

Supplementary

Table S1- Inclusion and exclusion criteria for all studies included.

	Inclusion Criteria	Exclusion Criteria
Study 1 (n=9)	<ul style="list-style-type: none"> • Age 18–40 years • BMI ≥ 18.5 and $< 30 \text{ kg.m}^{-2}$ • Weight not fluctuated more than $\pm 3\text{kg}$ in the last 6 months, • Recreationally active, but not elite 	<ul style="list-style-type: none"> • contraindication to exercise (e.g., ongoing, musculoskeletal injury, first-degree relative experienced severe cardiac event at early age [$< \sim 45$ years], breathlessness or dizziness on exertion, poor circulation, hypo- or hypertension), • excessive purposeful exercise (> 5 times \times 20-minute bouts of self-reported vigorous exercise performed per week, • weight instability ($> 3\text{kg}$ change in previous 6 months) • Use of any medications known to affect study outcomes
Study 2 (n=11)	<ul style="list-style-type: none"> • Age 50–74 years, • BMI $\geq 27.5 \text{ kg.m}^{-2}$ (White European) or $\geq 25 \text{ kg.m}^{-2}$ (South Asian) OR • Has had 2-hour glucose between 7.8 mmol.L^{-1} and 11.1 mmol.L^{-1} after an oral glucose tolerance test OR 	<ul style="list-style-type: none"> • Regular purposeful exercise ($\geq 3 \times 20$-minute bouts of self-reported vigorous exercise performed per week • Use of any glucose lowering medication, • contraindication to exercise (e.g., abnormal resting ECG, breathlessness or dizziness on exertion, poor circulation, hypo- or hypertension),

	<ul style="list-style-type: none"> • Has HbA1c between 5.70%–6.49% at baseline or at their most recent blood test within the previous 5 years, • Weight not fluctuated more than ± 5kg in the last 6 months 	<ul style="list-style-type: none"> • Significant renal or hepatic impairment defining parameters i.e., chronic kidney disease stage 3b, liver markers more than 3x greater than the normal range
Study 3 (n=23)	<ul style="list-style-type: none"> • Age 30–75 years, • $\geq 27.0 \text{ kg.m}^{-2}$ and $\leq 45.0 \text{ kg.m}^{-2}$ or $\geq 23.0 \text{ kg.m}^{-2}$ and $\leq 45.0 \text{ kg.m}^{-2}$ (South Asian), • Waist circumference ≥ 94 cm (or ≥ 90 cm if south Asian), • HbA1c $\geq 6.5\%$ and $<10\%$, • Clinically elevated liver fat ($\geq 5.56\%$ assessed via ^1H-MRS), • Additional criteria for participants with T2DM: HbA1c $< 6\%$, treatment via lifestyle or metformin only within the last 6 months, 	<ul style="list-style-type: none"> • Contraindication to magnetic resonance procedures, • Contraindication to exercise, • Participating in regular purposeful exercise training of vigorous intensity – frequency ≥ 3 sessions per week and intensity ≥ 6.0 metabolic equivalents, • Weight instability or planned/on-going dietary intervention, • Current smoker, • Uncontrolled hypertension- systolic blood pressure ≥ 160mmHg and/or diastolic blood pressure ≥ 100 mmHg, • Additional criteria for participants with T2DM: taking additional oral anti-diabetic medication to metformin (e.g., SGLT2i, GLP-1RA) within the last 6 months, taking insulin

Note: BMI, body mass index; ECG, electrocardiogram; HbA1c, glycosylated haemoglobin; ^1H -MRS, proton magnetic resonance spectroscopy; T2DM, type 2 diabetes

Study 1- All participants took part in Study 1 were included in Part A; Study 2- 48% of the participants (11/23 participants) within Study 2 were included in Part A, chosen to match the characteristics of Study 1; Study 3- 58% of all participants (23/40 participants) within Study 3 were included in Part A, chosen due to HbA1c $> 6.5\%$.

Supplementary Figure S1- A schematic of the experimental trials

