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Accelerometer-measured chronoactivity and type 2 diabetes risk: A prospective study in UK Biobank participants

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ABSTRACT

Objective: We assessed whether timing of physical activity, independent from the total activity amount, – which we refer to as chronoactivity – is associated with type 2 diabetes (T2D) risk.
Methods: We included UK Biobank participants with valid accelerometry data (UK, exposure measurement: 2013–2015, follow-up till November 2023) and without diabetes mellitus at baseline (N = 89,439; mean age: 61.7 [SD:7.9] years). Relative hourly physical activity was calculated by dividing the average hourly clock time physical activity by the average hourly physical activity in a week. Participants were categorized into different chronoactivity clusters using k-means cluster analysis on relative hourly physical activity. We used multivariable-adjusted cox-proportional hazard regressions to examine associations between relative hourly physical activity, chronoactivity clusters and T2D, adjusted for potential confounders, including BMI as a potential mediator.
Results: Over 7.8 (interquartile range: 7.2 to 8.3) years of follow-up, 2240 participants developed T2D. Higher relative hourly activity amounts during late morning (8:00–10:59) and late afternoon (15:00–15:59, 17:00–17:59) were associated with approximately 5 %–10 % lower T2D risk. Four clusters of chronoactivity patterns were identified, notably: midday (reference), early morning peak, late morning peak, and evening peak. Compared with participants exhibiting a midday pattern, those with a late morning peak had a lower T2D risk (Hazards Ratio: 0.88, 95 %CI: 0.79, 0.98). Overall, all observations attenuated after additional BMI adjustment.
Conclusions: Independent of the total amount of physical activity, specific timing of physical activity represents an additional dimension in T2D risk.

1. Introduction

The estimated prevalence of adults (20–79 years) living with diabetes worldwide was 537 million in 2021 (Federation, 2025) and over 90 % cases were type 2 diabetes (T2D) (Zheng et al., 2018). Multiple epidemiological studies (Aune et al., 2015; Smith et al., 2016) have reported that increased physical activity (both intensity and duration) plays a crucial role in the prevention and management of T2D, with weight loss mediating part of these observations (Magkos et al., 2020; Carbone et al., 2019). However, these studies largely relied on self-reported physical activity. Physical activity derived from accelerometry, are more accurate, unbiased, and could provide an additional

Abbreviations: MVPA, Moderate-to-vigorous physical activity; T2D, Type 2 diabetes; BMI, Body mass index.

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dimension: physical activity timing.

A study (Sato et al., 2019) performed in mouse models demonstrated that exercise at different times of day can lead to distinct metabolic responses, including alterations in glucose metabolism, lipid oxidation, and amino acid metabolism, which potentially affect glucose homeostasis and insulin sensitivity. Recent epidemiological and interventional studies have addressed the associations of moderate-to-vigorous physical activity (MVPA) timing with glycemic control (Qian et al., 2023; Savikj et al., 2019) and cardiovascular risk (Qian et al., 2021) in patients with diabetes. In addition, the associations between MVPA timing and diabetes-related biomarkers such as insulin resistance, body mass index (BMI), fasting glucose, fasting insulin and hemoglobin A1c (van der Velde et al., 2023; Albalak et al., 2022) have been studied in non-diabetic patients. All these studies provided evidence for a role of the physical activity timing -which we refer to as chronoactivity- in the prevention of T2D. However, to date, few studies (Tian et al., 2023; Xiao et al., 2025) investigated the relationship between chronoactivity and T2D, focusing on relatively broad time windows (morning, afternoon, evening) without considering influence of total physical activity level or using cross-sectional design. Chronoactivity patterns derived from accelerometry data provide precise time windows of peak diurnal physical activity, which we have exploited before and showed that a pattern of peak physical activity in the late morning was associated with a lower risk of coronary artery disease and ischemic stroke in the participants of the UK Biobank (Albalak et al., 2023). In addition, chronotype may impact the optimal timing of physical activity, which is not considered in most studies on this topic (Hower et al., 2018).

We hypothesized that chronoactivity, independent of the total amount of physical activity, plays a role in T2D incidence. To test this hypothesis, we performed a prospective cohort study in which we studied the association between accelerometer-measured relative hourly physical activity, chronoactivity patterns and incident T2D in middle-aged participants free of T2D at baseline.

2. Materials and methods

2.1. Study design and population

The present study was embedded in the UK Biobank, which included over 500,000 participants aged 40–70 years at recruitment (2006–2010) at multiple centers across England, Scotland and Wales. Extensive phenotyping has been performed, and collection of information on many health-related outcomes is still ongoing (Sudlow et al., 2015; Doherty et al., 2017). The UK-Biobank study was approved by the North-West Multi-center Research Ethics Committee. All participants in the UK Biobank provided written informed consent.

Between February 2013 and December 2015, a random group of 103,661 participants were invited to participate in the accelerometer substudy. Accelerometry data was collected between 2.8 and 9.7 years after the baseline assessment, which enabled assessment of hourly physical activity (Doherty et al., 2017). Exclusion criteria for accelerometry data were similar to those used previously (Albalak et al., 2023; Feng et al., 2023): (1) unexpectedly small or large size of the uncompressed dataset returned by the accelerometer device; (2) data from less than 72 h or lack of data for all 1-h periods within a 24-h cycle during the 7-day data collection; (3) data was not well-calibrated; (4) participants' data was recalibrated using the accelerometer record from the same device worn by a different participant; (5) data with a non-zero count of interrupted recording periods; (6) data with more than 768 (Q3 + 1.5 × IQR (interquartile range)) data recording errors; (7) daily mean acceleration adjusted for non-wear time bias was implausibly high (>100 milligravity). In total, 11,067 participants were excluded. Additionally, participants who were diagnosed with T2D before the accelerometer wear period date were excluded (3155; 3.04 %). Finally, 89,439 participants (86.28 %) with valid data were included in the current study (Supplementary Fig. 1).

2.2. Exposure

2.2.1. Assessment of physical activity

Physical activity was assessed at 100 Hz over up to seven days using the Axivity AX3 wrist-worn triaxial accelerometer with a dynamic range of ±8 g (Doherty et al., 2017). Acceleration is presented in milligravity (mg) (1 mg = 0.00981 m/s (Zheng et al., 2018)). Participants were advised to wear the accelerometer device continuously on their dominant wrist and to carry out their normal daily activities.

In the present study, we used hourly means across all measurement days. To investigate the timing effect independent of total physical activity amount, we calculated the relative hourly physical activity levels by dividing the average hourly clock time physical activity by the average hourly physical activity in a week. In addition, to group participants in clusters based on chronoactivity patterns, we used K-means cluster analysis using these 24-hourly relative physical activity levels. K-means cluster analysis is a machine learning technique for grouping data into clusters based on similarities, working by minimizing the variance within clusters while maximizing the differences between them. More details are described in our previous study (Albalak et al., 2023).

2.3. Ascertainment of T2D

T2D was defined using the International Classification of Disease (ICD-10) code E11. Incident T2D was ascertained mainly by the following sources: primary care data, hospital admissions death register and self-reported diagnoses, by a combination of expert consensus from practicing UK clinicians and review of existing literature. Data were collected until November 06, 2023. Detailed information on the ascertainment of T2D is available online at https://biobank.ctsu.ox.ac.uk/showcase/field.cgi?id=130708.

2.4. Covariates

BMI was calculated by dividing the body weight (kilograms) by height (meters) squared. The Townsend deprivation index, an area-based measure of socioeconomic status, was derived from the postal code of residence using the Townsend deprivation score (Townsend et al., 1988). Self-reported questionnaires were used to determine sex (women/men), ethnicity (European/others), smoking status (never/previous/current), alcohol intake frequency (never/less than three times a week/three or more times a week), educational status (College or University degree or above/any other qualification/no qualification), and family history of diabetes. Dietary information including fruit, whole grain, processed meat, red meat and sugar sweetened beverage consumption were estimated though a short food frequency questionnaire. All information described above was collected on average 5.9 years before the accelerometer assessment period. Age (continuous) was calculated in years from the date of birth and the date of wearing the accelerometer. The data on the season of accelerometer wear, chronotype (sleep midpoint<2:30 a.m.(Q1) / 2:30–3:34 a.m.(Q3)/ > 3:34 a.m.) and sleep duration (<7 h per day/7–8 h per day/> 8 h per day) were obtained from the accelerometer data.

2.5. Statistical analyses

We conducted multiple imputation by chained equations (MICE) to handle missing covariates, implemented in the "mice" package (v3.16.0) in R. Descriptive statistics were computed for the whole study population and for each chronoactivity cluster separately. Characteristics of the study population were presented as median (IQR) for continuous data or N. (%) for categorical data.

First, we examined associations between clock time hourly (e.g., 00:00–00:59 etc.) mean relative physical activity level and T2D incidence using Cox-proportional hazard models. In these analyses, we standardized the relative hourly physical activity level to allow

Table 1
Overall and chronoactivity cluster-specific characteristics of participants in the UK Biobank with accelerometry data measured from 2013 to 2015 (n = 89,439).

Characteristic, N(%)	Overall N = 89,439	Midday N = 27,681	Early morning N = 18,614	Late morning N = 23,299	Early evening N = 19,845
Age, years, Median (IQR)	62.8 (55.6, 68.0)	64.6 (58.9, 68.6)	59.4 (53.1, 66.1)	66.3 (61.3, 69.9)	56.9 (51.4, 63.5)
Female sex	51,014 (57)	15,775 (57)	10,394 (56)	13,590 (58)	11,255 (57)
European ethnicity	86,679 (97)	27,078 (98)	17,857 (96)	22,921 (98)	18,823 (95)
BMI, kg/m^2, Median (IQR)	25.9 (23.5, 28.8)	26.1 (23.7, 29.0)	25.9 (23.4, 28.9)	25.9 (23.6, 28.7)	25.6 (23.3, 28.7)
Townsend Deprivation Index, Median (IQR)	−2.5 (−3.8, −0.2)	−2.5 (−3.9, −0.4)	−2.3 (−3.7, 0.1)	−2.7 (−4.0, −0.8)	−2.2 (−3.7, 0.4)
Education level					
Degree or above	39,153 (44)	11,673 (42)	8317 (45)	8648 (37)	10,515 (53)
Any other qualification	43,012 (48)	13,490 (49)	9052 (48)	11,826 (51)	8644 (44)
No qualification	7274 (8)	2518 (9)	1245 (7)	2825 (12)	686 (3)
Smoking status					
Never	51,521 (58)	15,238 (55)	11,125 (60)	13,197 (57)	11,961 (60)
Previous	31,823 (35)	10,274 (37)	6328 (34)	8918 (38)	6303 (32)
Current	6095 (7)	2169 (8)	1161 (6)	1184 (5)	1581 (8)
Alcohol intake frequency					
≥3 times per week	46,170 (51.8)	14,891 (53.8)	8921 (47.9)	12,346 (53.0)	10,012 (50.4)
<3 times per week	42,924 (47.8)	12,705 (45.9)	9611 (51.7)	10,857 (46.6)	9751 (49.2)
Never	345 (0.4)	85 (0.3)	82 (0.4)	96 (0.4)	82 (0.4)
Sleep midpoint, Median (IQR)	3:02 (2:29, 3:34)	3:23 (2:52, 3:55)	2:27(1:59, 2:53)	2:57(2:29, 3:23)	3:13(2:44, 3:44)
Sleep duration, hours, Median (IQR)	7.0 (7.0, 8.0)	7.0 (7.0, 8.0)	7.0 (6.0, 8.0)	7.0 (7.0, 8.0)	7.0 (7.0, 8.0)
Season wearing accelerometer					
Spring	20,232 (23)	6143 (22)	4602 (25)	4922 (21)	4565 (23)
Summer	23,357 (26)	6973 (25)	4666 (25)	5706 (24)	6012 (30)
Autumn	26,737 (30)	8451 (31)	5529 (30)	7159 (31)	5598 (28)
Winter	19,113 (21)	6114 (22)	3817 (21)	5512 (24)	3670 (18)
Diabetes family history	14,207 (16)	4283 (15)	3166 (17)	3436 (15)	3322 (17)
Self-reported diet (weekly)					
Fruit intake (serving), Median (IQR)	21 (14, 28)	20 (13, 28)	21 (14, 28)	21 (14, 28)	20 (13, 28)
Whole grain intake (serving), Median (IQR)	10 (5, 17)	10 (5, 17)	10 (5, 17)	11 (5, 17)	10 (5, 17)
Processed meat frequency (2–4 times)	22,447 (25)	6947 (25)	4643 (25)	5706 (24)	5151 (26)
Red meat frequency (2–4 times)	39,393 (44)	12,741 (46)	7781 (42)	10,596 (45)	8275 (42)
Sugar sweetened beverage (Never)	12,481 (14)	3969 (14)	2581 (14)	3746 (16)	2185 (11)
Total physical activity (milli-gravity), Median (IQR)	27.2 (22.6, 32.6)	26.3 (21.9, 31.5)	28.4 (23.7, 33.9)	26.5 (22.1, 31.9)	28.1 (23.4, 33.5)
T2D incidence	2240 (2.5)	763 (2.8)	477 (2.6)	589 (2.5)	411 (2.1)

Abbreviations: BMI, Body Mass Index; T2D: Type 2 Diabetes; IQR: Interquartile Range.

comparison between the different hours. To account for individual differences in chronotype, we additionally examined the associations by using an hourly time window that was relative to the average sleep midpoint of each individual (e.g., 0–59 min after the sleep midpoint).

For our second analysis, chronoactivity patterns derived from K-means cluster analysis were used as independent variables in multivariable-adjusted Cox-proportional hazards regression models. The cluster representing a midday relative acceleration pattern which best represented the average acceleration of the entire study population (which was also the largest group), was used as reference. For this analysis, we adjusted the regression models for the factors that were considered potential confounders as indicated below. Model 1: sex, age, ethnicity, Townsend deprivation index, education, smoking status, alcohol intake frequency, sleep duration, chronotype, season of accelerometry wear and family history of diabetes. Based on observations done in a previous study (Boonpor et al., 2023), where BMI was found to mediate the effect of physical activity on T2D in UK Biobank participants, we additionally adjusted for BMI in model 2. Results were presented as HR with accompanying 95 % CI. R (version 4.3.2) statistical software was used to perform all statistical analyses (RC, 2025).

3. Results

3.1. Participant characteristics

Participant characteristics are shown in Table 1. A total of 89,439 participants were included of whom 57 % were women. The median (IQR) age of the total population was 62.8 (55.6, 68.0) years at the time of accelerometry data collection. The median BMI of the total group of participants at recruitment to UK Biobank was 25.9 (IQR: 23.5, 28.8) kg/m^2. A total of 14,207 (16 %) participants had a familial history of diabetes. Compared with the other clusters, cluster 3 (late morning peak group) had the lowest education level, and cluster 2 (early morning peak group) had a healthier lifestyle with less smoking, alcohol intake and an earlier midpoint time of sleep. The self-reported diet and sleep duration were generally similar between the clusters.

3.2. Hourly relative physical activity in relation to incident T2D

During a median follow-up of 7.8 years (IQR: 7.2–8.3), 2240 participants (2.5 %) developed T2D. The associations between relative hourly physical activity (by clock time and relative to sleep midpoint) and T2D risk are presented (Fig. 1, supplementary Fig. 2, and supplementary Table 1). Higher relative physical activity during the late evening, night, and early morning (21:00–6:59 and 6 h before until 4 h after sleep midpoint) were associated with higher T2D risk. Being more active in the late evening/before sleeptime (21:00–23:59 and 4–6 h before sleep midpoint) were associated with 5 % ~ 10 % higher T2D risk per 1 SD unit increase in relative activity level. In addition, being active at night and early morning (00:00–6:59 and three hours before until four hours after the sleep midpoint were associated with 9 % ~ 13 % higher T2D risk. In contrast, higher relative physical activity levels during the morning (8:00–10:59 and 6–10 h after sleep midpoint) were associated with 5 % ~ 10 % lower T2D risk. In addition, higher relative physical activity during the afternoon (15:00–15:59, 17:00–17:59 and 13–17 h after sleep midpoint) was also associated with 4 %–7 % lower risk. After adjusting for BMI, the associations between higher physical activity during the day and lower risk of T2D attenuated. Also, although the associations between nighttime activity and T2D risk remained after BMI adjustment, effect sizes attenuated here as well (5 % ~ 9 % higher T2D risk, compared to 9 %–16 % without BMI adjustment; Fig. 1 and Supplementary Table 1).

3.3. Clusters of physical activity and their characteristics

We determined that optimal intra- and inter-cluster variance was reached with four clusters: Standardized physical activity cluster 1 (N = 27,681) (Fig. 2), being the largest sample, represents an 'average midday pattern' of the total study population. Cluster 2 (N = 18,614) represents a group of individuals with a pattern of 'early morning physical activity peak', cluster 3 (N = 23,299) represents a pattern of 'late morning physical activity peak', and cluster 4 (N = 19,845) represents a pattern of 'early evening physical activity peak'. Participant characteristics per cluster are shown in Table 1.

Fig. 3 provides a visual representation of the associations between the clusters of chronoactivity patterns and risk of T2D in the total population. After adjusting for covariates in model 1, participants who were most active in the late morning had a lower T2D risk (HR 0.88; [95 % CI 0.79, 0.98]) compared to the reference group (cluster 1: midday). After additionally adjusting for BMI, the strength of the abovementioned association was attenuated (HR 0.92; [95 % CI 0.82, 1.02]).

4. Discussion

In our prospective cohort study, we observed associations between the physical activity timing and T2D risk, which were independent from the total physical activity amount. Particularly, we observed that being relatively more active during late morning and late afternoon were associated with lower risks of incident T2D, while being relatively more active in the late evening and night were associated with higher T2D risks. These associations were attenuated after adjusting BMI, suggesting a possible mediating effect of BMI. Unexpectedly, chronotype did not affect the observed associations.

A similar research question has been addressed previously using the same data from UK Biobank. In this previous study however, the authors

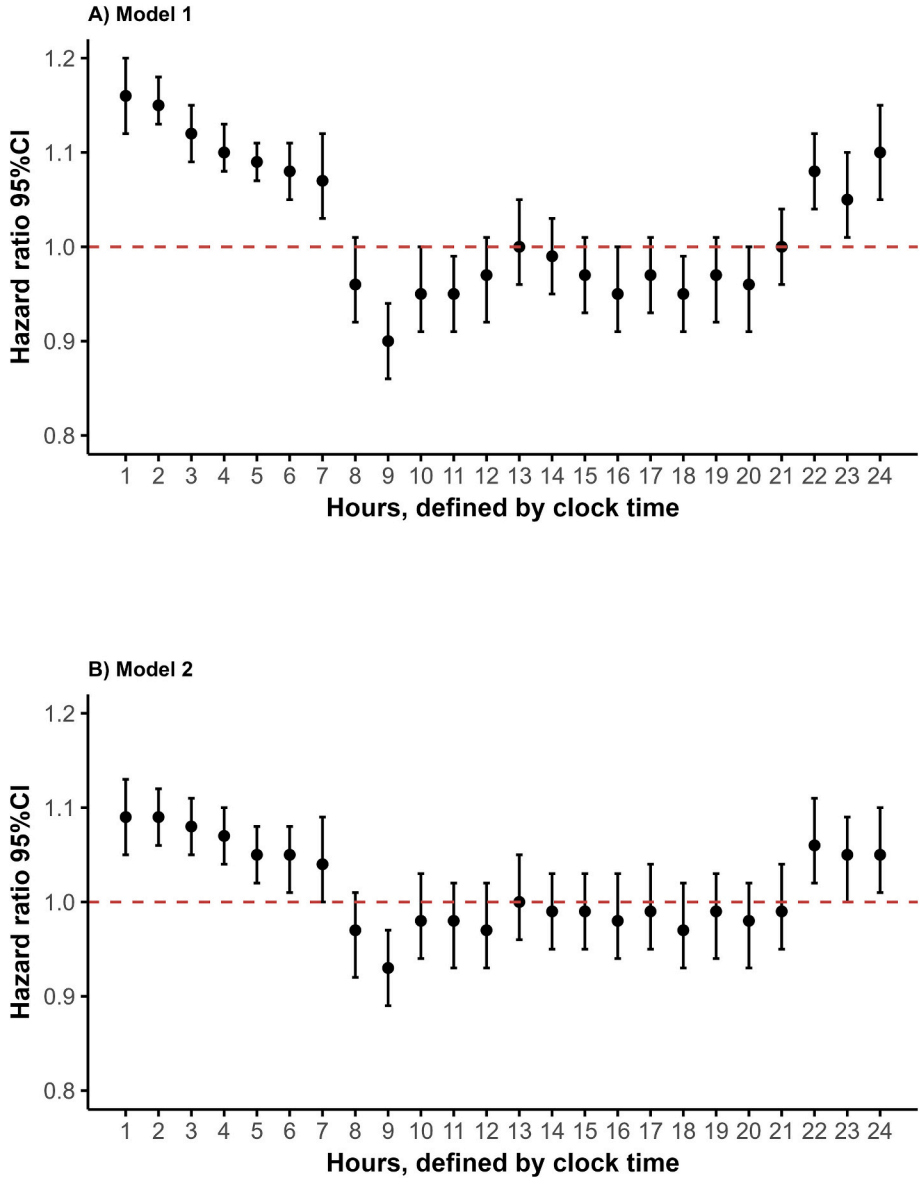

Fig. 1. Associations between relative hourly physical activity and type 2 diabetes risk presented as hazard ratios in the UK Biobank participants with accelerometry data measured from 2013 to 2015 (n = 89,439). Each hourly window was determined by clock time. Model 1 adjusted for sex, age, ethnicity, Townsend deprivation index, education, smoking status, alcohol intake frequency, chronotype, dietary information, sleep duration, season of accelerometry wear and family history of diabetes. Model 2 additionally adjusted baseline BMI. Physical activity was calculated as relative acceleration by dividing the each hourly mean of 24 h by the overall hourly mean (both are according mean of the entire recording period of each participant, and are adjusted for non-wear time bias) and was standardized. Abbreviations: CI: Confidence Interval.

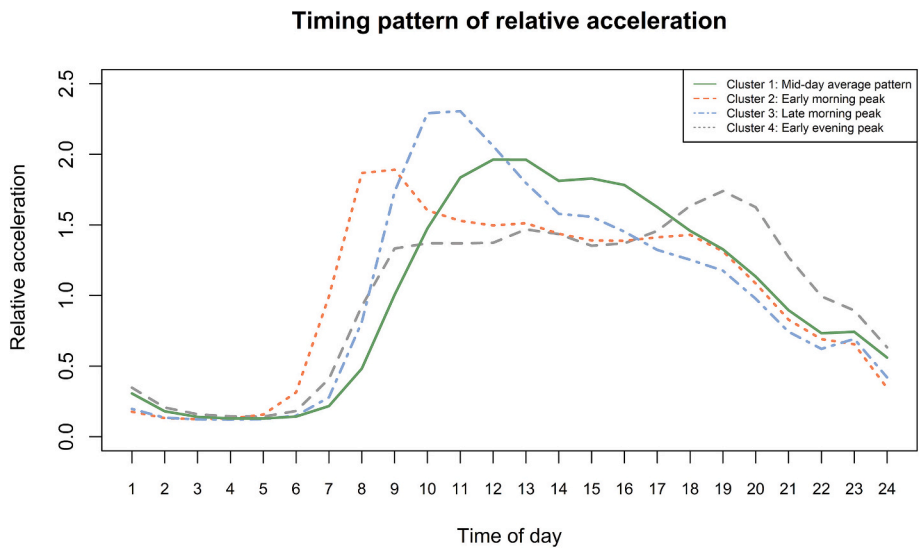

Fig. 2. Clusters patterns of relative acceleration in the UK Biobank participants with accelerometry data measured from 2013 to 2015 (n = 89,439). Mean relative physical activity pattern per cluster. Relative acceleration shown in milligravity (mg). Cluster definitions: cluster 1(N = 27,681), average pattern of acceleration close to the average pattern of the total UK-Biobank population; cluster 2 (N = 18,614), 'early morning peak'; cluster 3 (N = 23,299), 'late morning peak'; cluster 4(N = 19,845), 'early evening peak'.

Group	Cases	Noncases	Model1.HR.95.CI.	Model2.HR.95.CI.
Cluster 1	763	26918	1.00	1.00
Cluster 2	477	18137	1.06 (0.94, 1.20)	1.05 (0.93, 1.19)
Cluster 3	589	22710	0.88 (0.79, 0.98)	0.92 (0.82, 1.02)
Cluster 4	411	19434	0.95 (0.84, 1.08)	0.95 (0.84, 1.08)

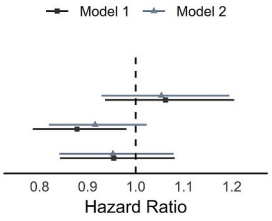

Fig. 3. Associations between physical activity timing and type 2 diabetes risk presented as adjusted hazard ratios for type 2 diabetes associated with each chronoactivity cluster in the UK Biobank participants with accelerometry data measured from 2013 to 2015 (n = 89,439). Model 1 is adjusted for sex, age, ethnicity, Townsend deprivation index, education, smoking status, alcohol intake frequency, chronotype, dietary information, sleep duration, season of accelerometry wear and family history of diabetes. Model 2 additionally adjusted baseline BMI. Cluster definitions: cluster 1(N = 27,681), average pattern of acceleration close to the average pattern of the total UK-Biobank population; cluster 2 (N = 18,614), 'early morning peak'; cluster 3 (N = 23,299), 'late morning peak'; cluster 4(N = 19,845), 'early evening peak'. Abbreviations: HR, Hazard Ratio; CI: Confidence Interval.

used three predefined time windows (morning, afternoon and evening), and did not consider total physical activity (to allow investigating timing-specific effects) and chronotype as covariates and/or effect modifiers. Here, the authors observed that physical activity was associated with lower risk of T2D during all time windows, with only weak evidence for evening physical activity, which likely reflects combined effects of both timing and amount of physical activity on T2D risk. While our results largely align with previous observations, our analyses focused additionally on isolating the effect of physical activity timing by minimizing the influence of physical activity amount. Moreover, we assessed in more detail the exact time windows showing the strongest T2D risk reductions (late morning and late afternoon). Furthermore, we extended this work by considering the individual chronotypes in combination with a data-driven approach to cluster participants into four chronoactivity patterns (midday, early morning peak, late morning peak and evening peak). Also, we recently published a study addressing a similar research question using cross-sectional data on glycemic measures from the National Health and Nutrition Examination Survey (2011–2014), and found similar trends as in the present study on incident T2D in UK Biobank. Therefore, our study further advances the understanding of the relationship between physical activity timing per se and T2D risk.

Studies on this research topic mainly focus on glycemic measures, and most of them showed a more beneficial effect of physical activity during the morning or afternoon. One epidemiological study (Albalak et al., 2022) observed that people with higher physical activity levels in the morning had lower fasting glucose, fasting insulin, and HOMA-IR. An intervention study (Teo et al., 2020) found that both morning and late afternoon (17:00–19:00) exercise improved glycemic control and postprandial glycemic responses. In contrast, several other studies (Qian et al., 2023; Savikj et al., 2019; van der Velde et al., 2023; Kerr et al., 2024) only found a beneficial effect of afternoon physical activity on glycemic control or glycemic markers. The results from different studies are somewhat heterogenous, which may be caused by limited sample size or differences in sample populations. However, together with the data from our study, these results do suggest that the physical activity timing can be an additional dimension through which the T2D risk can be modified. The potential role of physical activity timing in cardiometabolic risk modification is also supported by experimental work in mice using different physical activity timing interventions (Sato et al., 2019; Pendergrast et al., 2023). Various physiological processes display circadian rhythmicity including processes implicated in glucose metabolism and insulin sensitivity (Panda, 2016). Given that physical activity is well established to improve insulin sensitivity (Bird and Hawley, 2016), alignment of physical activity with circadian rhythms could further optimize metabolic outcomes (Peña Carrillo et al., 2024) and result in a larger decrease in T2D risk.

When we additionally adjusted for BMI, the associations between daytime physical activity patterns and T2D attenuated. These results are in line with previous studies showing that BMI may be mediating the

effect of total physical activity on T2D risk (Magkos et al., 2020; Carbone et al., 2019). However, we were unable to formally test for mediation because the BMI assessment was done some years before the data collection of the accelerometers and thus before the start of our follow-up.

Being relatively more active during the late evening and night was associated with higher T2D risk. Overall, research focused on activity during the late evening and night is scarce, and only one study (Albalak et al., 2022) showed that being active during the night was associated with higher BMI, which supports the findings from our study along with studies demonstrating unfavorable metabolic effects of nighttime eating which is often associated with nighttime activity (Hood et al., 2014; Gill and Panda, 2015). In addition, nighttime shift work has been established as a risk factor for developing T2D (Shan et al., 2018; Vetter et al., 2018). Furthermore, higher sleep fragmentation, and irregular sleep timing, possibly underlying a higher amount of physical activity during the night period, has been associated with T2D (Ogilvie and Patel, 2018; Rutters and Nefs, 2022; Reutrakul and Van Cauter, 2018; Antza et al., 2021). We therefore hypothesize that nighttime eating, lack of sleep or disrupted sleep during the night (Liu et al., 2022), or the effects of circadian disruption through shift work, are potential explanations for the higher T2D risk observed for relatively higher activity during the night period, rather than the level of night-time exercise-associated physical activity.

To consider individual differences in chronotype, we additionally examined the associations between relative hourly physical activity (relative to sleep midpoint) and T2D, we found for people who sleep early or late, being relatively more active during wake periods is linked to lower T2D risk, while being relatively more active during a few hours before sleep and sleep window is linked to higher T2D risk.

There are a number of strengths and limitations of the current study. Strengths include the prospective cohort design, large sample size, in combination with the accelerometer-measured physical activity measures in the UK Biobank. Furthermore, some limitations need to be mentioned when interpreting the study results. Firstly, some variables used as potential confounding factors, including BMI as potential mediator, were assessed some years before the exposure measurement and thus before initiation of the follow-up. As a result, the potential mediating effect of BMI cannot be formally tested, and the results could be confounded by prospective changes of the variables, despite the relative stability of key covariates over time. Secondly, despite selection bias in the UK Biobank, its large sample and diverse exposure measures enable valid inferences on exposure-health associations applicable to other populations (Fry et al., 2017). In addition, given the observational nature of the study, there still may be residual confounding. Given these limitations, we should be cautious to interpret the present results as being causal and more studies including intervention studies are required to further provide evidence supporting causality. Additionally, large-scale studies investigating the underlying mechanisms through genetic and molecular approaches, as well as exploring the determinants and causes of physical activity timing are warranted.

In conclusion, our study showed that independent of the total amount of physical activity, specific timing of physical activity seems to associate with different T2D risks. This indicates a possible role of physical activity timing as an additional dimension to be considered for the prevention of T2D.

CRediT authorship contribution statement

Qiuyu Feng: Writing – original draft, Formal analysis. **Gali Albalak:** Writing – review & editing, Methodology. **Ko Willems van Dijk:** Writing – review & editing, Supervision. **Jeroen H.P.M. van der Velde:** Writing – review & editing. **Qian Xiao:** Writing – review & editing. **Raymond Noordam:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Diana van Heemst:** Writing – review & editing, Supervision.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2025.108312.

Data availability

UK Biobank data are available through a procedure described at http://www.ukbiobank.ac.uk/using-the-resource/.

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