



Associations of Daily Steps and Step Intensity With Incident Diabetes in a Prospective Cohort Study of Older Women: The OPACH Study

Diabetes Care 2022;45:339–347 | <https://doi.org/10.2337/dc21-1202>

Alexis C. Garduno,^{1,2} Andrea Z. LaCroix,¹ Michael J. LaMonte,³ David W. Dunstan,^{4,5} Kelly R. Evenson,⁶ Guangxing Wang,⁷ Chongzhi Di,⁷ Benjamin T. Schumacher,^{1,2} and John Bellettiere¹

OBJECTIVE

The primary aim was to assess associations between total steps per day and incident diabetes, whereas the secondary aim was to assess whether the intensity and/or cadence of steps is associated with incident diabetes.

RESEARCH DESIGN AND METHODS

Women without physician-diagnosed diabetes ($n = 4,838$; mean [SD] age 78.9 [6.7] years) were followed up to 6.9 years; 395 developed diabetes. Hip-worn ActiGraph GT3X+ accelerometers worn for 1 week enabled measures of total, light-intensity, and moderate- to vigorous-intensity (MV-intensity) steps per day. Using Cox proportional hazards analysis we modeled adjusted change in the hazard rate for incident diabetes associated with total, light-intensity, and MV-intensity steps per day. We further estimated the proportion of the steps-diabetes association mediated by BMI.

RESULTS

On average, participants took 3,729 (SD 2,114) steps/day, of which 1,875 (791) were light-intensity steps and $1,854 \pm 1,762$ were MV-intensity. More steps per day were associated with a lower hazard rate for incident diabetes. Confounder-adjusted models for a 2,000 steps/day increment yielded hazard ratio (HR) 0.88 (95% CI 0.78–1.00; $P = 0.046$). After further adjustment for BMI, HR was 0.90 (95% CI 0.80–1.02; $P = 0.11$). BMI did not significantly mediate the steps-diabetes association (proportion mediated = 17.7% [95% CI –55.0 to 142.0]; $P = 0.09$). The relationship between MV-intensity steps per day (HR 0.86 [95% CI 0.74–1.00]; $P = 0.04$) and incident diabetes was stronger than for light-intensity steps per day (HR 0.97 [95% CI 0.73–1.29]; $P = 0.84$).

CONCLUSIONS

These findings suggest that for older adults, more steps per day are associated with lower incident diabetes and MV-intensity steps are most strongly associated with a lower hazard of diabetes. This evidence supports that regular stepping is an important risk factor for type 2 diabetes prevention in older adults.

Type 2 diabetes (T2D) is increasingly prevalent among older adults, with risk for developing T2D plateauing around age 85 years; one in five newly diagnosed cases

¹Herbert Wertheim School of Public Health and Human Longevity Science, University of California, San Diego, San Diego, CA

²Division of Epidemiology and Biostatistics, School of Public Health, San Diego State University, San Diego, CA

³Department of Epidemiology and Environmental Health, School of Public Health and Health Professions, University at Buffalo-SUNY, Buffalo, NY

⁴Baker Heart and Diabetes Institute, Melbourne, Victoria, Australia

⁵Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Victoria, Australia

⁶Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC

⁷Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, WA

Corresponding authors: Alexis C. Garduno, agarduno@health.ucsd.edu, and John Bellettiere, jbellettiere@health.ucsd.edu

Received 7 June 2021 and accepted 12 November 2021

This article contains supplementary material online at <https://doi.org/10.2337/figshare.17004046>.

This article is featured in a podcast available at diabetesjournals.org/journals/pages/diabetes-core-update-podcasts.

© 2022 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <https://www.diabetesjournals.org/journals/pages/license>.

are among adults older than 65 years old, 95% of which are diagnosed as type 2 (1,2). Older adults who develop diabetes are at higher risk for complications including cardiovascular and peripheral artery disease, worse renal function, and severe or fatal hypoglycemia (3).

Physical activity (PA) is a key modifiable behavior for diabetes prevention and management (4,5); many prevention studies have demonstrated that regular PA, along with improved diet, reduces the risk of diabetes in adults (5,6). Using movement sensors, such as pedometers and accelerometers, PA can be measured in terms of steps per day. Steps/day is a highly translatable metric that is familiar, memorable, and accessible with many wearable devices and smart phones (7), which have become ubiquitous. Accelerometers also measure steps taken over a spectrum of light activity to moderate- to vigorous-intensity activity, which can then be used to better understand the role of movement intensity in diabetes prevention (8–10). To the best of our knowledge, there are few studies examining the association between objectively measured steps per day and incident diabetes in a community-based setting (11).

The 2018 Physical Activity Guidelines Advisory Committee (12 and the update published a year later [10]) concluded that there was insufficient evidence to support an association of increased steps per day with reduced T2D risk, and called for more research on the topic from prospective cohort studies using objective measurements of daily steps (12,13). One of the few existing studies among older adults was the Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) trial, from which, in post hoc analyses, it was reported that each 2,000 steps/day increment (measured by pedometer) was associated with a 6% decrease in the hazard rate for incident T2D (14). Unfortunately, the publications for the NAVIGATOR trial have not yet reported on the intensity of stepping, which may be an important metric (15,16).

In this study, we analyzed data from a diverse cohort of older women without physician-diagnosed diabetes who had enrolled in the Objective Physical Activity and Cardiovascular Health (OPACH) Study and were followed for up to 6.9 years for

incident diabetes. The primary aim was to assess associations between total steps per day and incident diabetes, whereas the secondary aim was to assess whether the intensity and/or cadence of steps is associated with incident diabetes.

RESEARCH DESIGN AND METHODS

Study Population

The OPACH Study is a prospective, ancillary study of the Women's Health Initiative (WHI) aimed at characterizing PA and cardiovascular health in older women. In 2012, the OPACH Study recruited participants from the WHI extension study (2010–2015) and Long Life Study (2012–2013); details of the OPACH Study have previously been published (17). Briefly, 6,489 ambulatory women wore an accelerometer and 6,382 returned the device with evidence of human wear. We excluded prevalent cases of diabetes, those with a history of diabetes treated with medication prior to OPACH enrollment ($n = 1,358$), 173 women (3%) having <4 days with 10+ hours of awake wear time—a commonly recommended criteria for actigraphy processing (18), 10 women missing information on incident diabetes, and 3 individuals whose average daily steps (>30,000 steps/day) exceeded expected maximum values. The final analytic sample consisted of 4,838 women. The Institutional Review Board of the Fred Hutchinson Cancer Research Center (WHI coordinating center) approved all study protocols, and all participants gave informed consent prior to entry.

Measuring Steps Per Day

PA was measured with an ActiGraph GT3X+ worn 24 h/day over the right hip for 1 week, except when bathing or swimming. A nightly sleep diary was concurrently completed. Accelerometer movement was collected 30 times per second (i.e., 30 Hz) and then aggregated to 15-s epochs with use of ActiLife software (version 6). Steps for each 15-s epoch were derived using ActiLife's proprietary algorithm (17). The factory default (i.e., normal frequency) filter was used to process accelerometer data to compute steps, as has been done in similar studies (16,19). Awake wear time was defined as the time participants were wearing the device while awake; nonwear time was identified using the Choi algorithm (20) with a 90-min

window, 30-min stream frame, and 2-min tolerance; and awake time was identified using self-reported sleep logs. Out-of-bed periods were identified using sleep diaries. When at least one in-bed or out-of-bed time was missing, each woman's average in-bed and out-of-bed time was used if available; otherwise, the overall cohort mean in-bed (10:45 P.M.) and out-of-bed (7:22 A.M.) times were used.

We calculated steps per day by dividing cumulative steps over all included days by the total number of adherent device wear days. When accounting for interindividual differences in awake wear time, numbers of steps per day were residualized by regressing the number of steps per day on wear time. Residuals were added to the mean predicted value to obtain a wear time-adjusted measure of steps per day. We used this residual approach over traditional adjustment, since it allows for modeling the exposure in nonlinear models, or through use of quartiles or tertiles, and enables the nonwear time to be addressed as a measurement issue directly in those nonlinear parameterizations. Since we residualized for awake wear time, we effectively controlled for average sleep duration in our analyses. A total of 304 women were missing all sleep diary data; missing diary data were not related to incident diabetes ($P = 0.27$ [data not shown]), and in our previous work, use of alternate sleep time imputation methods (21) did not influence results (22). In addition to steps per day, three common measures of step cadence were computed (16). Peak 30-min cadence represented the mean steps per minute for the fastest 30 min each day. The average daily percentage of wear time with ≥ 40 steps/min was used to measure "purposeful stepping," which has been validated in adult populations (23). Lastly, we considered average steps per day that were accumulated in bouts (i.e., short, continuous periods) of at least 5 min or more.

In a separate, laboratory-based calibration study among 200 OPACH Study women, acceleration cut points for vector magnitude (VM) counts were identified for stratification of each 15-s epoch into sedentary time (<19 VM counts/epoch) and PA of light intensity (19–518 VM counts/epoch) and moderate to vigorous (MV) intensity (≥ 519 VM counts/epoch) (24). ActiLife software also

provided step counts for each 15-s epoch. Using both steps and counts, we computed “light steps” as the average daily number of steps that occurred while VM counts per 15 s were <519. “MV steps” were computed as the average daily number of steps that occurred while VM counts per 15 s were >518.

Diabetes Incidence

Incident diabetes and date of diagnosis were determined based on self-report of newly physician-diagnosed diabetes requiring insulin or oral hypoglycemic medication, queried on annual health updates administered in the national WHI. High validity was demonstrated for this case definition of diabetes in a separate study of >700 WHI participants; 82% of women reporting incident diabetes were classified by expert physicians as having incident diabetes following a medical record review, and reports of being without diabetes were concordant in 95% of women confirmed as not having diabetes (25). Note that a description of covariates and their measurement can be found in Supplementary Procedures.

Statistical Analyses

Baseline characteristics were summarized across quartiles of daily steps per day. χ^2 and *F* tests were used to test differences in baseline characteristics across steps per day quartiles for categorical and continuous variables, respectively. The Cox proportional hazards regression modeled the change in the hazard rate for incident diabetes for each 2,000-steps/day increment. Hazard ratios (HRs) approximate instantaneous relative risk, and are not risk ratios, and should be interpreted accordingly (26). We tested the Cox proportional hazards assumption in each outcome model using the Schoenfeld residuals and found no violations (Supplementary Material 1). As in previous WHI studies, time to event was computed as the number of days from accelerometry to the received date of the medical history update containing the first ever record of physician-diagnosed diabetes, with time for those without diabetes censored either at death or the date of the last received medical history update.

Restricted cubic splines were used to test nonlinear associations between steps per day and incident diabetes with 3-5 knots (rms; R package version

6.1-1). The estimated dose-response curve was nearly linear, and the result of the Wald test for the nonlinear functional form was not statistically significant (3 knots $P_{\text{nonlinear}} = 0.92$, $P_{\text{overall}} = 0.13$; 4 knots $P_{\text{nonlinear}} = 0.30$, $P_{\text{overall}} = 0.09$; 5 knots $P_{\text{nonlinear}} = 0.14$; $P_{\text{overall}} = 0.06$). Therefore, a continuous, linear functional form was used in the models (see Fig. 1). Three multivariable models were fit to evaluate the association between step measures and incident diabetes. The selection of covariates mirrored our previous study (27) and was based on existing literature in the fields of exercise science, epidemiology, and diabetes. To address the fact that we are studying an older population (average age ~80 years), we also took into account variables that were highly related to age, PA, and diabetes, including multimorbidity, physical functioning, and self-rated health. The first model included adjustment for age and race-ethnicity, as did the second model with addition of the following covariates to model 1: education, family history of diabetes, self-rated health, physical functioning, alcohol consumption, and smoking status. In the final model we added BMI, which is a potential mediator in the causal pathway between steps per day and diabetes. We then added an interaction term between total steps per day and each potential effect modifier selected a priori, including age, BMI, physical functioning, race-ethnicity, and family history of diabetes (28), to test for multiplicative interaction. Associations of step cadence (all three metrics, modeled separately) and steps taken at light or MV intensity (both metrics, modeled separately) with incident diabetes were examined with use of the same procedures described above.

We performed two sensitivity analyses to address the concern for reverse causation, whereby subclinical diabetes and its associated comorbidities may lead to reduced PA and fewer steps per day. First, we repeated the confounder-adjusted model after excluding 121 women who reported a diagnosis of diabetes within 2 years after accelerometry. Second, we excluded 170 women (37 of whom were subsequently diagnosed with incident diabetes [9.4% of total incident diabetes cases]) who had fasting glucose levels meeting the clinical threshold for diabetes diagnosis (29)

(>126 mg/dL, based on a single blood test at OPACH baseline) and repeated the confounder-adjusted Cox regression models.

All statistical tests were two tailed, $\alpha = 0.05$, with use of R, version 4.0.2 (2020-06-22; Vienna, Austria). Multiple imputation (mice package) was performed with 50 rounds of imputation over five iterations, and all models were executed with multiple imputation to avoid inducing selection bias by virtue of restriction to those with complete data (Supplementary Material). In addition, we further investigated whether BMI mediated the steps per day–diabetes association (Supplementary Procedures). Overall, there were minimal missing data for main analyses: BMI was the covariate with the most missing observations (6%); <1% of observations were missing for education, self-reported health, and physical functioning (Supplementary Table 1).

Data Availability

The data that support the findings of this study are available from A.Z.L. (alacroix@health.ucsd.edu) in accordance with the WHI publications and presentations policy.

RESULTS

Study participants were followed for a median of 5.7 years with a maximum follow-up of 6.9 years, during which 395 women (8.1%) developed diabetes, at a rate of 16.3 cases/1,000 person-years. Mean (SD) steps per day among OPACH women was 3,729 (2,114), of which 1,875 (791) were light steps and 1,854 (1,762) were MV steps. Peak 30-minute cadence was 36 (22) steps/min, whereas percentage of time spent in bouts >40 steps/min and total steps accumulated in bouts of 5+ minutes were 1% (2%) and 78 (1,214) steps, respectively. Among the 25% of women with the fewest steps per day, 75% were over >80 years in age, and this group was more likely to be White, have poor self-rated health, score below average for RAND-36 physical function score, and have three or more comorbidities (Table 1). Among participants in the highest steps per day quartile ($\geq 4,914$ steps/day), 72.0% of participants were younger than 80 years of age, and this group was more likely to have graduated college, report excellent/very good health, score above average for physical

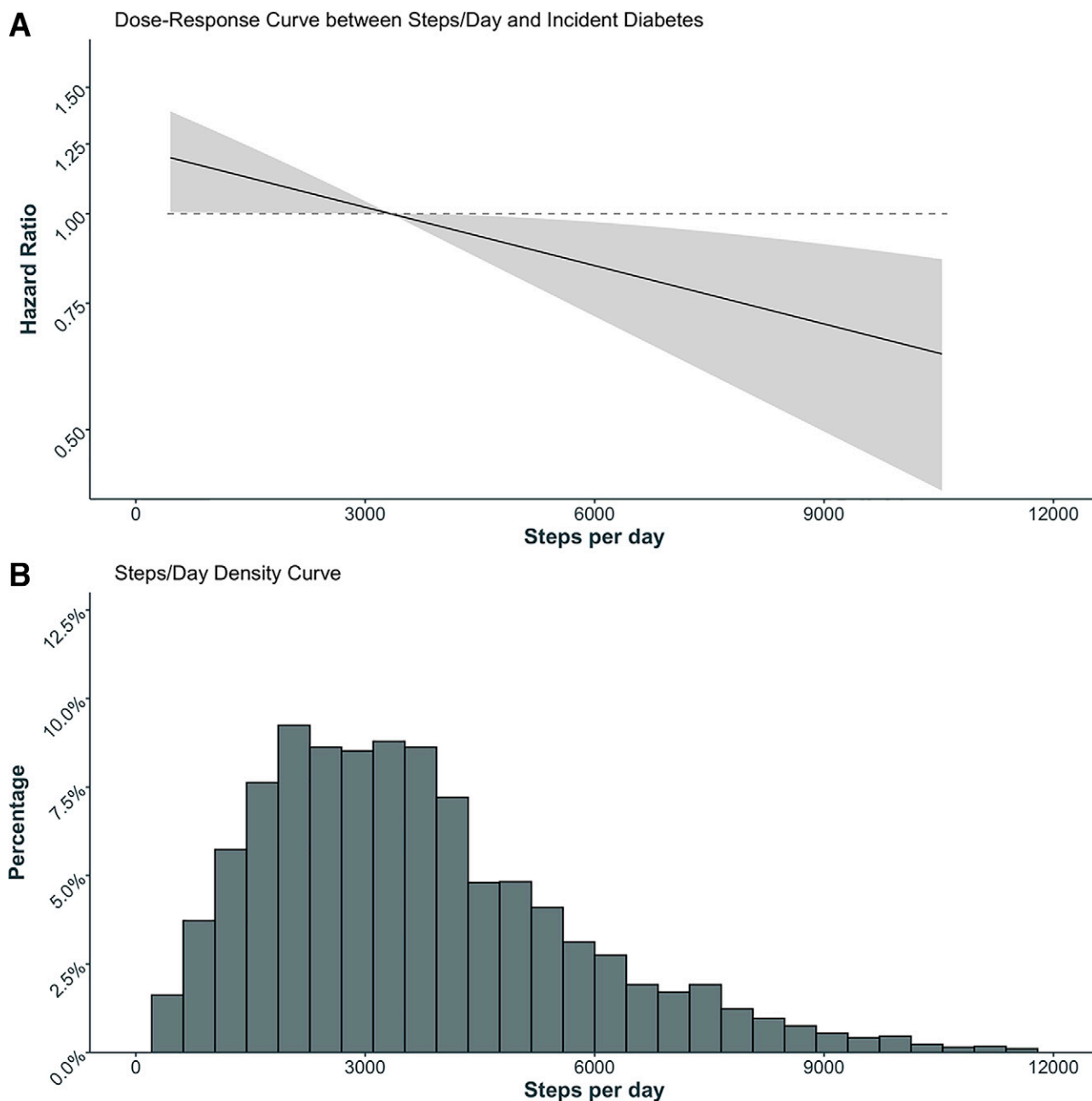


Figure 1—Dose-response trajectory for associations of incident diabetes and steps per day. HR and the 95% CI (shaded gray) are from Cox proportional hazards models with adjustment for age, race-ethnicity, education, general health status, family history of diabetes, number of chronic conditions, physical function, alcohol, and smoking status. *A*: The dose-response curve data trimmed at 1st and 99th percentiles. *B*: Density curve shows the number of participants at each increment of steps per day across the steps per day distribution.

functioning, drink >1 alcoholic drink/week, and have fewer total comorbidities.

More steps per day were associated with a decrease in the hazard rate for diabetes in this cohort of older women. The minimally adjusted HR for a 2,000 steps/day increment was equal to 0.86 (95% CI 0.80–0.92) (Table 2). Further adjustment for potential confounders (education, self-reported health, family history of diabetes, physical functioning,

alcohol consumption, and smoking) produced similar results (HR 0.88 [95% CI 0.78–1.00]; $P = 0.045$). After adjustment for BMI as a potential mediator, the association was slightly attenuated and the CIs widened to include the null value (HR 0.90 [95% CI 0.80–1.02]; $P = 0.11$). Results from complete-case analyses, which were similar to those from the multiple imputation analysis, are reported in Supplementary Tables 2 and 3. Accelerated failure time models demon-

strated that BMI did not significantly mediate the steps-diabetes association (proportion mediated 17.7% [95% CI –55.0 to 142.0]; $P = 0.09$). Tests for interaction of steps per day with age, race-ethnicity, BMI, physical functioning, or family history of diabetes were not statistically significant (all P values >0.60).

With stratification of steps per day into either light or MV intensity, the HRs for associations with light steps

Table 1—Baseline (2012–2014) characteristics for OPACH participants by quartile of steps per day

	Total (n = 4,838)	Steps per day quartiles*				P
		Quartile 1 (n = 1,210)	Quartile 2 (n = 1,210)	Quartile 3 (n = 1,209)	Quartile 4 (n = 1,209)	
Age, years, mean (SD)	78.92 (6.73)	82.75 (5.92)	79.95 (6.26)	77.81 (6.35)	75.19 (5.98)	<0.001
Age-group, ≥80 years, n (%)	2,487 (51.4)	907 (75.0)	706 (58.3)	536 (44.3)	338 (28.0)	<0.001
Race-ethnicity, n (%)						<0.001
White	2,568 (53.1)	803 (66.4)	662 (54.7)	581 (48.1)	522 (43.2)	
Black	1,469 (30.4)	325 (26.9)	397 (32.8)	398 (32.9)	349 (28.9)	
Hispanic	801 (16.6)	82 (6.8)	151 (12.5)	230 (19.0)	338 (28.0)	
Education, n (%)						<0.001
High school/GED	951 (19.8)	269 (22.4)	230 (19.1)	240 (20.1)	212 (17.6)	
Some college	1,817 (37.8)	474 (39.4)	475 (39.4)	447 (37.4)	421 (34.9)	
College graduate+	2,039 (42.4)	459 (38.2)	501 (41.5)	507 (42.5)	572 (47.5)	
Self-rated health, n (%)						<0.001
Excellent/very good	2,633 (54.6)	461 (38.3)	570 (47.2)	708 (58.8)	894 (74.1)	
Good	1,818 (37.7)	573 (47.6)	535 (44.3)	439 (36.5)	271 (22.5)	
Poor/very poor	371 (7.7)	171 (14.2)	102 (8.5)	57 (4.7)	41 (3.4)	
Light-intensity steps, mean (SD)	1,875 (7,901)	1,161 (444)	1,712 (506)	2,089 (602)	2,540 (814)	<0.001
MV steps, mean (SD)	1,854 (1,762)	460 (3,712)	1,027 (536)	1,815 (736)	4,115 (1,928)	<0.001
RAND-36 physical function score, mean (SD)	70.6 (25.1)	52.9 (25.7)	67.1 (24.4)	76.2 (20.4)	86.2 (16.1)	<0.001
Smoker status, smoker, n (%)	133 (2.7)	56 (4.6)	30 (2.5)	24 (2.0)	23 (1.9)	<0.001
Alcohol frequency, n (%)						<0.001
<1 drink/week	1,526 (31.5)	448 (37.0)	415 (34.3)	366 (30.3)	297 (24.6)	
≥1 drinks/week	1,546 (32.0)	395 (32.6)	392 (32.4)	387 (32.0)	372 (30.8)	
Nondrinker	1,390 (28.7)	241 (19.9)	310 (25.6)	373 (30.9)	466 (38.5)	
Unspecified	376 (7.8)	126 (10.4)	93 (7.7)	83 (6.9)	74 (6.1)	
Family history of diabetes, yes, n (%)	1,599 (33.2)	382 (31.7)	415 (34.5)	404 (33.6)	398 (33.0)	0.54
BMI, mean (SD)	27.58 (5.43)	28.30 (6.01)	28.42 (5.73)	27.58 (5.13)	26.05 (4.42)	<0.001
No. of comorbidities, n (%)#						<0.001
Zero	548 (11.3)	74 (6.1)	93 (7.7)	139 (11.5)	242 (20.0)	
One	1,660 (34.3)	355 (29.3)	368 (30.4)	444 (36.7)	493 (40.8)	
Two	1,719 (35.5)	444 (36.7)	489 (40.4)	433 (35.8)	353 (29.2)	
Three or more	911 (18.8)	337 (27.9)	260 (21.5)	193 (16.0)	121 (10.0)	

P value: χ^2 for categorical variables and trend test for continuous. GED, General Educational Development. *Steps per day is defined as quartiles: quartile 1, <2,337 steps/day; quartile 2, 2,337–3,396 steps/day; quartile 3, 3,396–4,914 steps/day; and quartile 4, >4,914 steps/day. #Chronic conditions used to compute this included cardiovascular disease, cancer, cognitive impairment, depression medication use, osteoarthritis, history of frequent falls, chronic obstructive pulmonary disease, hypertension, and cerebrovascular disease.

were weaker than those for MV steps. In the crude models, the HR for incident diabetes associated with a 2,000 steps/day increment of light steps was 0.87 (95% CI 0.66–1.15; $P = 0.33$) and of MV steps was 0.83 (95% CI 0.72–0.95; $P = 0.009$). In the confounder adjusted models, the HR for incident diabetes associated with a 2,000 steps/day increment of light steps was 0.97 (0.73–1.29; $P = 0.83$) and of MV steps was 0.86

(95% CI 0.74–1.00; $P = 0.04$). Dose-response trajectories for light and MV steps with model 2 are illustrated in Fig. 2. The complete-case analysis results for these step-intensity metrics can be found in Supplementary Table 3.

None of the step cadence measures were significantly associated with incident diabetes after adjustment for sociodemographic and lifestyle factors (Supplementary Table 5). The estimated hazard ratios

from models of peak 30-minute cadence suggested that faster step cadence was associated with a decrease in the hazard rate for diabetes, albeit not statistically significantly ($HR_{\text{per } 20 \text{ steps/min}} = 0.91$ [95% CI 0.81–1.02]; $P = 0.09$) (Supplementary Table 5).

In sensitivity analyses, in which women with high fasting glucose and diabetes onset within 2 years of baseline were removed separately, point estimates did

Table 2—Associations between steps per day (unit: 2,000 steps) and incident diabetes among older women who had accelerometry during 2012–2014 and follow-up through 28 February 2020

	HR (95% CI)	P
Model 1	0.86 (0.77–0.96)	0.007
Model 2	0.88 (0.78–1.00)	0.045
Model 3	0.90 (0.80–1.02)	0.11

n = 4,838; diabetes cases = 395. Model 1, adjustment for age and race-ethnicity; model 2, model 1 adjustments plus education, self-rated health, family history of diabetes, number of chronic conditions, physical functioning (RAND-36), alcohol consumption, and current smoking status; model 3, model 1 adjustments, model 2 adjustments, and BMI, which we consider to be in the steps per day and diabetes pathway.

not appreciably change for the observed relationship between steps per day and diabetes onset, though the CIs were wider (Supplementary Table 6).

CONCLUSIONS

In this racially and ethnically diverse cohort of community-dwelling women who were predominantly in their late 70s/early 80s, each 2,000 steps/day increment was associated with a 12% lower hazard rate after adjustment. Additionally, the steps per day–diabetes association was not modified by age, race-ethnicity, BMI, physical functioning, or family history of diabetes, which supports the generalizability of these findings to community-living older women. In analyses we found that the association between accelerometer-measured steps per day and diabetes was stronger for MV than for light stepping. This finding further supports emerging evidence that some PA on a regular basis is better than none and that moving more and at higher intensity is optimal for reducing one's risk of diabetes, irrespective of age (30).

The strength of the relationship between more steps and a lower hazard of diabetes observed in our study was slightly stronger than the relationship reported in earlier epidemiologic studies among older adults (14,31). In a post hoc analysis of the NAVIGATOR trial that followed participants for 6 years, each additional 2,000 steps/day increment, measured by a pedometer, was associated with a 6% decrease in the diabetes hazard rate. This relationship was linear only after exclusion of individuals with >10,000 steps/day. One possible explanation for observing a stronger inverse association with T2D in

our study population is that OPACH Study women are more closely aligned with a population-based study; e.g., the crude incidence of newly diagnosed cases of diabetes among adults 65 years old and older in the U.S. is 8.8 cases/1,000 (95% CI 6.5–11.9) (32), and the rate among the ~80-year-old OPACH Study population was 16.3 cases/1,000 person-years, while the crude incidence in the NAVIGATOR trial (among adults with impaired glucose tolerance and either cardiovascular disease or cardiovascular disease risk factors) was 350 cases/1,000 person-years (14). In addition to being at higher risk for diabetes, those participating in the NAVIGATOR trial, which was aimed at preventing clinical manifestations of impaired glucose homeostasis, were younger (~65 years old), were more active (average steps per day ~6,200), and received intense lifestyle modification or pharmaceutical intervention, both, or neither. In comparison, among OPACH Study women, on average age was 80 years and women took 3,700 steps/day, and women were community based (14).

In the prospective Health Ageing Initiative (HAI) study of 3,055 70-year-old Swedish men and women who were followed up to 2.6 years for incident diabetes (*n* = 81 cases), there was a nonlinear, inverse dose-response relationship with accelerometer-measured steps (19). The HAI cohort took notably more steps per day than OPACH women (HAI_{mean steps} = 7,139, OPACH_{mean steps} = 3,729, OPACH 70-year-olds_{mean steps} = 5,087) and had lower overall incidence of diabetes (HAI_{incidence rate} = 10.2/1,000 person-years, OPACH_{incidence rate} = 16.3/1,000 person-years). In HAI, the diabetes hazard rate among older adults with >7,445

steps/day was flat and ~2.5 to 3.0 times lower than the hazard rate for those with steps per day around the OPACH average of 3,729. This finding suggests a possible threshold above which additional steps per day are not related to further decrements in the diabetes hazard rate in older adults. The apparent threshold is, however, far beyond the usual stepping levels of these older OPACH women, among whom just 5% had steps per day above the 7,445 threshold suggested in the HAI study.

In four cross-sectional studies of adults who on average were 55–65 years old, investigators found that more steps per day were associated with lower odds of diabetes (33,34) and metabolic syndrome (36), smaller waist circumference (33), and lower 2-h glucose measures (36). In addition, results of a prospective study with use of an Omron pedometer with 5-year follow-up among 458 middle-aged adults in Australia showed that 1,000 more steps per day were associated with 13% lower odds of incident dysglycemia, a precursor to T2D (37). This study also showed that more steps per day were associated with lower 5-year fasting blood glucose but not with lower 2-h plasma glucose (37).

Our findings with respect to MV and light stepping are in line with the 2020 World Health Organization guidelines on PA that some PA on a regular basis is better than none and that moving more at higher intensity is optimal for improving health outcomes (30). It is well-known that intense lifestyle intervention can delay or prevent diabetes, especially when the intervention includes diet modification (5,38). An important note is that MV PA is attainable even among older women with severe mobility limitations, as demonstrated in our previous study where women with very low physical function (defined as having a Short Physical Performance Battery [SPPB] score <4) had on average 30 min per day of MV PA (39). MET values assigned to walking pace in the compendium are based on middle-aged adults; older women achieve MV PA intensity at a slower pace. This difference in classifying PA is partially due to older adults having a lower resting metabolic rate and higher energy cost of movement. For example, most older women achieve MV-intensity steps

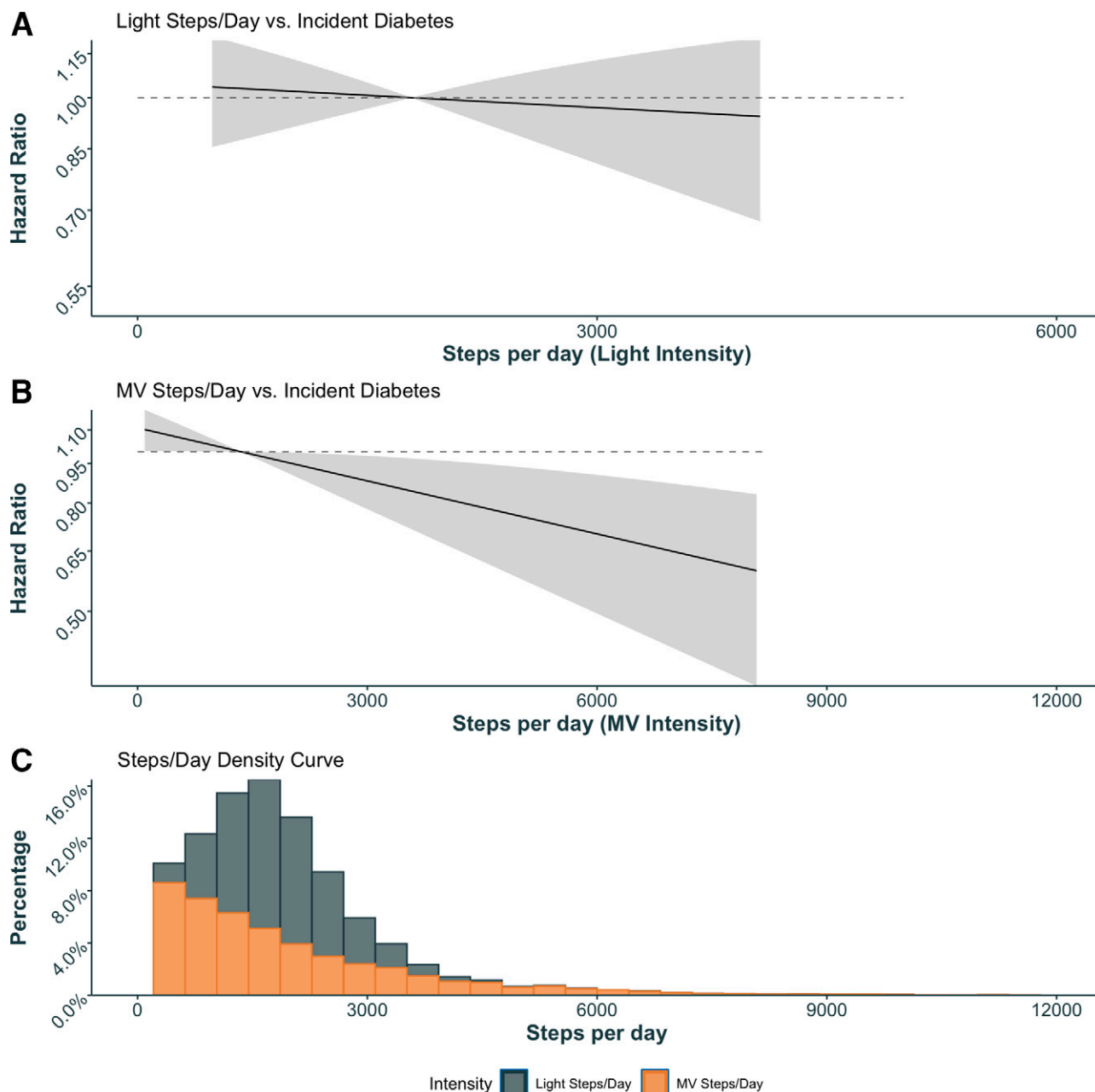


Figure 2—Dose-response trajectory for associations of light and MV steps per day and incident diabetes. *A*: Dose-response trajectory for steps taken at light stepping intensity. *B*: Dose-response trajectories for steps taken at MV stepping intensity. HR and the 95% CI (shaded gray) are from Cox proportional hazards models with adjustment for age, race-ethnicity, education, general health status, family history of diabetes, total chronic conditions, physical function, alcohol, and smoking status. *y*-axes are trimmed to the 1st and 99th percentiles. *C*: Light- and MV-intensity steps per day density curves are overlaid for all participants, showing the number of participants for each light- and MV-intensity steps per day increment across the respective distributions.

during a usual paced 400-m walk (one lap around a track) (24).

Strengths and Limitations

This study was limited in several respects. Our diabetes outcome measure and the corresponding diagnosis date were self-reported, which may lead to misclassification. Though the case definition does not distinguish between type 1 diabetes

and T2D, T2D accounts for 95% of total diagnosed diabetes in U.S. older adults (2). In addition, our self-reported outcome has demonstrated high accuracy when compared with physician adjudication using medication inventories and medical record review (25).

A total of 938 women consented to OPACH but did not return accelerometers with sufficient data, and in the

current study 183 women were excluded from analyses due to missing exposure or outcome data. As shown in our previous study (40) and Supplementary Table 1, women who were excluded had lower PA including fewer steps, higher BMI, and higher fasting glucose, increasing the likelihood for incident diabetes. Any selection bias resulting from these exclusions would likely bias our results toward

the null, meaning that the steps and diabetes association may be stronger than reported in the current study.

Although we performed sensitivity analyses to address reverse causation, others have reported in studies of PA and mortality that exclusion of the first 5 years of follow-up is needed to reduce the bias of undiagnosed disease elevating mortality risk and interfering with an individual's engagement in PA (41,42). In the context of modeling risk for diabetes, additional research is needed to determine the exclusion period that may reduce the potential for reverse causation for select disease-specific outcomes. Our study includes up to 5.9 years of follow-up, so we did not exclude longer periods of follow-up that went beyond the first 2 years. In addition, there is a competing potential for increasing the influence of survival bias and/or the misclassification of exposure in excluding earlier cases. For example, excluding cases that occur in the first few years of follow-up increases the likelihood that the PA exposure changed from its initial measurement (41), especially among older adults.

ActiGraph GT3X+ accelerometers when worn over the hip acceptably measure steps per day compared with direct observation but only at speeds >2.0 miles/h (43,44). This measurement feature might lead to an underestimation of steps per day for older people who tend to walk slower—and if older people are more likely to walk <2.0 miles per hour, and are more likely to have diabetes, differential measurement error could bias results toward the null, indicating that our estimate of a 12% lower hazard rate for each 2,000 steps/day increment might be lower than the unbiased HR. This measurement error could also play a role in our null findings related to light steps per day. Another potential limitation is that the absence of an association seen for low-intensity stepping and diabetes could be attributed to measurement error, since steps were measured with a hip-worn accelerometer and processed with the default filter in ActiLife, which misses steps taken at a low cadence (18,44,45). In a separate analysis by our team (E.T. Hyde, S. Nguyen, F. Tuz-Zahra, C.C. Moore, M.A. Greenwood-Hickman, R.L. Walker, L. Natarajan, D. Rosenberg, J.B., unpublished data, 2021) of data from 952 older adults who concurrently wore an ActiGraph GT3X+ and activPAL micro3 it was found that the number of steps

measured using low-frequency extension filter was high and lacked face validity for an older adult population and was discordant with those measured by the activPAL inclinometer (mean [SD] steps per day with ActiGraph normal filter 4,981 [3,099], ActiGraph low-frequency filter 11,800 [4,273], activPAL 6,832 [3,507]). Results from this separate analysis were similar to those from the study of Tudor-Locke et al. (46) in 2015, which demonstrated an average of 6,200 more steps per day with application of the low-frequency filter than with use of the normal filter. As a result, our team did not process OPACH Study steps data using the low frequency extension. Future studies with use of devices or data-processing methods that are not limited in measuring steps at low cadence should be prioritized for replicating our findings.

Furthermore, evidence demonstrating the validity and reliability of step cadence measures with use of the ActiGraph is limited, and so additional studies are needed to investigate possible measurement error. Measurement error may also have had a role in our inability to assess whether step cadence was associated with a lower diabetes hazard rate independent of total step volume due to multicollinearity ($r > 0.90$) resulting from the strong interrelationship between step volume and cadence among the older women in our study. However, it may be that older women who take fewer steps per day also have lower stepping intensity.

There are several key strengths of this study. Our cohort of older community-living women was relatively large and diverse, and this study relied on objective measures of steps per day, step cadence, and step intensity that were specifically calibrated (22) for older women. Our period of follow-up coincides with the known period of the life course during which diabetes incidence continues to increase, peaking at 85 years of age (1). Together, the research-quality measures of steps per day and the prospective study design are essential to adding to our understanding of steps per day and diabetes in older adults. In addition, our sensitivity analyses reduce concern that the findings presented in this study can be attributed to reverse causation.

Conclusion

This study provides evidence supporting an association between steps per day and lower incident diabetes, evidence that the 2018 Physical Activity Guidelines Advisory Committee found lacking. While further work is needed to identify whether there is a minimum number of steps per day that results in a clinically significant reduction of diabetes and to evaluate the role that step intensity plays in diabetes etiology for older adults, findings from this study suggest that MV-intensity steps may be more important than lower-intensity steps with respect to incident diabetes. Steps per day-based interventions are needed to advance diabetes prevention science in older adults.

Acknowledgments. The authors thank Sandy Liles, University of California, San Diego, for editorial assistance in reviewing for grammar and clarity. The authors appreciate the WHI participants for their dedication to the advancement of science and to helping the authors learn about how movement is associated with diabetes in older age. The full list of WHI investigators responsible for the overarching project in which this study was nested is available from <https://www-who-org.s3.us-west-2.amazonaws.com/wp-content/uploads/WHI-Investigator-Short-List.pdf>.

Funding. The study was supported by R01HL105065 (to A.Z.L.) and 5R01CA227122 (to K.R.E.). J.B. was funded by National Institute on Aging grant P01 AG052352, the National Institute of Diabetes and Digestive and Kidney Diseases (R01 DK114945), and the Tobacco-Related Disease Research Program (T31KT1501). This work was also supported by an NIH-funded predoctoral fellowship to A.C.G. (T32MH122376). The WHI program is funded by the National Heart, Lung, and Blood Institute, NIH, U.S. Department of Health and Human Services (HHSN268-201100046C, HHSN268201100001C, HHSN26820-1100002C, HHSN268201100003C, HHSN26820-1100004C, and HHSN271201100004C).

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. J.B. and A.C.G. contributed to development of study concept and design. A.C.G., G.W., and J.B. contributed to data preparation. A.C.G., B.T.S., and J.B. contributed to statistical analysis. A.C.G., A.Z.L., M.J.L., D.W.D., K.R.E., C.D., and J.B. contributed to interpretation of data. A.C.G. and J.B. contributed to drafting of the manuscript. All authors contributed to critical revision of the manuscript for important intellectual content. A.Z.L., M.J.L., and K.R.E. obtained funding. A.C.G. and J.B. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

References

- Sinclair A, Dunning T, Rodriguez-Mañas L. Diabetes in older people: new insights and remaining challenges. *Lancet Diabetes Endocrinol* 2015;3:275–285
- American Diabetes Association. 12. Older adults: *Standards of Medical Care in Diabetes—2020*. *Diabetes Care* 2020;43(Suppl. 1):S152–S162
- Meneilly GS, Tessier D. Diabetes in elderly adults. *J Gerontol A Biol Sci Med Sci* 2001;56:M5–M13
- LaMonte MJ, Blair SN, Church TS. Physical activity and diabetes prevention. *J Appl Physiol* (1985) 2005;99:1205–1213
- Colberg SR, Sigal RJ, Yardley JE, et al. Physical activity/exercise and diabetes: a Position Statement of the American Diabetes Association. *Diabetes Care* 2016;39:2065–2079
- Zhang Y, Pan XF, Chen J, et al. Combined lifestyle factors and risk of incident type 2 diabetes and prognosis among individuals with type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. *Diabetologia* 2020; 63:21–33
- Tryon WW. *Activity Measurement in Psychology and Medicine*. New York, Springer Science & Business Media, 2013
- Tudor-Locke C, Bassett DR Jr. How many steps/day are enough? Preliminary pedometer indices for public health. *Sports Med* 2004; 34:1–8
- Marshall SJ, Levy SS, Tudor-Locke CE, et al. Translating physical activity recommendations into a pedometer-based step goal: 3000 steps in 30 minutes. *Am J Prev Med* 2009;36:410–415
- Kraus WE, Janz KF, Powell KE, et al.; 2018 Physical Activity Guidelines Advisory Committee. Daily step counts for measuring physical activity exposure and its relation to health. *Med Sci Sports Exerc* 2019;51:1206–1212
- Cleven L, Krell-Roesch J, Nigg CR, Woll A. The association between physical activity with incident obesity, coronary heart disease, diabetes and hypertension in adults: a systematic review of longitudinal studies published after 2012. *BMC Public Health* 2020;20:726
- 2018 Physical Activity Guidelines Advisory Committee. *2018 Physical Activity Guidelines Advisory Committee Scientific Report*. Washington, DC, U.S. Department of Health and Human Services, 2018
- LaCroix AZ, Bellettiere J, Rillamas-Sun E, et al.; Women's Health Initiative (WHI). Association of light physical activity measured by accelerometry and incidence of coronary heart disease and cardiovascular disease in older women. *JAMA Netw Open* 2019;2:e190419
- Kraus WE, Yates T, Tuomilehto J, et al. Relationship between baseline physical activity assessed by pedometer count and new-onset diabetes in the NAVIGATOR trial. *BMJ Open Diabetes Res Care* 2018;6:e000523
- Mañas A, Del Pozo Cruz B, Ekelund U, et al. Association of accelerometer-derived step volume and intensity with hospitalizations and mortality in older adults: a prospective cohort study. *J Sport Health Sci* 2021:S2095-2546(21) 00052-1
- Lee IM, Shiroma EJ, Kamada M, Bassett DR, Matthews CE, Buring JE. Association of step volume and intensity with all-cause mortality in older women. *JAMA Intern Med* 2019;179:1105–1112
- LaCroix AZ, Rillamas-Sun E, Buchner D, et al. The Objective Physical Activity and Cardiovascular Disease Health in Older Women (OPACH) Study. *BMC Public Health* 2017;17:192
- Miguelo JH, Cadenas-Sanchez C, Ekelund U, et al. Accelerometer data collection and processing criteria to assess physical activity and other outcomes: a systematic review and practical considerations. *Sports Med* 2017;47:1821–1845
- Ballin M, Nordström P, Niklasson J, et al. Daily step count and incident diabetes in community-dwelling 70-year-olds: a prospective cohort study. *BMC Public Health* 2020;20:1830
- Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. *Med Sci Sports Exerc* 2011;43:357–364
- Bellettiere J, Zhang Y, Berardi V, et al. Parameterizing and validating existing algorithms for identifying out-of-bed time using hip-worn accelerometer data from older women. *Physiol Meas* 2019;40:075008
- Bellettiere J, LaMonte MJ, Evenson KR, et al. Sedentary behavior and cardiovascular disease in older women: the Objective Physical Activity and Cardiovascular Health (OPACH) Study. *Circulation* 2019;139:1036–1046
- Tudor-Locke C, Camhi SM, Leonardi C, et al. Patterns of adult stepping cadence in the 2005–2006 NHANES. *Prev Med* 2011;53:178–181
- Evenson KR, Wen F, Herring AH, et al. Calibrating physical activity intensity for hip-worn accelerometry in women age 60 to 91 years: The Women's Health Initiative OPACH Calibration Study. *Prev Med Rep* 2015;2:750–756
- Jackson JM, DeFor TA, Crain AL, et al. Validity of diabetes self-reports in the Women's Health Initiative. *Menopause* 2014;21:861–868
- De Neve J, Gerds TA. On the interpretation of the hazard ratio in Cox regression. *Biom J* 2020;62:742–750
- Bellettiere J, LaMonte MJ, Healy GN, et al. Sedentary behavior and diabetes risk among women over the age of 65 years: the OPACH Study. *Diabetes Care* 2021;44:563–570
- Bellettiere J, Healy GN, LaMonte MJ, et al. Sedentary behavior and prevalent diabetes in 6,166 older women: the Objective Physical Activity and Cardiovascular Health Study. *J Gerontol A Biol Sci Med Sci* 2019;74:387–395
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2013;36(Suppl. 1):S67–S74
- Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med* 2020;54:1451–1462
- Huffman KM, Sun JL, Thomas L, et al. Impact of baseline physical activity and diet behavior on metabolic syndrome in a pharmaceutical trial: results from NAVIGATOR. *Metabolism* 2014;63:554–561
- Centers for Disease Control and Prevention. Estimates of diabetes and its burden in the United States. In *National Diabetes Statistics Report, 2020*. Atlanta, GA, Centers for Disease Control and Prevention, 2020
- Colpani V, Oppermann K, Spritzer PM. Association between habitual physical activity and lower cardiovascular risk in premenopausal, perimenopausal, and postmenopausal women: a population-based study. *Menopause* 2013;20:525–531
- Johnson ST, Eurich DT, Lytvak E, et al. Walking and type 2 diabetes risk using CANRISK scores among older adults. *Appl Physiol Nutr Metab* 2017;42:33–38
- Newton RL Jr, Han H, Johnson WD, et al. Steps/day and metabolic syndrome in African American adults: the Jackson Heart Study. *Prev Med* 2013;57:855–859
- Yates T, Henson J, Khunti K, et al. Effect of physical activity measurement type on the association between walking activity and glucose regulation in a high-risk population recruited from primary care. *Int J Epidemiol* 2013;42:533–540
- Ponsonby A-L, Sun C, Ukoumunne OC, et al. Objectively measured physical activity and the subsequent risk of incident dysglycemia: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Diabetes Care* 2011;34:1497–1502
- Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393–403
- Bellettiere J, Lamonte MJ, Unkart J, et al. Short physical performance battery and incident cardiovascular events among older women. *J Am Heart Assoc* 2020;9:e016845
- Jain P, Bellettiere J, Glass N, et al. The relationship of accelerometer-assessed standing time with and without ambulation and mortality: the WHI OPACH Study. *J Gerontol A Biol Sci Med Sci* 2021;76:77–84
- Tarp J, Hansen BH, Fagerland MW, Steene-Johannessen J, Anderssen SA, Ekelund U. Accelerometer-measured physical activity and sedentary time in a cohort of US adults followed for up to 13 years: the influence of removing early follow-up on associations with mortality. *Int J Behav Nutr Phys Act* 2020;17:39
- Singh PN, Wang X. Simulation study of the effect of the early mortality exclusion on confounding of the exposure-mortality relation by preexisting disease. *Am J Epidemiol* 2001; 154:963–971
- Nuss KJ, et al. Comparison of energy expenditure and step count measured by Acti-Graph accelerometers among dominant and nondominant wrist and hip sites. *J Meas Phys Behav* 2020;3:315–322
- Moore CW, McCullough AK, Aguiar EJ, Ducharme SW, Tudor-Locke C. Toward harmonized treadmill-based validation of step-counting wearable technologies: a scoping review. *J Phys Act Health* 2020;17:1–13
- Bezuidenhout L, Thurston C, Hagströmer M, Moolaee Conradsson D. Validity of hip and ankle worn Actigraph accelerometers for measuring steps as a function of gait speed during steady state walking and continuous turning. *Sensors (Basel)* 2021;21:3154
- Tudor-Locke C, Barreira TV, Schuna JM Jr. Comparison of step outputs for waist and wrist accelerometer attachment sites. *Med Sci Sports Exerc* 2015;47:839–842