

Supplementary Information

Title: Association of Timing of Moderate-to-Vigorous Physical Activity with Changes in Glycemic Control over 4 Years in Adults with Type 2 Diabetes from the Look AHEAD Trial

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Supplementary Methods

Study design and participants.

We included both control and intervention groups in the analyses, since either group has at least 19% of participants achieving PA goal of $\geq 150 \text{ min} \cdot \text{wk}^{-1}$ of bout-related moderate-to-vigorous physical activity (bMVPA) at year 1¹. Descriptive data for this accelerometer subgroup (compared with the entire Look AHEAD sample) have been reported previously¹.

Interventions.

The interventions have been described in detail previously^{2,3}. The ILI group included a combination of group and individual sessions, contact via telephone or e-mail, motivational campaigns, and refresher campaigns. For months 1–6, the intervention included group and individual sessions. During months 7–12, the ILI group were offered two group sessions and one individual session per month. Monthly in-person contact and one telephone or e-mail contact were offered during months 13–48, along with two annual refresher campaigns.

The dietary intervention focused on reducing energy intake to 1200 to 1500 kcal/d for persons $< 114 \text{ kg}$ (250 pounds) and 1500 to 1800 kcal/d for individuals $\geq 114 \text{ kg}$, with maximum dietary fat intake prescribed at 30% of total energy intake with 10% consumed as saturated fat. Commercially available liquid shakes and snack bars were provided to replace two meals per day at no cost to participants during weeks 3–20, and thereafter, one shake and one snack bar per day were provided, along with detailed meal plans of conventional foods for their daily meals.

Participants were instructed to progressively increase nonsupervised physical activity from 50 min/week to at least 175 min/week by week 26 of the intervention. Physical activity accumulated in bouts of $\geq 10 \text{ min}$ was counted toward the activity goal. Physical activity was recommended to be performed at a moderate-to-vigorous intensity, which was anchored as activity performed at an intensity similar to brisk walking. Resistance exercise was encouraged and could contribute to up to 25% of the prescribed activity goal each week. The physical activity program principally relies on unsupervised (at-home) exercise.

Participants assigned to DSE were offered three group sessions during years 1–4 that focused on diet, physical activity, or social support, but did not include specific behavioral strategies regarding diet or physical activity that would result in weight loss or change in fitness. For both the ILI and DSE groups, medical care and diabetes treatment continued to be provided by the participant's health care provider. Only temporary adjustments to diabetes medications were permitted by the local site to prevent episodes of hypoglycemia that may result from the intervention.

Assessments.

Demographic characteristics, including age, sex, race/ethnicity, education, and duration of diabetes were assessed by questionnaire at baseline. Participants reported their smoking and alcohol consumption status at baseline and follow-up visits. Certified staff members measured weight, height, and body mass index, assessed medication use, and obtained HbA1c and fasting serum glucose at annual visits as previously described^{4,5}. All participants (and with their permission, their PCPs) were provided with results from annual HbA1c assessments. Data on race/ethnicity was obtained by self-report, based on the questions: Are you Latino, Hispanic, or of Spanish origin? For those answering no, a further question asked: Which best describes you? (multiple choices were allowed): African American/Black, American Indian/Alaskan Native, Asian, Native Hawaiian or Pacific Islander, White, or Other. 'Other' includes both participants who chose 'other' and participants who chose multiple race categories. Due to small numbers, Asian, Native Hawaiian or Pacific Islander have been combined with Other. Each participant's physician handled all medication changes. However, to reduce the risk of hypoglycemia, study staff managed diabetes medications according to preset algorithms during the initial intervention period.

Accelerometry data.

The participants were instructed to wear the RT3 triaxial accelerometer during all waking hours for 7 consecutive days, removing it only for periods of bathing, showering, or other water-based activities. Participants were also instructed not to alter their typical physical activity pattern while wearing this device. Total energy expenditure per minute (kcal/min) and estimated resting energy expenditure (kcal/min) were provided by the StayHealthy® software that accompanied the RT3 accelerometer. Using these data, METs per minute were computed by dividing the estimated total energy expenditure per minute by the estimated resting energy expenditure ($\text{METs} = \text{total energy expenditure}$

per minute/estimated resting energy expenditure)^{1,6}. Moderate- and vigorous-intensity activity were defined as ≥ 3 METS and ≥ 6 METS respectively⁷.

Bout-related MET \times mins per week was calculated by summing the MET values for each minute identified as part of an MVPA bout and then adjusted for the number of valid days. Data for a given day were considered valid if the accelerometer was worn for ≥ 10.5 h on that day. Non-wear time was defined by an interval ≥ 60 consecutive minutes of no activity counts, with allowance for 1-2 min of activity ≤ 1.5 METs. We excluded participants with < 4 valid wear days, high nocturnal activity ($> 10\%$ activity counts between 1-4AM), and spurious long total duration of MVPA ($\geq \text{median} + 3.5 \times \text{interquartile ranges}$ [~ 180 min MVPA/day, top 0.6%]).

Missing data imputation.

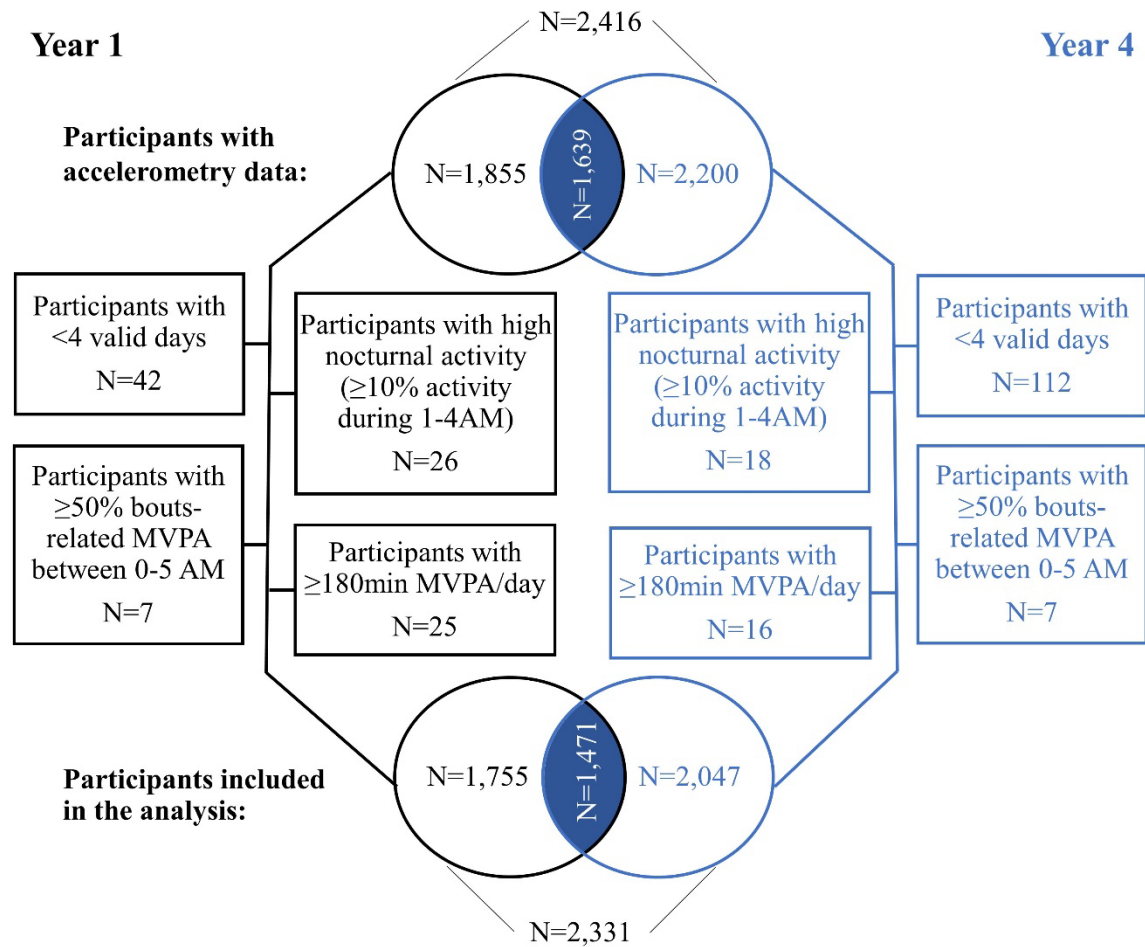
Less than 1.5% covariate data (including anthropometric data, smoking status, etc.) were missing at random. We imputed 5 data sets with the use of multiple imputation by chained equation⁸. Missing data on HbA1c, fasting glucose, glucose-lowering medication (when used as outcome) and exposure (bMVPA timing) were not imputed.

Statistical Analysis

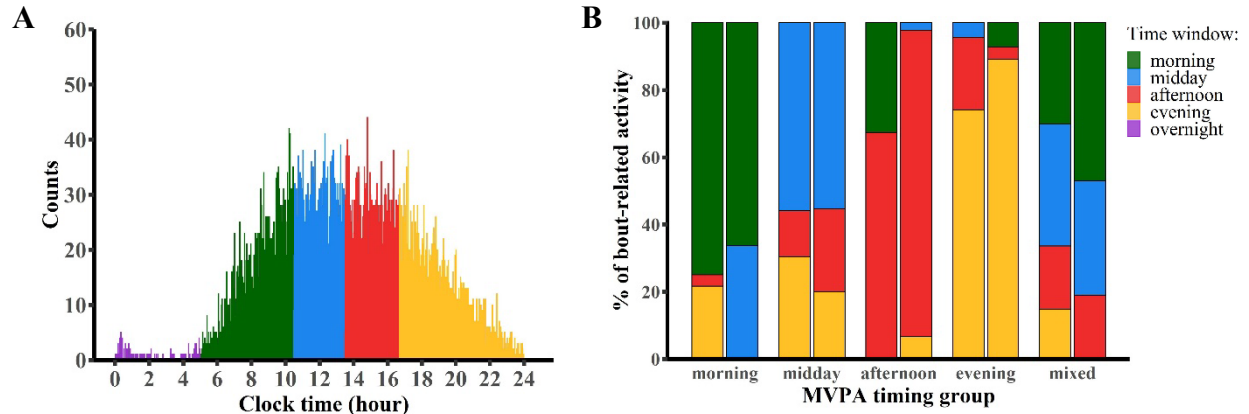
For the completeness of analyses on glucose-lowering medication, we also included all glucose-lowering medications (includ. insulin) in all participants in the supplementary analysis. Given that HbA1c varied across the bMVPA timing groups at baseline, we assessed the sensitivity of the results by using proportional changes in HbA1c as the outcome. To confirm the group differences were not mostly attributed to the inactive group vs. other active groups, we performed a sensitivity analysis on the primary outcome excluding the inactive group.

Supplementary References

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6. Jakicic JM, Gregg E, Knowler W, et al. Activity patterns of obese adults with type 2 diabetes in the look AHEAD study. *Med Sci Sports Exerc* 2010; **42**(11): 1995-2005.
7. King AC, Powell KE, Kraus WE. The US Physical Activity Guidelines Advisory Committee Report-Introduction. *Med Sci Sports Exerc* 2019; **51**(6): 1203-5.
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Supplementary Figure 1. Consort Diagram. We excluded participants with <4 valid wear days, high nocturnal activity ($>10\%$ activity counts between 1-4AM), spurious long total duration of MVPA ($\geq \text{median} + 3.5 \times \text{interquartile ranges}$ [$\sim 180\text{min}$ MVPA/day, top 0.6%]), and $\geq 50\%$ of their bMVPA amount between 0:00 and 4:59.



Time Window	Timing of bMVPA groups (Year 1)				
	Mixed	Morning	Midday	Afternoon	Evening
Morning	26.5 (24.7)	70.1 (26.2)	4.3 (18.4)	0 (9.8)	0 (9.5)
Midday	26.6 (23)	6.3 (19.6)	65.6 (24.4)	8.8 (22.8)	3.2 (19.2)
Afternoon	26.7 (21.3)	0 (12.4)	3.8 (18.7)	67.5 (20.3)	3.2 (16.8)
Evening	23.6 (24.3)	0 (13.2)	0 (18)	0 (18.4)	68.8 (24.7)

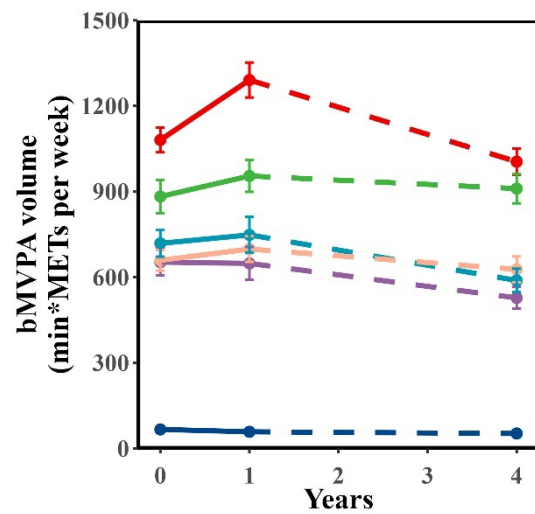
Time Window	Timing of bMVPA groups (Year 4)				
	Mixed	Morning	Midday	Afternoon	Evening
Morning	25.8 (24.2)	71.4 (27.2)	0 (17)	0 (10.4)	0 (10.6)
Midday	25.5 (22.4)	1 (15.2)	64.2 (21.3)	0 (17.4)	0 (17.4)
Afternoon	26.3 (23.1)	0 (16.1)	0 (20.8)	67.3 (22.1)	5.5 (20)
Evening	24.7 (25)	0 (14.4)	0 (16.4)	3.2 (23.2)	66.5 (23.9)

Note: Data are median (interquartile range) of the percentage of bMVPA spent in each time window. The bMVPA timing groups were defined by accelerometry data collected at Year 1 (top) or at Year 4 (bottom). Inactive group is not included, since the low overall activity made all values zero.

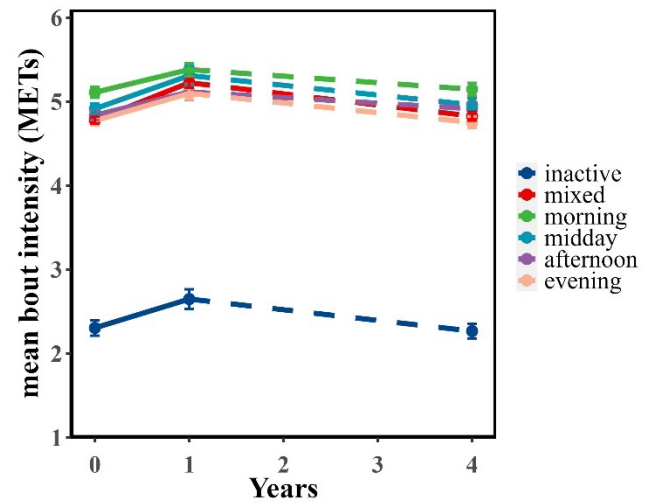
Supplementary Figure 2. Temporal distribution of bout-related MVPA. (A) The distribution of the 11,104 MVPA bouts at year 1 from all included participants ($n=1,762$, see method for details) across 24-h clock time. The overnight time window (purple, 0:00-4:59AM) has the lowest number of bouts per hour (<20). The remaining 19 hours (5:00 AM-11:59 PM) were divided into quartiles based on the number of bouts within each time window: morning (yellow, 5:00 AM-11:29 AM), the midday (red, 11:30 AM-1:29 PM), the afternoon (green, 1:30 PM-4:42PM), the evening (blue, 4:43PM-11-59PM). (B) Representative participants who are classified into the morning, the midday, the afternoon, the evening, and the mixed group. The stacked bar plot presents the proportion of bout-related MET \times min MVPA they performed in each time windows as defined in (A). (C) Median percentage of bout-related MET \times min MVPA spent in each time window (i.e., morning, midday, afternoon, and evening) across the timing of bMVPA groups.

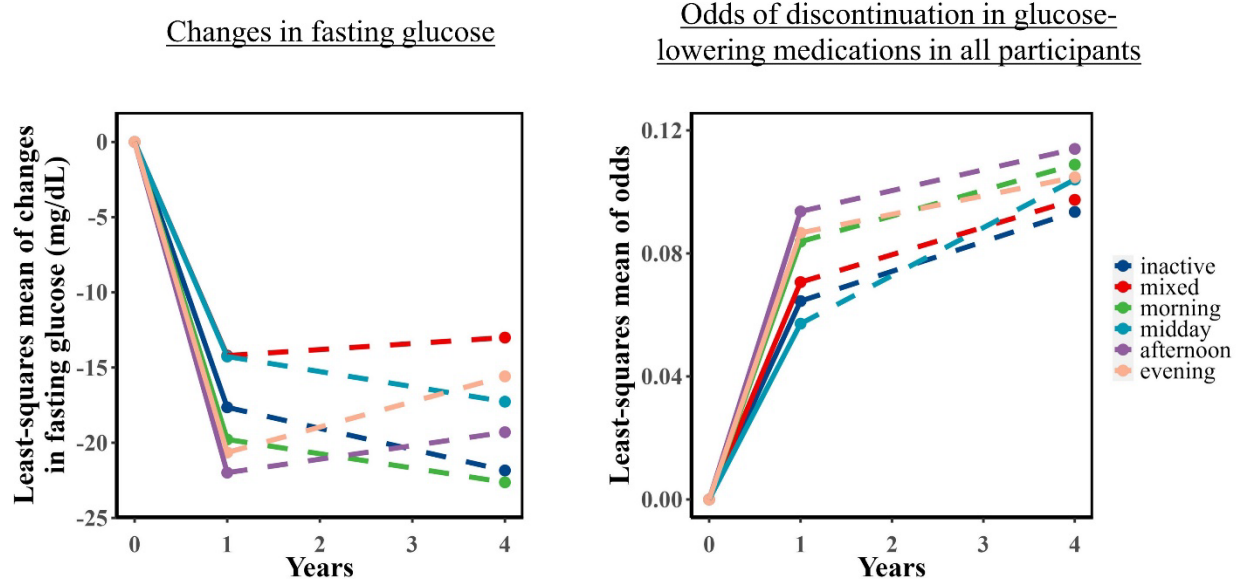
Supplementary Figure 3. Total amount of bMVPA per week (A) and average bout intensity (B) by bMVPA timing groups across 4 years.

A



B





Supplementary Figure 4. Changes in glycemic measurements by bMVPA timing groups. (A) Least-squares means of changes in fasting glucose over 4 years. **(B)** Least-squares means of changes in odds of discontinuation versus maintain or initiation in glucose-lowering medications in all participants over 4 years. Means are estimated using linear mixed effect model for continuous measures and multinomial generalized estimated equation model for reported medication use. Models 4 are used here and adjusted as indicated in Suppl. Tables 5 and 6. Since the bMVPA timing group included different participants at year 1 vs. year 4, changes from year 1 to year 4 were presented as dashed line.

Supplementary Table 1. Baseline characteristics of the study population.

Baseline Characteristics of All Participants (n=2,331)	
<i>Sociodemographic factors</i>	
Age (years)	59.2 (6.9)
Sex, n (%), men/women	1009 (43)/ 1322 (57)
Treatment Arm, n (%), DSE/ILI	1159 (49.7)/ 1172 (50.3)
Race/ethnicity, n (%)	
African American	451 (19)
Hispanic/Latino	107 (5)
Non-Hispanic white	1681 (72)
Other	92 (4)
Education, n (%)	
High school or others	434 (19)
Some college	861 (37)
College graduate	349 (15)
Graduate school	687 (29)
<i>Health and medication</i>	
History of cardiovascular diseases, n (%)	347 (15)
Insulins, n (%)	345 (15)
Glucose-lowering medications, n (%)	1998 (86)
<i>Lifestyle factors</i>	
Current smoking, n (%)	89 (4)
alcohol consumption, n (%)	849 (36)
bout-related MVPA, MET × mins/week	608.6 (774.6)
MVPA bout intensity (METs/min)	4.1 (1.9)
<i>Metabolic measurements</i>	
BMI, kg/m ²	36.3 (5.9)
Duration of diabetes, years	6.8 (6.4)
HbA1c, %	7.2 (1.1)
Fasting glucose, mg/dL	150.7 (44.1)

Data are n (%) or mean (SD).

Supplementary Table 2. Baseline characteristics in the Look AHEAD study population with valid accelerometry recordings at Year 4.

	bMVPA timing groups (n=2,047)						<i>P-value*</i>
	Inactive	Morning	Midday	Afternoon	Evening	Mixed	
	n=767	n=261	n=226	n=169	n=218	n=406	
<i>Sociodemographic factors</i>							
Age (years)	60.4 (7)	59.6 (6.7)	58.9 (6.8)	58.5 (7.3)	57.4 (6.6)	57.6 (6.3)	<0.0001
Sex, n (%), men/women	253 (33)/ 514 (67) #	132 (50.6)/ 129 (49.4)	95 (42)/ 131 (58)	84 (49.7)/ 85 (50.3)	100 (45.9)/ 118 (54.1)	227 (55.9)/ 179 (44.1)	<0.0001
Treatment Arm, n (%), DSE/ILI	407 (53.1)/ 360 (46.9) #	114 (43.7)/ 147 (56.3)	103 (45.6)/ 123 (54.4)	89 (52.7)/ 80 (47.3)	94 (43.1)/ 124 (56.9)	201 (49.5)/ 205 (50.5)	0.02
Race/ethnicity, n (%)							0.38
African American	169 (22)	46 (17.6)	35 (15.5)	31 (18.3)	38 (17.4)	74 (18.2)	
Hispanic/Latino	36 (4.7)	7 (2.7)	12 (5.3)	10 (5.9)	11 (5)	21 (5.2)	
Non-Hispanic white	539 (70.3)	195 (74.7)	169 (74.8)	122 (72.2)	160 (73.4)	287 (70.7)	
Other	23 (3)	13 (5)	10 (4.4)	6 (3.6)	9 (4.1)	24 (5.9)	
Education, n (%)							0.10
High school or other	71 (17.5)	159 (20.7)	46 (17.6)	38 (16.8)	29 (17.2)	34 (15.6)	
Some college	134 (33)	300 (39.1)	87 (33.3)	83 (36.7)	72 (42.6)	79 (36.2)	
College graduate	67 (16.5)	98 (12.8)	53 (20.3)	33 (14.6)	26 (15.4)	33 (15.1)	
Graduate school	134 (33)	210 (27.4)	75 (28.7)	72 (31.9)	42 (24.9)	72 (33)	
<i>Health and diabetes medication</i>							
History of cardiovascular diseases, n (%), yes	121 (15.8)	44 (16.9)	24 (10.6)	21 (12.4)	25 (11.5)	56 (13.8)	0.2
Insulins, n (%), yes	111 (14.8)	44 (17.5)	30 (13.8)	24 (14.8)	23 (11)	64 (16.2)	0.12
glucose-lowering drugs, n (%), yes	664 (87.4)	232 (89.9)	194 (86.6)	133 (79.6)	186 (86.1) #	336 (83)	0.02
<i>Lifestyle factors</i>							
Current smoking, n (%), yes	34 (4.4)	3 (1.2) #	7 (3.1)	5 (3)	14 (6.5)	13 (3.2)	0.05
alcohol consumption, n (%), yes	311 (40.5) #	93 (35.6)	75 (33.2)	58 (34.3)	66 (30.3)	133 (32.8)	0.02
bout-related MVPA, MET×mins/week	191.1 [517.4]	518.4 [850.5]	410.9 [772.3]	318 [712.6]	444 [713.8]	554.6 [1071.8]	<0.0001
MVPA bout intensity, METs/min	4.2 [1.1]	4.7 [1.3]	4.7 [1.2]	4.5 [1.3]	4.7 [1.3]	4.7 [1.2]	<0.0001
<i>Metabolic measurements</i>							
BMI, kg/m ²	36.8 (6.1)	35.4 (6)	36.3 (5.5)	35.5 (5.1)	36.3 (5.9)	35.8 (6.1)	0.002
Duration of diabetes, years	6.7 (6.4)	7.3 (7.3)	6.4 (6)	6.9 (6.5)	6.2 (6)	6.3 (5.8)	0.77
HbA1c, %	7.3 (1.1)	7 (1)	7.2 (1.1)	7.1 (1.2)	7.1 (1.2)	7.3 (1.1)	0.009
Fasting glucose, mg/dL	151.7 (43.9)	145.5 (43.1)	146.9 (41.5)	149.1 (41.8)	143.4 (40.3)	155.2 (45.7)	0.003

Data are n (%), mean (SD) or median [IQR], shown according to the temporal distribution of bout-related MVPA. DSE, diabetes support and education (control); ILI, intensive lifestyle intervention.

* P values obtained with the Kruskal-Wallis test for continuous variables and χ^2 test for categorical variables. P values refer to heterogeneity across temporal distribution of bout-related MVPA categories.

refers to the most contributing cells to the total χ^2 score.

Supplementary Table 3. Mean changes in HbA1c% from baseline to years 1 and year 1 to year 4 across bMVPA timing groups (excluding inactive group, N_{total}=1,788).

	Model 1		Model 2		Model 3	
	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4
Mixed	<i>reference</i>		<i>reference</i>		<i>reference</i>	
Morning	-0.07 (-0.22, 0.08)	-0.1 (-0.29, 0.08)	-0.06 (-0.2, 0.09)	-0.09 (-0.28, 0.09)	-0.05 (-0.2, 0.1)	-0.03 (-0.27, 0.21)
Midday	0.04 (-0.12, 0.2)	-0.09 (-0.28, 0.1)	0.02 (-0.13, 0.18)	-0.08 (-0.27, 0.12)	0.01 (-0.14, 0.17)	-0.11 (-0.36, 0.14)
Afternoon	-0.28 (-0.44, -0.12) ^a	0.03 (-0.18, 0.24)	-0.28 (-0.44, -0.12) ^a	0.02 (-0.19, 0.24)	-0.29 (-0.45, -0.13) ^b	0.31 (0.04, 0.58)
Evening	-0.07 (-0.22, 0.09)	0.14 (-0.05, 0.34)	-0.06 (-0.21, 0.09)	0.16 (-0.04, 0.36)	-0.06 (-0.22, 0.09)	0.21 (-0.04, 0.46)
<i>P</i> value	0.01	0.17	0.01	0.17	0.005	0.22

Data are expressed as least-squares mean differences (95% CI). Unit in %. Sample size: N=1267 for BL to Y1, N=1256 for Y1 to Y4. Model 1 adjusted for age, sex, race, education, smoking, alcohol consumption, diabetes duration, and medication. Model 2 further adjusted for treatment arm. Model 3 further adjusted for body mass index (BMI), bout-related METs × min/week and average bout intensity.

P values indicate significant differences among groups.

^a indicates that $P_{FDR} < 0.05$ vs. Midday and Mixed groups in pairwise post-hoc comparisons.

^b indicates that $P_{FDR} < 0.05$ vs. Morning, Midday, Evening, and Mixed groups in pairwise post-hoc comparisons.

Supplementary Table 4. Mean percentage changes in HbA1c% from baseline to years 1 and year 1 to year 4 across bMVPA timing groups (N_{total} = 2,299).

	Model 1		Model 2		Model 3	
	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4
inactive	<i>reference</i>		<i>reference</i>		<i>reference</i>	
morning	-1.0 (-2.8, 0.8)	-1.0 (-3.4, 1.3)	-0.8 (-2.6, 1)	-0.8 (-3.2, 1.6)	-0.1 (-2.0, 1.8)	-0.1 (-2.6, 2.4)
midday	-0.1 (-2.0, 1.8)	-1.1 (-3.6, 1.5)	-0.3 (-2.2, 1.6)	-0.9 (-3.4, 1.7)	0.3 (-1.7, 2.3)	-0.5 (-3.1, 2.1)
afternoon	-3.3 (-5.3, -1.3) ^a	1.3 (-1.5, 4.2)	-3.3 (-5.2, -1.3) ^a	1.2 (-1.7, 4)	-2.7 (-4.8, -0.7) ^a	1.8 (-1.2, 4.7)
evening	-1.4 (-3.3, 0.5)	3.2 (0.7, 5.8)	-1.2 (-3.1, 0.6)	3.6 (0.9, 6.2)	-0.6 (-2.6, 1.3)	3.9 (1.2, 6.6) ^c
mixed	-0.4 (-2.0, 1.2)	0.7 (-1.4, 2.8)	-0.4 (-2.0, 1.2)	0.7 (-1.4, 2.8)	0.6 (-1.2, 2.4)	1.6 (-0.7, 3.8)
<i>P</i> value	0.03	0.06	0.03	0.06	0.04	0.04

Data are expressed as least-squares mean differences (95% CI). Unit in %. Sample size: N=1750 for BL to Y1, N=2003 for Y1 to Y4. Model 1 adjusted for age, sex, race, education, smoking, alcohol consumption, diabetes duration, and medication. Model 2 further adjusted for treatment arm. Model 3 further adjusted for body mass index (BMI), bout-related METs × min/week and average bout intensity.

P values indicate significant differences among groups.

^a indicates that $P_{FDR} < 0.05$ vs. Inactive, Midday and Mixed groups in pairwise post-hoc comparisons.

^b indicates that $P_{FDR} < 0.05$ vs. Inactive, Morning, and Midday groups in pairwise post-hoc comparisons.

^c indicates that $P_{FDR} < 0.05$ vs. Inactive and Midday groups in pairwise post-hoc comparisons.

Supplementary Table 5. Mean changes in HbA1c% from baseline to years 1 and 4 across MVPA timing groups in men and women, separately.

Interaction effect of sex and bMVPA timing group: $P=0.67$				
subgroup analysis by sex:				
	Model 1		Model 2	
	Men			
	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4
Inactive	reference		reference	
Morning	0.05 (-0.18, 0.28)	-0.12 (-0.36, 0.13)	-0.09 (-0.27, 0.1)	0.03 (-0.21, 0.28)
Midday	0.13 (-0.11, 0.37)	0.11 (-0.16, 0.38)	-0.04 (-0.24, 0.16)	-0.16 (-0.4, 0.08)
Afternoon	-0.2 (-0.46, 0.05)	0.13 (-0.15, 0.42)	-0.3 (-0.5, -0.1)	-0.02 (-0.31, 0.27)
Evening	-0.09 (-0.34, 0.16)	0.35 (0.08, 0.62)	-0.02 (-0.2, 0.17)	0.07 (-0.19, 0.33)
Mixed	0.05 (-0.15, 0.26)	0.11 (-0.1, 0.32)	0.01 (-0.16, 0.19)	-0.03 (-0.25, 0.19)
$P\ value^*$	0.34	0.12	0.26	0.08
	Women			
	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4
Inactive	reference		reference	
Morning	0.11 (-0.13, 0.36)	-0.05 (-0.31, 0.21)	-0.03 (-0.23, 0.17)	0.1 (-0.16, 0.36)
Midday	0.18 (-0.07, 0.43)	0.16 (-0.12, 0.44)	-0.01 (-0.22, 0.2)	-0.13 (-0.38, 0.13)
Afternoon	-0.15 (-0.42, 0.11)	0.19 (-0.1, 0.48)	-0.27 (-0.48, -0.06)	0.01 (-0.3, 0.31)
Evening	-0.03 (-0.29, 0.23)	0.4 (0.12, 0.68)	0.02 (-0.18, 0.21)	0.1 (-0.17, 0.37)
Mixed	0.12 (-0.1, 0.34)	0.18 (-0.05, 0.41)	0.1 (-0.1, 0.29)	0.03 (-0.2, 0.26)
$P\ value^*$	0.16	0.99	0.12	0.99

Data are expressed as least-squares mean differences (95% CI). Unit in %. Sample size: N=759 men and N=996 women for BL to Y1; N=891 men and N=1,156 women for Y1 to Y4. Model 1 adjusted for age, treatment arm, race, education, smoking, alcohol consumption, diabetes duration, and medication. Model 2 further adjusted for BMI, bout-related METs \times min/week and average bout intensity. Interaction effect of sex and bMVPA timing group was tested under Model 1 plus sex as fixed effect.

* P-value in stratified analyses was Bonferroni adjusted.

Supplementary Table 6. Mean changes in fasting glucose from baseline to years 1 and year 1 to year 4 across bMVPA timing groups. (N=2,300)

	Model 1		Model 2		Model 3	
	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4
Inactive	<i>reference</i>		<i>reference</i>		<i>reference</i>	
Morning	-5.0 (-11.3, 1.4)	-1.6 (-8.3, 5.2)	-4.9 (-11.3, 1.4)	-1.4 (-8.2, 5.5)	-2.1 (-8.9, 4.6)	1.3 (-5.9, 8.6)
Midday	1.4 (-5.4, 8.1)	-1.2 (-8.3, 5.9)	0.8 (-5.9, 7.6)	-1 (-8.2, 6.1)	3.4 (-3.7, 10.4)	1.2 (-6.3, 8.7)
Afternoon	-6.5 (-13.6, 0.5)	4.8 (-3.3, 12.8)	-6.5 (-13.5, 0.5)	4.3 (-3.8, 12.4)	-4.3 (-11.6, 2.9)	6.9 (-1.5, 15.3)
Evening	-5.4 (-12, 1.2)	7.0 (-0.4, 14.3)	-5.4 (-12.1, 1.2)	7.2 (-0.2, 14.6)	-3.0 (-9.9, 3.9)	9.3 (1.6, 17)
Mixed	0.7 (-5.1, 6.4)	2.9 (-3, 8.8)	0.5 (-5.2, 6.2)	2.8 (-3.1, 8.7)	3.4 (-2.8, 9.7)	5.4 (-1, 11.8)
<i>P value</i>	0.10	0.28	0.13	0.31	0.16	0.14

Data are expressed as mean β -coefficient (95% CI). Unit in mg/dl. Sample size: N=1744 for BL to Y1, N= 2003 for Y1 to Y4. Model 1 adjusted for age, sex, race, education, smoking, alcohol consumption, diabetes duration, and medication. Model 2 further adjusted for treatment arm. Model 3 further adjusted for BMI, bout-related METs \times min/week and average bout intensity. P values indicate significant differences among groups.

Supplementary Table 7. Odds ratio for discontinuation vs. continuation or initiation of glucose-lowering medications in non-insulin users (N_{total}=1,939).

	Initiate/Continue/Discontinue incidence (%)		Model 1		Model 2		Model 3	
	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4
Inactive	15/311/18 (4.4/90.4/5.2)	55/505/13 (9.6/88.1/2.3)	<i>reference</i>		<i>reference</i>		<i>reference</i>	
Morning	4/172/18 (2.1/88.7/9.3)	23/164/11 (11.6/82.8/5.6)	1.77 (1.06, 2.93)	1.17 (0.68, 2.01)	1.61 (0.97, 2.68)	1.14 (0.66, 1.97)	1.28 (0.76, 2.16)	0.88 (0.49, 1.58)
Midday	8/148/11 (4.8/88.6/6.6)	9/155/6 (5.3/91.2/3.5)	1.07 (0.61, 1.88)	1.7 (1.02, 2.82)	1.09 (0.62, 1.9)	1.66 (1, 2.75)	0.88 (0.49, 1.59)	1.33 (0.78, 2.27)
Afternoon	2/127/15 (1.4/88.2/10.4)	17/106/6 (13.2/82.2/4.7)	2.13 (1.29, 3.52) ^a	0.73 (0.42, 1.26)	1.96 (1.18, 3.25)	0.73 (0.42, 1.26)	1.64 (0.97, 2.78)	0.6 (0.34, 1.07)
Evening	3/161/14 (1.7/90.4/7.9)	23/132/6 (14.3/82/3.7)	1.62 (0.99, 2.64)	0.8 (0.48, 1.34)	1.51 (0.92, 2.45)	0.79 (0.47, 1.32)	1.22 (0.73, 2.04)	0.62 (0.36, 1.09)
Mixed	9/260/26 (3.1/88.1/8.8)	27/250/10 (9.4/87.1/3.5)	1.52 (0.95, 2.41)	1.04 (0.68, 1.6)	1.43 (0.9, 2.27)	1.06 (0.68, 1.63)	1.14 (0.69, 1.87)	0.84 (0.52, 1.36)
<i>P value</i>			0.04	0.16	0.13	0.18	0.39	0.16

Data are expressed as OR (95% CI) unless indicated otherwise.

Sample size: N=1,322 for BL to Y1, N=1,518 for Y1 to Y4.

Model 1 adjusted for age, sex, race, education, smoking, alcohol consumption, and diabetes duration. Model 2 further adjusted for treatment arm. Model 3 further adjusted for BMI, bout-related METs × min/week and average bout intensity. P values indicate significant differences among groups.

^a indicates that $P_{FDR} < 0.05$ vs. Inactive group in pairwise post-hoc comparison.

Supplementary Table 8. Odds ratio for discontinuation vs. continuation or initiation of glucose-lowering medications in all participants. (N=2,261)

	Initiate/Continue/Discontinue incidence (%)		Model 1		Model 2		Model 3	
	Year 1	Year 4	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4	BL to Y1	Y1 to Y4
Inactive	19/433/23 (4/91.2/4.8)	63/655/15 (8.6/89.4/2)	<i>reference</i>		<i>reference</i>		<i>reference</i>	
Morning	5/229/20 (2/90.2/7.9)	26/219/11 (10.2/85.5/4.3)	1.76 (1.10, 2.81)	1.13 (0.69, 1.85)	1.60 (1.00, 2.56)	1.09 (0.67, 1.79)	1.30 (0.79, 2.13)	0.86 (0.51, 1.46)
Midday	8/193/11 (3.8/91/5.2)	9/200/9 (4.1/91.7/4.1)	1.06 (0.64, 1.78)	2.02 (1.23, 3.33)	1.07 (0.64, 1.79)	1.96 (1.19, 3.21)	0.89 (0.52, 1.52)	1.62 (0.96, 2.73)
Afternoon	3/172/15 (1.6/90.5/7.9)	17/139/7 (10.4/85.3/4.3)	1.85 (1.15, 2.96)	0.84 (0.49, 1.43)	1.73 (1.07, 2.79)	0.84 (0.49, 1.45)	1.45 (0.88, 2.41)	0.70 (0.40, 1.23)
Evening	3/205/17 (1.3/91.1/7.6)	25/174/6 (12.2/84.9/2.9)	1.73 (1.11, 2.71)	0.80 (0.50, 1.28)	1.61 (1.03, 2.52)	0.77 (0.48, 1.24)	1.34 (0.83, 2.16)	0.62 (0.38, 1.03)
Mixed	10/331/27 (2.7/89.9/7.3)	27/343/12 (7.1/89.8/3.1)	1.47 (0.95, 2.26)	1.15 (0.77, 1.71)	1.36 (0.89, 2.10)	1.14 (0.77, 1.70)	1.10 (0.68, 1.75)	0.92 (0.59, 1.43)
<i>P value</i>			0.04	0.052	0.13	0.06	0.45	0.06

Data are expressed as OR (95% CI) unless indicated otherwise. Sample size: N=1724 for BL to Y1, N=1957 for Y1 to Y4. Model 1 adjusted for age, sex, race, education, smoking, alcohol consumption, and diabetes duration. Model 2 further adjusted for treatment arm. Model 3 further adjusted for BMI, bout-related METs × min/week and average bout intensity. P values indicate significant differences among groups.