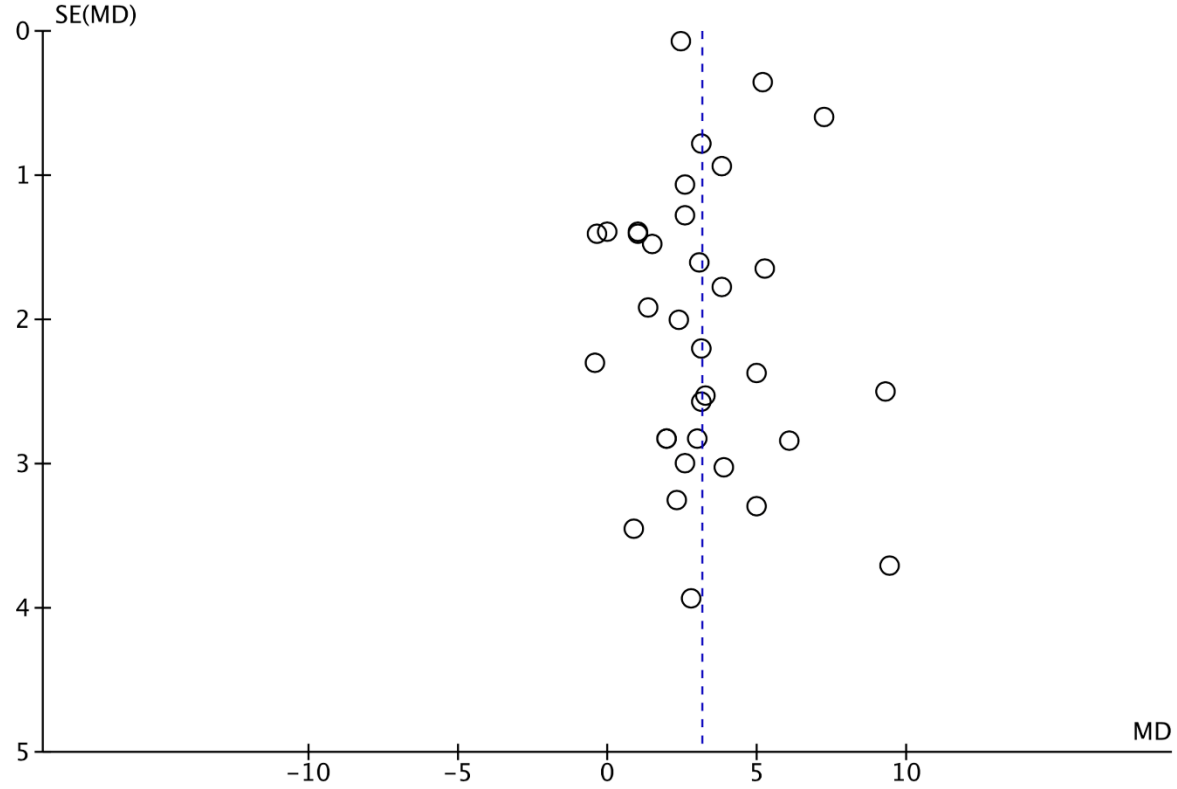
Supplementary Fig. 23: Forest plot of the effect of HIIT on VO2max (subgroup analysis for BMI). SD: standard deviation; 95% CI: 95% confidence interval



Supplementary Fig. 24: Forest plot of the effect of HIIT on VO2max (subgroup analysis for health status). SD: standard deviation; 95% CI: 95% confidence interval



Supplementary Fig. 25: Funnel plot of the effects of HIIT on VO2max of overweight and obese people. MD: mean difference; SE: standard error



Supplementary Table 3: GRADE analysis [33,34]

		Evaluation components to lower quality						Evaluation components to higher quality		
Quality of evidence (GRADE)	**Outcome**	Methodological design start point	Risk of bias	Inconsistencey of results	Indirectness	Imprecision	Publication bias	Large effect	Dose response	Confounding
Very Low ⊕◯◯◯	HIIT on citrate synthase vs. Control	Most of the studies invervetional without randomization: **Low quality**	>67% of the components of the included studies display low risk of bias and not applicable risk (RoB #1 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=38%, p=0.03, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect does not exclude the "favor control" values. The confidence interval represents the true underlying effect. Downgrade 1 level	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= $(\pi/\sqrt{3})*$SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20% (ACR=0.2). The outcome showed a RR=1.24	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(RR<2). No upgrade		
Low ⊕⊕◯◯	HIIT on cytochrome c vs. Control	Most of the studies invervetional without randomization: **Low quality**	>64% of the components of the included studies display low risk of bias and not applicable risk (RoB #2 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=0%, p>0.05, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect excludes however, the "favor control" values. The confidence interval represents the true underlying effect. No downgrade	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= $(\pi/\sqrt{3})*$SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.57 (RR<2). No upgrade		
Low ⊕⊕◯◯	HIIT on β-HAD vs. Control	Most of the studies invervetional without randomization: **Low quality**	>63% of the components of the included studies display low risk of bias and not applicable risk (RoB #3 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=61%, p<0.01, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect excludes however, the "favor control" values. The confidence interval represents the true underlying effect. No downgrade	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= $(\pi/\sqrt{3})*$SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.32 (RR<2). No upgrade		
Low ⊕⊕◯◯	HIIT on PGC-1a vs. Control	50% of the studies are randomized controlled trials: **Moderate quality**	>61% of the components of the included studies display low risk of bias and not applicable risk (RoB #4 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=68%, p<0.01, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect does not exclude the "favor control" values. The confidence interval represents the true underlying effect. Downgrade 1 level	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= ($\pi/\sqrt{3}$)*SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.08 (RR<2). No upgrade		
Very Low ⊕◯◯◯	HIIT on COMPLEX I vs. Control	Most of the studies invervetional without randomization: **Low quality**	>63% of the components of the included studies display low risk of bias and not applicable risk (RoB #5 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=66%, p<0.01, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect does not exclude the "favor control" values. The confidence interval represents the true underlying effect. Downgrade 1 level	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= ($\pi/\sqrt{3}$)*SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.39 (RR<2). No upgrade		
Low ⊕⊕◯◯	HIIT on COMPLEX II vs. Control	Most of the studies invervetional without randomization: **Low quality**	>64% of the components of the included studies display low risk of bias and not applicable risk (RoB #6 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=0%, p>0.05, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect excludes however, the "favor control" values. The confidence interval represents the true underlying effect. No downgrade	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= $(\pi/\sqrt{3})*$SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.26 (RR<2). No upgrade		
Low ⊕⊕◯◯	HIIT on COMPLEX III vs. Control	40% of the studies are randomized controlled trials: **Moderate quality**	>60% of the components of the included studies display low risk of bias and not applicable risk (RoB #7 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=31%, p>0.05, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect does not exclude the "favor control" values. The confidence interval represents the true underlying effect. Downgrade 1 level	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= ($\pi/\sqrt{3}$)*SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.77 (RR<2). No upgrade		
Low ⊕⊕◯◯	HIIT on COMPLEX IV vs. Control	40% of the studies are randomized controlled trials: **Moderate quality**	>60% of the components of the included studies display low risk of bias and not applicable risk (RoB #8 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=68%, p<0.01, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect does not exclude the "favor control" values. The confidence interval represents the true underlying effect. Downgrade 1 level	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= ($\pi/\sqrt{3}$)*SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.26 (RR<2). No upgrade		
Moderate ⊕⊕⊕◯	HIIT on COMPLEX V vs. Control	50% of the studies are randomized controlled trials: **Moderate quality**	>58% of the components of the included studies display low risk of bias and not applicable risk (RoB #9 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=0%, p>0.05, no substantial heterogeneity. No downgrade	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is <800, therefore, the optimal information size is not met. 2. The confidence interval of the overall effect excludes however, the "favor control" values. The confidence interval represents the true underlying effect. No downgrade	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= $(\pi/\sqrt{3})*$SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=0.21 (RR<2). No upgrade		
Moderate ⊕⊕⊕◯	HIIT on VO2max vs. Control	Most of the studies invervetional without randomization: **Low quality**	>66% of the components of the included studies display low risk of bias and not applicable risk (RoB #10 sheet). Therefore, it is unlikely to increase the overall risk of bias. No downgrade	Even though we used a random effect model meta-analysis, we consider heterogeneity as an index of inconsistency. I2=78%, p<0.01, Substantial heterogeneity. Downgrade 1 level	All of the studies do display as a primary aim, very similar to the systematic review aim. Therefore, the available evidence is applicable to our research question. No downgrade	1. The overall sample size is >800, therefore, the optimal information size is met. 2. The confidence interval of the overall effect excludes however, the "favor control" values. The confidence interval represents the true underlying effect. No downgrade	Most studies in this meta-analysis do not suffer from important limitations, the evidence is direct and consistent. No major funding from the industry. No publication bias in the funnel plots. No downgrade	Given that the data are skewed, we converted SMD to Odds ratio (OR) using the equation LogOR= (π/√3)*SMD and we converted the LogOR into Risk Ratio (RR) using the equation RR= OR/ (1- Absolute Control Risk)*(1-OR). We assumed an absolute control risk reduction of 20%	No robust evidence for a dose response effect. No upgrade	We found no confounding factors that indicate upgrading

								(ACR=0.2). The outcome showed a RR=33.43 (RR>5). Upgrade 2 levels		

Supplementary Table 4: PRISMA checklist [35]

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 1-2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 2-3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 2, figure S1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplement Page 2-6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 2-3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 3

Section and Topic	Item #	Checklist item	Location where item is reported
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 3, Table S1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 3
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 3
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 3
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 3
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 3
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 3
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 3
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 2-3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 3
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	NA

Section and Topic	Item #	Checklist item	Location where item is reported
Study characteristics	17	Cite each included study and present its characteristics.	Page 4 Table S1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 4, Table S2, Figure S2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table S1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 4, Table S2, Figure S2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 4-8, Table 1 Figure 1,2 Figure S3-S25
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 4-8, Table 1 Figure 1,2, Figure S3-S25
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 8, Table 2
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 4, Table S2, Figure S2
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 4-8, Table 1 Figure 1,2, Figure S3-

Section and Topic	Item #	Checklist item	Location where item is reported
			S25
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 8
	23b	Discuss any limitations of the evidence included in the review.	Page 8-9
	23c	Discuss any limitations of the review processes used.	Page 9
	23d	Discuss implications of the results for practice, policy, and future research.	Page 9-10
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 1, 2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 1, 2
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 10
Competing interests	26	Declare any competing interests of review authors.	Page 10
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 10-13

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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1. Page MJ, McKenzie JE, Bossuyt PM *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372.

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