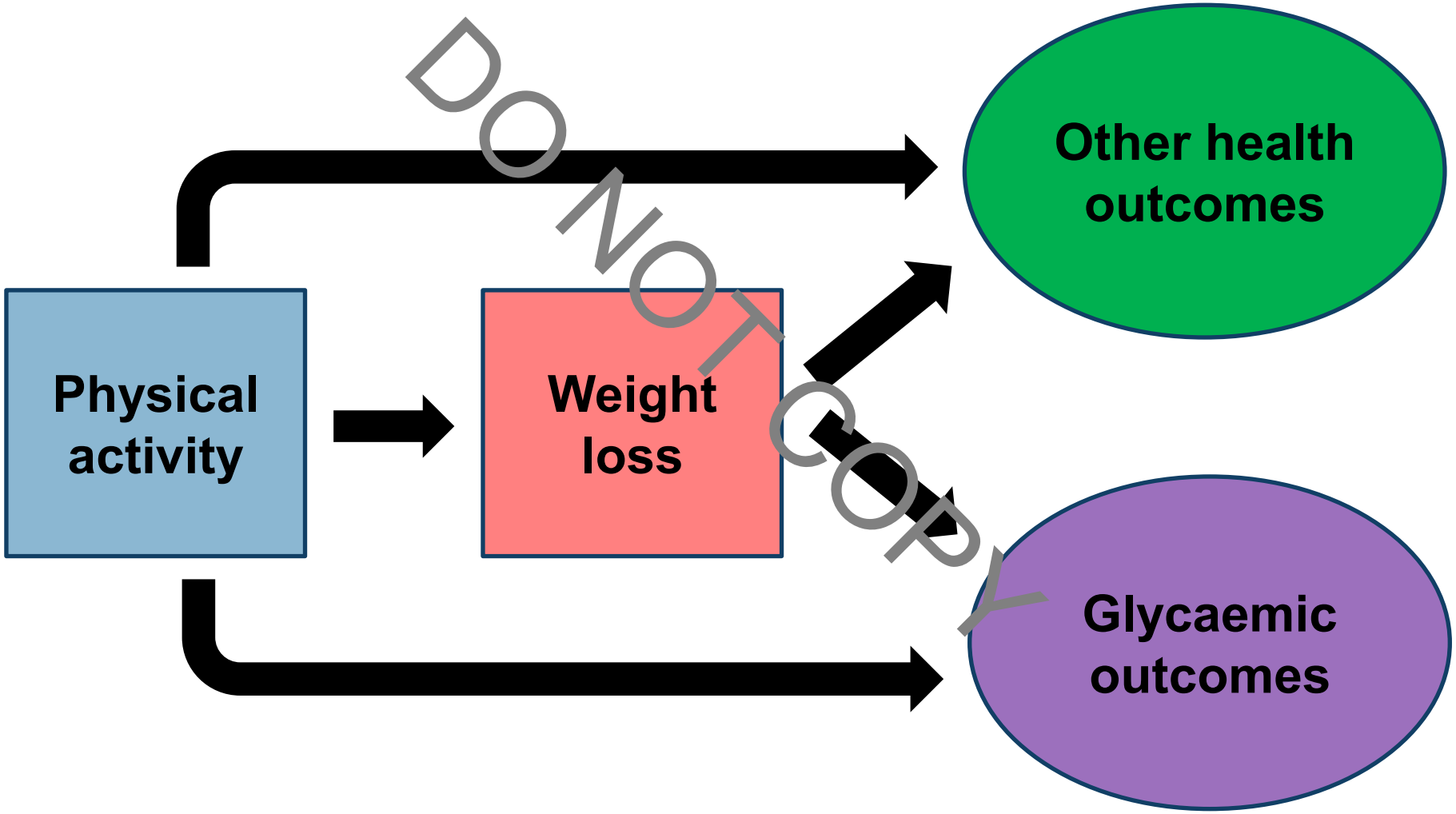
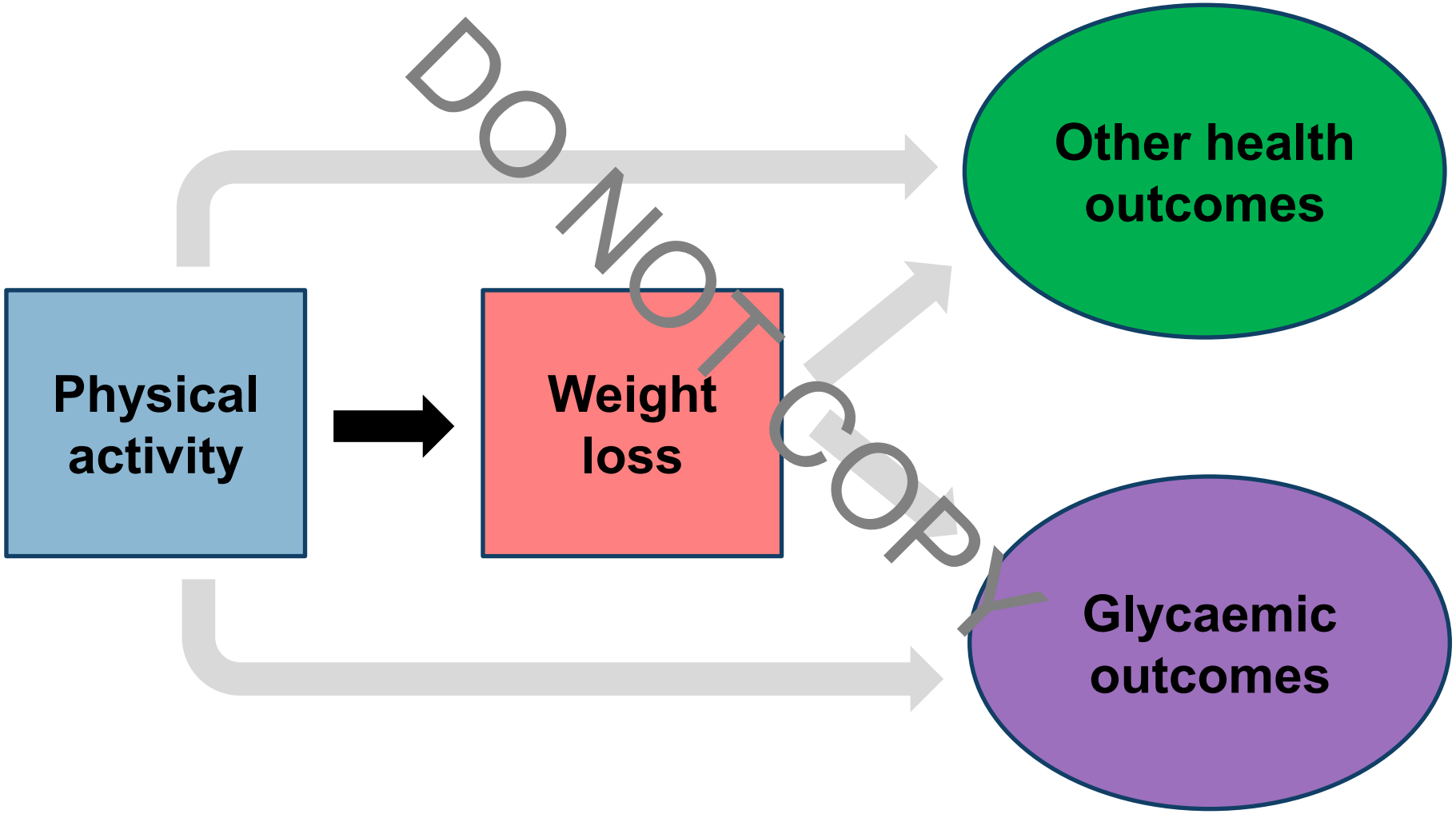
An update on physical activity in type 2 diabetes: is it all about weight loss?

Prof Jason Gill
University of Glasgow


Other health outcomes
Physical activity
Weight loss
Glycaemic outcomes


Physical activity
Weight loss
Other health outcomes
Glycaemic outcomes
DO NOT COPY

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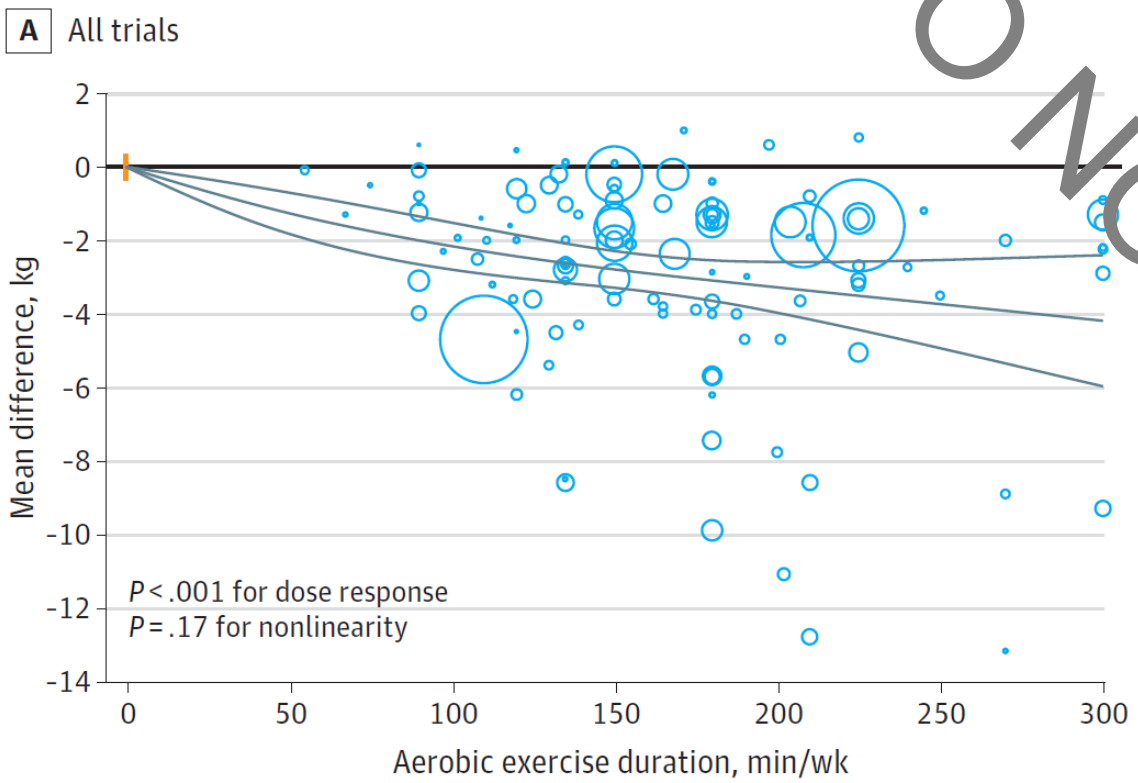
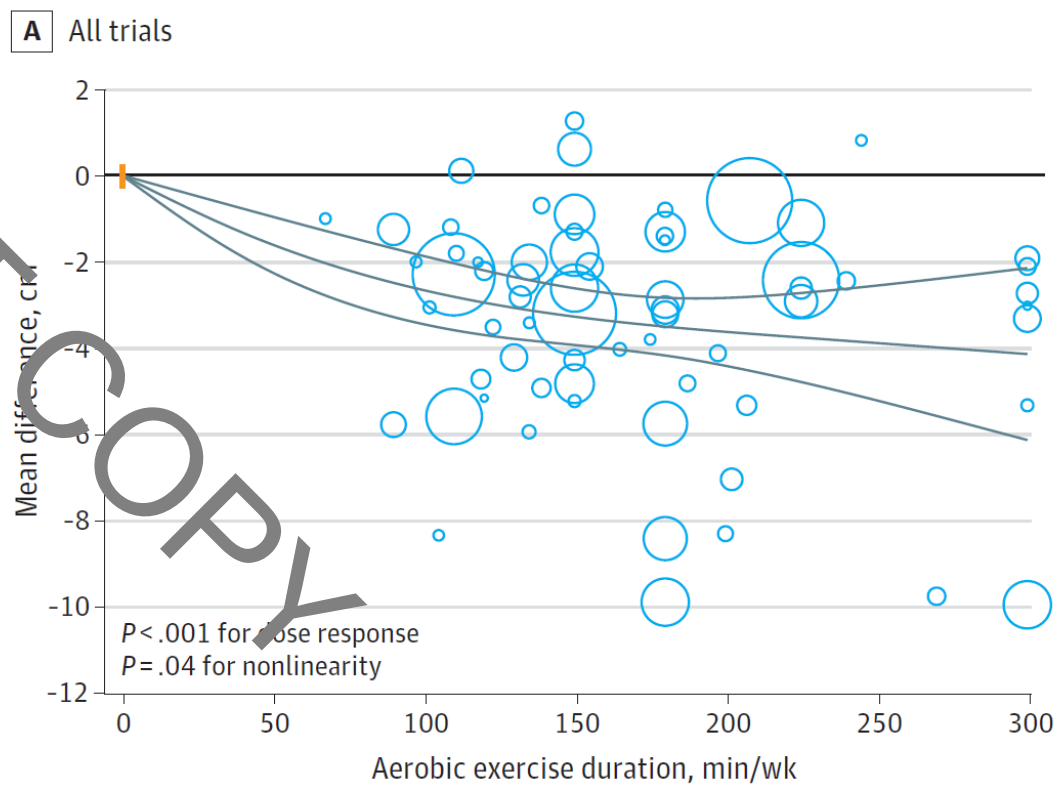
Aerobic exercise and weight loss in adults: dose-response meta-analysis

Weight



Waist



Jayedi et al (2024) JAMA Network Open 7(12):e2452185

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Long term effects of diet and/or exercise on weight loss: network meta-analysis

	Diet vs Exercise
Body weight (kg)	-2.93 (-4.18, -1.68)
Waist circumference (cm)	-1.75 (-4.12, 0.62)
Fat mass (kg)	-2.20 (-3.75, -0.66)
Waist-to-hip ratio	-0.00 (-0.01, 0.01)
Total cholesterol (mg/dl)	-3.91 (-8.11, 0.30)
LDL cholesterol (mg/dl)	-3.19 (-6.85, 0.48)
HDL cholesterol (mg/dl)	-0.96 (-1.88, -0.04)
Triglyceride (mg/dl)	-3.80 (-12.21, 4.62)
Diastolic BP (mmHg)	-1.33 (-3.00, 0.35)
Systolic BP (mmHg)	-2.19 (-4.23, -0.15)
VO_2max (ml/kg/min)	-1.16 (-2.42, 0.09)

Studies at least 12 months in duration, values mean difference (95% CI)

Schwingshackl et al (2014) Syst Rev, 3:130

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Long term effects of diet and/or exercise on weight loss: network meta-analysis

	Diet vs Exercise	Diet & Exercise vs Diet
Body weight (kg)	-2.93 (-4.18, -1.68)	-1.38 (-1.98, -0.79)
Waist circumference (cm)	-1.75 (-4.12, 0.62)	-1.68 (-2.66, -0.70)
Fat mass (kg)	-2.20 (-3.75, -0.66)	-1.65 (-2.81, -0.49)
Waist-to-hip ratio	-0.00 (-0.01, 0.01)	-0.01 (-0.02, -0.01)
Total cholesterol (mg/dl)	-3.91 (-8.11, 0.30)	-2.19 (-7.84, 3.46)
LDL cholesterol (mg/dl)	-3.19 (-6.85, 0.48)	-0.93 (-6.14, 4.27)
HDL cholesterol (mg/dl)	-0.96 (-1.88, -0.04)	1.62 (0.28, 2.95)
Triglyceride (mg/dl)	-3.80 (-12.21, 4.62)	-10.08 (-17.38, -2.79)
Diastolic BP (mmHg)	-1.33 (-3.00, 0.35)	-1.20 (-2.26, -0.15)
Systolic BP (mmHg)	-2.19 (-4.23, -0.15)	-0.24 (-1.45, 0.97)
VO_2max (ml/kg/min)	-1.16 (-2.42, 0.09)	3.61 (2.07, 5.14)

Studies at least 12 months in duration, values mean difference (95% CI)

Schwingshackl et al (2014) Syst Rev, 3:130

Physical activity and long-term weight maintenance

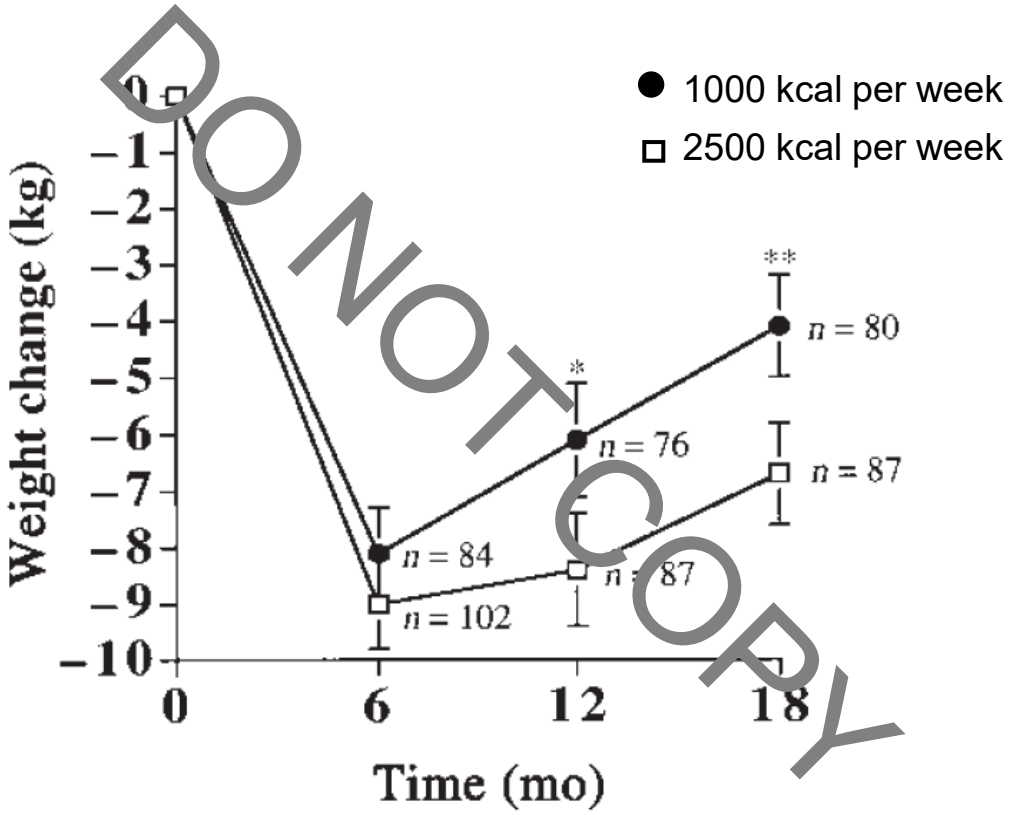
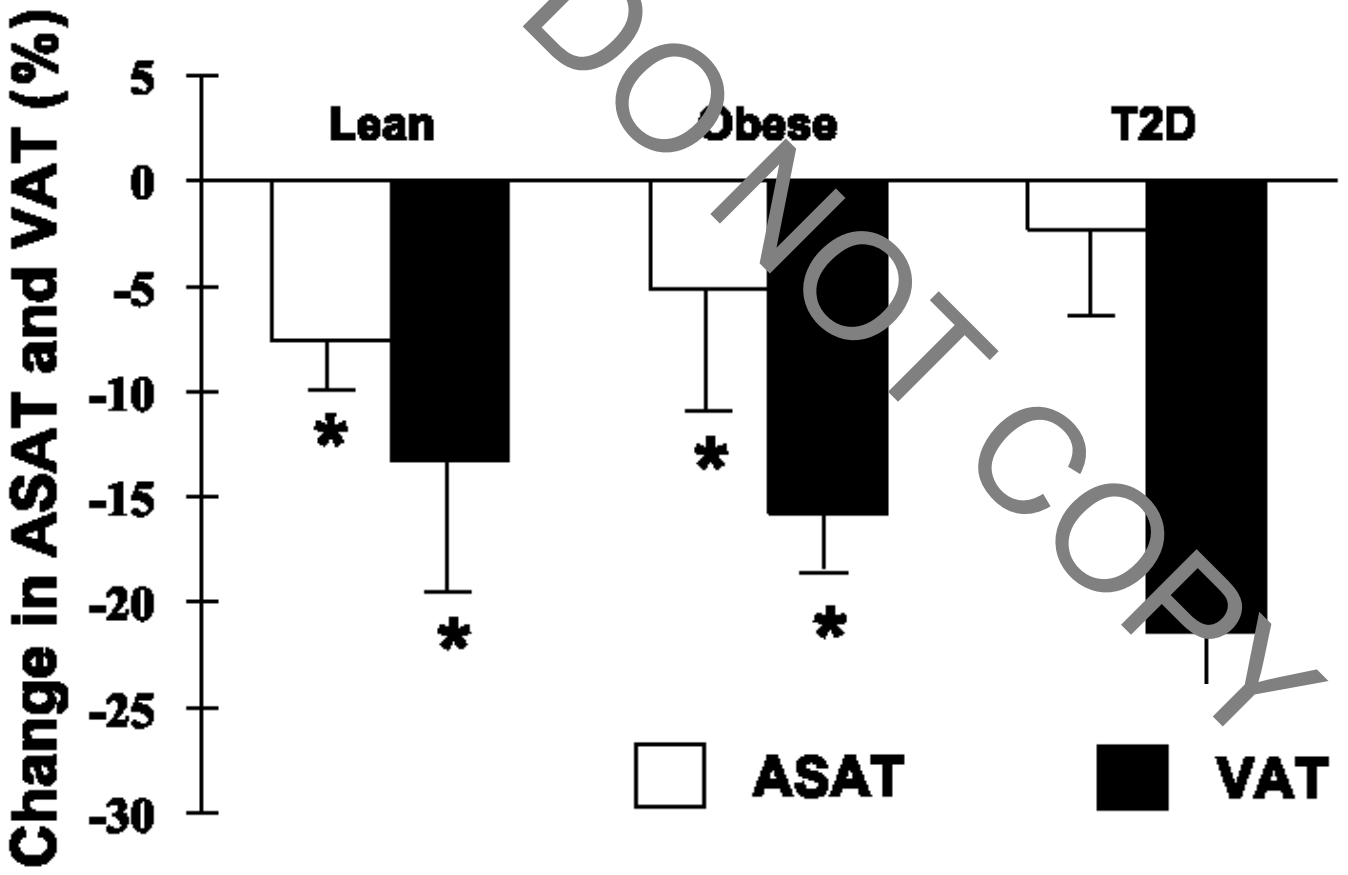
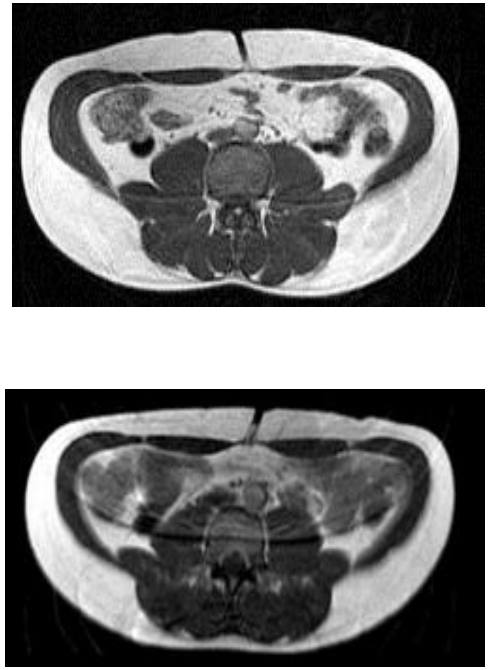


FIGURE 2. Mean (±SEM) weight change over time by treatment group (●, standard behavior therapy group; □, high physical activity treatment group). *,**Significantly different from the HPA treatment group (SAS GLM procedure): *$P = 0.07$, **$P = 0.04$.

Jeffery et al (2003) AJCN, 78:684-9

Effects of exercise training, without weight loss, on body fat





Lee et al (2005) J Appl Physiol 99:1220-1225

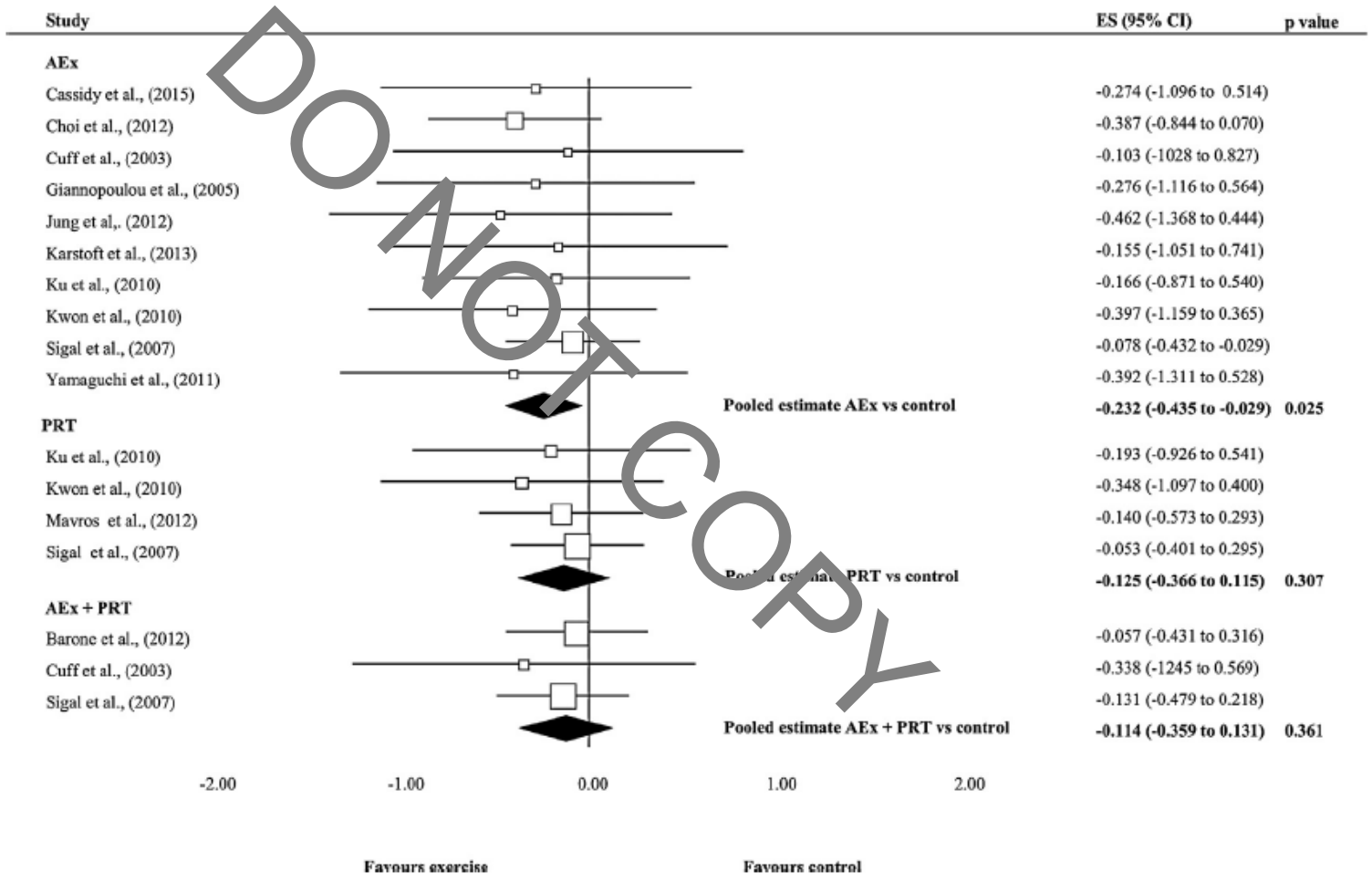
60 min moderate exercise, 5 x per week for 13 weeks

Exercise and visceral fat in type 2 diabetes: systematic review and meta-analysis

Aerobic exercise

Resistance exercise

Combined exercise



Sabag et al (2017) Diabetes & Metabolism 19:1446-1459

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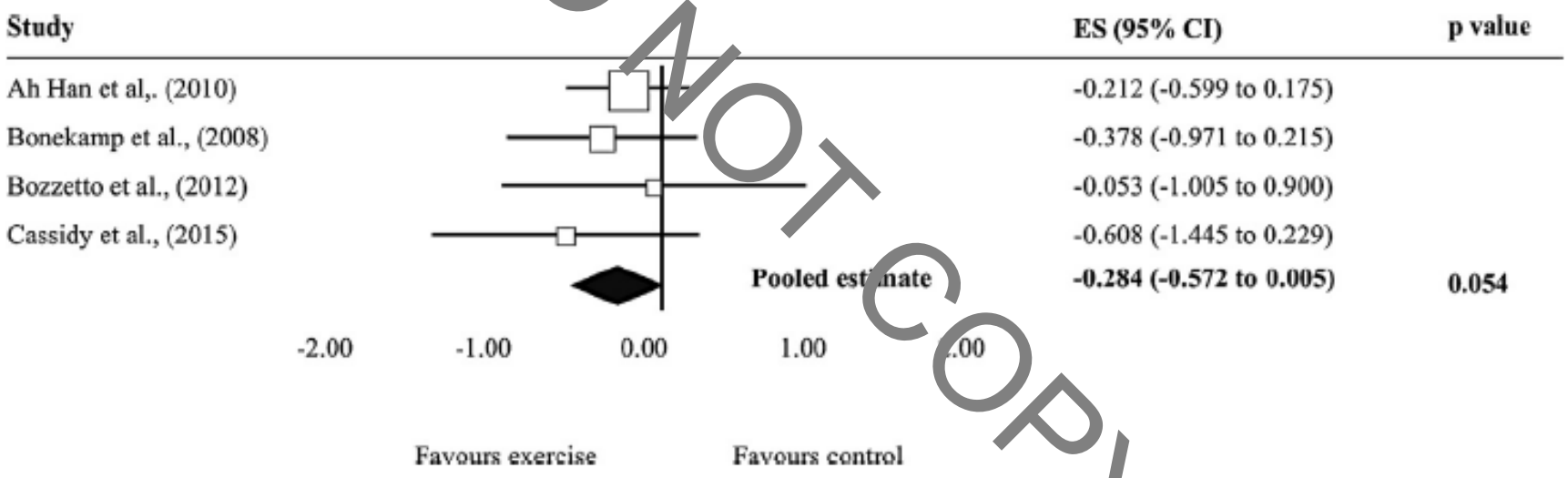
Exercise and liver fat in type 2 diabetes: systematic review and meta-analysis



Sabag et al (2017) Diabetes & Metabolism 19:1446-1459

Exercise training and intrahepatic TG in NAFLD: systematic review and meta-analysis

No significant weight loss

Significant weight loss

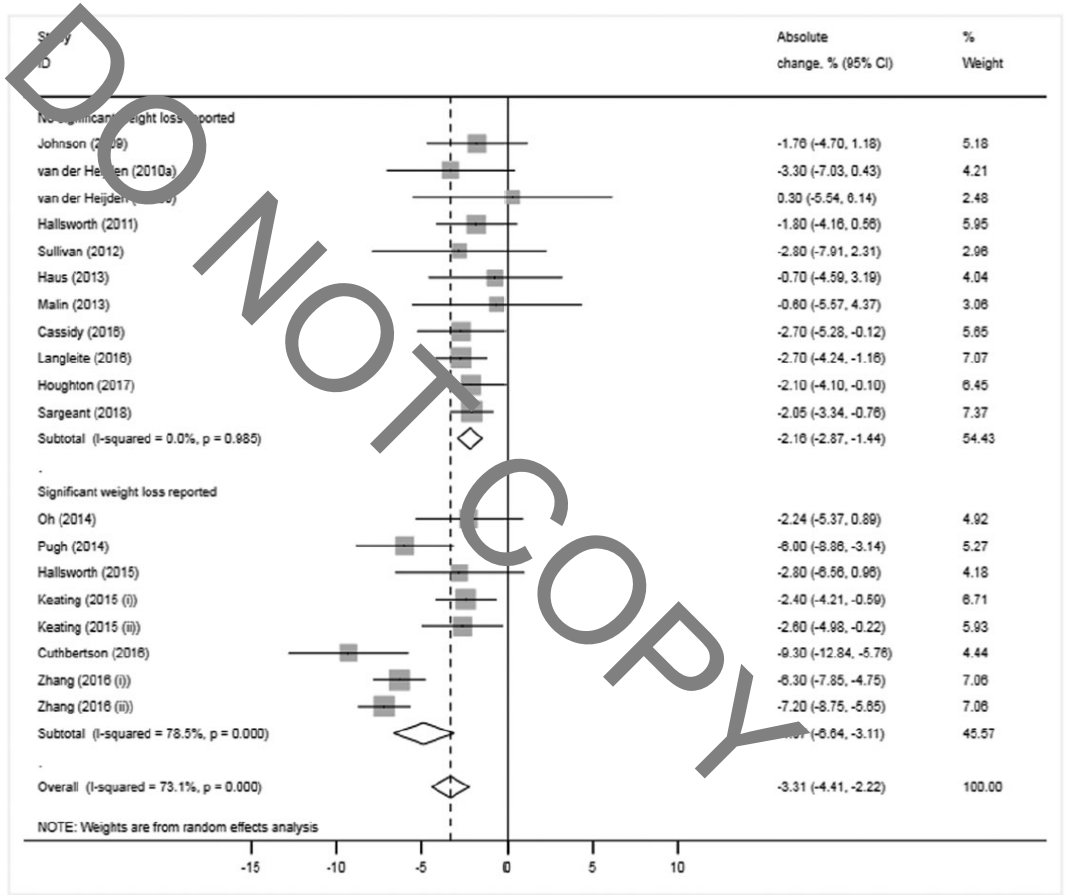


Figure 3 Meta-analysis of the pooled effect of exercise training on IHTG from pre-training to post-training in all exercise groups of all eligible studies when studies are grouped into those that elicited weight loss versus those that did not. IHTG, intrahepatic triglyceride; 95% CI, 95% confidence interval.

Sargeant et al (2018) Obesity Reviews 43:195-210

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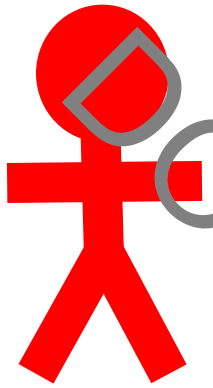
Is the relationship between physical activity and adiposity the same in everyone?

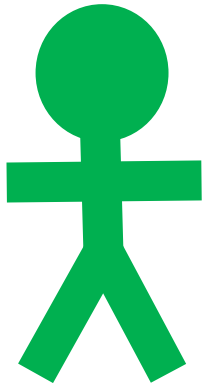
Physical activity, genetic predisposition to obesity and BMI in UK Biobank

High genetic obesity risk (top 25%)



~4.2 kg heavier

Low genetic obesity risk (bottom 25%)



Celis-Morales et al (2019) Int J Obes https://doi.org/10.1038/s41366-019-0381-5

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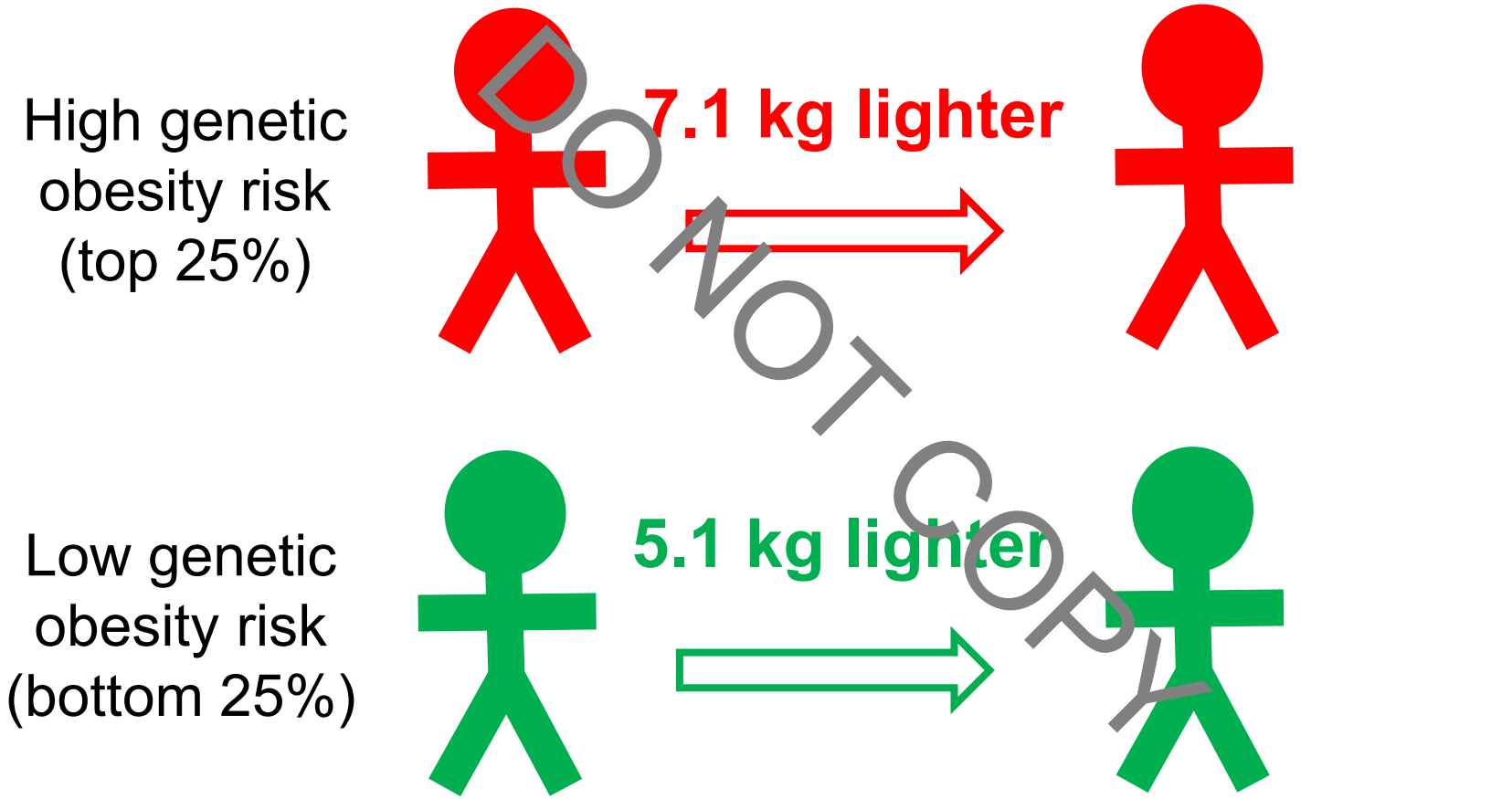
Physical activity, genetic predisposition to obesity and BMI in UK Biobank



Celis-Morales et al (2019) Int J Obes https://doi.org/10.1038/s41366-019-0381-5

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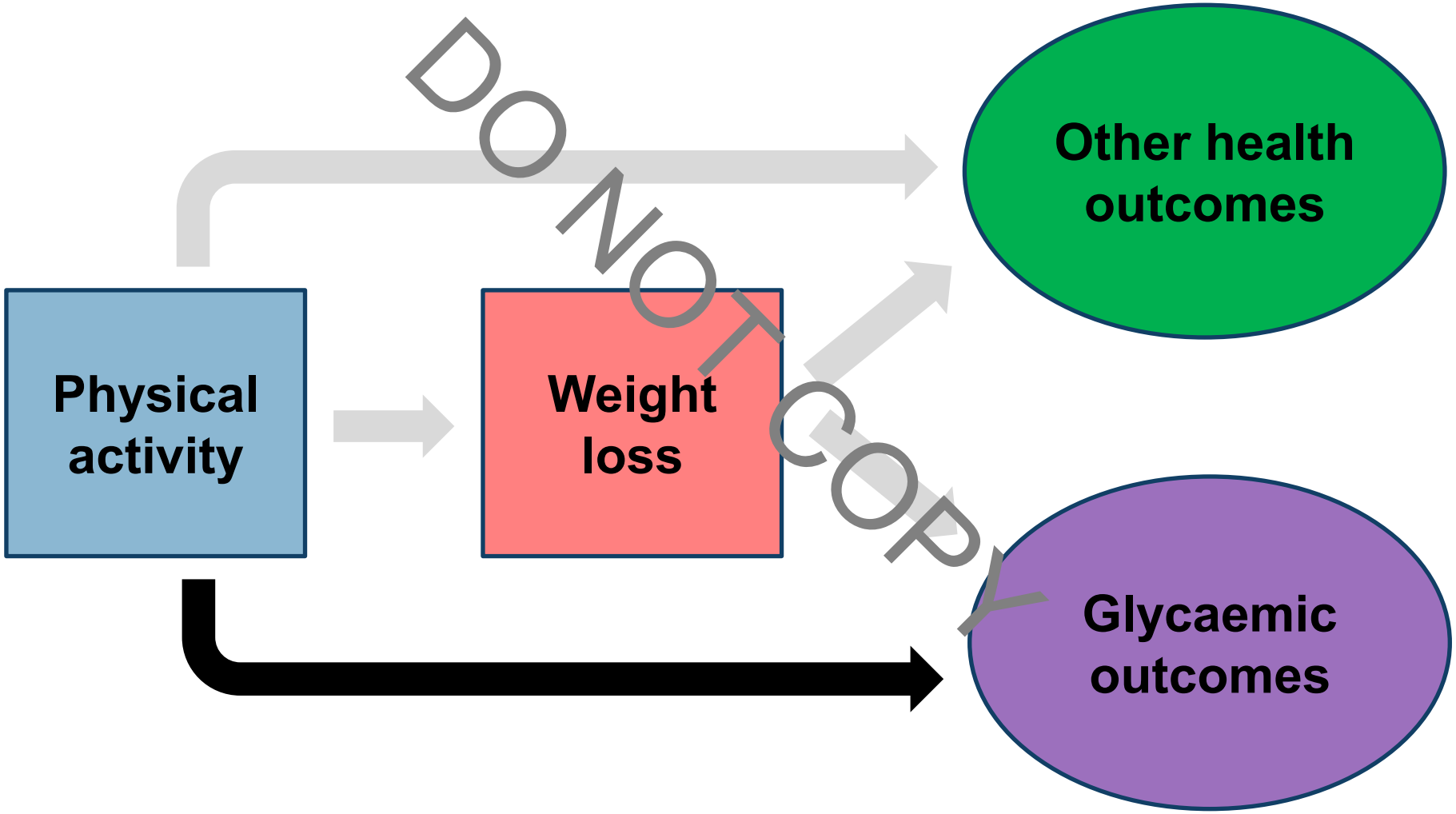
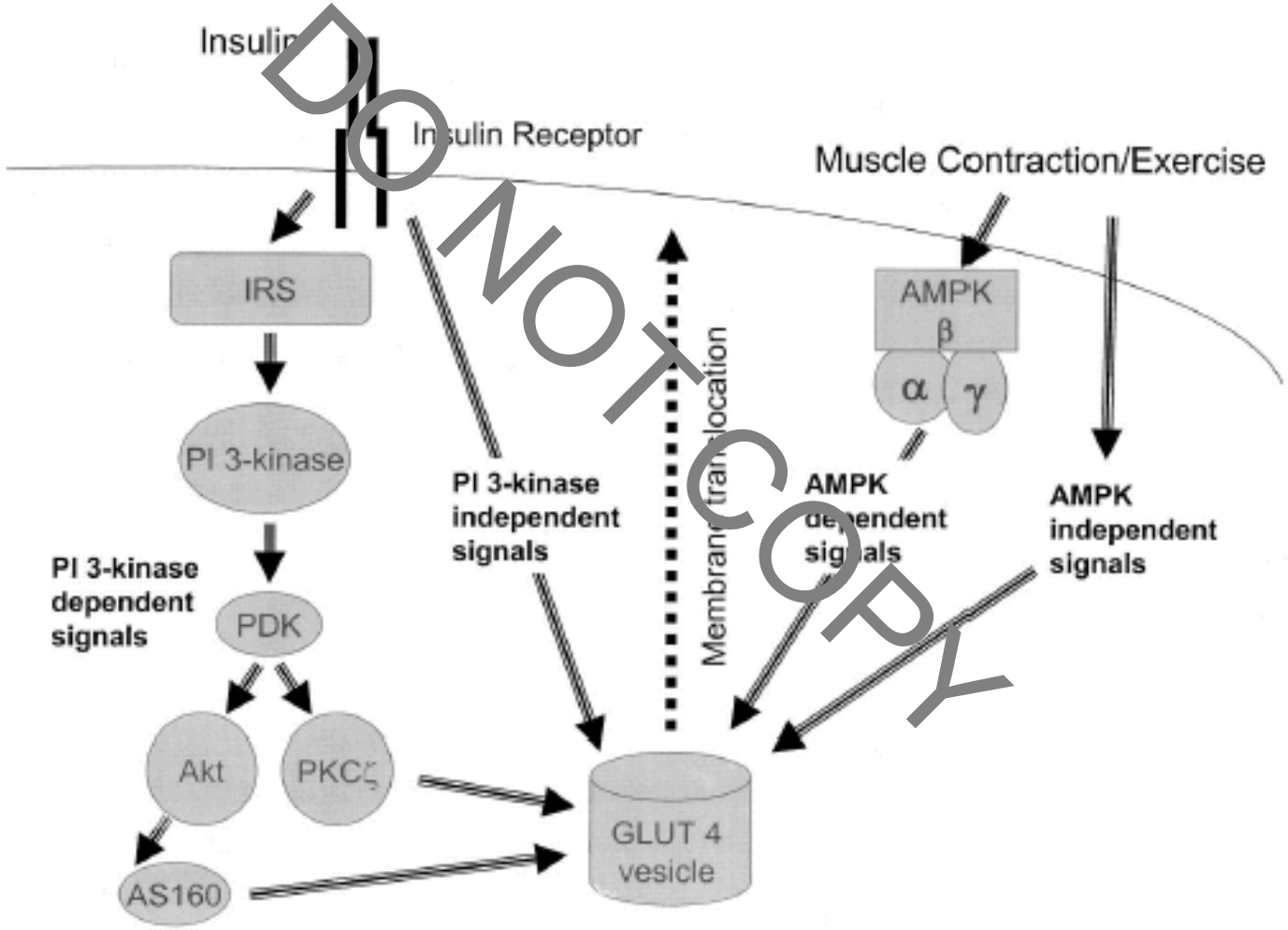
Benefits of being more physically active on body weight are greater in those with high genetic risk of obesity

Key messages
Physical activity and weight loss

- Physical activity intervention alone has modest effects on bodyweight
- Effects of physical activity plus diet on bodyweight are greater than the effects of diet alone
- Even without weight loss, physical activity can substantially reduce body fat, visceral and liver fat – the scales don't tell the full story
- Effects of physical activity on body weight are greater in those with high genetic predisposition to obesity


Other health outcomes
Physical activity
Weight loss
Glycaemic outcomes

Contraction and insulin mediated glucose uptake



Krook et al (2004) Med Sci Sports Exerc 36:1212-17

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Effects of prior exercise on insulin-stimulated glucose uptake across the leg

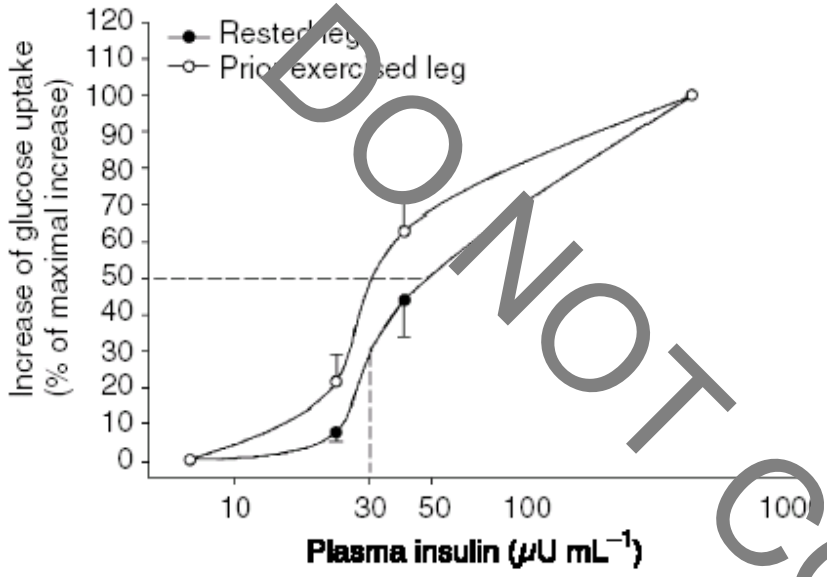
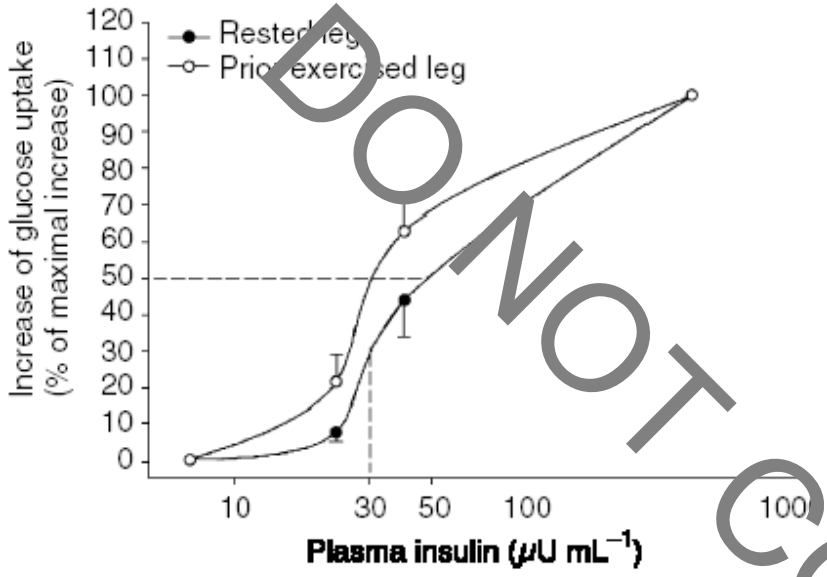


Figure 2 Exercise-improved insulin sensitivity of glucose uptake in human muscle. Prior one-legged exercise enhances sensitivity of glucose uptake to insulin in the exercised compared with the rested leg, in healthy human subjects as indicated by the decreased insulin concentration eliciting a half maximal glucose uptake response, when glucose uptake is given as percentage of maximal increase. The figure is reproduced from Wojtaszewski *et al.* (2002c) with permission. Data are extracted from Richter *et al.* (1989) and represent mean ± SE for $n = 6$.

Data from Richter et al (1989) J Appl Physiol 66:876-885

Effects of prior exercise on insulin-stimulated glucose uptake across the leg



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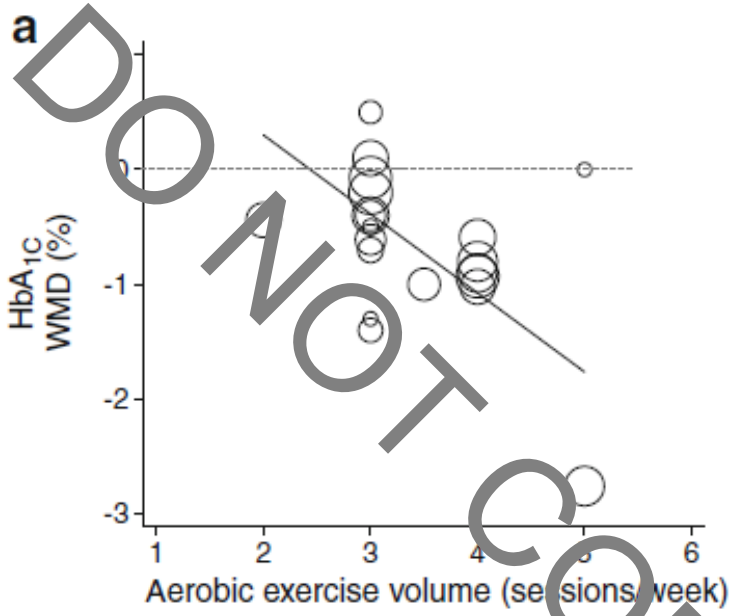
Acute effect:

- Present for ~48-72 hours
- Enhanced by exercise training

Data from Richter et al (1989) J Appl Physiol 66:876-885

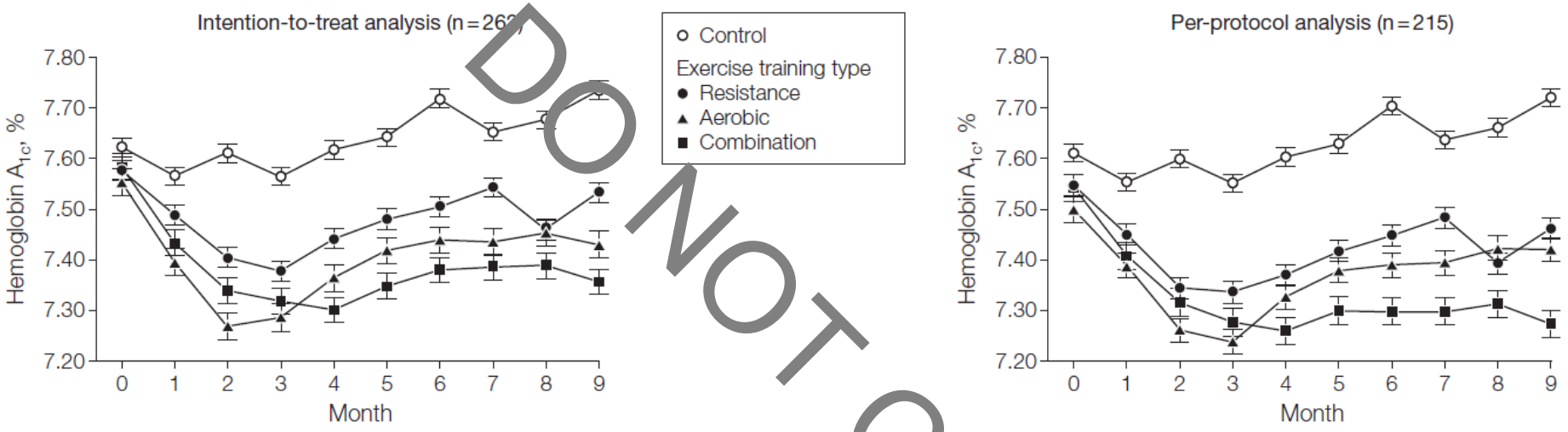
Effects of supervised exercise training on glycaemic control in T2D: a meta-regression



Covariates	Coefficient	95% CI	*p*	Adjusted R^2
Supervised aerobic training[b]				
Intensity (% HR_{max}), $n=13$	−0.003	−0.07, 0.058	0.9	NS
Frequency (sessions/week), $n=20$	−0.69	−1.03, −0.35	<0.001	62.3%
Weekly volume (min/week), $n=20$	−0.007	−0.014, 0.0005	0.07	NS

Umpierre et al (2013) Diabetologia 56:242-251

Aerobic training, resistance training or both on glycaemic control in type 2 diabetes



- Control group (n = 41) – no exercise
- Aerobic training group (n = 72) – 12 kcal/kg/week aerobic exercise over 3 sessions/week
- Resistance training group (n = 73) – 2-3 sets of 9 resistance exercises 3 x per week
- Combined training group (n = 76) – 12 kcal/kg/week aerobic exercise over 3 sessions/week PLUS 1 set of 9 resistance exercises in each session

SIMILAR EXERCISE TIME FOR THE 3 INTERVENTION GROUPS (~130-150 MIN/WEEK)

Church et al (2010) JAMA, 304(20):2253-2262

Comparison of different exercise types in patients with T2D: systematic review and network metaanalysis

Nutrition, Metabolism & Cardiovascular Diseases (2021) 31, 1985–1992

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

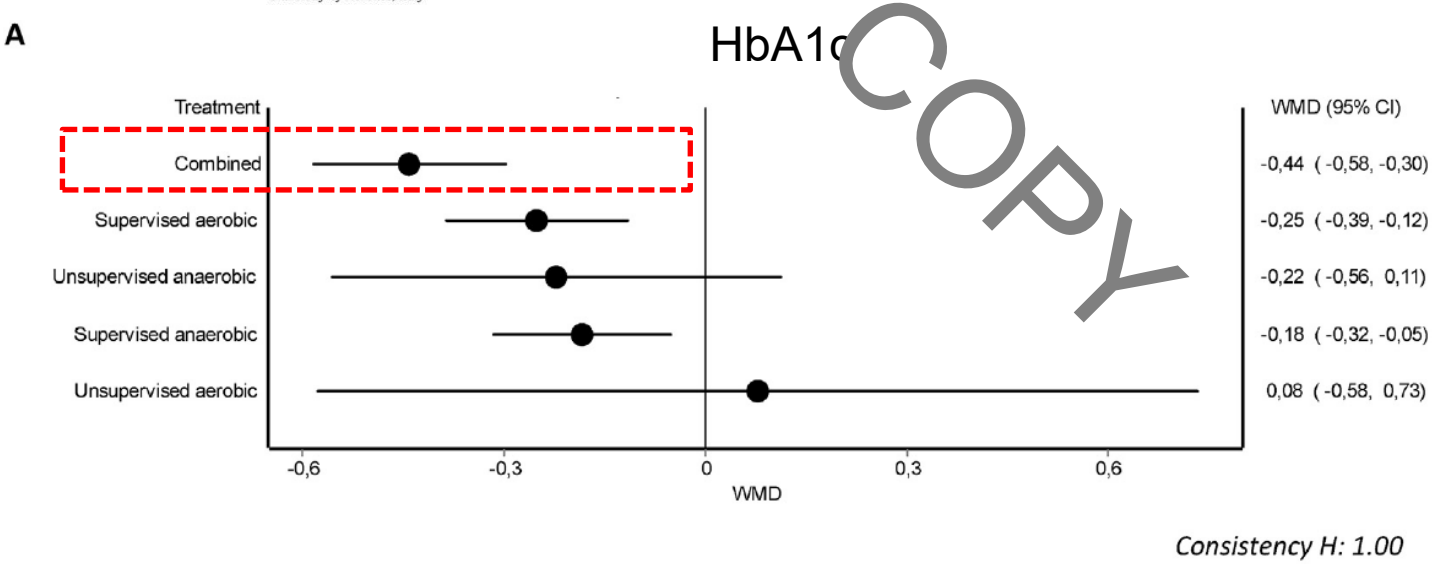
journal homepage: www.elsevier.com/locate/nmcd

SYSTEMATIC REVIEWS AND META-ANALYSIS

Comparison between different types of exercise training in patients with type 2 diabetes mellitus. A systematic review and network metanalysis of randomized controlled trials

Edoardo Mannucci [a,b], Allegra Bonifazi [b], Matteo Monami [a]

[a] Diabetology, Careggi Hospital, Florence, Italy
[b] University of Florence, Italy



Mannucci et al (2021) Nutr Metab Cardiovasc Dis 31:1985-1993

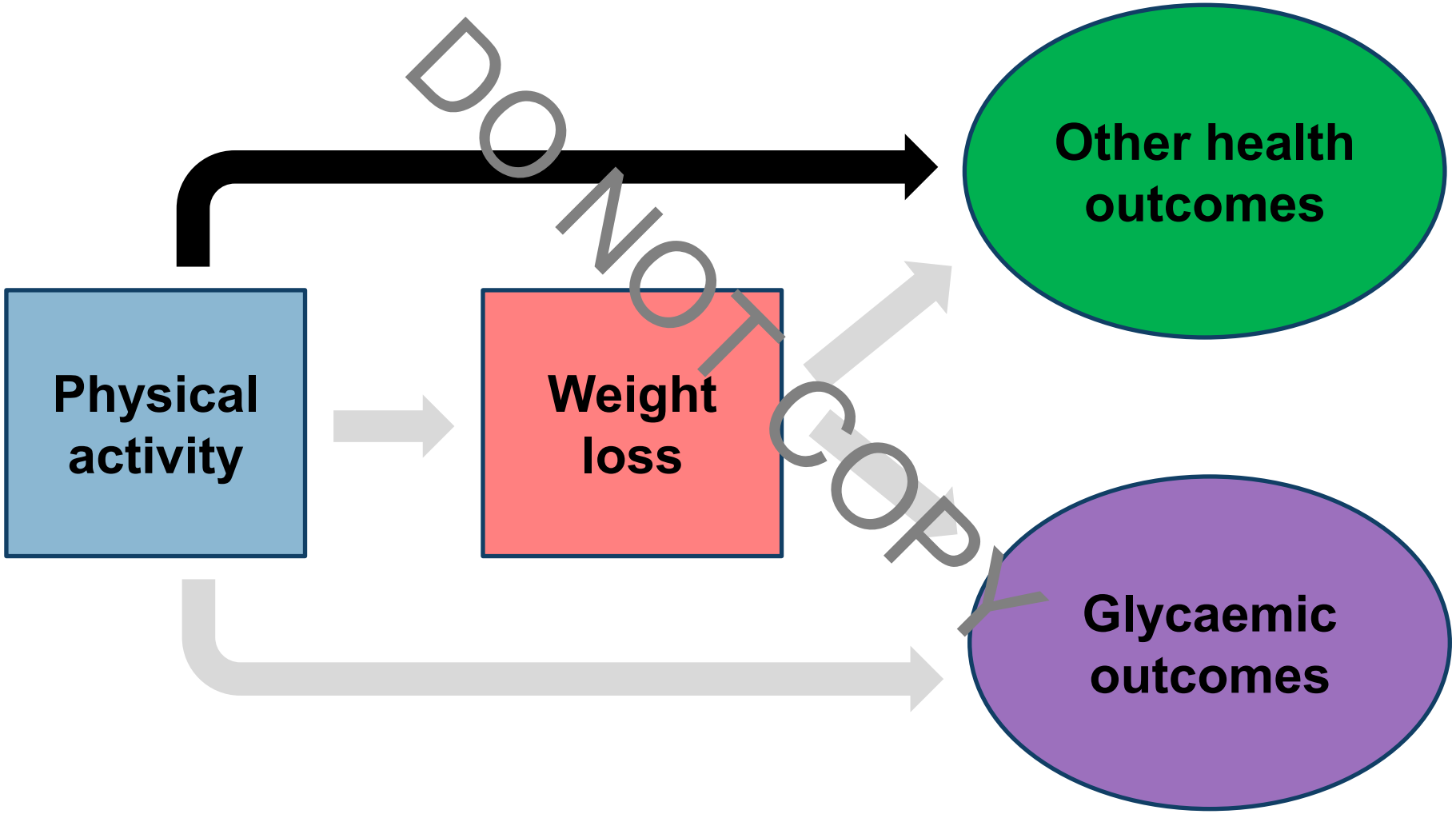
ACSM/ADA recommendations for Physical activity in treatment of type 2 diabetes

- Persons with type 2 diabetes should undertake at least 150 min/week of moderate to vigorous aerobic exercise spread out during at least 3 days during the week, with no more than 2 consecutive days between bouts of aerobic activity.
- In addition to aerobic training, persons with type 2 diabetes should undertake moderate to vigorous resistance training at least 2–3 days/week.
- Supervised and combined aerobic and resistance training may confer additional health benefits, although milder forms of PA (such as yoga) have shown mixed results. Persons with type 2 diabetes are encouraged to increase their total daily unstructured PA. Flexibility training may be included but should not be undertaken in place of other recommended types of PA.

Colberg et al (2010) Diabetes Care, 33:e147-e167

Key messages
Physical activity and glycaemic control

- Exercise acutely improves insulin sensitivity for 48-72 hours
- Frequency of physical activity is more important than intensity or volume for effects on HbA1c in patients with type 2 diabetes
- A combination of aerobic and resistance exercise is more effective for HbA1c reduction in patients type 2 diabetes than either type of exercise alone


Other health outcomes
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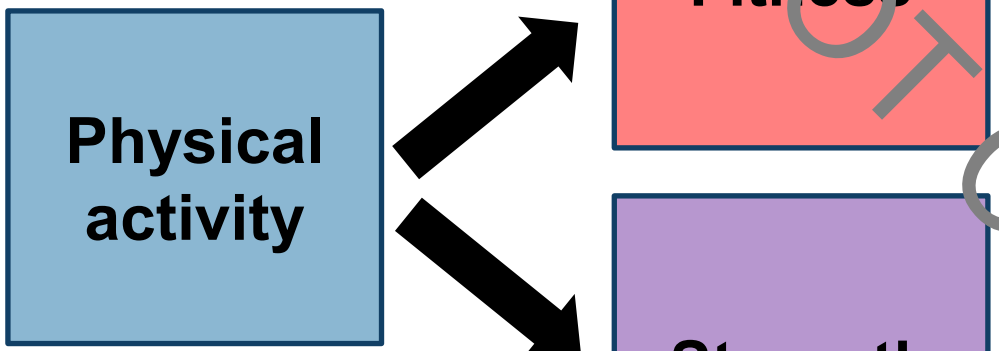
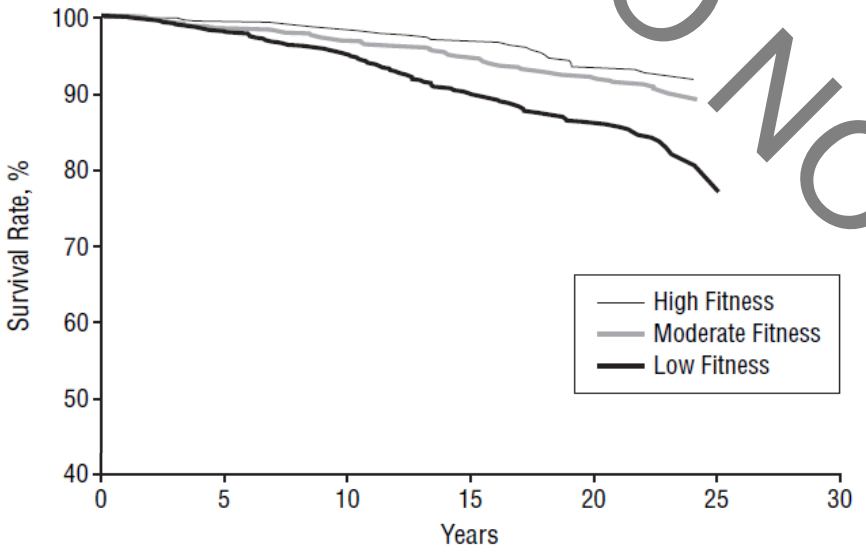
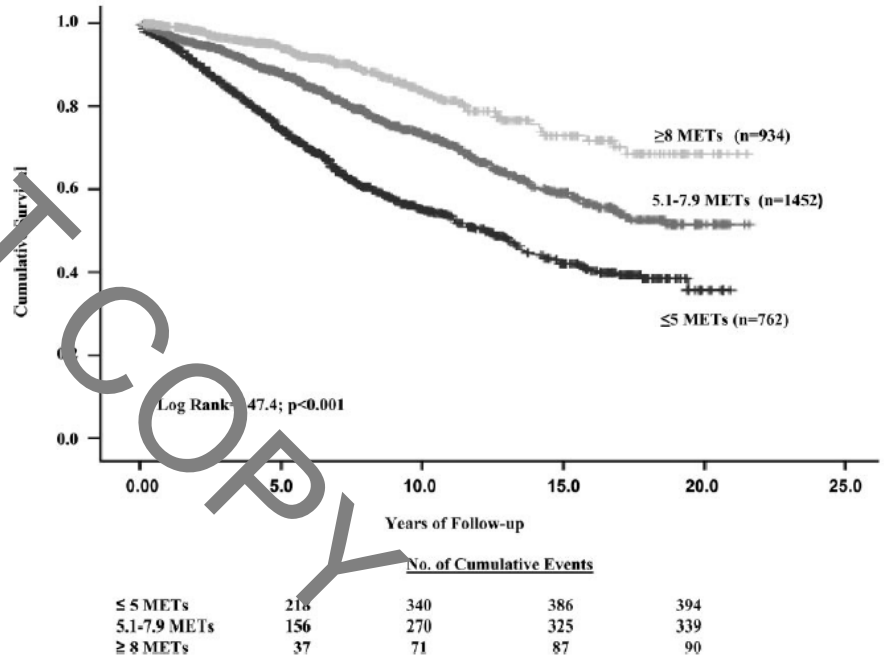


Fitness and risk of CVD mortality in patients with type 2 diabetes

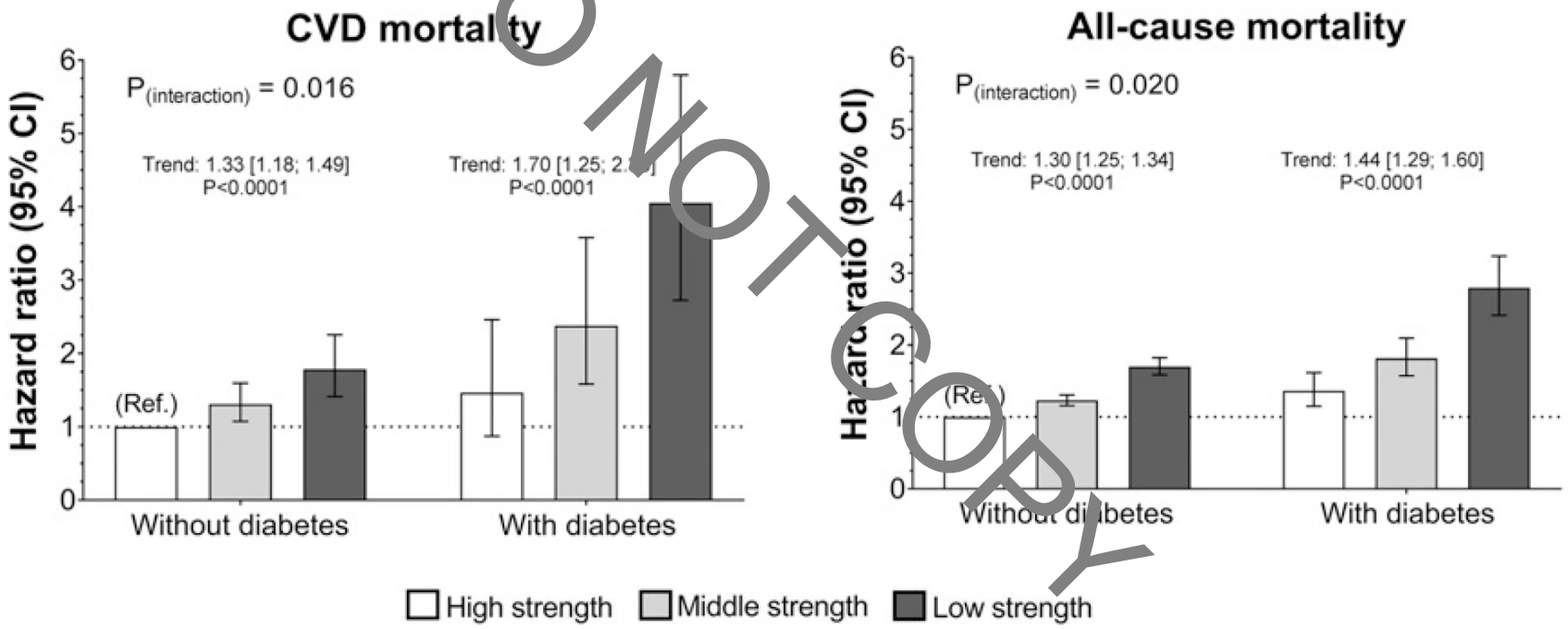




Church et al (2005) Arch Intern Med, 165:2114-2120

Kokkinos et al (2009) Diabetes Care, 32:623-628

Grip strength and risk of CVD and all-cause mortality in people with and without T2D



Celis-Morales et al (2017) Diabetes Care, 40:1710–1718

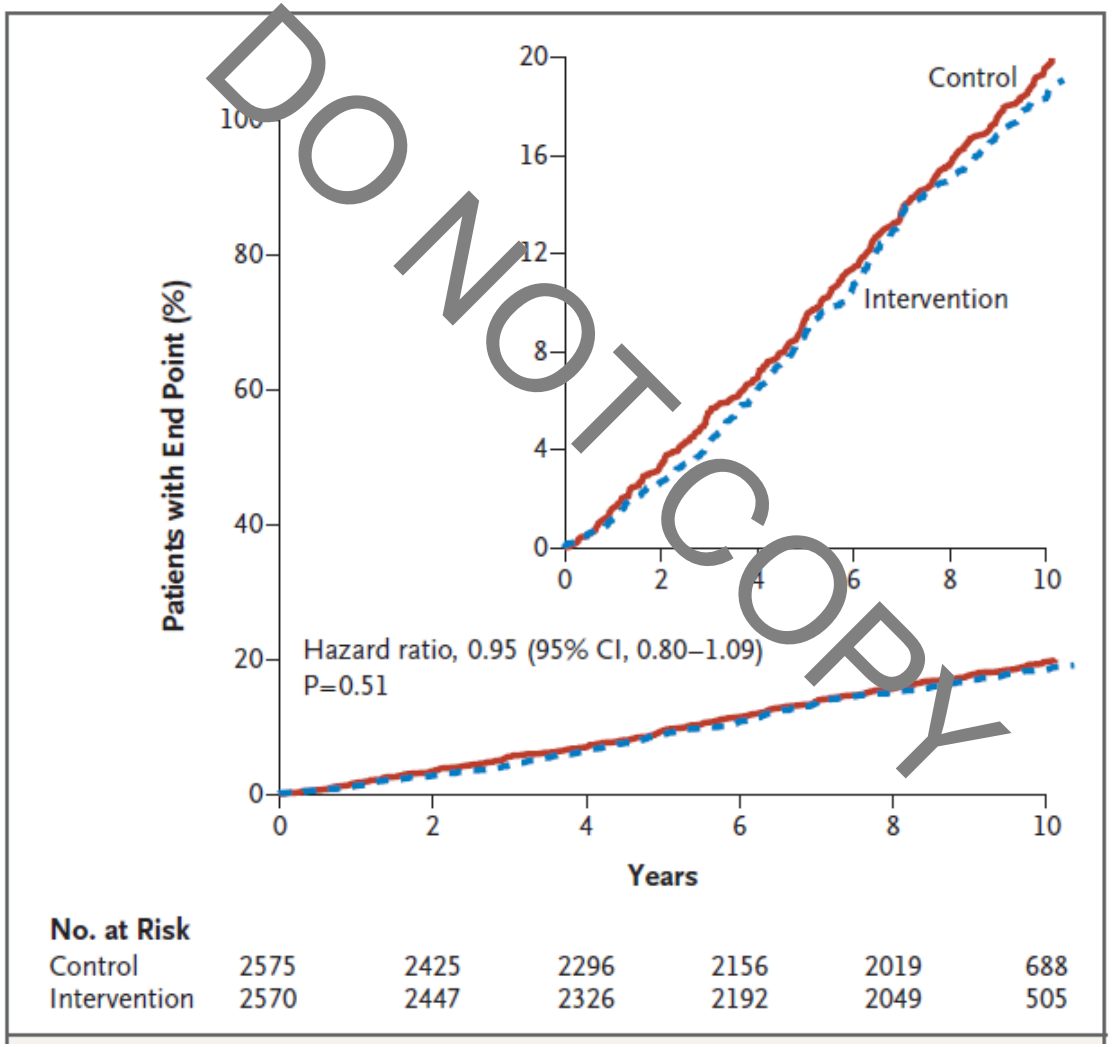
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

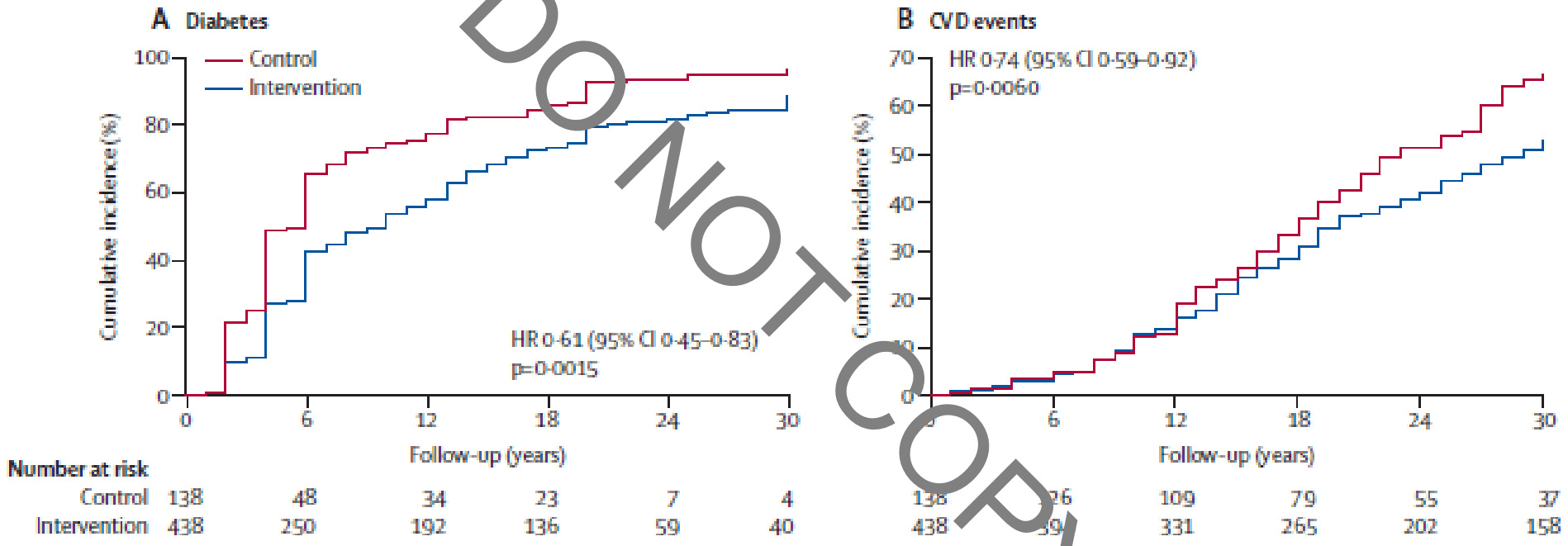
The Look AHEAD Research Group*

Long-term effects of lifestyle intervention on CVD events in type 2 diabetes: the Look AHEAD trial



The Look AHEAD Research Group (2013) NEJM, 369(2):145-54

Morbidity and mortality after lifestyle intervention in people with IGT: The Da Qing Study 30-year follow-up

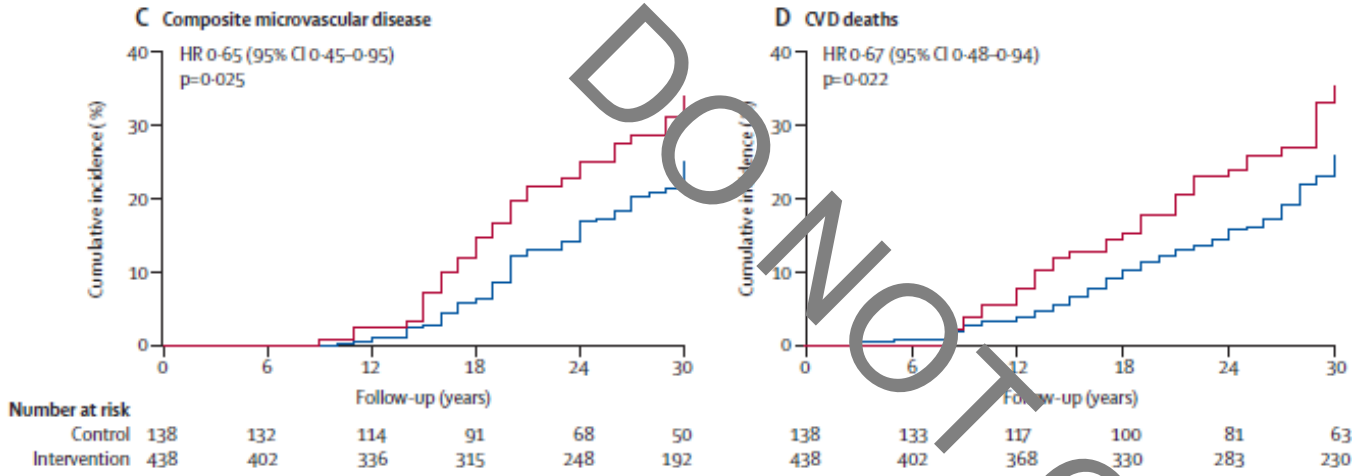


Immediate and sustained effect on diabetes risk

Delayed effect on CVD risk

Gong et al (2019) Lancet Diabetes Endo, 7:452-461

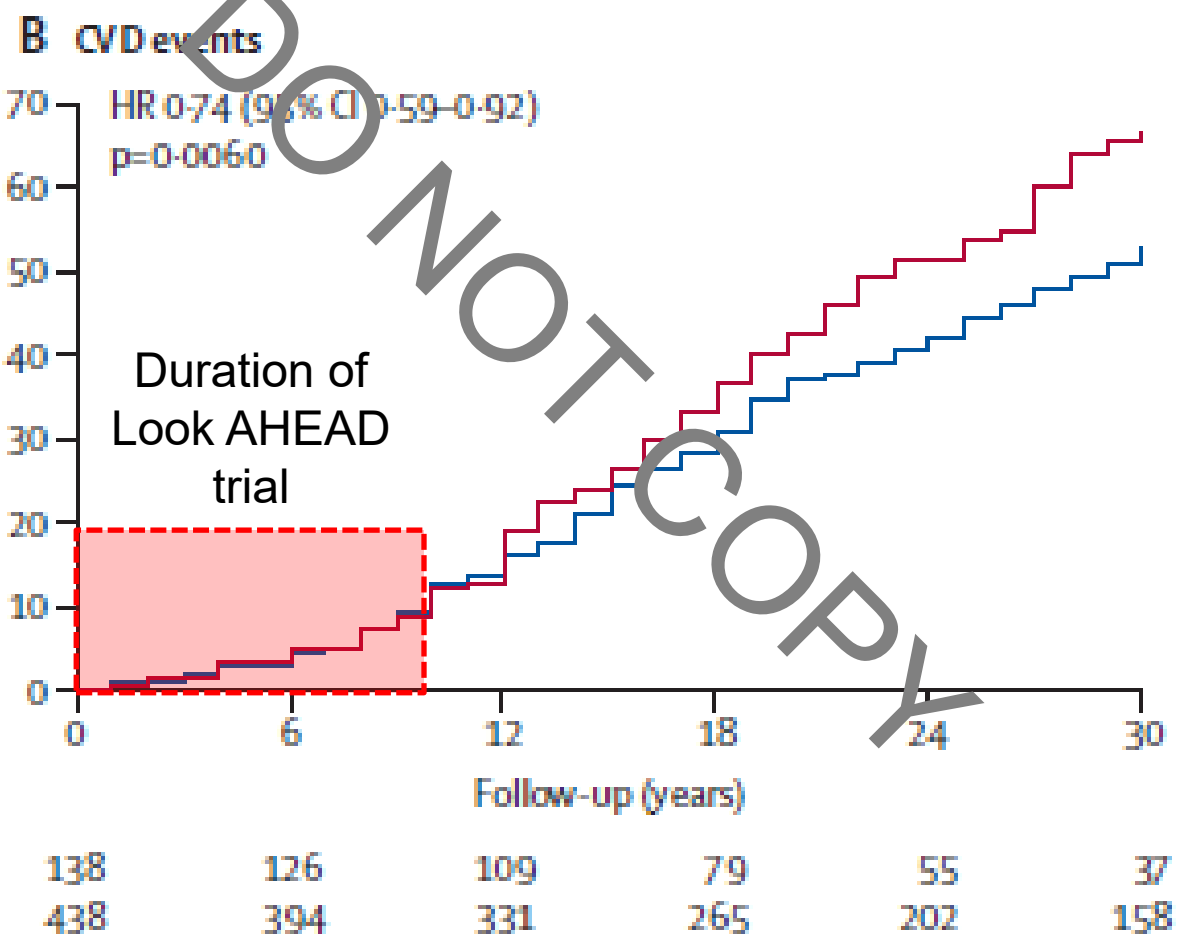
Morbidity and mortality after lifestyle intervention in people with IGT: The Da Qing Study 30-year follow-up



	Median delay, years (95% CI)	Mean number of event-free years (95% CI)	Number needed to treat (95% CI)
Diabetes	3·[illegible] p=0·0047)	4·07 (1·46 to 6·68; p=0·0022)	10 (7 to 23)
CVD events	4·64 (1·05 to 8·22; p=0·011)	1·77 (0·18 to 3·36; p=0·029)	9 (5 to 36)
Composite microvascular disease outcome	5·17 (–0·56 to 10·90; p=0·077)	0·96 (–0·12 to 2·03; p=0·080)	10 (5 to 193)
CVD deaths	7·25 (–0·18 to 14·67; p=0·056)	1·06 (0·10 to 2·23; p=0·074)	10 (5 to 72)
All-cause mortality	4·82 (1·48 to 8·15; p=0·0047)	1·44 (0·20 to 2·68; p=0·023)*	10 (6 to 25)

Gong et al (2019) Lancet Diabetes Endo, 7:452-461

Morbidity and mortality after lifestyle intervention in people with IGT: The Da Qing Study 30-year follow-up



Gong et al (2019) Lancet Diabetes Endo, 7:452-461

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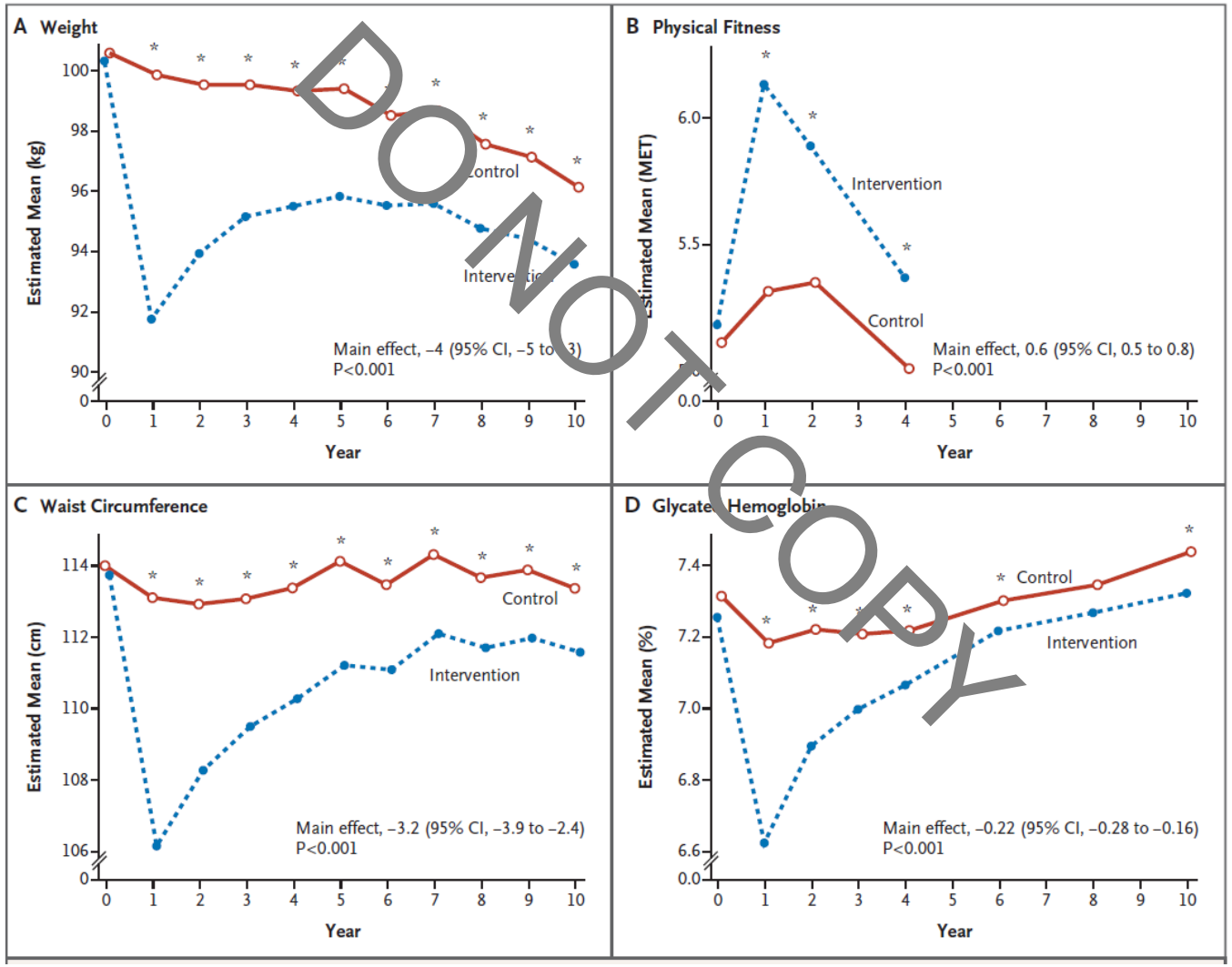
Long-term effects of lifestyle intervention on weight & CVD risk in type 2 diabetes: the Look AHEAD trial



The Look AHEAD Research Group (2013) NEJM, 369(2):145-54

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Magnitude of change weight loss and change in fitness and CVD outcomes in the Look AHEAD trial

	Weight-change categories (percentage weight loss in first year; n=4834)					Fitness-change categories (change in metabolic equivalents in first year; n=4406)				
	Gain or stable (<2% loss)	Small loss (≥2–<5%)	Medium loss (≥5–<10%)	Large loss (≥10%)	p value	Loss or stable (<0·5 loss)	Small gain (≥0·5–<1·0)	Medium gain (≥1·0–<2·0)	Large gain (≥2·0)	p value
Primary outcome										
Events per person-years	289/17 075	141/7870	154/857	128/8942	..	347/19 997	95/6091	102/7183	72/5312	..
Crude rate per 100 person-years	1·69	1·79	1·80	1·43	..	1·74	1·56	1·42	1·36	..
Unadjusted hazard ratio (95% CI)	1·00	1·07 (0·88–1·31)	1·07 (0·88–1·31)	0·83 (0·67–1·02)	0·21	1·00	0·88 (0·70–1·10)	0·80 (0·64–1·00)	0·76 (0·59–0·98), p=0·032*	0·009
Adjusted hazard ratio†(95% CI)	1·00	1·08 (0·88–1·33)	1·16 (0·95–1·42)	0·79 (0·64–0·98), p=0·034*	0·17	1·00	0·87 (0·68–1·10)	0·83 (0·66–1·05)	0·78 (0·60–1·03), p=0·079*	0·03
Secondary outcome										
Events per person-years	422/16 699	206/7657	203/8411	186/8792	..	504/19 596	131/5996	145/7056	100/5220	..
Crude rate per 100 person-years	2·53	2·69	2·41	2·12	..	2·57	2·18	2·05	1·92	..
Unadjusted hazard ratio (95% CI)	1·00	1·08 (0·91–1·27)	0·96 (0·81–1·13)	0·83 (0·70–0·99), p=0·035*	0·04	1·00	0·83 (0·69–1·01)	0·79 (0·65–0·95), p=0·012*	0·73 (0·59–0·91), p=0·005*	0·0005
Adjusted hazard ratio† (95% CI)	1·00	1·05 (0·88–1·25)	0·97 (0·82–1·16)	0·76 (0·63–0·91), p=0·003*	0·006	1·00	0·84 (0·69–1·02)	0·79 (0·65–0·96), p=0·019*	0·77 (0·61–0·96), p=0·023*	0·0031

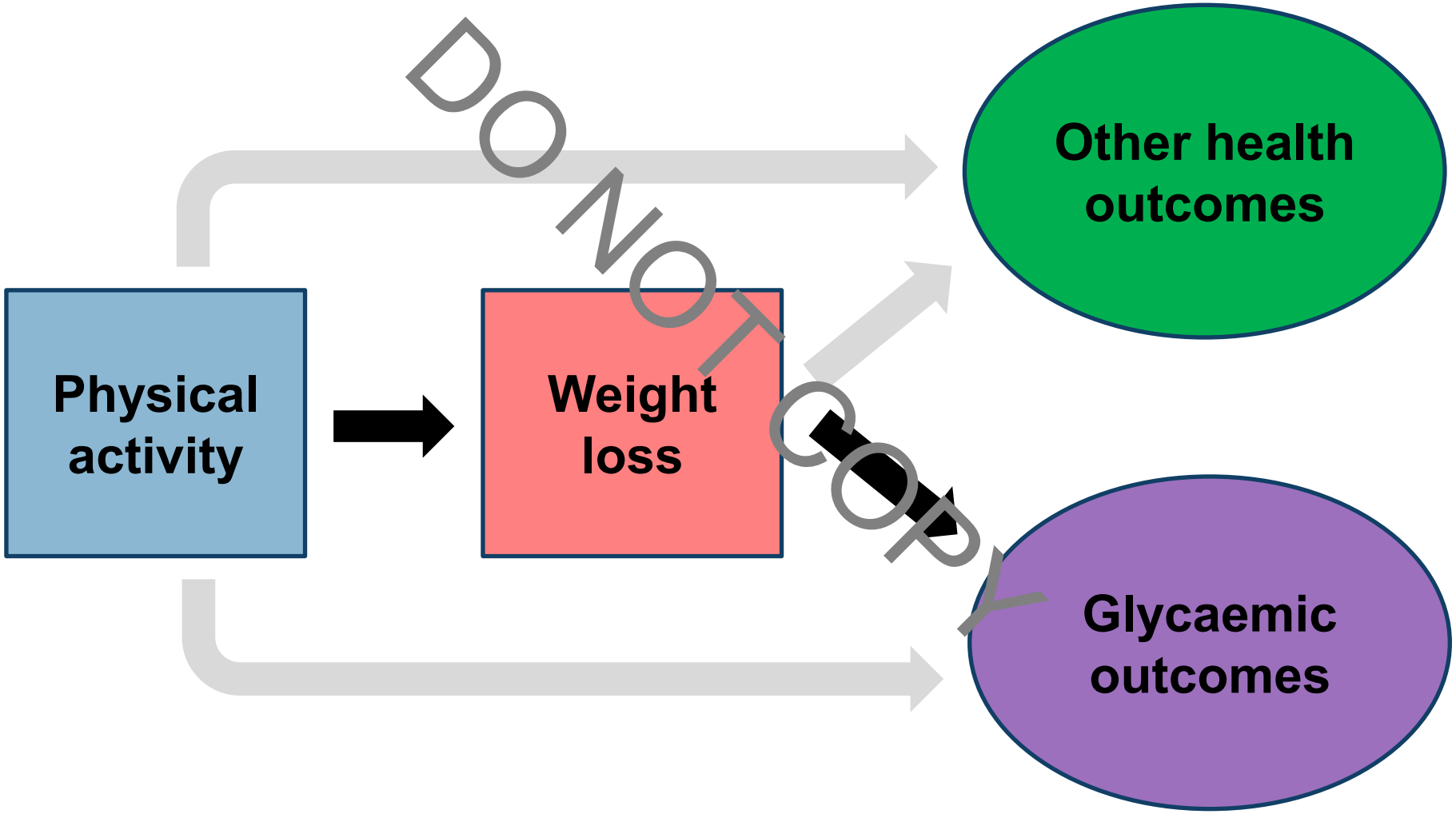
Data are for the overall study population (intensive lifestyle intervention and diabetes support and education [control] groups combined). *p value refers to pairwise comparison with referent group (gain or stable weight loss in weight-change analyses and loss or stable fitness gain in fitness change analyses). †Adjusted for sex, age, baseline weight (from weight-change models), baseline fitness (from fitness-change models), history of cardiovascular disease, insulin use, diabetes duration, smoking status, LDL cholesterol, systolic blood pressure, and diastolic blood pressure.

Table 2: **Primary and secondary outcomes associated with changes in weight and fitness (overall study population)**

The Look AHEAD Research Group (2016) Lancet Diabetes Endocrinol 4:913-21

Key messages
Physical activity and other health outcomes

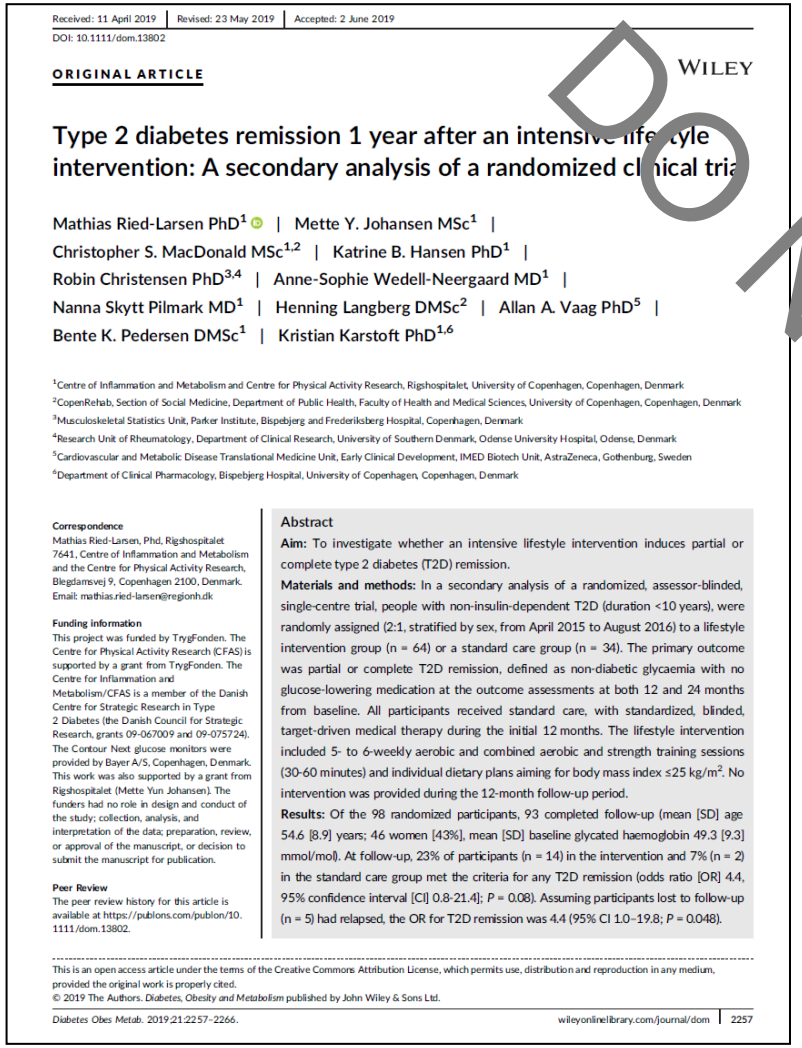
- High cardiorespiratory fitness and high muscular strength are associated with lower risk of mortality in patients with type 2 diabetes
- In Look Ahead, participants who increased cardiorespiratory fitness reduced incidence of adverse CVD outcomes
- We need to develop better interventions to help support people to sustain long-term behaviour change (years to decades)


Physical activity
Weight loss
Other health outcomes
Glycaemic outcomes
DO NOT COPY

University of Glasgow

Can diabetes remission be achieved through lifestyle interventions focused on physical activity?

U-TURN – Secondary analysis for diabetes remission at 12 and 24 months



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ORIGINAL ARTICLE

WILEY

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- 98 T2DM patients with <10 years disease duration, HbA1c ≤ 56 mmol/mol and not on insulin
- Randomised 2:1 into lifestyle intervention (n = 64) or standard care (n = 34).
- All received standardised blinded target-driven medical therapy during first 12 months
- Lifestyle intervention group received:
  - 5-6 sessions/week of aerobic & strength training (30-60 mins/session) for 12 months.
  - Diet plan with energy intake restriction for first 4 months (followed by energy balance diet).
- **No intervention provided after 12 months**

Ried-Larsen et al (2019) Diabetes Obes Metab 21:2257-2266

U-TURN – Secondary analysis for diabetes remission at 12 and 24 months

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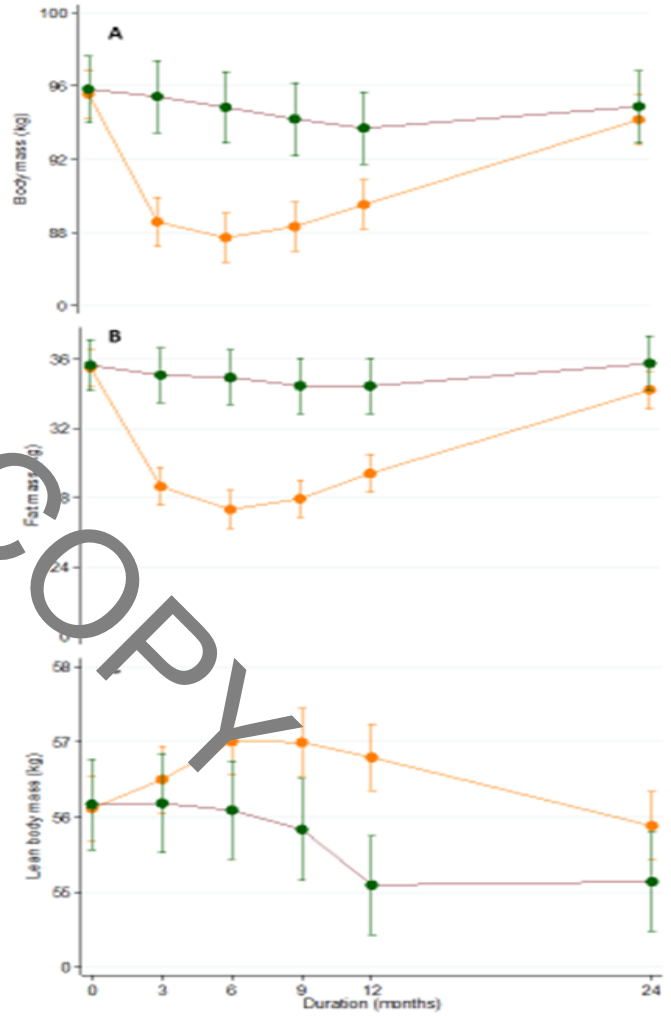
Body mass

Fat mass

Lean mass



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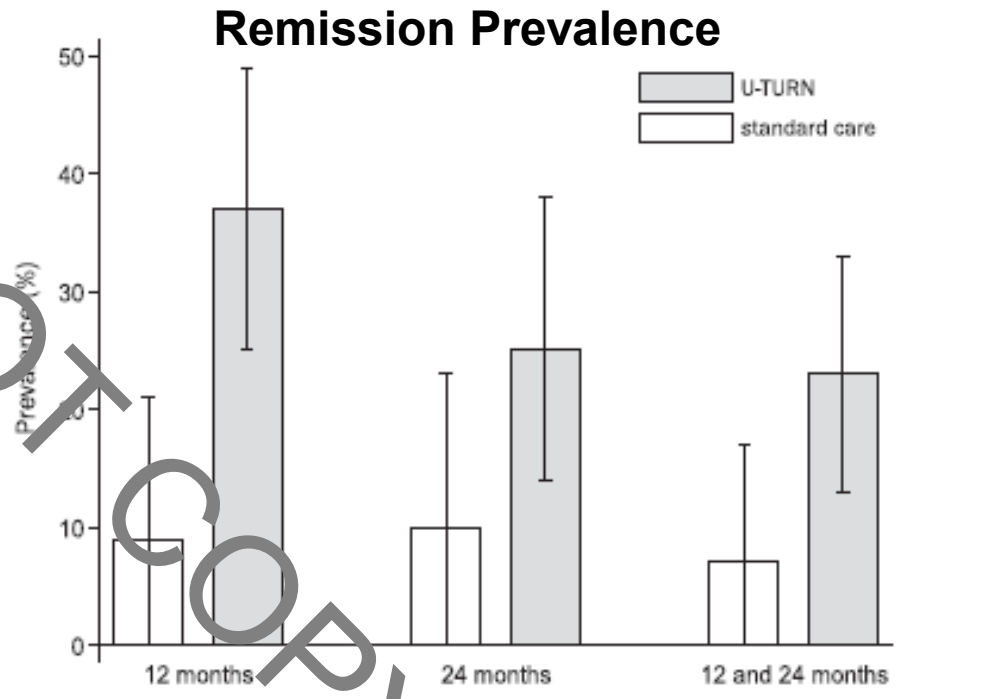

23% of intervention group and **7%** of control group achieved remission* at 12 & 24 months.
Odds Ratio 4.4 (0.8-21.4), p = 0.08.

*HbA1c <48 mmol/mol with no glucose lowering medication

Ried-Larsen et al (2019) Diabetes Obes Metab 21:2257-2266

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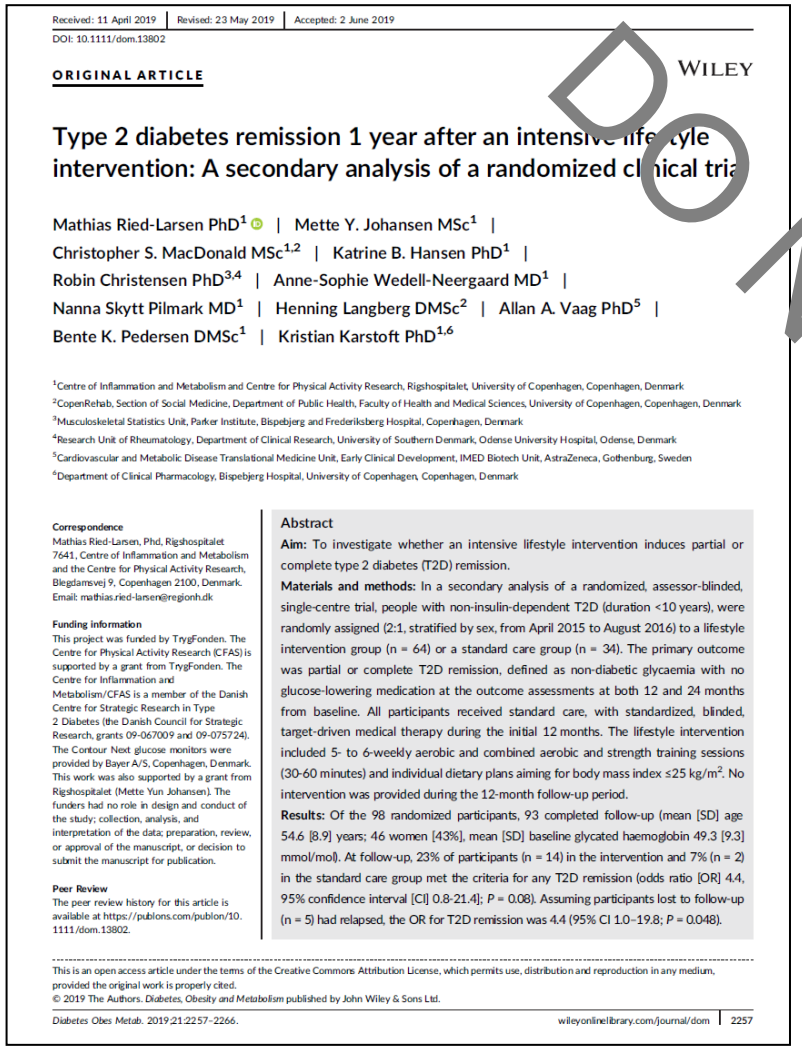
U-TURN



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Remission associated with:

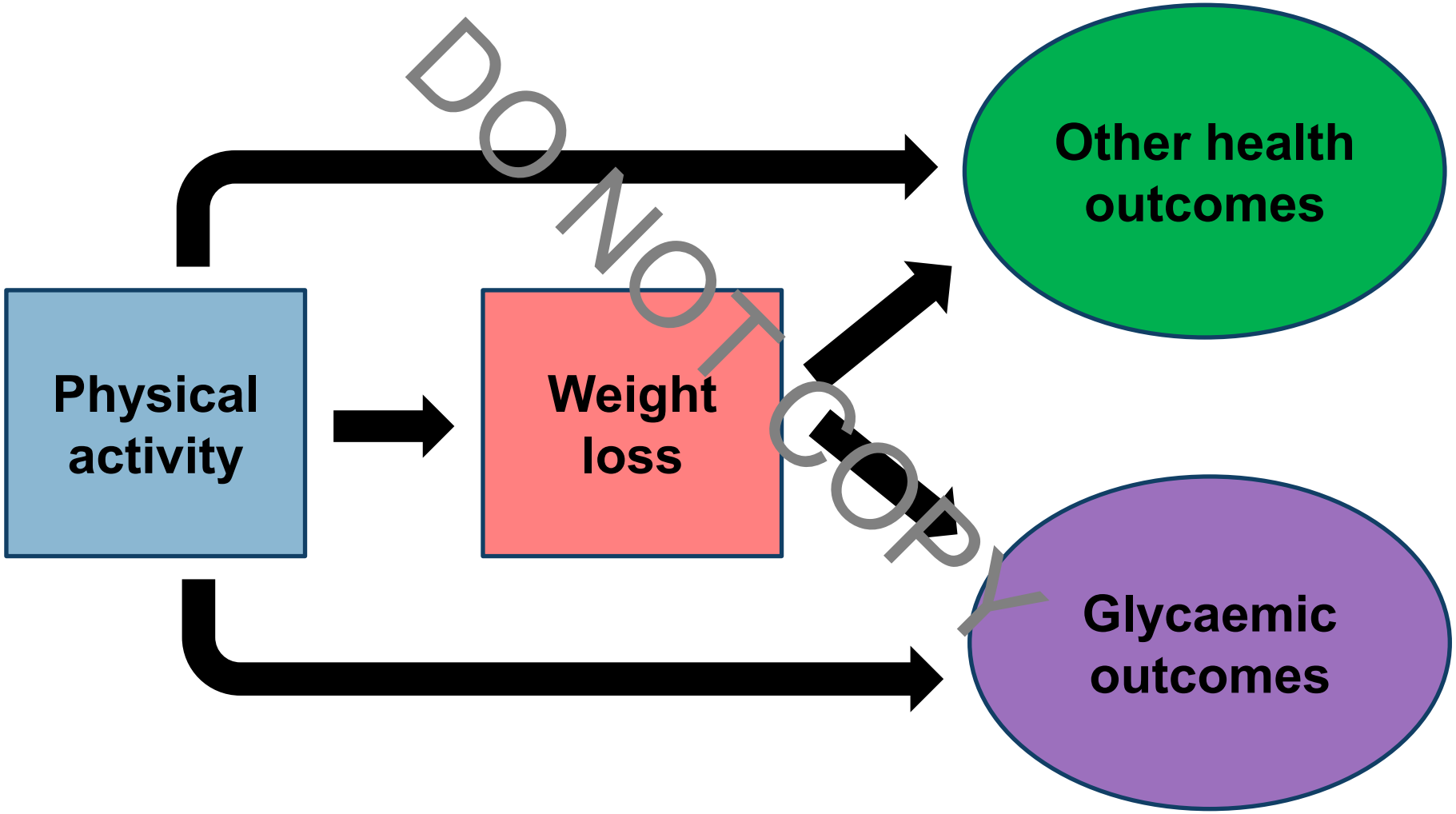
- Greater reduction in fat mass
- Greater reduction in abdominal fat mass
- Achieving 10% body weight reduction
- Greater increases in cardiorespiratory fitness

Ried-Larsen et al (2019) Diabetes Obes Metab 21:2257-2266

Key messages
Physical activity, weight and glycaemic control

- With an intense enough exercise-focused intervention, substantial weight loss is possible, leading to diabetes remission in some

- This approach may be appealing to some (probably a minority) of patients with type 2 diabetes


Other health outcomes
Physical activity
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Glycaemic outcomes

Device-measured VILPA and risk of mortality

nature medicine

Article

Association of wearable device-measured vigorous intermittent lifestyle physical activity with mortality

Received: 3 March 2022

Accepted: 21 October 2022

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Check for updates

Emmanuel Stamatakis[1], Matthew N. Ahmadi[1], Jason M. R. Gill[2], Cecilie Thøgersen-Ntoumani[3], Martin J. Gibala[4], Aiden Doherty[5] & Mark Hamer[6]

Wearable devices can capture unexplored movement patterns such as brief bursts of vigorous intermittent lifestyle physical activity (VILPA) that is embedded into everyday life, rather than being done as leisure time exercise. Here, we examined the association of VILPA with all-cause, cardiovascular disease (CVD) and cancer mortality in 25,241 nonexercisers (mean age 61.8 years, 14,178 women/11,063 men) in the UK Biobank. Over an average follow-up of 6.9 years, during which 852 deaths occurred, VILPA was inversely associated with all three of these outcomes in a near-linear fashion. Compared with participants who engaged in no VILPA, participants who engaged in VILPA at the sample median VILPA frequency of 3 length-standardized bouts per day (lasting 1 or 2 min each) showed a 38%–40% reduction in all-cause and cancer mortality risk and a 48%–49% reduction in CVD mortality risk. Moreover, the sample median VILPA duration of 4.4 min per day was associated with a 26%–30% reduction in all-cause and cancer mortality risk and a 32%–34% reduction in CVD mortality risk. We obtained similar results when repeating the above analyses for vigorous physical activity (VPA) in 62,344 UK Biobank participants who exercised (1,552 deaths, 35,290 women/27,054 men). These results indicate that small amounts of vigorous nonexercise physical activity are associated with substantially lower mortality. VILPA in nonexercisers appears to elicit similar effects to VPA in exercisers, suggesting that VILPA may be a suitable physical activity target, especially in people not able or willing to exercise.

Physical activity is associated with reduced mortality risk[1], and reduced risk of CVD[1] and certain cancers[2–4]. Recently updated guidelines[4,5], based mostly on questionnaire-derived evidence, recommend 150–300 min of moderate-intensity activity or 75–150 min of vigorous-intensity physical activity (≥6 metabolic equivalents) per week. New emphasis is placed on 'all activity counts' occurring across all life domains and regardless of bout duration. This recommendation contrasts with previous guidelines[4,7] that did not recognize the health value of physical activity bouts

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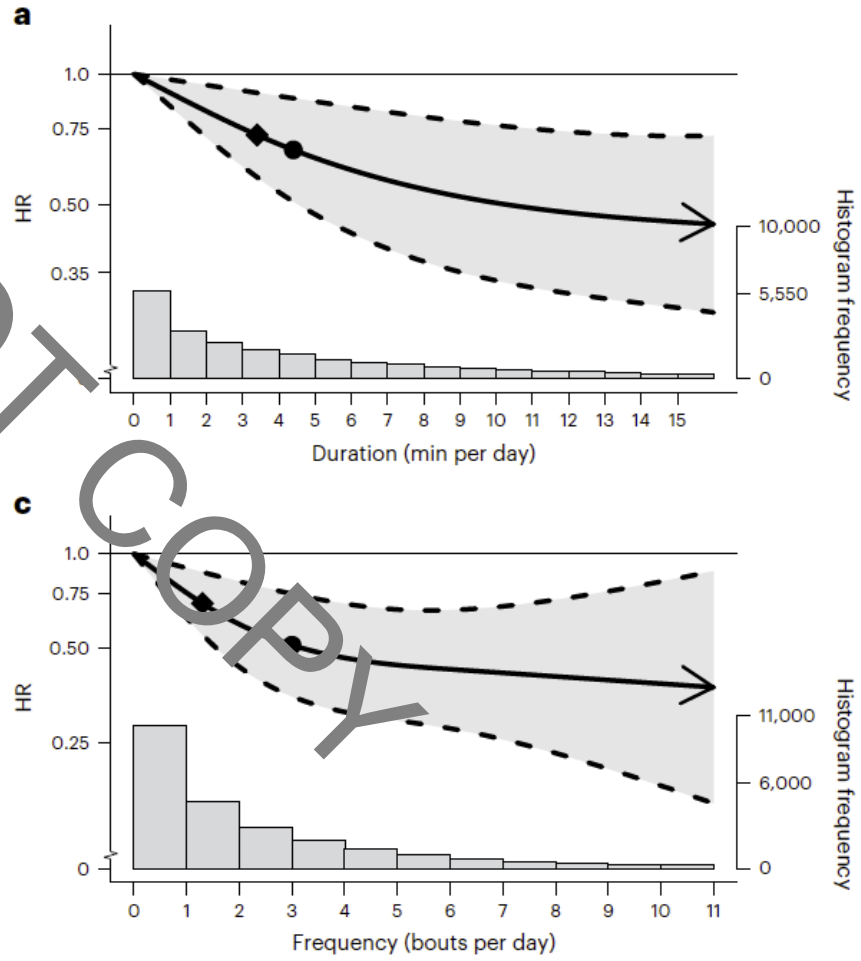

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University of Glasgow

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