

Objectively Measured Physical Activity and the Subsequent Risk of Incident Dysglycemia

The Australian Diabetes, Obesity and Lifestyle Study (AusDiab)

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OBJECTIVE—To investigate pedometer-measured physical activity (PA) in 2000 and change in PA over 5 years with subsequent risk of dysglycemia by 2005.

RESEARCH DESIGN AND METHODS—This prospective cohort study in Tasmania, Australia, analyzed 458 adults with normal glucose tolerance and a mean (SD) age of 49.7 (12.1) years in 2000. Variables assessed in 2000 and 2005 included PA, by pedometer and questionnaire, nutrient intake, and other lifestyle factors. Incident dysglycemia was defined as the development of impaired fasting glucose or impaired glucose tolerance revealed by oral glucose tolerance testing in 2005, without type 2 diabetes.

RESULTS—Incident dysglycemia developed in 26 participants during the 5-year period. Higher daily steps in 2000 were independently associated with a lower 5-year risk of incident dysglycemia (adjusted odds ratio [AOR] 0.87 [95% CI 0.77–0.97] per 1,000-step increment). Higher daily steps in 2005, after controlling for baseline steps in 2000 (thus reflecting change in steps over 5 years), were not associated with incident dysglycemia (AOR 1.02 [0.92–1.14]). Higher daily steps in 2000 were also associated with lower fasting blood glucose, but not 2-h plasma glucose by 2005. Further adjustment for BMI or waist circumference did not remove these associations.

CONCLUSIONS—Among community-dwelling adults, a higher rate of daily steps is associated with a reduced risk of incident dysglycemia. This effect appears to be not fully mediated through reduced adiposity.

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The number of people with type 2 diabetes will escalate from 285 to 438 million between 2010 and 2030 (1). Preventive strategies targeting modifiable factors, such as physical activity (PA), are a priority. Current public health policy is limited by an inability to quantify the magnitude of the apparent beneficial effect of PA due to a lack of studies

measuring PA objectively and incident dysglycemia. Incident dysglycemia includes individuals who newly develop impaired fasting glucose (IFG) but who have a normal response to a glucose load, and/or individuals with a normal fasting glucose but impaired glucose tolerance (IGT) (2). Incident dysglycemia is associated with increased risk of type 2

diabetes, cardiovascular disease, and death (3–6).

Although evidence is emerging that the increasing prevalence of type 2 diabetes and its precursor, dysglycemia, is partly attributed to a physically inactive lifestyle, few prospective studies have used objectively measured PA to evaluate this association. Two recent cohort studies reported conflicting findings regarding the associations of accelerometer-measured moderate and vigorous activity with insulin resistance (7,8).

A review conducted predominantly in individuals at higher risk of diabetes, with a mean (SD) fasting blood glucose of 7.09 (2.09) mmol/L at baseline, reported that pedometer-measured PA was not associated with fasting glucose level (β -0.03 mmol/L; $P = 0.70$) (9). The lack of an association could be explained by 1) the relatively small sample size in these studies (a pooled sample of 211 participants), 2) the intervention length and follow-up being insufficient to assess longer-term metabolic change, or 3) nondetection of a glucose metabolic effect that the oral glucose tolerance test (OGTT) would have detected.

We have recently reported that lower daily steps at baseline and a reduction in daily steps by follow-up are both associated with impaired insulin sensitivity at a 5-year follow-up (10). Here, we examine the longitudinal association between PA (using pedometer-measured and self-reported activity) and incident dysglycemia, defined by repeated OGTT in the population-based Australian Diabetes, Obesity and Lifestyle Study (AusDiab).

RESEARCH DESIGN AND METHODS

Study population

The AusDiab is a large population-based study designed to investigate the national prevalence of diabetes and related risk factors in 2000 (11,12). Baseline testing was conducted in 2000, and the study recruited 11,247 adults aged ≥ 25 years, with $>85\%$ being born in Australia, New

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Zealand, or the U.K. In the state of Tasmania, AusDiab included six random census collection districts based on the 1996 Australian Census. Of those who completed a questionnaire, 40% participated in the physical examination. An OGTT was administered at baseline and at follow-up, unless the participants were pregnant or being treated with oral hypoglycemic medication. Of 1,611 participants who had a baseline OGTT result, 592 provided 2-day pedometer data at baseline and at follow-up (10,13). Of these, we excluded 38 who had impaired fasting glucose (IFG) and 75 who had impaired glucose tolerance (IGT) on the basis of their initial OGTT, and we further excluded 2 who developed type 2 diabetes at follow-up and 19 with no follow-up glycemic status data. Thus, 458 participants were available for the assessment of incident dysglycemia and 460 for the assessment of type 2 diabetes.

The study was approved by the International Diabetes Institute Ethics Committee and the Human Research Ethics Committee of the University of Tasmania. Informed consent was obtained from all participants.

Study measures

Participants were invited to attend a local testing site where physical measurements and a fasting venous blood sample were obtained at baseline and follow-up.

Questionnaire assessment of recent PA time

Information on the frequency and duration of PA in the previous week was collected using the Active Australia Questionnaire (14). A weighted sum of the responses (with vigorous-intensity activity given double-weighting) was calculated to quantify total hours of PA (14).

Objective pedometer assessment of PA

The pedometer (Omron HJ-003 and Omron HJ-102; Omron Healthcare, Inc., Bannockburn, IL) protocol has been previously described (10,13). Pedometer data were collected for 2 consecutive days in 2000, and only readings that included at least 1 weekday were used. In 2005, participants were asked to wear pedometers during weekdays and weekends for 7 consecutive days. To provide comparability with the 2000 pedometer measures, only the first 2 consecutive days of the 2005 pedometer measures were used where at least 1 day was a

weekday (10,13). The intraclass correlations are 0.71–0.84 for any 2 days of recording (15). Pedometers are simpler and cheaper than accelerometers and thus have been generally more applicable in large population-based studies. Although accelerometers provide information about pattern, intensity, and type of PA, which will not all be captured by pedometers, the intraclass correlation coefficient relating their step measures has been estimated at 0.74 to 0.86 for 7 days of recording (16).

Diet, other lifestyle, and demographic attributes

We collected self-reported information on current smoking status (defined as current or past/never) and education level (≤ 12 years vs. >12 years). A self-administered validated food frequency questionnaire, developed by the Cancer Council of Victoria, was used to assess dietary and alcohol intake during the previous 12 months at both phases based on the Nutrient Data Table for Use in Australia 1995 (11).

Physical examination

Height was measured to the nearest 0.5 cm without shoes, and weight was recorded to the nearest 0.1 kg. Waist circumference was measured halfway between the lower border of the ribs and the iliac crest on the horizontal plane. BMI (kg/m^2) and waist circumference were used as adiposity measures (11,12).

Fasting plasma glucose and 2-h plasma glucose

Fasting blood samples were collected and centrifuged on site and transported daily to the central laboratory. Serum insulin (samples stored at -80°C) was measured using a human insulin-specific radioimmunoassay kit (Linco Research, St. Charles, MO) for participants aged >35 years in 2000, and a chemiluminescence method was used for all participants in 2005 (12). We assessed OGTT in both phases. Fasting plasma glucose (FPG) levels were determined using an Olympus AU600 automated analyzer (Center Valley, PA) in 2000 and spectrophotometric-hexokinase methods (Roche Diagnostics, Indianapolis, IN) in 2005 (12).

IFG, IGT, or type 2 diabetes were defined according to 1999 World Health Organization diabetes criteria. Participants who reported a history of physician-diagnosed diabetes and who were receiving treatment with oral hypoglycemic

agents and/or insulin, or had a fasting plasma glucose (FPG) level ≥ 7.0 mmol/L or 2-h plasma glucose (2-hPG) level ≥ 11.1 mmol/L were classified as having type 2 diabetes. Participants who did not have diabetes were classified as having (in mmol/L) IFG (FPG ≥ 6.1 and <7.0 , with 2-hPG <7.8), IGT (2-hPG ≥ 7.8 and <11.1 , with FPG <7.0), or normal glucose tolerance (FPG <6.1 and 2-hPG <7.8).

Statistical analysis

The primary outcome of interest was incident dysglycemia, defined as participants who had no dysglycemia or type 2 diabetes at baseline who had developed IFG or IGT—but not type 2 diabetes—by the 5-year follow-up. Type 2 diabetes was excluded in our main analyses because this reflects a different disease end point and the numbers were too small to study type 2 diabetes alone. We also, however, used a secondary outcome with an expanded definition to also incorporate the two individuals with type 2 diabetes. Because previous studies have reported different pathophysiologic processes may underlie the etiology of IFG and IGT, we also used FPG and 2-hPG levels at follow-up as continuous outcome variables, enabling exploration in a parallel analysis.

Categorical variables are described using percentages and continuous variables using means and SD or medians and interquartile ranges, if not normally distributed. Using logistic regression models, we examined the prospective association between baseline PA and glucose metabolism in 2005, without adjusting for follow-up PA (17). To assess change of PA in relation to dysglycemia, PA in 2000 and 2005 were both included in the logistic regression model. In such a model, the odds ratio (OR) for PA in 2005 could therefore be interpreted as the OR for change in activity after 5 years because baseline activity was included (18).

A range of potential confounders measured in 2000 were considered in model building. We used relatedness of potential confounders to exposures and outcomes and change-in-estimate criterion to select potential confounders in the multivariable model. We investigated whether the effect of daily steps on dysglycemia was mediated through reduced adiposity by additionally adjusting for BMI or waist circumference in 2000 and 2005. We also examined change in PA in other ways by using a categorical ordinal variable (13). We classified daily steps into five categories: persistent low steps

(the lowest third tertile of daily steps in both 2000 and 2005), decreasing steps (dropped by one or two categories between 2000 and 2005), persistent moderate steps (middle third at both waves), increasing steps (increase of one or two categories), and persistent high steps (highest third at both waves).

In a sensitivity analysis, population-weighted models were fitted to determine whether the results were influenced by differences on demographic characteristics between the 458 participants analyzed in this report and those who were excluded. Weights were used to adjust the analyzed sample to be representative of the reference group (all Tasmanian AusDiab participants at baseline, excluding those with dysglycemia/type 2 diabetes) with respect to sex and age, BMI in 2000, and socioeconomic status. The weights were the inverse of the probability of being analyzed in this report and were calculated using the probabilities obtained after fitting a logistic regression of whether analyzed in this report (0 = not analyzed; 1 = analyzed) compared with the reference group (19). We used STATA 11 software (StataCorp, College Station, TX) for all analyses.

RESULTS—The mean (SD) age of the study sample was 49.7 (12.1) years at baseline with 55.9% women. Of the 458 people free of type 2 diabetes or dysglycemia at baseline, dysglycemia had developed in 26 (5.7%) by follow-up. Among these, 11 (42.3%) were classified as IFG and 15 (57.7%) as IGT. Type 2 diabetes developed in a further 2. At baseline, the median number (interquartile range) of daily steps was 10,733 (7,695–13,833). Median change in daily steps over 5 years was –1,469 (–5,068 to 1,315). Median self-reported PA in the past week at baseline was 4 (1–8) h and median self-reported vigorous activity was 0 (0–1) h. Participants who developed dysglycemia were older, were more likely to be men, had a larger waist circumference, were more overweight, and were less likely to smoke (Table 1).

Higher baseline daily steps were associated with lower incident dysglycemia, after adjusting for age and sex (adjusted OR [AOR] 0.87 [95% CI 0.77–0.97] per 1,000-step increment, Table 2). The independent association of higher daily steps at baseline with lower risk of dysglycemia remained unchanged after additionally adjusting for BMI at baseline and follow-up (AOR 0.87 [0.78–0.98])

Table 1—Baseline characteristics comparing participants who did and did not develop 5-year incident dysglycemia

Variable	Incident dysglycemia	
	Did not develop n = 432	Developed n = 26
Age (years)	49.4 (0.6)	54.9 (2.3)
Women (%)	56.7 (245/432)	42.3 (11/26)
Waist circumference (cm)	86.7 (0.6)	92.9 (2.0)
Weight (kg)	74.2 (0.7)	80.7 (3.2)
Height (cm)	168.6 (0.4)	170.9 (2.1)
BMI (kg/m ²)	26.0 (0.2)	27.4 (0.6)
Weight class by BMI (kg/m ²)		
Overweight, >25 to <30 (%)	43.0 (185/430)	69.2 (18/26)
Obese, ≥30 (%)	14.7 (63/430)	15.4 (4/26)
Current cigarette smoking (%)	12.9 (55/427)	3.9 (1/26)
Alcohol consumption (g/day)*	6.3 (0.8–16.8)	8.0 (0.9–23.2)

Data show crude mean (SD), proportions (n/N), or *median (interquartile range).

or waist circumference (0.88 [0.79–0.99]). Change in daily steps over 5 years was not associated with incident dysglycemia, after adjusting for baseline daily steps, age, and sex (AOR 1.02 [0.92–1.14]). Neither self-reported baseline PA nor self-reported change in PA was associated with incident dysglycemia (data not shown).

An inverse linear relationship was found between daily steps at baseline and 5-year FPG and 2-hPG. Fractional polynomial modeling (20) was used to assess any departure from linearity, and indicated the linear model was appropriate. In the multivariable analysis, a 1,000-step increment at baseline was significantly associated with a 0.01 mmol/L (95% CI –0.018 to –0.003, P = 0.006) lower 5-year FPG, after adjusting for age and sex (Table 3). The association of baseline daily steps with 5-year FPG was partly attenuated after further controlling for BMI at baseline and follow-up (β –0.008 [95% CI –0.016 to –0.001], P = 0.03) or baseline and follow-up waist circumference (β –0.007 [–0.015 to

–0.000], P = 0.06). Again, change in daily steps was not associated with 5-year FPG. Neither baseline daily steps nor change in step activity was associated with the 5-year 2-hPG.

Overall, self-reported PA was not associated with 5-year FPG or 2-hPG. Change in self-reported vigorous activity over 5 years was positively associated with lower 5-year 2-hPG (β –0.001 [95% CI –0.002 to –0.000] mmol/L, P = 0.04), after adjusting for baseline self-reported vigorous activity, age, and sex. This association was substantially attenuated and became nonsignificant after further adjustment for BMI at baseline and follow-up (β –0.0006 [–0.002 to 0.000] mmol/L, P = 0.21), indicating the association between change in self-reported vigorous activity and 2-hPG may be partly mediated through the associated beneficial reduction in adiposity.

The additional individual adjustment for family history of diabetes; socioeconomic status; current smoking (cigarettes/day); alcohol (g/day), total energy (kJ/day), protein (g/day), carbohydrate

Table 2—Relationship of pedometer-measured PA with 5-year incident dysglycemia

Variable	Unadjusted		Adjusted	
	OR (95% CI)	P	OR (95% CI)	P
Daily steps (1,000 steps/day)				
Baseline	0.85 (0.76–0.95)	0.004	0.87 (0.77–0.97)*	0.01
Follow-up	1.01 (0.91–1.12)†	0.87	1.02 (0.92–1.14)‡	0.65

*Multivariable model for baseline daily steps adjusted for age and sex. †Adjusted for baseline daily steps as the crude model for follow-up activity (reflecting change in activity). ‡Multivariable model for follow-up daily steps (reflecting change in activity) adjusted for baseline daily steps, age, and sex.

Table 3—Relationships of pedometer-measured PA with 5-year FPG and 2-hPG

Outcome Variable	Unadjusted		Adjusted*	
	Mean difference (95% CI)	P	Mean difference (95% CI)	P
FPG				
Daily steps, 1,000-step increase/day				
Baseline	−0.011 (−0.019 to −0.004)	0.004	−0.01 (−0.018 to −0.003)*	0.006
Follow-up	0.004 (−0.006 to 0.013)†	0.45	0.004 (−0.006 to 0.013)‡	0.46
2-hPG				
Daily steps, 1,000-step increase/day				
Baseline	−0.021 (−0.043 to 0.001)	0.06	−0.014 (−0.036 to 0.008)*	0.22
Follow-up	−0.005 (−0.033 to 0.023)†	0.72	0.003 (−0.025 to 0.031)‡	0.84

*Multivariable model for baseline daily steps adjusted for age and sex. †Adjusted for baseline daily steps in this crude model for follow-up daily steps (thus reflects change in activity). ‡Multivariable model for follow-up daily steps (thus reflects change in activity) adjusted for baseline daily steps, age, and sex.

(g/day), or fat intake (g/day) collected at baseline did not alter the magnitude of the association between daily steps in 2000 and incident dysglycemia by more than 3% (Table 2). Similarly, the associations reported in Table 3 were not altered by further adjustment for these factors. Furthermore, inclusion of the two participants with type 2 diabetes as additional dysglycemia cases did not alter the findings in Tables 2 and 3. For this expanded classification of dysglycemia (type 2 diabetes, IFG, and IGT), higher daily steps in 2000 remained independently associated with a lower 5-year risk of incident dysglycemia (AOR 0.86 [95% CI 0.77–0.96] per 1,000-step increment), after adjusting for age and sex. Higher daily steps in 2005, after controlling for baseline steps in 2000 (thus reflecting change in steps over 5 years), were also not associated with this expanded classification of dysglycemia (AOR 1.00 [0.90–1.11]). Higher daily steps in 2000 were also associated with lower FPG ($P = 0.003$), but not 2-hPG by 2005 ($P = 0.15$). When change in PA was analyzed using a categorical ordinal variable, participants with persistent low daily steps in both 2000 and 2005 were significantly more likely to have incident dysglycemia by 2005 (AOR 2.98 [1.27–6.97]) than those who did not. There was no significant variation in risk across the other categories of activity (test of trend, $P = 0.30$). The associations between 1) higher baseline daily steps and risk of dysglycemia or between 2) higher baseline steps and FPG were altered little by accounting for the nonresponse bias using inverse probability weighting.

CONCLUSIONS—This study provides the first evidence, to our knowledge, that objectively measured higher PA is associated with reduced risk of dysglycemia over

5 years. In a parallel analysis, using blood glucose measures as an outcome with a continuous scale, higher baseline daily steps remained an independent predictor of lower FPG levels 5 years later.

The strengths of the study include its population-based sample, prospective design, objective pedometer measurement of PA, long follow-up, use of repeated OGTTs to accurately classify glycemic status, and the collection of a variety of potential confounders. The associations observed are prospective, but the timing of the incident occurrence is unavailable. The exposure measure, however, was daily steps at baseline, and because glycemic status rather than overt diabetes was the focus, participants would be likely to be asymptomatic and unaware of their conditions and, thus, would be less likely to modify factors, such as adiposity, by follow-up.

The number of incident cases was not large. However, similar patterns were observed in the parallel analysis using daily steps in 2000 and continuous glucose measures in 2005. The small case number and low magnitude of any change in PA, with an average decline of less than 1,500 steps, may explain the lack of association between a change in daily steps and dysglycemia risk. We were able to address the issue of loss to follow-up in this cohort study by weighting the results for the loss that occurred. This did not affect the estimate of association between daily steps and dysglycemia. Finally, we cannot fully rule out residual confounding due to unmeasured confounders (e.g., genetic factors) or potentially misclassified measures.

Previous data from the AusDiab have shown that 1) self-reported PA is associated with a reduced prevalence of impaired glucose metabolism (21) and 2) inactivity is associated with an

increased incidence of type 2 diabetes (12). Some studies have demonstrated a rapid short-term effect of PA on fasting insulin and glucose concentration (22,23). Results from this current study suggest that PA may also have a relatively longer-term effect on glucose metabolism. Studies for direct comparison are not available at present, although a recent review showed little effect of interventions to increase daily steps on FPG concentration (9).

The reason higher daily steps was associated with incident dysglycemia here, but not in the studies included in the review (9), may be that PA has a longer-term effect on dysglycemia, which was reflected by PA in 2000 but not PA in 2005 being associated with dysglycemia, and that persistently low average daily steps had the highest risk. Alternatively, the use of repeated OGTTs here may have provided more sensitive detection. Also, most studies included in the review were conducted among highly selected groups. Furthermore, our finding that PA, when measured objectively rather than self-reported, was associated with subsequent dysglycemia and FPG levels, together with the previous report that a lower magnitude of association was observed for the prospective association between self-report PA and insulin sensitivity (10), indicates that objective measures such as pedometers may capture PA better by inclusion of incidental activity and reduced measurement error.

We estimated that every increment of 1,000 daily steps resulted in a 13% lower odds of 5-year incident dysglycemia. In the parallel analysis, an inverse association remains between baseline daily steps and 5-year FPG. For this later association the beneficial changes may be partly mediated through a reduced BMI or waist circumference. A similar result was

observed when waist circumference was used as an alternative adiposity measure.

Our data are consistent with a recent systematic review that revealed that higher self-reported PA is associated with lower risk of type 2 diabetes, even after accounting for BMI (BMI-adjusted relative risk 0.83 [95% CI 0.76–0.90]) (24). Findings from this current study add to the broader evidence base on the importance of increasing PA through its direct beneficial effect on future glucose metabolism.

The findings here of a significant association between daily steps in 2000 and incident dysglycemia are consistent with a recent report from the same cohort that daily steps in 2000 were associated with improved insulin sensitivity in 2005 (10). Although our previous study demonstrated that an increase in daily steps in 2000 compared with 2005 was associated with improved insulin sensitivity (10), this current study did not show that it was associated with a reduction in the risk of incident dysglycemia, raising the possibility that PA has a longer-term effect on dysglycemia than insulin sensitivity. In addition, the current findings suggest that an increase in self-reported vigorous activity over 5 years may have a different effect on aspects of glucose metabolism than daily steps alone.

This study has allowed us to quantify the magnitude of the effect. An increase from being essentially sedentary to meeting the goal of 10,000 steps (25)—a 10,000-step increase—would be associated with 76% lower odds of developing dysglycemia 5 years later, based on the magnitude of associations observed in this study (AOR 0.24 [95% CI 0.08–0.73]). Alternatively, from any average daily steps, an additional 2,000 steps would be associated with a 25% reduction in developing incident dysglycemia over the subsequent 5 years (AOR 0.75 [0.60–0.94] per 2,000 steps). Our findings indicate that if the type 2 diabetes cases were additionally included in an expanded definition of dysglycemia, a similar magnitude of effect would be expected.

To conclude, higher daily steps is an important predictor of a lower 5-year risk of dysglycemia among an adult population, and such an effect appears to be not fully mediated by reduced adiposity.

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