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Extremely short duration interval exercise improves 24-h glycaemia in men with type 2 diabetes

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Abstract

Purpose: Reduced-exertion high-intensity interval training (REHIT) is a genuinely time-efficient exercise intervention that improves aerobic capacity and blood pressure in men with type 2 diabetes. However, the acute effects of REHIT on 24-h glycaemia have not been examined.

Methods: Eleven men with type 2 diabetes (mean \pm SD: age, 52 \pm 6 years; BMI, 29.7 \pm 3.1 kg/m²; HbA_{1c}, 7.0 \pm 0.8 %) participated in a randomised, four-trial crossover study, with continual interstitial glucose measurements captured during a 24 h dietary standardized period following either: (1) no exercise (CON); (2) 30 min of continuous exercise (MICT); (3) 10 x 1 min at \sim 90 HR_{max} (HIIT; time commitment, \sim 25 min); and (4) 2 x 20 s ‘all-out’ sprints (REHIT; time commitment, 10 min).

Results: Compared to CON, mean 24-h glucose was lower following REHIT (mean \pm 95%CI: -0.58 \pm 0.41 mmol/L, $p=0.008$, $d=0.55$) and tended to be lower with MICT (-0.37 \pm 0.41 mmol/L, $p=0.08$, $d=0.35$), but was not significantly altered following HIIT (-0.37 \pm 0.59 mmol/L, $p=0.31$, $d=0.35$). This seemed to be largely driven by a lower glycaemic response (area under the curve) to dinner following both REHIT and MICT (-11%, $p<0.05$ and $d>0.9$ for both) but not HIIT (-4%, $p=0.22$, $d=0.38$). Time in hyperglycaemia appeared to be reduced with all three exercise conditions compared with CON (REHIT: -112 \pm 63 min, $p=0.002$, $d=0.50$; MICT: -115 \pm 127 min, $p=0.08$, $d=0.50$; HIIT -125 \pm 122 min, $p=0.04$, $d=0.54$), whilst indices of glycaemic variability were not significantly altered.

Conclusion: REHIT may offer a genuinely time-efficient exercise option for improving 24-h glycaemia in men with type 2 diabetes and warrants further study.

Key Words:

Exercise; High-Intensity Interval Training; Postprandial Glucose; Continuous Glucose Monitoring; Type 2 diabetes

Abbreviations:

ADA, American Diabetes Association; AUC, area under the curve; iAUC, incremental area under the curve; BMI, body mass index; CGM, continuous glucose monitoring; CONGA, continuous net overlapping glucose action; HbA_{1c}, glycated hemoglobin; HIIT, high-intensity interval training; HR, heart rate; HRmax, maximal heart rate; MAGE, mean amplitude of glucose excursions; MICT, moderate intensity continuous training; PA, physical activity; PAL, physical activity level; REHIT, reduced-exertion high-intensity interval training; SIT, sprint interval training; VO₂, oxygen uptake; VO_{2peak}, peak oxygen uptake; Wmax, peak power output.

1 **Introduction**

2 Exaggerated postprandial glycaemic excursions are strongly correlated with type 2 diabetes-
3 related complications, including cardiovascular disease, which is a major cause of morbidity
4 and mortality (Monnier and Colette, 2015). However, studies employing continuous glucose
5 monitoring (CGM) have shown that, despite pharmacological intervention, a large proportion
6 of patients with type 2 diabetes (and even those well controlled according to HbA_{1c}) still spend
7 significant portions of the day in hyperglycaemia (van Dijk et al., 2011). This emphasises the
8 importance of a multi-component treatment approach in type 2 diabetes, incorporating regular
9 exercise, which is an effective strategy for lowering postprandial glucose excursions (Van Dijk
10 et al., 2013) and HbA_{1c} (Church et al., 2010) over and above improvements seen with first line
11 drug therapies. Whilst exercise training induced adaptations may result in an additive and more
12 prolonged improvement in insulin sensitivity (i.e. >72 h post training) (Dela et al., 1995), it is
13 generally accepted that the cumulative impact of regular (i.e. daily) acute exercise on glycaemic
14 control (van Dijk et al., 2012) is of greater clinical importance for the long-term management
15 of glycaemic control in type 2 diabetes (Colberg et al., 2016).

16 The exercise recommendations for individuals with type 2 diabetes are similar as for the
17 general population, suggesting a minimum of 150 minutes of moderate-vigorous intensity
18 aerobic exercise each week (Colberg et al., 2016, Garber et al., 2011). However, self-report
19 data suggest that adherence to these guidelines is poor in the general population (Allender et
20 al., 2008, Hallal et al., 2012) and potentially even lower in those with type 2 diabetes (Morrato
21 et al., 2007). The reasons for poor exercise adherence are numerous and complex, but a
22 perceived lack of time is consistently reported as one of the important barriers in people with
23 type 2 diabetes (Korhonen et al., 2009). In response to this, submaximal high-intensity
24 interval training (HIIT) and supramaximal sprint interval training (SIT) have been proposed as

25 time-efficient alternative exercise options for improving glycaemic control. Acute studies in
26 overweight individuals (Little et al., 2014) and people with type 2 diabetes (Terada et al., 2016)
27 have shown superior improvements in glycaemic control with HIIT compared with 30-60 mins
28 of traditional MICT. Despite the case for a superior clinical benefit, the total time commitment,
29 including recovery intervals, means that most HIIT protocols are not as time-efficient as often
30 claimed. To date, the protocols studied generally require 20-60 min (Terada et al., 2016, Little
31 et al., 2011, Gillen et al., 2012), which is no different (and in some cases, exceeds) current
32 exercise recommendations for MICT (Colberg et al., 2016, Garber et al., 2011). Moreover,
33 there is currently vigorous debate about whether either HIIT or SIT would be appropriate
34 exercise strategies for recommendation to the general population or specific patient
35 populations, based on the hypothesised potential for ‘unpleasant’ perceptual responses (e.g.
36 high perceived exertion and negative affect) to lead to low exercise adherence (Hardcastle et
37 al., 2014). The total time commitment and potential for unpleasant perceptual responses
38 increase as a function of the number and duration of high-intensity efforts (Townsend et al.,
39 2017). Thus, it is important to examine whether HIIT/SIT protocols, with fewer and shorter
40 high-intensity efforts, remain efficacious for improving insulin sensitivity and glycaemic
41 control in type 2 diabetes (Vollaard and Metcalfe, 2017).

42 There is evidence that HIIT/SIT protocols with fewer and/or shorter sprints can improve
43 glucose tolerance in healthy sedentary individuals (Metcalfe et al., 2016, Metcalfe et al., 2012,
44 Gillen et al., 2016). For example, we previously demonstrated that a modified SIT intervention,
45 consisting of 10 min of low-intensity cycling interspersed with two 20 s ‘all-out’ sprints
46 (termed ‘reduced-exertion high-intensity interval training’ [REHIT]), was effective at
47 improving insulin sensitivity in sedentary men over 6 weeks (Metcalfe et al., 2012).
48 Importantly, these benefits were observed despite the low time commitment (10 min per
49 session) and acceptable session ratings of perceived exertion (‘somewhat hard’). Ruffino et al

50 (Ruffino et al., 2017) recently applied REHIT in type 2 diabetes and observed superior
51 improvements in aerobic capacity and similar changes in resting blood pressure compared with
52 a moderate intensity walking intervention over an 8 week training period. REHIT did not
53 improve insulin sensitivity or reduce 24 h mean glucose in this study, however, responses were
54 captured 3 days following training cessation and improvements may have been lost at this time
55 point (Ruffino et al., 2017). Nevertheless, 8 weeks of REHIT did lower plasma fructosamine
56 concentrations (a marker of average blood glucose levels in the preceding 2-4 week period),
57 suggesting improved glycaemic control during the training intervention (Ruffino et al., 2017).
58 Yet, the acute effects of REHIT on post-exercise glycaemic control in people with type 2
59 diabetes have not been explored. Thus, the primary aim of this study was to examine the effect
60 of a single bout of REHIT on 24 h glycaemia in men with type 2 diabetes relative to a no-
61 exercise control trial using continuous glucose monitors. Our primary hypothesis was that
62 REHIT would improve glycaemic control relative to no-exercise. We also studied the effects
63 of a single bout of MICT and a single bout of HIIT compared with no exercise, as both have
64 previously been shown to improve glycaemic control (Gillen et al., 2012, van Dijk et al., 2012).

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72 **Methods**

73 **Ethical approval**

74 This randomised-controlled acute cross-over trial was conducted at Ulster University, Northern
75 Ireland (UK), between October 2016 and August 2017 (ClinicalTrials.gov registration:
76 NCT03082859). The experimental protocol was approved by the Office for Research Ethics in
77 Northern Ireland (RECA ref: 16/NI/0115) and conducted in accordance with the Declaration
78 of Helsinki.

79 **Participants**

80 Eleven ($n=11$) men, diagnosed with type 2 diabetes mellitus by a clinician 4 ± 3 (range 0.5 to
81 8) years previously, completed the full experimental procedures (Fig. 1 and Table 1). Exclusion
82 criteria included exogenous insulin therapy, currently taking more than two glucose-lowering
83 medications, $BMI \geq 40$ kg/m², classification as highly active on the International Physical
84 Activity Questionnaire (IPAQ) (Craig et al., 2003), and any contraindications to exercise,
85 including any history of cardiovascular or cerebrovascular disease, impaired renal or liver
86 function, and hypertension not well controlled by standard medication. All participants were
87 informed about the study, both verbally and in writing, before providing their written consent
88 to participate. Eligible participants completed a twelve-lead exercise stress test on a cycle
89 ergometer (Lode Corival; Lode, Groningen, Netherlands) and received clearance for vigorous
90 intensity exercise from a clinical cardiac physiologist. At baseline, all medication was recorded
91 and participants were instructed to maintain their usual dose/timing/type of medication
92 throughout the study period.

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94 **Pre-experimental procedures**

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96 Following health screening, participants completed a maximal incremental cycling test to
97 volitional exhaustion to determine peak oxygen uptake ($\dot{V}O_{2\text{peak}}$), peak power output (W_{max})
98 and peak heart rate (HR_{max}). Following a 5 min warm up at 50 W, the intensity was increased
99 by 15 W/min until cadence could not be maintained at ≥ 50 rpm (Lode Corival). $\dot{V}O_{2\text{peak}}$ was
100 determined as the highest ten-breath rolling average, $\dot{V}O_2$ measured using an online gas
101 analysis system (Cosmed Quark; CPET, Rome, Italy), and accepted if two or more of the
102 following criteria were met: 1) volitional exhaustion, 2) a plateau in $\dot{V}O_2$ despite increasing
103 intensity, 3) $RER > 1.15$, and 4) maximal heart rate within 10 beats of the age-predicted
104 maximum (i.e. $220 - \text{age}$) (Howley et al., 1995). This was the case for all participants.
105 Participants also completed two familiarisation sessions, on separate days, each lasting
106 approximately 20 min, to introduce participants to the technique and effort required to perform
107 all-out cycling sprints.

108 **Main experimental protocol**

109 Each participant completed four main experimental trials (CON, REHIT, HIIT and MICT) in
110 a randomised order (envelope method), with each trial taking place over 3 days. During each
111 trial, participants underwent 24 h of continuous glucose monitoring under standardised dietary
112 intake and the following experimental conditions: 1) a no-exercise control condition (CON);
113 2) a single bout of high-intensity interval training (HIIT); 3) a single bout of reduced-exertion
114 high-intensity interval training (REHIT); and 4) moderate–vigorous intensity continuous
115 exercise (MICT). Each trial was separated by at least 5 days, and prior to each trial, participants
116 were asked to avoid any structured exercise for 2 days. This was confirmed via physical activity
117 monitoring using synchronised accelerometry and heart rate monitoring with branched model
118 equations (Actiheart, Cambridge Neurotechnology Ltd., Cambridge, UK). The Actiheart is a
119 non-invasive physical activity monitor that is both reliable and valid, can accurately estimate
120 energy expenditure across low, moderate and high intensity physical activities, and provides

121 useful quantitative data on patterns of physical activity, allowing a comprehensive
122 characterisation of physical activity status (Thompson et al., 2006). Participants wore the
123 monitor continuously (day and night) and were instructed to only remove it when showering
124 or bathing. There were no differences in physical activity across the 2 days prior to each
125 experimental trial ($p>0.05$ for all main effects of condition, respectively; Table 2). The
126 Actiheart monitors were also worn throughout each main 24-h monitoring period.

127 Participants attended the lab between 15:00 and 18:00 hours on day 1 for insertion of a
128 subcutaneous glucose sensor (Enlite, Medtronic Inc., Minneapolis, USA) and CGM in the
129 abdomen (iPro2, Medtronic Inc. Minneapolis, USA). Sensors were inserted approximately 5
130 cm from the umbilicus and on the opposite side from which participants tended to sleep on.
131 The iPro2 measures glucose in the interstitial fluid every 5 min and values are subsequently
132 converted to blood glucose using capillary measurements taken by each participant before each
133 main meal and before sleep (Accu-Check; Roche Diagnostics, Basel, Switzerland). It has
134 previously shown good validity and reliability when compared to blood glucose measured
135 simultaneously from an intravenous cannula (Bailey et al., 2014). Participants then returned
136 home but were provided with a standardised evening meal and snack (Table 2).

137 Participants returned to the laboratory the following morning (day 2) between 07:00 and 08:30
138 hours to consume breakfast and complete the exercise session (30 min post breakfast). During
139 CON, participants remained sedentary throughout this entire period (i.e. ~2 h). Participants
140 then returned to their normal daily routine but were provided with standardised meals (lunch,
141 evening meal, snacks, to be consumed at standardised times (Table 2). Participants returned to
142 the laboratory the following morning for removal of the CGM.

143 **Dietary standardisation**

144 Participants were provided with a standardised food and (energy containing) drinks package
145 containing meals, snacks and drinks for each 42 h trial period (~18:00 hours on day 1 to ~12:00
146 hours on day 3; Table 3). The diet was designed to meet resting metabolic rate (determined
147 using the Harris and Benedict equation (Harris and Benedict, 1918)) multiplied by a PA level
148 of 1.4. The macronutrient content was composed according to the 2008 ADA dietary
149 recommendations for type 2 diabetes (Bantle et al., 2008) and consisted of three meals and
150 snacks per full day. The contents of the dietary package was self-selected by participants (in
151 consultation with the principle investigator) from a pre-determined list of foods available from
152 a local supermarket. In this way, individual food preferences and tolerances were taken into
153 account but the investigators were able to ensure appropriate energy and macronutrient content
154 (Bantle et al., 2008). The food and drinks were ingested at pre-determined times for each
155 participant so that a completely standardised diet was consumed during all four experimental
156 trials. In addition to any energy containing drinks provided to participants in food packages,
157 participants were allowed to consume water *ad libitum* throughout each trial.

158 **Exercise bouts**

159 **REHIT** The REHIT bout was performed on a mechanically braked cycle ergometer (Monark
160 Peak Bike; Monark, Vansbro, Sweden) and was based on the protocol used in previous studies
161 (Metcalf et al., 2012, Metcalf et al., 2016, Ruffino et al., 2017, Metcalf et al., 2015). It
162 consisted of 10 min of unloaded pedalling interspersed with two ‘all-out’ sprints against a
163 resistance equivalent to 5% of body mass. Just before each sprint, participants increased their
164 pedal cadence to their maximal speed, the braking force was applied to the ergometer and
165 participants maintained the highest possible cadence against the resistance for 20 s. Sprints
166 were performed at 2 min 40 s and 6 min 40 s into the 10 min exercise session.

167 **HIIT** The HIIT bout was performed on an electronically braked cycle ergometer (Lode
168 Corival; Lode, Groningen, Netherlands) and involved 10 × 60 s cycling efforts interspersed

169 with 60 s of low intensity recovery (25 W) as previously described (Little et al., 2011, Gillen
170 et al., 2012). Individual workloads were set at 85% W_{\max} , as pilot work has suggested this was
171 appropriate for achieving ~90% maximal heart rate (HR_{\max}) during the final intervals.

172 **MICT** MICT was performed on an electronically braked cycle ergometer (Lode Corival; Lode,
173 Groningen, Netherlands) and involved 30 min of continuous cycling at an intensity equivalent
174 to 50% of W_{\max} with a 2-min warm up and cool down (25 W) as previously described (van
175 Dijk et al., 2012).

176 **Calculations**

177 The 24 h period of interest for continuous glucose measurements commenced at the start of the
178 breakfast period on day 2. The continuous glucose data were exported to Excel (Microsoft,
179 Washington, USA), the relevant 288, 5-min replicate values were isolated, and subsequently
180 converted in summary variables including mean 24 h glucose (primary outcome), and
181 secondary outcomes including glycaemic variability, proportion of time in hyperglycaemia, 24
182 h incremental (above fasting; calculated from the mean glucose 30-min prior to breakfast) AUC
183 (iAUC), and the total AUC for 3 h breakfast, lunch and dinner responses. AUC was calculated
184 using the trapezoid rule. The 3-h postprandial glucose (3-h PPG) was defined as mean glucose
185 150-180 mins following each main meal. The glycaemic range, the mean amplitude of
186 glycaemic excursions (MAGE) and the continuous overall net glycaemic action (CONGA)
187 were calculated as measures of glycaemic variability (Rodbard, 2009) using a freely available
188 Excel Macro (Easy GV 9.0; available at www.easygv.co.uk). The hyperglycaemic threshold
189 was defined as ≥ 9 mmol/l based on the published International Diabetes Federation criteria
190 (International Diabetes Federation, 2014).

191 For the analysis of the Actihearts, minute by minute energy expenditure was calculated using
192 the manufacturers software (Actiheart, Cambridge Neurotechnology Ltd., Cambridge, UK) and

193 subsequently exported to Microsoft Excel for determination of physical activity summary
194 variables including total 24-hour energy expenditure (TEE), physical activity level (PAL; total
195 energy expenditure / resting energy expenditure), sedentary time (mins <1.5 METs), time in
196 light PA (mins >1.5 METs but <3 METs), time in moderate PA (mins >3 METs and <6 METs)
197 and time in vigorous PA (mins >6 METs) (Haskell et al., 2007, Pate et al., 2008).

198 **Statistical analysis**

199 All statistical analysis was performed in GraphPad Prism 7 for Mac OS X. Differences between
200 conditions for exercise responses (i.e. power output and exercise energy expenditure), as well
201 as for 24-h CGM and PA summary variables, were compared using a one factor (condition)
202 repeated measures ANOVA. ANOVA was performed regardless of any minor deviances from
203 a normal distribution and with the Greenhouse-Geisser correction applied in cases of violated
204 sphericity (Maxwell and Delaney, 2004). If significant main effects were observed for 24-h
205 CGM and PA variables, then to address our planned primary aim and hypothesis we compared
206 each of the three exercise conditions to control with a paired t-test and a Bonferroni correction
207 for multiple comparisons. For comparisons of exercise responses, the one-way ANOVA was
208 followed up with Bonferroni corrected t-tests to locate differences between exercise conditions.
209 Statistical significance was set at $p \leq 0.05$ (two-tailed) and, unless stated otherwise, data is
210 presented as mean \pm SD. Cohens d was calculated as a measure of effect size with the following
211 thresholds: small ($d = 0.2$), medium ($d = 0.6$) and large ($d = 1.2$) effect.

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216 **Results**

217 **Exercise Characteristics / Intervention Fidelity**

218 All participants successfully completed the three exercise sessions. During the exercise work
219 intervals, mean power output was lowest during MICT (97 ± 17 W), higher during HIIT (165 ± 28
220 W, $p<0.05$ vs MICT), and higher still following REHIT (417 ± 49 W, $p<0.05$ vs HIIT and
221 MICT). On the other hand, Actiheart estimated energy expenditure during exercise was, on
222 average, lowest during REHIT (251 ± 94 kJ), higher during HIIT (921 ± 279 kJ, $p<0.05$ vs
223 REHIT), and tended to be highest during MICT (1076 ± 378 kJ, $p<0.05$ vs. REHIT, $p=0.07$ vs
224 HIIT). During REHIT, peak, average and end power output were 5.9 ± 0.7 , 4.8 ± 0.6 and 3.7 ± 0.6
225 W/kg for the first sprint, and 5.6 ± 0.5 , 4.4 ± 0.5 and 3.2 ± 0.6 W/kg for the second sprint,
226 respectively.

227 MICT elicited a mean exercise heart rate of $80\pm 5\%$ of the HR_{max} achieved during the VO_2 peak
228 test, whilst during the HIIT work intervals there was a progressive increase in heart rate, which
229 reached $89\pm 5\%$, $90\pm 5\%$, $91\pm 5\%$, $92\pm 4\%$ and $94\pm 5\%$ of HR_{max} during intervals 6-10
230 respectively (Figure 2). Heart rate during REHIT peaked at $86\pm 4\%$ and $91\pm 3\%$ of HR_{max} during
231 sprint 1 and 2, respectively, but mean exercise heart rate during REHIT was $74\pm 12\%$ of HR_{max}
232 (Figure 2).

233 The impact of the four trial conditions on 24-h physical activity energy expenditure derived
234 from the Actihearts is shown in Table 2. There were significant main effects of condition for
235 all PA parameters ($p<0.05$ for all). Both HIIT and MICT appeared to increase total 24-h energy
236 expenditure ($p<0.05$ for both), light PA ($p<0.05$ for both), moderate PA ($p=0.06$ for both), and
237 decrease sedentary time ($p<0.05$ for both), when compared with CON. Vigorous PA was
238 significantly increased with HIIT compared with CON only ($p<0.05$). Although 24-h TEE,
239 light PA, moderate PA, and vigorous PA were higher, and sedentary time lower, on average

240 with REHIT compared with CON, the differences were smaller and (with the exception of light
241 PA ($p<0.05$)) not statistically significant.

242 **Effects of exercise on glycaemic parameters**

243 ***24-hour Summary Variables***

244 The mean effect of exercise on 24-hour glycaemic summary variables is shown in Table 4 with
245 individual participant change scores (exercise minus control) for key summary variables shown
246 in Figure 3. There were significant effects of condition for mean 24-hour glucose ($p=0.05$),
247 time in hyperglycaemia ($p=0.04$) and for 24-h iAUC ($p=0.02$). Mean 24-h glucose was lower
248 during REHIT ($p=0.008$, $d=0.55$) and tended to be lower during MICT ($p=0.08$, $d=0.35$) when
249 compared to CON, but there was no statistically significant change observed with HIIT
250 ($p=0.31$, $d=0.35$). Time spent in hyperglycaemia appeared to be lower following all three
251 exercise conditions compared with CON (REHIT: $p=0.002$, $d=0.50$; MICT: $p=0.08$, $d=0.50$;
252 HIT: $p=0.04$, $d=0.54$), whilst 24-h iAUC was significantly reduced following MICT only
253 ($p=0.02$, $d=0.89$). There were no significant changes in 24-hour SD, glycaemic range, MAGE
254 or CONGA with any of the exercise conditions ($p>0.05$ for all main effects, respectively; Table
255 4).

256 ***Meal Responses***

257 The 3-hour glycaemic responses to breakfast, lunch and dinner are shown in Figure 4 with
258 additional postprandial summary variables in Table 4. There were no differences between
259 conditions in the glycaemic response to breakfast or lunch (both $p>0.05$, respectively).
260 However, there was a significant effect of condition on the AUC for dinner ($p=0.004$), with
261 lower AUC following REHIT (-11%, $p=0.018$, $d=1.05$) and MICT (-11%, $p=0.006$, $d=0.99$)
262 compared with CON. The glycaemic response to dinner was not significantly affected by HIIT

263 (-4%, $p=0.22$, $d=0.38$). There were no significant main effects of condition on any other
264 postprandial variable (Table 4).

265 **Adverse Events**

266 One participant reported subjective symptoms of hypoglycaemia between lunch and dinner
267 during the HIIT trial, however, glucose recorded via the CGM appeared to be within the normal
268 range (between 5-6 mmol/l). There were no other adverse events.

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287 **Discussion**

288 This study examined the acute effects of three discordant exercise strategies, performed after
289 breakfast, on CGM-derived 24 h glycaemic control in 11 men with type 2 diabetes. We
290 replicate the findings of numerous previous studies that have shown the beneficial effects of a
291 single 30 min bout of MICT on the 24 h glycaemic profile in type 2 diabetes (van Dijk et al.,
292 2013, van Dijk et al., 2012), and provide the first evidence to suggest that a modified SIT
293 protocol (REHIT), requiring 40 s of high-intensity exercise within a total time commitment of
294 10 min, is also associated with positive glycaemic effects in the post-exercise period. This
295 finding is both novel and of potential significance, as it provides the first evidence for a
296 genuinely time-efficient exercise option to improve glycaemic control in individuals with type
297 2 diabetes who currently perceive lack of time as a barrier to performing regular structured
298 exercise (Korkeakangas et al., 2009).

299 REHIT was associated with small (Cohens d between 0.2 to 0.6) but significant beneficial
300 decreases in 24-hour mean glucose and the prevalence of hyperglycaemia relative to a no-
301 exercise control trial. This appears to have been predominantly driven by a marked reduction
302 in the glycaemic response to the evening meal, as the breakfast and lunch responses were not
303 significantly affected. Importantly, the improvements in glycaemic control were observed *in*
304 *addition* to the impact of participants' current medication, given the response to the no exercise
305 (i.e. medication only) control trial. It is well established that hyperglycaemia is associated with
306 endothelial cell stress and subsequent vascular dysfunction (Paneni et al., 2013), whilst
307 improving glycaemic control reduces the risk of microvascular complications in type 2 diabetes
308 (Stolar, 2010). This is largely based on analysis of fasting glucose concentrations, OGTT
309 glucose responses, or HbA_{1c}, as estimates of glycaemic control, so it's difficult to draw direct
310 comparisons on relative risk reduction for microvascular complications based on CGM
311 variables (Monnier and Colette, 2015). For example, a reduction in mean 24 h glucose can

312 reflect changes during both ‘ambient’ and ‘postprandial’ periods (Monnier and Colette, 2015).
313 Nevertheless, it is reasonable to suggest that the ~0.5 mmol/l average reduction in 24 h mean
314 glucose and ~2-hour reduction in the prevalence of postprandial hyperglycaemia (per day)
315 observed with REHIT, when performed on a regular basis, would make a meaningful impact
316 on overall glycaemia (i.e. HbA_{1c}) and hence long-term risk (Monnier and Colette, 2015). The
317 lower glucose AUC (-11%) observed following dinner further supports this assertion, given
318 that the relative contribution of postprandial hyperglycaemia to overall glycaemic exposure is
319 greater in patients with HbA_{1c} ≤ 7.3% (Monnier and Colette, 2015).

320 There is also a strong correlation between postprandial hyperglycaemia and the risk of adverse
321 cardiovascular events (Coutinho et al., 1999). However, whether intervening to improve
322 glycaemic control lowers cardiovascular risk over the long term is currently contentious (Wing
323 et al., 2013). Nonetheless, combined with evidence that REHIT improves cardiorespiratory
324 fitness and resting blood pressure with 8 weeks of thrice weekly training sessions (Ruffino et
325 al., 2017), the current study provides further (tentative) evidence that REHIT favourably
326 modifies the cardiovascular risk profile in those with type 2 diabetes. The lack of improvement
327 in insulin sensitivity and glycaemic control reported 3 days after the final training session by
328 Ruffino et al (2017) suggests that the positive acute effects on glycaemic control are short lived.
329 Future research should determine the optimal frequency of REHIT to maintain the acute
330 benefits on glycaemic control.

331 The fact we could largely replicate the findings of previous studies on MICT and glycaemic
332 control (van Dijk et al., 2012, van Dijk et al., 2013) validates our methodology and strengthens
333 these preliminary findings with REHIT. However, it should be highlighted that the magnitude
334 of the effects observed with both MICT and REHIT in the present study are smaller than in
335 previous studies (van Dijk et al., 2012, van Dijk et al., 2013). We suspect that this is explained

336 by the fact that our participants' type 2 diabetes was relatively well controlled according to
337 HbA_{1c}. Van Dijk et al (Van Dijk et al., 2013) demonstrated that reductions in, for example,
338 mean 24 h glucose were lower (-0.6 mmol/l vs -1.2 mmol/l) in well controlled (HbA_{1c} <7.0%)
339 compared with sub-optimally controlled (HbA_{1c} >7%) individuals with type 2 diabetes,
340 respectively. The mean reductions in 24-h glucose of ~0.6 mmol/l with REHIT and ~0.4
341 mmol/l with MICT in the present study are, therefore, in line with the literature (Van Dijk et
342 al., 2013).

343 The lack of statistically significant improvement in most glycaemic parameters with HIIT is an
344 unexpected finding, particularly given the improvements observed with REHIT. Gillen et al
345 (2012) used a comparable HIIT protocol, trial design, and participants (n=7) of similar diabetic
346 status, and reported that HIIT markedly lowered average post-meal glucose spikes, as well as
347 the glucose concentrations 60-120 min after the 3 post-exercise meals. In contrast, we observed
348 no significant change in the AUC to any post-exercise meal or in any other marker of
349 postprandial glycaemia. Similar, however, was the lower prevalence of hyperglycaemia despite
350 no significant change in mean 24-hour glucose (Gillen et al., 2012). It is important to highlight
351 that the mean change for several of the glycaemic variables assessed with HIIT were in a
352 favourable direction in the current study, but there was greater variation in individual change
353 scores than with REHIT and MICT. It is possible that with an increased sample size and greater
354 statistical power we would have observed effects of HIIT on other glycaemic parameters.
355 Considering the accumulating evidence for beneficial training effects with this HIIT protocol
356 in type 2 diabetes (Little et al., 2011, Francois et al., 2017), we would encourage larger
357 definitive studies of the acute effects on glycaemic control.

358 There are several considerations in the study design and employed techniques that should be
359 acknowledged. First, although we provided standardised food packages during all trials, and

360 asked participants to record the time of their medication, the study was otherwise free-living
361 and (although this is also a strength of the study) we only have participants' self-reported
362 compliance. In addition, although CGM captures of glycaemic data outside of the laboratory
363 and has shown good agreement with responses measured simultaneously in venous blood
364 (Bailey et al., 2014), the coefficient of variation for some parameters can be high (Terada et
365 al., 2014). The fact we could detect differences despite this lower level of control is
366 encouraging, but we acknowledge that our small sample size, although consistent with
367 numerous other studies on this topic (van Dijk et al., 2012, van Dijk et al., 2013, Manders et
368 al., 2010), is a key limitation and our data should be interpreted with caution in that context.
369 Larger free-living CGM studies combined with more controlled laboratory assessments will be
370 required to confirm our preliminary findings. We were also only able to capture postprandial
371 glucose responses in this study and can provide no mechanistic insight, and so future
372 investigations should aim to provide a more holistic and mechanistic assessment of
373 carbohydrate and lipid metabolism following REHIT in both men and women with type 2
374 diabetes.

375 In conclusion, this study suggests that a brief bout of REHIT improves markers of postprandial
376 glycaemic control over the following 24 h period when compared with no exercise. We
377 conclude that REHIT may offer a genuinely time-efficient exercise option for men with type 2
378 diabetes and warrants further study.

379

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385 **Data availability** The raw data for this study is available from the corresponding author on
386 reasonable request.

387
388 **References**

389
390 Allender, S., Scarborough, P., Peto, V., Rayner, M., Leal, J., Luengo-Fernandez, R. and Gray,
391 A. 2008. European Cardiovascular Disease Statistics. European Heart Network,
392 Brussels, England.

393 Bailey, T. S., Ahmann, A., Brazg, R., Christiansen, M., Garg, S., Watkins, E., Welsh, J. B.
394 and Lee, S. W. (2014) 'Accuracy and acceptability of the 6-day Enlite continuous
395 subcutaneous glucose sensor', *Diabetes Technol Ther*, 16(5), pp. 277-83.

396 Bantle, J. P., Wylie-Rosett, J., Albright, A. L., Apovian, C. M., Clark, N. G., Franz, M. J.,
397 Hoogwerf, B. J., Lichtenstein, A. H., Mayer-Davis, E., Mooradian, A. D., Wheeler,
398 M. L. and Association, A. D. (2008) 'Nutrition recommendations and interventions for
399 diabetes: a position statement of the American Diabetes Association', *Diabetes Care*,
400 31 Suppl 1, pp. S61-78.

401 Church, T. S., Blair, S. N., Cocroham, S., Johannsen, N., Johnson, W., Kramer, K., Mikus, C.
402 R., Myers, V., Nauta, M., Rodarte, R. Q., Sparks, L., Thompson, A. and Earnest, C. P.
403 (2010) 'Effects of aerobic and resistance training on hemoglobin A1c levels in
404 patients with type 2 diabetes: a randomized controlled trial', *JAMA*, 304(20), pp.
405 2253-62.

406 Colberg, S. R., Sigal, R. J., Yardley, J. E., Riddell, M. C., Dunstan, D. W., Dempsey, P. C.,
407 Horton, E. S., Castorino, K. and Tate, D. F. (2016) 'Physical Activity/Exercise and
408 Diabetes: A Position Statement of the American Diabetes Association', *Diabetes*
409 *Care*, 39(11), pp. 2065-2079.

410 Coutinho, M., Gerstein, H. C., Wang, Y. and Yusuf, S. (1999) 'The relationship between
411 glucose and incident cardiovascular events. A metaregression analysis of published
412 data from 20 studies of 95,783 individuals followed for 12.4 years', *Diabetes Care*,
413 22(2), pp. 233-40.

- 414 Craig, C. L., Marshall, A. L., Sjoström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E.,
415 Pratt, M., Ekelund, U., Yngve, A., Sallis, J. F. and Oja, P. (2003) 'International
416 physical activity questionnaire: 12-country reliability and validity', *Med Sci Sports
417 Exerc*, 35(8), pp. 1381-95.
- 418 Dela, F., Larsen, J. J., Mikines, K. J., Ploug, T., Petersen, L. N. and Galbo, H. (1995) 'Insulin-
419 stimulated muscle glucose clearance in patients with NIDDM. Effects of one-legged
420 physical training', *Diabetes*, 44(9), pp. 1010-20.
- 421 Francois, M. E., Durrer, C., Pistawka, K. J., Halperin, F. A., Chang, C. and Little, J. P. (2017)
422 'Combined Interval Training and Post-exercise Nutrition in Type 2 Diabetes: A
423 Randomized Control Trial', *Front Physiol*, 8, pp. 528.
- 424 Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M.,
425 Nieman, D. C., Swain, D. P. and Medicine, A. C. o. S. (2011) 'American College of
426 Sports Medicine position stand. Quantity and quality of exercise for developing and
427 maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently
428 healthy adults: guidance for prescribing exercise', *Med Sci Sports Exerc*, 43(7), pp.
429 1334-59.
- 430 Gillen, J. B., Little, J. P., Punthakee, Z., Tarnopolsky, M. A., Riddell, M. C. and Gibala, M. J.
431 (2012) 'Acute high-intensity interval exercise reduces the postprandial glucose
432 response and prevalence of hyperglycaemia in patients with type 2 diabetes', *Diabetes
433 Obes Metab*, 14(6), pp. 575-7.
- 434 Gillen, J. B., Martin, B. J., MacInnis, M. J., Skelly, L. E., Tarnopolsky, M. A. and Gibala, M.
435 J. (2016) 'Twelve Weeks of Sprint Interval Training Improves Indices of
436 Cardiometabolic Health Similar to Traditional Endurance Training despite a Five-
437 Fold Lower Exercise Volume and Time Commitment', *PLoS One*, 11(4), pp.
438 e0154075.
- 439 International Diabetes Federation Guideline Development Group (2014) 'Guideline for
440 management of postmeal glucose in diabetes', *Diabetes Res Clin Pract*, 103(2), pp.
441 256-68.

- 442 Hallal, P. C., Andersen, L. B., Bull, F. C., Guthold, R., Haskell, W., Ekelund, U. and Group,
443 L. P. A. S. W. (2012) 'Global physical activity levels: surveillance progress, pitfalls,
444 and prospects', *Lancet*, 380(9838), pp. 247-57.
- 445 Hardcastle, S. J., Ray, H., Beale, L. and Hagger, M. S. (2014) 'Why sprint interval training is
446 inappropriate for a largely sedentary population', *Front Psychol*, 5, pp. 1505.
- 447 Harris, J. A. and Benedict, F. G. (1918) 'A Biometric Study of Human Basal Metabolism',
448 *Proc Natl Acad Sci U S A*, 4(12), pp. 370-3.
- 449 Haskell, W. L., Lee, I. M., Pate, R. R., Powell, K. E., Blair, S. N., Franklin, B. A., Macera, C.
450 A., Heath, G. W., Thompson, P. D. and Bauman, A. (2007) 'Physical activity and
451 public health: updated recommendation for adults from the American College of
452 Sports Medicine and the American Heart Association', *Med Sci Sports Exerc*, 39(8),
453 pp. 1423-34.
- 454 Howley, E. T., Bassett, D. R. and Welch, H. G. (1995) 'Criteria for maximal oxygen uptake:
455 review and commentary', *Med Sci Sports Exerc*, 27(9), pp. 1292-301.
- 456 Korkiakangas, E. E., Alahuhta, M. A. and Laitinen, J. H. (2009) 'Barriers to regular exercise
457 among adults at high risk or diagnosed with type 2 diabetes: a systematic review',
458 *Health Promot Int*, 24(4), pp. 416-27.
- 459 Little, J. P., Gillen, J. B., Percival, M. E., Safdar, A., Tarnopolsky, M. A., Punthakee, Z.,
460 Jung, M. E. and Gibala, M. J. (2011) 'Low-volume high-intensity interval training
461 reduces hyperglycemia and increases muscle mitochondrial capacity in patients with
462 type 2 diabetes', *J Appl Physiol*, 111(6), pp. 1554-60.
- 463 Little, J. P., Jung, M. E., Wright, A. E., Wright, W. and Manders, R. J. (2014) 'Effects of
464 high-intensity interval exercise versus continuous moderate-intensity exercise on
465 postprandial glycaemic control assessed by continuous glucose monitoring in obese
466 adults', *Appl Physiol Nutr Metab*, 39(7), pp. 835-41.
- 467 Manders, R. J., Van Dijk, J. W. and van Loon, L. J. (2010) 'Low-intensity exercise reduces
468 the prevalence of hyperglycemia in type 2 diabetes', *Med Sci Sports Exerc*, 42(2), pp.
469 219-25.

470 Maxwell, S. E. and Delaney, H. D. (2004) *Designing experiments and analyzing data : a*
471 *model comparison perspective*. 2nd ed. edn. Mahwah, N.J. ; London: Lawrence
472 Erlbaum Associates.

473 Metcalfe, R. S., Babraj, J. A., Fawkner, S. G. and Vollaard, N. B. (2012) 'Towards the
474 minimal amount of exercise for improving metabolic health: beneficial effects of
475 reduced-exertion high-intensity interval training', *Eur J Appl Physiol*, 112(7), pp.
476 2767-75.

477 Metcalfe, R. S., Koumanov, F., Ruffino, J. S., Stokes, K. A., Holman, G. D., Thompson, D.
478 and Vollaard, N. B. (2015) 'Physiological and molecular responses to an acute bout of
479 reduced-exertion high-intensity interval training (REHIT)', *Eur J Appl Physiol*,
480 115(11), pp. 2321-34.

481 Metcalfe, R. S., Tardif, N., Thompson, D. and Vollaard, N. B. (2016) 'Changes in aerobic
482 capacity and glycaemic control in response to reduced-exertion high-intensity interval
483 training (REHIT) are not different between sedentary men and women', *Appl Physiol*
484 *Nutr Metab*, 41(11), pp. 1117-1123.

485 Monnier, L. and Colette, C. (2015) 'Postprandial and basal hyperglycaemia in type 2 diabetes:
486 Contributions to overall glucose exposure and diabetic complications', *Diabetes*
487 *Metab*, 41(6 Suppl 1), pp. 6S9-6S15.

488 Morrato, E. H., Hill, J. O., Wyatt, H. R., Ghushchyan, V. and Sullivan, P. W. (2007) 'Physical
489 activity in U.S. adults with diabetes and at risk for developing diabetes, 2003',
490 *Diabetes Care*, 30(2), pp. 203-9.

491 Paneni, F., Beckman, J. A., Creager, M. A. and Cosentino, F. (2013) 'Diabetes and vascular
492 disease: pathophysiology, clinical consequences, and medical therapy: part I', *Eur*
493 *Heart J*, 34(31), pp. 2436-43.

494 Pate, R. R., O'Neill, J. R. and Lobelo, F. (2008) 'The evolving definition of "sedentary",
495 *Exerc Sport Sci Rev*, 36(4), pp. 173-8.

496 Rodbard, D. (2009) 'New and improved methods to characterize glycemic variability using
497 continuous glucose monitoring', *Diabetes Technol Ther*, 11(9), pp. 551-65.

498 Ruffino, J. S., Songsorn, P., Haggett, M., Edmonds, D., Robinson, A. M., Thompson, D. and
499 Vollaard, N. B. (2017) 'A comparison of the health benefits of reduced-exertion high-
500 intensity interval training (REHIT) and moderate-intensity walking in type 2 diabetes
501 patients', *Appl Physiol Nutr Metab*, 42(2), pp. 202-208.

502 Stolar, M. (2010) 'Glycemic control and complications in type 2 diabetes mellitus', *Am J*
503 *Med*, 123(3 Suppl), pp. S3-11.

504 Terada, T., Loehr, S., Guigard, E., McCargar, L. J., Bell, G. J., Senior, P. and Boulé, N. G.
505 (2014) 'Test-retest reliability of a continuous glucose monitoring system in
506 individuals with type 2 diabetes', *Diabetes Technol Ther*, 16(8), pp. 491-8.

507 Terada, T., Wilson, B. J., Myette-Côté, E., Kuzik, N., Bell, G. J., McCargar, L. J. and Boulé,
508 N. G. (2016) 'Targeting specific interstitial glycemic parameters with high-intensity
509 interval exercise and fasted-state exercise in type 2 diabetes', *Metabolism*, 65(5), pp.
510 599-608.

511 Thompson, D., Batterham, A. M., Bock, S., Robson, C. and Stokes, K. (2006) 'Assessment of
512 low-to-moderate intensity physical activity thermogenesis in young adults using
513 synchronized heart rate and accelerometry with branched-equation modeling', *J Nutr*,
514 136(4), pp. 1037-42.

515 Townsend, L. K., Islam, H., Dunn, E., Eys, M., Robertson-Wilson, J. and Hazell, T. J. (2017)
516 'Modified sprint interval training protocols. Part II. Psychological responses', *Appl*
517 *Physiol Nutr Metab*, 42(4), pp. 347-353.

518 Van Dijk, J. W., Manders, R. J., Canfora, E. E., Mechelen, W. V., Hartgens, F., Stehouwer,
519 C. D. and Van Loon, L. J. (2013) 'Exercise and 24-h glycemic control: equal effects
520 for all type 2 diabetes patients?', *Med Sci Sports Exerc*, 45(4), pp. 628-35.

521 van Dijk, J. W., Manders, R. J., Hartgens, F., Stehouwer, C. D., Praet, S. F. and van Loon, L.
522 J. (2011) 'Postprandial hyperglycemia is highly prevalent throughout the day in type 2
523 diabetes patients', *Diabetes Res Clin Pract*, 93(1), pp. 31-7.

524 van Dijk, J. W., Manders, R. J., Tummers, K., Bonomi, A. G., Stehouwer, C. D., Hartgens, F.
525 and van Loon, L. J. (2012) 'Both resistance- and endurance-type exercise reduce the
526 prevalence of hyperglycaemia in individuals with impaired glucose tolerance and in

527 insulin-treated and non-insulin-treated type 2 diabetic patients', *Diabetologia*, 55(5),
528 pp. 1273-82.

529 van Dijk, J. W., Venema, M., van Mechelen, W., Stehouwer, C. D., Hartgens, F. and van
530 Loon, L. J. (2013) 'Effect of moderate-intensity exercise versus activities of daily
531 living on 24-hour blood glucose homeostasis in male patients with type 2 diabetes',
532 *Diabetes Care*, 36(11), pp. 3448-53.

533 Vollaard, N. B. and Metcalfe, R. S. (2017) 'Research into the Health Benefits of Sprint
534 Interval Training Should Focus on Protocols with Fewer and Shorter Sprints', *Sports*
535 *Med*, 47(12), pp. 2443–2451.

536 Wing, R. R., Bolin, P., Brancati, F. L., Bray, G. A., Clark, J. M., Coday, M., Crow, R. S.,
537 Curtis, J. M., Egan, C. M., Espeland, M. A., Evans, M., Foreyt, J. P., Ghazarian, S.,
538 Gregg, E. W., Harrison, B., Hazuda, H. P., Hill, J. O., Horton, E. S., Hubbard, V. S.,
539 Jakicic, J. M., Jeffery, R. W., Johnson, K. C., Kahn, S. E., Kitabchi, A. E., Knowler,
540 W. C., Lewis, C. E., Maschak-Carey, B. J., Montez, M. G., Murillo, A., Nathan, D.
541 M., Patricio, J., Peters, A., Pi-Sunyer, X., Pownall, H., Reboussin, D., Regensteiner, J.
542 G., Rickman, A. D., Ryan, D. H., Safford, M., Wadden, T. A., Wagenknecht, L. E.,
543 West, D. S., Williamson, D. F., Yanovski, S. Z. and Group, L. A. R. (2013)
544 'Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes', *N Engl J*
545 *Med*, 369(2), pp. 145-54.

Figure legends

Fig. 1 Flow of participants through the study

Fig. 2 Heart rate responses over time with each exercise session. Data is presented as mean and SEM for visual clarity.

Fig. 3 Effect of exercise on 24-h CGM summary variables. Data is presented as mean change (bars) with individual change scores (dots) compared with CON.

Fig. 4 Glucose time responses (a, c, e) and AUC (b, d, f) for breakfast (a and b), lunch (c and d) and dinner (e and f). * denotes $p < 0.05$ vs. CON. Glucose time responses are presented as means only for clarity, whilst AUC's are presented as mean change (bars) with individual change scores (dots) compared with CON.