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Dose–Response Associations of Intermittent Lifestyle Physical Activity Micropatterns and Incident Type 2 Diabetes

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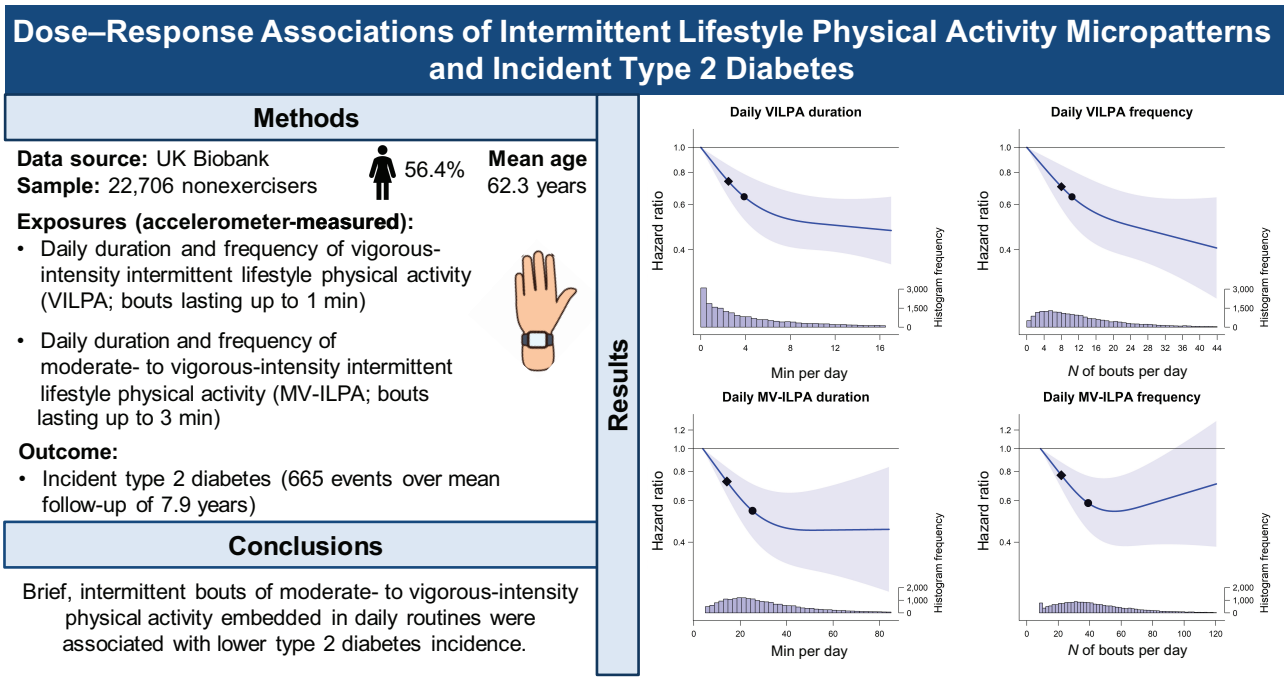

ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  Intermittent lifestyle physical activity micropatterns have demonstrated beneficial associations with various health outcomes, but their association with incident type 2 diabetes is unknown.

- **What is the specific question(s) we wanted to answer?**
  Are daily duration and frequency of vigorous intermittent lifestyle physical activity (VILPA) and its moderate- to vigorous-intensity equivalent (MV-ILPA) associated with lower incidence of type 2 diabetes?

- **What did we find?**
  Both daily duration and frequency of VILPA and MV-ILPA were inversely associated with incident type 2 diabetes in a dose–response manner.

- **What are the implications of our findings?**
  Our results support integrating brief, regular bursts of higher-intensity incidental physical activity into daily routines as a promising strategy for preventing type 2 diabetes.

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ORIGINAL ARTICLE

OBJECTIVE

To examine dose–response associations of vigorous intermittent lifestyle physical activity (VILPA; bouts ≤1 min) and its moderate- to vigorous-intensity equivalent (MV-ILPA; bouts ≤3 min) with incident type 2 diabetes.

RESEARCH DESIGN AND METHODS

Prospective data from UK Biobank accelerometry substudy participants who reported no leisure-time exercise and had no type 2 diabetes at baseline were analyzed. Daily duration and frequency of VILPA and MV-ILPA were derived from wrist-worn accelerometers. Incident type 2 diabetes was ascertained through linked primary care, hospital, and death records. Dose–response associations were examined using multivariable-adjusted Fine-Gray subdistribution hazard models accounting for competing risks.

RESULTS

Among 22,706 participants (mean age 62.3 years; 56.4% female), 665 developed type 2 diabetes over an average follow-up of 7.9 years. Daily durations of VILPA and MV-ILPA showed inverse, nonlinear L-shaped associations with incident type 2 diabetes. Median durations of 3.9 min/day of VILPA and 25.3 min/day of MV-ILPA were associated with 36% and 46% lower risks of type 2 diabetes, respectively, compared with no VILPA or 3.9 min/day of MV-ILPA. Daily VILPA frequency showed a near-linear inverse association, with 10.4 bouts/day (median) corresponding to a hazard ratio (HR) of 0.64 (95% CI 0.51–0.81) compared with 0 bouts/day. Daily MV-ILPA frequency showed a U-shaped pattern, with risk reductions plateauing at approximately 56 bouts/day (HR 0.54; 95% CI 0.39–0.76).

CONCLUSIONS

Among adults who do not engage in leisure-time exercise, accruing brief, intermittent bouts of moderate- to vigorous-intensity physical activity during day-to-day routines may be a promising strategy for prevention of type 2 diabetes.

Type 2 diabetes is a global public health concern, with its prevalence projected to increase from 5.9% in 2021 to 9.5% in 2050, affecting more than 1.27 billion people worldwide (1). Physical inactivity is a well-recognized modifiable risk factor, contributing at least 7.4% of global disability-adjusted life-years (DALYs) attributable to type 2 diabetes in 2021 (1). Increasing regular physical activity, especially of moderate to vigorous intensity, is therefore widely recommended as a first-line strategy for type 2 diabetes prevention (2,3).

Compared with other forms of physical activity, structured (leisure-time) exercise has long been regarded as the key behavioral strategy for preventing and managing type 2 diabetes (4,5). Despite its well-documented efficacy, evidence of long-term health effects is limited, largely because of persistently low adherence in real-world settings (6). This reality supports the need to shift from an emphasis on exercise (which is planned and structured) toward a more holistic approach to physical activity promotion that better reflects real-world behavior. In this context, incidental physical activity, defined as an unstructured, unplanned activity of daily living performed as a by-product of an action with a different primary purpose (e.g., walking to the bus stop, gardening, or carrying groceries/goods) (7), may offer a practical alternative for the majority of the adult population (>85%) (8,9) who do not engage in exercise regularly. This approach has strong potential to increase overall physical activity levels by leveraging behaviors that already make up the majority of daily movement. This is supported by a global survey showing that 88% of daily moderate- to vigorous-intensity physical activity is accumulated through activities undertaken in the work, household, and travel domains (10).

Most evidence to date of the beneficial health associations of physical activity has been derived from questionnaire-based data that typically capture only activity accrued through longer bouts (e.g., ≥10 min) and performed during leisure time (11). Recent advances in wearable technology and machine learning methods have enabled a more granular examination of physical activity micropatterns, such as activity accrued through brief and sporadic bursts of incidental activity occurring throughout the day (12,13). Specifically, a series of wearable-based studies using UK Biobank and National Health and Nutrition Examination Survey data have demonstrated steep beneficial health associations of vigorous intermittent lifestyle (i.e., incidental) physical activity (VILPA; bouts lasting no more than 1 min) (12,14–16) and its moderate- to vigorous-intensity equivalent (MV-ILPA; bouts lasting no more than 3 min) (13). For example, accumulating 4.4 min/day or 3.0 bouts/day of VILPA was associated with 27% or 39% lower risk of all-cause mortality, respectively, compared with no VILPA (12). Similarly, all-cause mortality risk was 34% lower among individuals who accumulated MV-ILPA in bouts lasting 1 to <3 min when compared with bouts <1 min (13). However, micropattern-accrued physical activity has not been examined in relation to incident type 2 diabetes. Addressing this gap could help inform future clinical and public health guidelines by determining whether brief, incidental bursts of higher-intensity activity offer a practical and accessible strategy for preventing type 2 diabetes, particularly for individuals who are unable or unwilling to engage in leisure-time exercise.

The aim of this study was to examine the dose–response associations of daily duration and frequency of VILPA and MV-ILPA with incident type 2 diabetes in a large cohort of U.K. adults.

RESEARCH DESIGN AND METHODS

Study Design and Participants

Data were drawn from the UK Biobank, a prospective population-based cohort of adults aged 40 to 69 years in the U.K. Detailed descriptions of the study design and methods have been published elsewhere (17). Briefly, participants were recruited via postal invitations and attended baseline assessments between 2006 and 2010. Additionally, between June 2013 and December 2015, a subsample of 103,684 participants were mailed an Axivity AX3 accelerometer (Newcastle Upon Tyne, U.K.) and instructed to wear it on their dominant wrist for 7 consecutive days (24 h/day) to measure physical activity (18). The UK Biobank received ethical approval from the National Research Ethics Service of the U.K. National Health Service (11/NW/0382), and all participants provided written informed consent.

For the current study, we included participants with valid accelerometry data (≥16 h/day of wear time) for at least 3 days, including at least 1 weekend day. As previously described (12,13,15), nonexerciser status of participants was defined by excluding those who reported engaging in leisure-time exercise or recreational walking more than once a week at baseline (relevant questions reported Supplementary Table 1). We further excluded participants who reported an inability to walk, had prevalent type 2 diabetes or were receiving exogenous insulin therapy (ascertained from self-reports, primary care records, or hospital records) at or before accelerometry assessment, or had missing covariate data. To minimize reverse causation bias, participants who registered an event within the first 2 years of follow-up were excluded. The participant selection process is summarized in Supplementary Fig. 1.

Physical Activity Assessment and Processing

Before mailing, all AX3 accelerometers were initialized to collect data at a sampling frequency of 100 Hz with a dynamic range of ±8 *g* (18). In this study, raw data files were calibrated, and nonwear time was identified using standard procedures (19,20). Physical activity was classified using a validated two-stage machine learning–based random forest activity classifier (84.6% accuracy across all four intensities) (21), as detailed in the Supplementary Methods. Briefly, each 10-s window was first classified into one of four activity classes (sedentary, standing utilitarian movement, walking, or running/high-energy activity), which were then assigned to one of four intensity levels: sedentary (≤1.5 metabolic equivalents [METs]), light (1.6 to <3 METs), moderate (3 to <6 METs), or vigorous (≥6 METs).

In this study, we defined VILPA as that accumulated in bouts lasting no more than 1 min and MV-ILPA as that accumulated in bouts lasting no more than 3 min. The bout length selection was informed by *1*) laboratory data, where the average time to elicit VILPA was 76.7 [SD 6.8] s based on physiological responses (i.e., percentage of VO_{2max} measured by indirect calorimetry and percentage of maximal heart rate) and perceived exertion (22), and *2*) naturally occurring bout lengths observed in the UK Biobank sample, where 89.1% of incidental vigorous-intensity (15) and 87.2% of incidental moderate- to vigorous-intensity activities (13) were accrued in bouts lasting no more than 1 and 3 min, respectively.

Type 2 Diabetes Ascertainment

The primary outcome of this study was incident type 2 diabetes, ascertained from multiple data sources (i.e., primary care records, hospital inpatient records, and death registries) using Read Code versions 2 and 3 for primary care records and the ICD-10 E11 code for hospital and death records (Supplementary Table 2). Participants were observed through 30 November 2022, with deaths obtained

via linkage with the National Health Service Digital of England and Wales or the National Health Service Central Register and National Records of Scotland. Inpatient hospitalization data were obtained from the Hospital Episode Statistics for England, the Patient Episode Database for Wales, or the Scottish Morbidity Record for Scotland. Follow-up time was calculated as the time in years from accelerometry assessment to the first diagnosis of type 2 diabetes, death, or censoring, whichever occurred first.

Potential Confounders

Potential confounders were selected based on prior knowledge of variables associated with exposures and outcomes and previous analog analyses using UK Biobank data (23–25). Specifically, we adjusted for demographic characteristics (age, sex, ethnicity, and education level), health-related behaviors (smoking status, alcohol consumption, fruit and vegetable consumption, discretionary screen time, and accelerometer-estimated sleep duration), medical history (use of cholesterol- or blood pressure–lowering medication, previous diagnosis of cancer, or cardiovascular disease [CVD]), and familial/genetic risk (parental history of cancer, CVD, or type 2 diabetes), all of which may influence physical activity and diabetes risk through behavioral, metabolic, or socioeconomic pathways (24,25). In addition, models were adjusted for physical activity energy expenditure volume from nonexposure physical activity components to account for confounding by physical activity performed at intensities other than VILPA or MV-ILPA. For example, analyses with VILPA duration or frequency as the main exposure were adjusted for physical activity energy expenditure estimated from any light- or moderate-intensity activity and from vigorous-intensity activity in bouts lasting >1 min. This ensured that the observed associations reflected the independent contributions of VILPA/MV-ILPA rather than overall physical activity volume (21). Complete covariate definitions are listed in Supplementary Table 3.

Statistical Analysis

Participant characteristics were summarized by tertiles of daily MV-ILPA duration using means and SDs or medians and interquartile ranges for continuous variables and counts and percentages for categorical variables. To minimize the influence of sparse data and outliers, the upper ranges of VILPA and MV-ILPA values were winsorized at the 97.5th percentile, and the lower range of MV-ILPA values were winsorized at the 2.5th percentile (12,14, 15). We estimated the dose–response absolute risk between daily VILPA/MV-ILP+A duration and frequency with incident type 2 diabetes (expressed as events per 10,000 person-years) using Poisson regression (14). Consistent with previous analogous analyses (13,14), we applied restricted cubic splines to demonstrate the dose–response curves, with knots placed at the 10th, 50th, and 90th percentiles of the exposures (26). We assessed time-to-event associations of daily VILPA/MV-ILPA duration and frequency with incident type 2 diabetes using Fine-Gray subdistribution hazards models to account for competing risks from deaths from non–type 2 diabetes causes (e.g., cancer, CVD, or respiratory disease) that precluded the occurrence of the primary outcome (27). Departure from linearity was assessed with a Wald test. Proportional hazards assumptions were tested using Schoenfeld residuals in the models, and no violations were observed (all $P > 0.05$). We calculated the minimum effective dose (ED_{50}) (28), defined as the daily VILPA/MV-ILPA duration and frequency associated with 50% of the optimal risk reduction, and reported the corresponding point estimates (hazard ratios [HRs] and 95% CIs) for median daily duration and frequency of VILPA/MV-ILPA. In all analyses, the minimum data point of the exposure was used as the reference (VILPA 0 min/day and 0 bouts/day; MV-ILPA 3.9 min/day and 8.7 bouts/day).

We calculated E values to assess the plausibility of bias from unmeasured confounding (29). To ensure the robustness of our findings, several sensitivity analyses were performed. We repeated main analyses with additional adjustment for cardiometabolic biomarkers that may be potential mediators: BMI, waist circumference, LDL, HDL, triglycerides, and systolic and diastolic blood pressure. To further reduce the possibility of reverse causation bias, we excluded participants who were underweight (BMI <18.5 kg/m^2), reported poor self-rated health, or had a frailty index ≥3 (on a 0–5 scale) at baseline and those who had prevalent cancer or CVD (24,25). We also tested the influence of analytical decisions by repeating the main analyses using the 25th percentile of the exposure distribution (VILPA 1.3 min/day and 5.4 bouts/day; MV-ILPA 15.3 min/day and 25.6 bouts/day) as the referent and by applying an alternative spline specification, with knots at the 10th, 33rd, and 67th percentiles to account for potential data skewness. Finally, considering prior evidence of sex differences in the health associations of VILPA with CVD (15), we investigated potential effect modification by sex and conducted sex-stratified analyses of VILPA and MV-ILPA with incident type 2 diabetes.

All analyses were performed in R (version 4.5.1) using the rms (version 8.0-0) and survival (version 3.8.3) packages. This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplementary Table 4).

Data and Resource Availability

UK Biobank data were obtained under application 25813. UK Biobank data are available to researchers with an approved request (https://www.ukbiobank.ac.uk/register-apply/).

RESULTS

Participant Characteristics

The final analytical sample comprised 22,706 nonexercising adults (mean age 62.3 [SD 7.6] years; 56.4% female), with 665 incident type 2 diabetes cases occurring over an average follow-up period of 7.9 (SD 1.0) years. The sample was predominantly White (99.1%), with 37% having a college or university degree, 55.7% having never smoked, and 59.3% reporting alcohol consumption within current U.K. guidelines (≤14 units/week). Daily median (interquartile range) duration and frequency were 3.9 (1.5–8.9) min/day and 10.4 (5.4–17.9) bouts/day for VILPA and 25.3 (15.3–40.8) min/day and 39.0 (25.6–57.4) bouts/day for MV-ILPA, respectively. Participant characteristics by tertile of daily MV-ILPA duration are listed in Table 1.

Dose–Response Association of VILPA and Type 2 Diabetes Incidence

The multivariable-adjusted models of absolute risk (Supplementary Fig. 2*A*) and relative HRs (Fig. 1*A*) showed that daily VILPA duration was associated with lower type 2 diabetes risk in an L-shaped manner. The median daily VILPA duration (3.9 min/day) was associated with an absolute risk of

Table 1—Participant characteristics by tertile of daily MV-ILPA duration

	Tertile, min/day			
	3.8–18.4	18.4–34.4	>34.4	Full sample
Sample size, *n*	7,561	7,562	7,583	22,706
Follow-up, mean (SD), years	7.8 (1.2)	7.9 (1.0)	8.0 (0.9)	7.9 (1.0)
Age, mean (SD), years	63.9 (7.4)	62.1 (7.6)	60.8 (7.6)	62.3 (7.6)
Male sex	3,213 (42.5)	3,298 (43.6)	3,397 (44.8)	9,908 (43.6)
Non-White ethnicity	67 (0.9)	66 (0.9)	57 (0.8)	190 (0.9)
Education level				
College or university degree	2,890 (38.2)	2,950 (39.0)	2,708 (35.7)	8,548 (37.6)
A/AS level	1,013 (13.4)	905 (12.0)	948 (12.5)	2,866 (12.6)
General certificate of secondary education	1,604 (21.2)	1,693 (22.4)	1,754 (23.1)	5,051 (22.2)
Certificate of secondary education	320 (4.2)	331 (4.4)	499 (6.6)	1,150 (5.1)
National Vocational Qualifications, Higher National Diploma, or Higher National Certificate	464 (6.1)	480 (6.3)	482 (6.4)	1,426 (6.3)
Other	1,270 (16.8)	1,203 (15.9)	1,192 (15.7)	3,665 (16.1)
Smoking status				
Current	816 (10.8)	644 (8.5)	604 (8.0)	2,064 (9.1)
Never	4,038 (53.4)	4,264 (56.4)	4,349 (57.4)	12,651 (55.7)
Previous	2,707 (35.8)	2,654 (35.1)	2,630 (34.7)	7,991 (35.2)
Alcohol consumption*				
Never	304 (4.0)	279 (3.7)	268 (3.5)	851 (3.7)
Former	258 (3.4)	252 (3.3)	234 (3.1)	744 (3.3)
Within guidelines	4,497 (59.5)	4,503 (59.5)	4,475 (59.0)	13,475 (59.3)
Above guidelines	2,502 (33.1)	2,528 (33.4)	2,606 (34.4)	7,636 (33.6)
Fruit and vegetable consumption, mean (SD), servings/day	7.4 (4.3)	7.3 (4.1)	7.5 (4.2)	7.4 (4.2)
Medication				
Cholesterol lowering	1,430 (18.9)	1,134 (15.0)	866 (11.4)	3,430 (15.1)
Blood pressure lowering	1,824 (24.1)	1,403 (18.6)	1,097 (14.5)	4,324 (19.0)
Prevalent cancer	689 (9.1)	604 (8.0)	487 (6.4)	1,780 (7.8)
Prevalent CVD	1,121 (14.8)	881 (11.7)	683 (9.0)	2,685 (11.8)
Parental history of cancer	2,671 (35.3)	2,594 (34.3)	2,348 (31.0)	7,613 (33.5)
Parental history of CVD	4,515 (59.7)	4,419 (58.4)	4,181 (55.1)	13,115 (57.8)
Parental history of type 2 diabetes	1,277 (16.9)	1,271 (16.8)	1,288 (17.0)	3,836 (16.9)
BMI, mean (SD), kg/m^2	28.4 (5.2)	27.3 (4.7)	26.5 (4.4)	27.4 (4.8)
Waist circumference, mean (SD), cm	92.9 (13.9)	90.1 (13.2)	88.0 (12.6)	90.3 (13.4)
Biomarkers				
HDL, mmol/L	1.4 (0.4)	1.4 (0.4)	1.5 (0.4)	1.4 (0.4)
LDL, mmol/L	3.6 (0.9)	3.6 (0.8)	3.6 (0.8)	3.6 (0.9)
Triglycerides, mmol/L	1.8 (1.0)	1.8 (1.0)	1.7 (1.0)	1.8 (1.0)
Systolic blood pressure, mmHg	141.2 (19.6)	138.8 (18.8)	138.1 (18.8)	139.4 (19.1)
Diastolic blood pressure, mmHg	83.2 (10.7)	82.3 (10.6)	81.9 (10.5)	82.5 (10.6)
Poor self-rated health	434 (5.7)	286 (3.8)	218 (2.9)	938 (4.1)
High frailty index†	441 (6.2)	242 (3.4)	210 (2.9)	893 (4.2)
Discretionary screen time, h/day	4.0 (3.0–5.5)	4.0 (2.5–5.0)	3.5 (2.5–5.0)	4.0 (2.5–5.0)
Sleep duration, min/day	441.0 (396.8–480.9)	439.1 (397.6–475.9)	437.3 (397.7–473.3)	439.1 (397.4–476.5)
Sedentary behavior, min/day	696.6 (647.3–749.6)	656.0 (606.8–706.1)	598.4 (544.9–649.9)	651.5 (593.4–710.2)
Physical activity, min/day				
Light intensity	68.7 (49.7–99.3)	90.9 (62.8–132.8)	128.2 (82.9–179.4)	91.4 (61.1–140.1)
Moderate intensity	10.3 (6.7–13.7)	23.0 (19.1–27.7)	46.4 (36.7–63.6)	23.3 (13.5–38.2)
Vigorous intensity	1.4 (0.5–3.5)	4.2 (1.9–9.0)	8.5 (3.6–18.1)	3.9 (1.3–9.6)

Continued on p. 1090

Table 1—Continued

	Tertile, min/day			
	3.8–18.4	18.4–34.4	>34.4	Full sample
VILPA	1.4 (0.5–3.2)	4.0 (1.8–8.0)	7.8 (3.5–15.4)	3.9 (1.5–8.9)
MV-ILPA	11.8 (8.0–15.2)	25.3 (21.7–29.5)	49.7 (40.8–66.6)	25.3 (15.3–40.8)
Physical activity, bouts/day				
VILPA	4.9 (2.6–8.1)	10.9 (7.0–15.9)	19.2 (12.5–28.3)	10.4 (5.4–17.9)
MV-ILPA	20.9 (14.9–26.7)	39.3 (33.9–45.6)	67.0 (55.9–84.6)	39.0 (25.6–57.4)
Physical activity energy expenditure, kJ/kg/day				
Light intensity	6.5 (4.8–8.9)	9.1 (6.7–12.3)	13.4 (9.4–17.4)	9.1 (6.4–13.3)
Moderate intensity	1.8 (1.2–2.4)	4.1 (3.4–5.0)	8.5 (6.6–11.6)	4.2 (2.4–7.0)
Vigorous intensity	0.4 (0.2–0.8)	1.1 (0.6–1.9)	2.1 (1.1–3.6)	1.0 (0.4–2.1)
Type 2 diabetes incidence	309 (4.1)	202 (2.7)	154 (2.0)	665 (2.9)

MV-ILPA, moderate-to-vigorous intermittent lifestyle physical activity; VILPA, vigorous intermittent lifestyle physical activity. Data are given as *n* (%) or median (interquartile range) unless otherwise indicated. *Defined based on U.K. guidelines of ≤14 units of alcohol per week (1 unit = 8 g of pure ethanol). †Frailty index of ≥3 (on 0–5 scale).

15.2 (95% CI 11.7–19.7) per 10,000 person-years (Supplementary Fig. 2*A*). Compared with the minimum referent data point (0 min/day), we observed a nonlinear dose–response association (nonlinear P = 0.007) between daily VILPA duration and incident type 2 diabetes, with the curve plateauing at approximately 8.0 min/day (HR 0.52; 95% CI 0.41–0.67) (Fig. 1*A*). The ED_{50} of VILPA duration was 2.5 min/day, corresponding to an HR of 0.73 (95% CI 0.64–0.85). The median daily VILPA duration was associated with an HR of 0.64 (95% CI 0.52–0.79).

Daily VILPA frequency showed a more linear dose–response association with incident type 2 diabetes compared with the association of daily duration. The median daily VILPA frequency (10.4 bouts/day) was associated with an absolute risk of 15.9 (95% CI 12.4–20.5) per 10,000 person-years (Supplementary Fig. 2*B*). Compared with the minimum referent data point (0 bouts/day), there was a near-linear dose–response association (nonlinear P = 0.060) with lower incident type 2 diabetes (Fig. 1*B*). The ED_{50} of daily VILPA frequency was 8.0 bouts/day (HR 0.70; 95% CI 0.58–0.85), and the median daily frequency was associated with an HR of 0.64 (95% CI 0.51–0.81).

Dose–Response Association of MV-ILPA and Type 2 Diabetes Incidence

Daily MV-ILPA duration showed a similar dose–response pattern to VILPA duration, but with a steeper slope. The median daily MV-ILPA duration (25.3 min/day) was

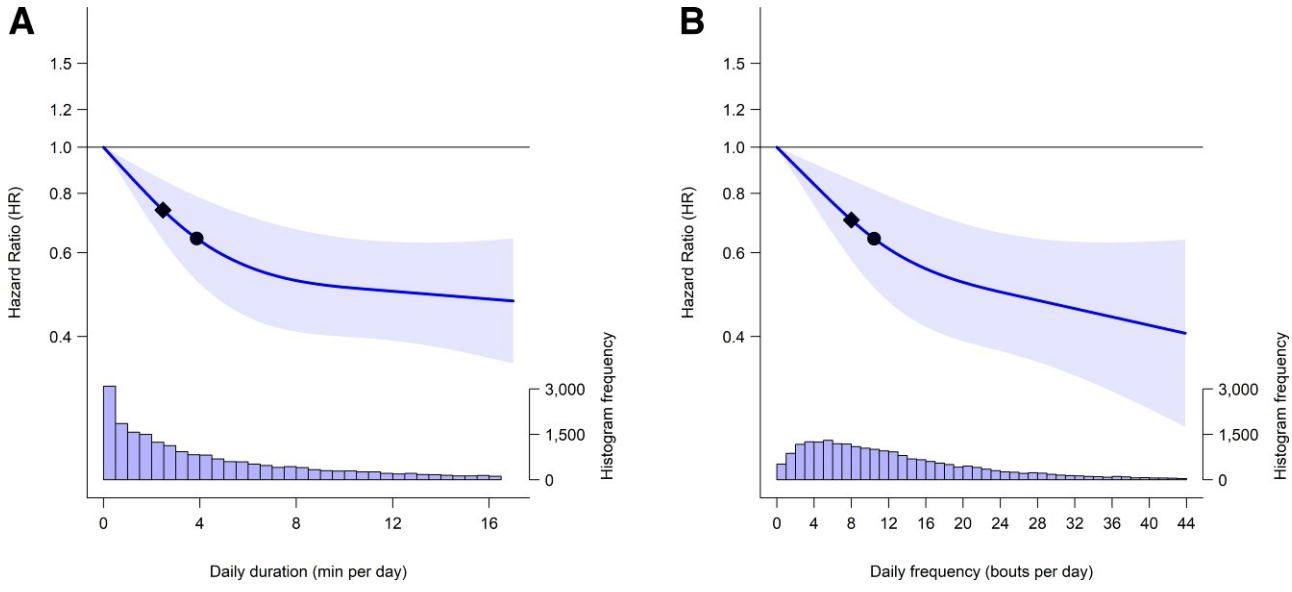

Figure 1—Multivariable-adjusted dose–response curves of daily VILPA duration and frequency with incident type 2 diabetes (n = 22,706; n of events = 665). Lines represent HRs and shaded areas represent 95% CIs associated with increasing daily duration (*A*) and frequency (*B*) of VILPA. Diamonds indicate minimal VILPA duration/frequency dose (as indicated by ED_{50} statistics) associated with 50% of optimal risk reduction, and circles indicate HRs associated with median duration/frequency of VILPA. Histograms show sample distribution. Model was adjusted for sex, age, education level, ethnicity, fruit and vegetable consumption, smoking status, alcohol consumption, sleep duration, discretionary screen time, medication use (cholesterol and blood pressure lowering), prevalent cancer, prevalent CVD, parental history of cancer, CVD, or type 2 diabetes, and physical activity energy expenditure volume of nonexposure physical activity components (light-, moderate-, and vigorous-intensity incidental physical activity [excluding VILPA]). Reference points were the minimum data points of VILPA duration (0 min/day) and frequency (0 bouts/day).

associated with an absolute risk of 15.2 (95% CI 11.8–19.6) per 10,000 person-years (Supplementary Fig. 3*A*). Compared with the minimal referent data point (3.9 min/day), daily MV-IPA duration was nonlinearly associated with incident type 2 diabetes (nonlinear $P = 0.003$), with the curve plateauing at approximately 40 min/day (HR 0.46; 95% CI 0.32–0.65) (Fig. 2*A*). The ED_{50} of MV-ILPA duration was 14.2 min/day, corresponding to an HR of 0.73 (95% CI 0.63–0.83). The median daily MV-ILPA duration was associated with an HR of 0.54 (95% CI 0.42–0.71).

For daily MV-ILPA frequency, both absolute (Supplementary Fig. 3*B*) and relative risk (Fig. 2*B*) analyses demonstrated a U-shaped nonlinear dose–response association with incident type 2 diabetes. The median daily MV-ILPA frequency (39.0 bouts/day) was associated with an absolute risk of 15.2 (95% CI 11.8–19.6) per 10,000 person-years (Supplementary Fig. 3*B*). Compared with the minimum referent data point (8.7 bouts/day), the nonlinear dose–response curve for MV-ILPA frequency (nonlinear $P < 0.001$) began to plateau at approximately 56 bouts/day, the data point corresponding to the lowest estimate (HR 0.54; 95% CI 0.39–0.76), followed by a gradual upward slope at higher frequencies (Fig. 2*B*). The ED_{50} of MV-ILPA frequency was 21.9 bouts/day (HR 0.77; 95% CI 0.68–0.86), and the median daily frequency was associated with an HR of 0.59 (95% CI 0.45–0.77).

Sensitivity Analyses

The E values ranged from 1.78 (lower 95% CI 1.48) to 2.05 (1.63) for VILPA and from 1.69 (1.42) to 2.42 (1.86) for MV-ILPA, suggesting that a moderate degree of unmeasured confounding would be required to nullify the observed associations with incident type 2 diabetes (Supplementary Table 5). Additional adjustment for BMI, waist circumference, and other cardiometabolic biomarkers showed similar results for VILPA (Supplementary Figs. 4 and 5) but attenuated dose–response associations for MV-ILPA (Supplementary Figs. 6 and 7) compared with the main analyses. Excluding participants who were underweight or reported poor self-rated health (n = 1,360 [including 330 with missing values]) or had a high frailty index (n = 2,271 [including 1,378 with missing values]) resulted in clearer and slightly steeper dose–response associations for both VILPA (Supplementary Figs. 8 and 9) and MV-ILPA (Supplementary Figs. 10 and 11) with type 2 diabetes incidence. Similarly, excluding participants with prevalent cancer or CVD (n = 4,326) produced clearer and steeper dose–response curves for both VILPA (Supplementary Fig. 12) and MV-ILPA (Supplementary Fig. 13), with VILPA frequency showing a more linear pattern. When setting the referent to the 25th percentile of exposure, the association pattern remained consistent for both VILPA (Supplementary Fig. 14) and MV-ILPA (Supplementary Fig. 15). Using alternative knot placements generated similar dose–response curves, but with a stronger magnitude of association for both exposures compared with the main analyses (Supplementary Figs. 16 and 17). Finally, there was only weak evidence of effect modification by sex for VILPA (interaction P for duration and frequency = 0.334 and 0.364, respectively) (Supplementary Fig. 18) and MV-ILPA (interaction P for duration and frequency = 0.823 and 0.682, respectively) (Supplementary Fig. 19).

CONCLUSIONS

To our knowledge, this is the first study to investigate the associations of physical activity micropatterns with incident type 2 diabetes. We found that daily

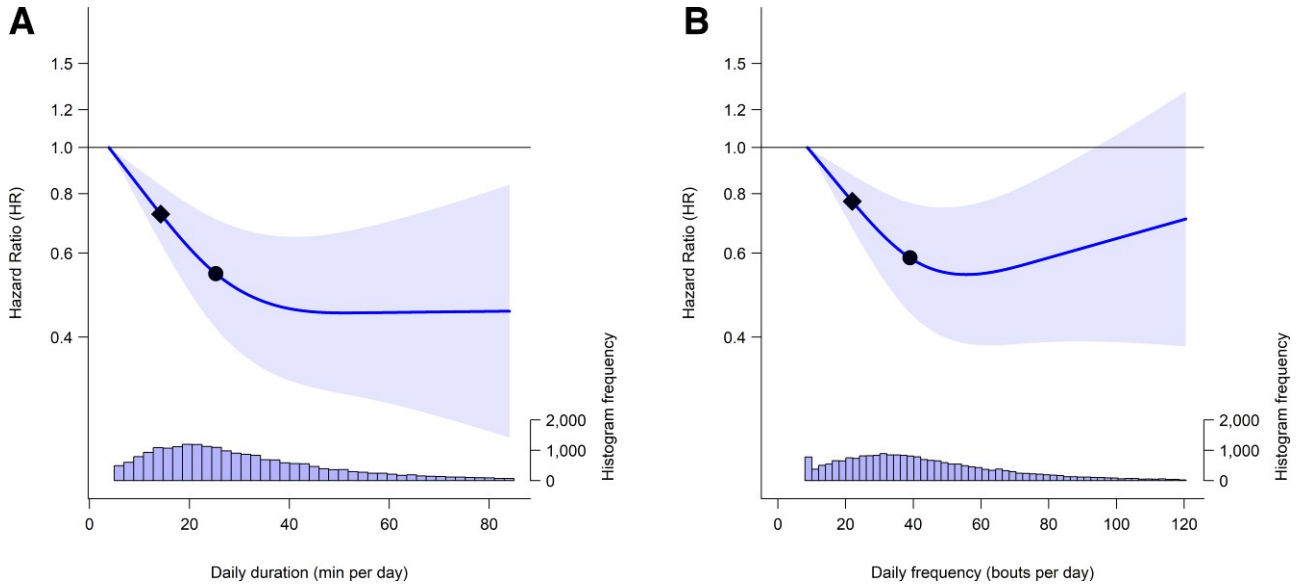

Figure 2—Multivariable-adjusted dose–response curves of daily MV-ILPA duration and frequency with incident type 2 diabetes (n = 22,706; n of events = 665). Lines represent HRs and shaded areas represent 95% CIs associated with increasing daily duration (*A*) and frequency (*B*) of MV-ILPA. Diamonds indicate minimal MV-ILPA duration/frequency dose (as indicated by ED_{50} statistics) associated with 50% of optimal risk reduction, and circles indicate HRs associated with median duration/frequency of MV-ILPA. Histograms show sample distribution. Model was adjusted for sex, age, education level, ethnicity, fruit and vegetable consumption, smoking status, alcohol consumption, sleep duration, discretionary screen time, medication use (cholesterol and blood pressure lowering), prevalent cancer, prevalent CVD, parental history of cancer, CVD, or type 2 diabetes, and physical activity energy expenditure volume of nonexposure physical activity components (light-, moderate-, and vigorous-intensity incidental physical activity [excluding MV-ILPA]). Reference points were the minimum data points of MV-ILPA duration (3.9 min/day) and frequency (8.7 bouts/day).

durations of both VILPA and MV-ILPA were inversely associated with incident type 2 diabetes in an L-shaped manner, with the sample median durations (VILPA 3.9 min/day; MV-ILPA 25.3 min/day) corresponding to 36% and 46% lower risks of incident type 2 diabetes, respectively. We also found a near-linear inverse association between daily frequency of VILPA and type 2 diabetes incidence, indicating progressively lower risk with increasing numbers of bouts daily. In contrast, daily frequency of MV-ILPA was inversely associated with incident type 2 diabetes in a U-shaped manner, with the strongest risk reduction (46%) observed at approximately 55.7 bouts/day. Our sensitivity analyses showed that these associations were broadly consistent across a range of measures against reverse causation (e.g., excluding prevalent cancer and CVD and setting the 25th percentile as referent data point) and other analytical assumptions (e.g., using different reference points or knot placements). Collectively, these findings suggest that brief bursts of higher-intensity incidental physical activity integrated into daily routines may be a time-efficient and potentially more behaviorally sustainable promising approach for prevention of type 2 diabetes.

Current type 2 diabetes prevention and management guidelines tend to focus on structured exercise as the primary behavioral intervention (4), despite its persistently low rates of uptake and adherence in real-world settings (6). Our analyses showed that regular brief bouts of moderate- to vigorous-intensity activity embedded within daily routines may offer comparable benefits for individuals who do not formally engage in structured exercise. Specifically, accumulating VILPA equivalent to the median of 3.9 min/day (i.e., 36.4% of the World Health Organization weekly recommended duration of vigorous physical activity) (2) or 10.4 bouts/day was associated with a 36% lower risk of developing type 2 diabetes compared with no VILPA. Furthermore, the near-linear pattern observed with daily VILPA frequency may indicate that integrating brief, frequent VILPA bouts into daily routines could offer more consistent benefits than accumulating longer daily durations alone in the context of type 2 diabetes prevention. The observed lower type 2 diabetes risk associated with greater micropattern-accrued physical activity may be partly explained by physiological adaptations analogous to those elicited by structured exercise, including maintenance and improvement of cardiorespiratory fitness, insulin sensitivity, and glycemic control (30,31).

Consistent with the dose–response pattern observed for VILPA, daily MV-ILPA duration showed a similar nonlinear trend, with the median duration of 25.3 min/day associated with a 46% lower risk of type 2 diabetes. The observed beneficial associations with MV-ILPA could possibly be due to moderate-intensity activity eliciting physiological adaptations that complement those induced by vigorous-intensity activity (32,33), which together may strengthen insulin sensitivity and overall cardiometabolic function. In contrast to VILPA frequency, we found a U-shaped association between daily MV-ILPA frequency and incident type 2 diabetes, suggesting that excessively high numbers of MV-ILPA bouts (beyond approximately 56 bouts/day) may not be associated with further risk reduction. Because there is no plausible underlying mechanism for such a dose–response pattern, the U-shaped part of the curve likely reflects data sparsity and reduced precision at the upper end of the bout frequency distribution. Notably, the estimated risk remained substantially lower than the referent level (8.7 bouts/day), even at the highest observed frequencies (e.g., approximately 30–40% lower at >80 bouts/day), indicating an overall consistent pattern across the sample.

Notably, the ED_{50} of MV-ILPA duration (14.2 min/day) corresponded to the same type 2 diabetes risk reduction (27%) as that of VILPA duration (2.5 min/day), suggesting that comparable risk reductions may be achieved through longer daily durations of incidental activity at moderate to vigorous intensity. This finding aligns with previous health equivalence analyses showing that each minute of incidental activity accrued at vigorous intensity may offer CVD risk reductions equivalent to 2.8 to 3.4 min of moderate-intensity incidental activity (21). This demonstrates the flexibility in how incidental activity can be accumulated across moderate to vigorous intensities with similar protective effects, providing a range of feasible and potentially behaviorally sustainable options for type 2 diabetes prevention. In contrast to previously reported sex-specific associations of VILPA and major adverse cardiovascular events (15), we found little evidence of effect modification by sex for the association of either VILPA or MV-ILPA with incident type 2 diabetes. Specifically, sex-specific dose–response curves were materially consistent and largely overlapped across most of the exposures' distribution.

Our findings are consistent with previous literature showing substantial risk reductions (approximately 16–45% lower risk) for VILPA and MV-ILPA across multiple health outcomes, including all-cause mortality (12,16), cancer mortality (12) and incidence (14), and major adverse cardiovascular events (13,15). Collectively, this evidence highlights the potential of incidental physical activity to offer a practical alternative for adults who do not exercise regularly, with previous qualitative work indicating that VILPA aligns well with individuals' daily routines and priorities (34). This approach slightly differs from exercise snacks, which typically comprise planned and structured short bouts of higher-intensity activity that are more deliberately incorporated into daily routines (35). Furthermore, recent pilot micropattern-focused interventions have demonstrated the feasibility and acceptability of promoting VILPA through brief, behaviorally informed strategies codesigned with adults transitioning into retirement (36) and women from socioeconomically diverse backgrounds (37). These interventions have focused on creating awareness of the health benefits of micropattern activities, helping individuals identify feasible VILPA opportunities across different contexts within their existing daily routines (e.g., climbing stairs or walking briskly to the shop) and providing support through personalized goal setting, which may also be translatable to clinical settings (e.g., through brief consultations that emphasize awareness and opportunity recognition). Our recent work also demonstrated the potential to quantify micropattern bouts using step cadence data derived from consumer-grade wearable devices (37), highlighting the feasibility of monitoring such behaviors in interventions. Although larger-scale trials are needed, these preliminary findings suggest the integration of brief bursts of vigorous- and/or moderate-intensity incidental physical activity into everyday life is a promising alternative strategy in type 2 diabetes prevention. Importantly, because our findings are based on daily averages of VILPA and MV-ILPA, the

observed risk reductions likely reflect consistent day-to-day accumulation patterns, reinforcing the importance of habitual physical activity in preventing noncommunicable disease (2).

The strengths of our study include the use of high-resolution data from accelerometers to capture physical activity micropatterns and the unique focus on nonexercising adults, which enabled investigation of the health associations of short bouts of intermittent physical activity embedded in daily living. The use of a validated two-stage machine learning–based activity classifier also improved the precision of incidental activity type and intensity classification (21), although underestimation of VILPA/MV-ILPA remains possible because of the inherent limitations of wrist-worn accelerometers in capturing certain activities (e.g., walking uphill or while carrying heavy loads). Accelerometry also cannot capture the resistive load or perceived exertion associated with activities (e.g., the weight of the grocery bags being carried), which may lead to residual confounding. Despite the long follow-up period and extensive sensitivity analyses, the possibility of reverse causation bias (e.g., arising from undiagnosed prediabetes at baseline) cannot be fully ruled out. There was a median lag of 5.5 years between the baseline questionnaire data collection (including self-reported leisure-time exercise and other covariates) and accelerometry measurements; however, previous studies have shown that nonexerciser status (82–88% retained this status based on reexamination data) (12) and most covariates (38) are generally stable over time. Although the UK Biobank had a very low response rate (5.5%) and may be susceptible to a healthy volunteer selection bias (i.e., participants were generally healthier and more socioeconomically advantaged than the broader U.K. population), the heterogeneity of exposures still allows for valid inferences about exposure–health associations that may be generalizable to other populations, as shown by previous empirical work (39,40). Nonetheless, additional studies in other populations and settings are warranted to confirm our findings. Finally, given the observational design, our findings cannot provide definitive evidence of the causality of the observed associations.

In summary, we found that micropattern-accrued incidental physical activity of higher intensities was consistently associated with lower type 2 diabetes incidence in a dose–response manner. These findings support the promotion of short, regular bouts of incidental physical activity at moderate and/or vigorous intensity as part of daily routines, offering a promising strategy for type 2 diabetes prevention.

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