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Predictors of the Acute Postprandial Response to Breaking Up Prolonged Sitting

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ABSTRACT

HENSON, J., C. L. EDWARDSON, C. A. CELIS-MORALES, M. J. DAVIES, D.W. DUNSTAN, D.W. ESLIGER, J. M. R. GILL, A. KAZI, K. KHUNTI, J. KING, M. MCCARTHY, N. SATTAR, D. J. STENSEL, L. VELAYUDHAN, F. ZACCARDI, and T. YATES. Predictors of the Acute Postprandial Response to Breaking Up Prolonged Sitting. *Med. Sci. Sports Exerc.*, Vol. 52, No. 6, pp. 1385–1393, 2020. **Purpose:** To identify predictors of favorable changes to postprandial insulin and glucose levels in response to interrupting prolonged sitting time with standing or light-intensity physical activity. **Methods:** Data were combined from four similarly designed randomized acute cross-over trials (n = 129; body mass index [BMI] range, 19.6–44.6 kg·m^{-2}; South Asian = 31.0%; dysglycemia = 27.1%). Treatments included: prolonged sitting (6.5 h) or prolonged sitting broken-up with either standing or light-intensity physical activity (5 min every 30 min). Time-averaged postprandial responses for insulin and glucose were calculated for each treatment (mean ± 95% confidence interval). Mutually adjusted interaction terms were used to examine whether anthropometric (BMI), demographic (age, sex, ethnicity [white European vs South Asian]) and a cardiometabolic variable (Homeostatic Model Assessment of Insulin Resistance)-modified responses. **Results:** Postprandial insulin and glucose were reduced when individuals interrupted prolonged sitting with bouts of light physical activity, but not with standing. Reductions in time-averaged postprandial insulin were more pronounced if individuals were South Asian compared with white European (−18.9 mU·L^{-1} [−23.5%] vs −8.2 mU·L^{-1} [−9.3%]), female compared with male (−15.0 mU·L^{-1} [−21.2%] vs −12.1 mU·L^{-1} [−17.6%]) or had a BMI ≥27.2 kg·m^{-2} (−20.9 mU·L^{-1} [−22.9%] vs −8.7 mU·L^{-1} [−18.2%]). Similarly, being female (−0.4 mmol·L^{-1} [−0.6 mmol·L^{-1}, −0.2 mmol·L^{-1}], −6.8% vs –0.1 mmol·L^{-1} [−0.3 mmol·L^{-1}, 1 mmol·L^{-1}], −1.7%) or having a BMI ≥27.2 kg·m^{-2} (−0.4 mmol·L^{-1} [−0.6 mmol·L^{-1}, −0.2 mmol·L^{-1}], −6.7% vs –0.2 mmol·L^{-1} [−0.4 mmol·L^{-1}, 0.0 mmol·L^{-1}], −3.4%) modified the postprandial glucose response. No significant interactions were found for Homeostatic Model Assessment of Insulin Resistance or age. **Conclusions:** Being female, South Asian, or having a higher BMI, all predicted greater reductions in postprandial insulin, whereas being female and having a higher BMI predicted greater reductions in postprandial glucose when sitting was interrupted with light physical activity. These results could help to guide personalized interventions in high-risk participants for whom breaking prolonged sitting time with light activity may yield the greatest therapeutic potential.
Key Words: POSTPRANDIAL, PHYSICAL ACTIVITY, SEDENTARY BEHAVIOR, RISK FACTORS, INSULIN, GLUCOSE

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Postprandial hyperglycemia plays a significant role in the development of cardiovascular disease (CVD) in people with type 2 diabetes mellitus (T2DM) (1). The postprandial phase is characterized by a rapid and large increase in blood glucose and insulin levels. Observational evidence suggests that postprandial hyperglycemia, even in the absence of fasting hyperglycemia, is associated with higher risks of future cardiometabolic disease (2,3). Similarly, a hyperinsulinemic response is closely associated with a number of CVD and T2DM-related outcomes (4). Therefore, if these links are in part causal, establishing effective and pragmatic interventions that reduce postmeal hyperglycemic and hyperinsulinemic excursions could be important therapeutic targets for the prevention of T2DM and CVD, particularly as individuals spend a large proportion of the day in a postprandial state (5).

Physical activity is known to enhance health and improve postprandial hyperglycemia (6). Current physical activity guidelines recommend that adults engage in ≥150 min of moderate-intensity physical activity or ≥75 min of vigorous activity and two to three resistance exercise sessions per week (7). In addition, current physical activity guidelines now include specific recommendations to reduce and interrupt prolonged sitting (6,8). These guidelines have been informed by emerging research, suggesting that sitting time *per se* is an independent risk factor for cardiometabolic morbidity and mortality (9,10). Over recent years, epidemiological research has been complemented by acute experimental studies showing that breaking up bouts of prolonged sitting with standing or light-intensity activity elicits significant benefits on markers of metabolic health (11–15).

These results are important as light-intensity activities are behaviorally more ubiquitous than moderate to vigorous physical activity and may therefore be appealing interventional targets in the promotion of metabolic health, while also being more culturally acceptable to high-risk groups (e.g., South Asian women). However, the interindividual variability in the effectiveness of such interventions is likely to be large. For example, previous experimental research has shown that the magnitude of postprandial dysglycemia in response to prolonged sitting and the subsequent reduction after breaks may differ considerably according to ethnicity or the degree of underlying insulin resistance (13,16).

Therefore, to ensure future T2DM prevention strategies are stratified and targeted at those who could derive the greatest benefit, it is necessary to determine the factors that may predict a favorable response to breaking up prolonged sitting with a low-intensity intervention. As such, the aim was to determine whether commonly measured demographic, anthropometric, or clinical factors are associated with the postprandial insulin and glucose response when breaking up prolonged sitting, with short bouts of either standing or physical activity, at a light intensity.

METHODS

Study Design

We performed a pooled analysis of data collected from 129 individuals across four separate acute, randomized, crossover experimental studies conducted within the Leicester Diabetes Centre (University of Leicester) (n = 99) and the University of Glasgow (n = 30), UK (2015–2018); all of which followed the same protocols and standard operating procedures for data collection and the same treatment methodology of breaking sitting time with 5 min of standing or light physical activity every 30 min (see Figure, Supplemental Digital Content 1, protocols and standard operating procedures for data collection, http://links.lww.com/MSS/B865). The research design and methods have been published in detail elsewhere (11–14). Briefly, participants were recruited from studies previously conducted within the Leicester Diabetes Centre (ACUTE, ARMING HEALTH, STAND UP) or from the public via strategic placement and distribution of promotional materials (STAND UP, FIT2SIT). Detailed inclusion and exclusion criteria can be found in Supplementary Digital Content Table 1 (see Table, Supplemental Digital Content 2, Inclusion and exclusion criteria, http://links.lww.com/MSS/B867).

Participants attended up to four separate visits to their corresponding center. One week to 2 wk after an initial familiarization visit, participants were randomized to the following treatment conditions: 1) prolonged sitting (6.5 h; plus 60 min steady state), 2) prolonged sitting broken up with standing for 5 min every 30 min, or 3) prolonged sitting broken up with physical activity (either walking or arm ergometry) for 5 min every 30 min. As an acute bout of physical activity may enhance insulin sensitivity for up to 48 h, we used a minimum wash-out period of 7 d between each condition.

All studies were registered with clinicaltrials.gov (ACUTE: NCT02135172; STAND UP: NCT02453204; ARMING HEALTH: NCT02909894; FIT2SIT: NCT02493309). Written informed consent was obtained from all eligible participants and the individual studies had full ethical and governance approval.

Participants

In total, 147 participants were randomized. Causes of drop out between familiarization and randomization are detailed in Figure 1. A further 18 individuals were excluded after randomization: due to cessation of the venous cannula line which resulted in less than 50% of data collection (n = 11), illness (n = 2), inability to tolerate the standardized meal (n = 2), unable to commit time (n = 2), or a change in personal circumstance (n = 1). This left 129 participants that were included in the analysis.

Familiarization Visit

Before participating in the experimental protocol, participants visited the Leicester Diabetes Centre or University of Glasgow for a familiarization visit in which they were accustomed to the required power output for the arm ergometry or walking speed (self-perceived light intensity). Participants were instructed to walk at a pace they felt was comfortable and registered between 10 and 12 on the Borg RPE scale (17). Body mass (Tanita TBE 611; Tanita, West Drayton, UK) and

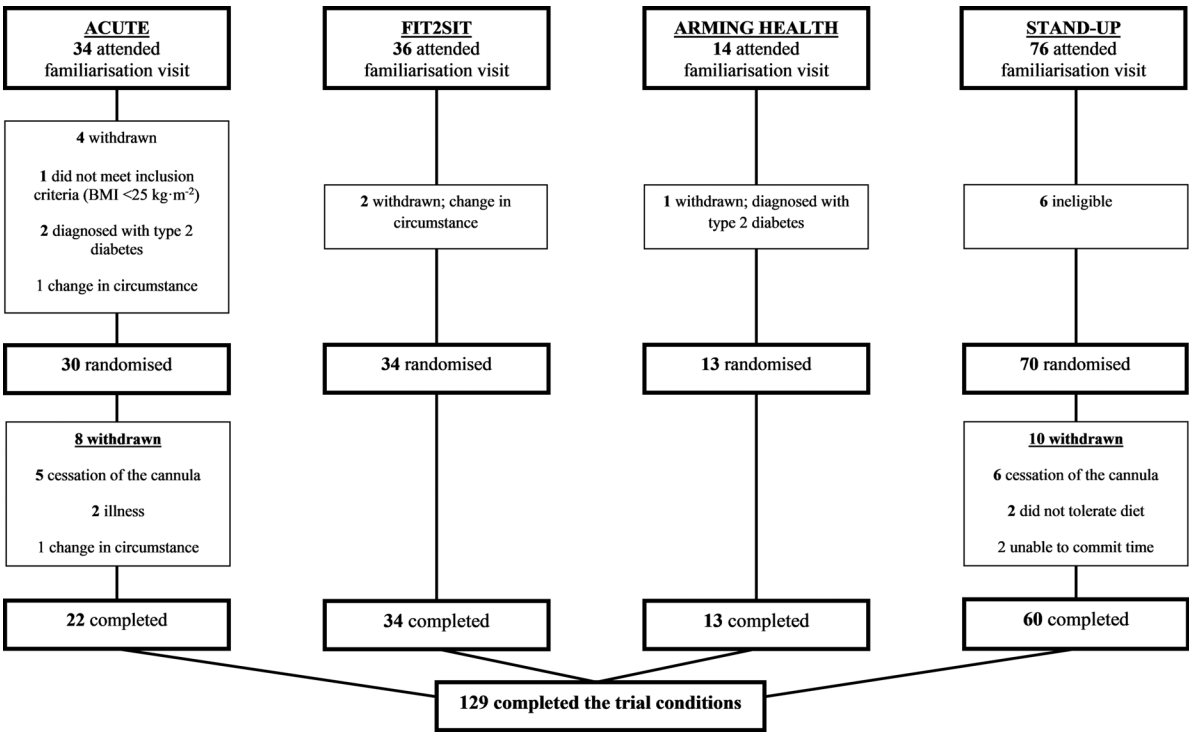

FIGURE 1—Study CONSORT Diagram.

height were measured to the nearest 0.1 kg and 0.5 cm, respectively. Information regarding demographic variables (age and ethnicity) was collected after an interview administered protocol. For the ACUTE and ARMING HEALTH studies, nondiabetic hyperglycemia was defined as 2-h postchallenge glucose ≥7.8 mmol·L^{-1} to <11.1 mmol·L^{-1} after a standard oral glucose tolerance test or HbA1c 39 to 46 mmol·mol^{-1} (5.7%–6.4%) inclusive (18), identified within the 12 months before the initial invitation letter being sent (see Table, Supplemental Digital Content 1, inclusion and exclusion criteria, http://links.lww.com/MSS/B866).

Experimental Treatment Overview

Participants were asked to record all food and drink consumed the day before the first experimental condition. They were then asked to replicate this diet before subsequent treatments. Participants were also requested to avoid alcohol, caffeine, and any moderate to vigorous physical activity for 2 d before each experimental condition (11–14).

Participants arrived at the laboratory after a 10-h fast and had a cannula fitted into an accessible arm vein and then asked to sit quietly for 60 min. A fasting blood sample (9 mL) was then taken (time point, 0 h) for the quantification of insulin and glucose. Participants were provided with a standardized breakfast that was typical of a westernized diet. Across the four studies, this consisted of 45.0% ± 12.7% carbohydrate, 40.7% ± 11.5% fat, and 14.3% ± 1.3% protein of energy intake (11–14). The time taken to consume the meal (≤15 min) was recorded and replicated in subsequent conditions. Blood was sampled at 30, 60, 120, and 180 min postprandially. Lunch, with an identical nutrient composition to breakfast, was consumed at 180 min with blood samples taken again at 30, 60, 120, and 210 min postprandially (see Figure, Supplemental Digital Content 1, protocols for treatment conditions, http://links.lww.com/MSS/B866). The research staff supervised participants throughout each study cycle to ensure full compliance with the trial protocols. Participants consumed water *ad libitum* during the first of the experimental conditions and were asked to replicate the volume ingested in subsequent conditions.

Experimental Conditions

Figure, Supplemental Digital Content 1 highlights the experimental conditions undertaken during each of the four included studies (see Figure, Supplemental Digital Content 1, protocols for treatment conditions, http://links.lww.com/MSS/B866).

Prolonged sitting (6.5 h) (ACUTE, STAND UP, ARMING HEALTH, FIT2SIT). All four studies included a prolonged sitting condition (11–14), where walking and standing was restricted (lavatory visits were conducted via a wheelchair). Participants sat in a designated room equipped with a chair, desk, laptop, and access to books and magazines.

Standing: Sitting (total, 5.5 h) + standing (total, 60 min) (ACUTE, STAND UP). Two studies used a standing protocol (13,14) which followed the same procedure as the sitting condition, except that participants were instructed to break their sitting time by standing close to their chair for 5 min, every 30 min. Individuals were asked to stand in the same, fixed position. In total, individuals accumulated 12 bouts (60 min) of standing.

Physical Activity

Walking: Sitting (total 5.5 h) + walking (total 60 min) (ACUTE, STAND UP, FIT2SIT). Three studies employed a walking protocol (12–14) which was similar to the standing condition, but participants conducted 5-min bouts of walking at a light intensity. Walking speed ranged from 1.5 to 4.4 $km \cdot h^{-1}$. In total, individuals accumulated 12 bouts (60 min) of walking. For the ACUTE and FIT2SIT trials, the walking breaks were carried out on a treadmill (Spazio Forma Folding Treadmill/Excite 700; TechnoGym U.K. Ltd., Bracknell, UK). For the STAND UP trial, participants were instructed to walk up and down a marked track in the laboratory.

Arm ergometry: Sitting (total, 5.5 h) + arm ergometry (total, 60 min) (ARMING HEALTH). One study used upper-body physical activity through arm ergometry (11). The power output (watts) necessary to elicit the desired energy expenditure during the main experimental condition (equivalent to walking at 3 $km \cdot h^{-1}$) was established during the familiarization visit (11). The subsequent power output was implemented for 5 min, every 30 min. In total, individuals accumulated 12 bouts (60 min) of arm ergometry.

Cardiometabolic Variables

For the studies conducted solely at the Leicester Diabetes Centre (11,12,14), all samples were analyzed within the same location. Plasma glucose was determined using standard enzymatic techniques with commercially available kits (Beckman, High Wycombe, UK) and using stable methodology standardized to external quality assurance reference values. Insulin and glucose samples underwent centrifugation to separate plasma within 15 min of collection. Plasma derived from insulin was stored at −80°C and analyzed at the end of data collection using an enzyme immunoassay (Mercodia, Uppsala, Sweden). Each sample was analyzed in duplicate to ensure reliability of readings. Sample values with ≥20% variability were reanalyzed.

All samples for STAND UP (13) were analyzed at the University of Glasgow. Glucose was analyzed using clinically validated automated biochemistry platforms (c311; Roche Diagnostics, Burgess Hill, UK). Insulin and glucose samples underwent identical preparation (centrifugation and storage) to the Leicester samples and were measured with an equivalent immunoassay platform (e411; Roche Diagnostics). The analyzers were calibrated and quality controlled using the manufacturer's materials. Coefficient of variation over two levels of controls was less than 3% for biochemistry assays and less than 6% for insulin.

All measurements and analysis were undertaken by individuals blinded to experimental condition.

Statistical Analyses

Missing outcome data for participants included in this analysis were imputed using a regression model with key predictor variables (baseline body mass index [BMI], age, fasting values, ethnicity and treatment) for each time point and outcome. Imputation was used to correct for verification bias (19). Across all experimental conditions, 3.5% of data values (148/4248) were missing and imputed.

Generalized estimating equations (GEE) with an exchangeable correlation matrix were used, considering repeated measures across treatments. Due to the right-skewed distributions of positive values, insulin was analyzed using a gamma distribution with an identity link. Total area under the curve (AUC) was first calculated by applying the trapezium rule, and time-averaged AUC (i.e., AUC divided by the 6.5 h, to give an average postprandial response) was then used as a summary measure for postprandial insulin and glucose, which can be interpreted as the average glucose or insulin concentration (not including the initial 60 min steady state). Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated as fasting insulin ($mU \cdot L^{-1}$) × fasting glucose ($mmol \cdot L^{-1}$)/22.5, using baseline values. This model is commonly used as an index of insulin resistance, and the validity of estimates in relation to gold standard measures has been examined in several epidemiological studies, in a wide variety of populations (20).

All models included, as independent variables, study and treatment (sitting, standing, light physical activity), along with age (continuous), sex, ethnicity, HOMA-IR (continuous), and BMI (continuous). In addition, interaction terms with treatment were entered simultaneously into the same model to investigate whether the effect of treatment was modified by anthropometric (BMI), demographic (age, sex, ethnicity) or cardiometabolic (HOMA-IR) variables independently to the other factors. Significant interactions were then stratified by dichotomous categories or using the median split.

To highlight the direction of significant interactions, modeling responses for insulin values were estimated in white European and South Asian men and women, age 60 yr, at BMI levels of 25 $kg \cdot m^{-2}$ (normal), 30 $kg \cdot m^{-2}$ (overweight) and 35 $kg \cdot m^{-2}$ (obese).

All data were analyzed using SPSS (version 24.0). A P value less than 0.05 was considered statistically significant for main effects and $P < 0.1$ for interactions. Descriptive data are reported as mean (95% confidence interval [CI]) in text and tables, unless otherwise stated.

Sensitivity Analyses

In order to aid interpretation and assess the robustness of the outcome, we investigated whether results were affected by removing the ARMING HEALTH participants ($n = 13$), as this protocol did not involve a change in posture. Furthermore, to ascertain whether factors that were found to modify the treatment effect for postprandial responses were driven by higher control values (postprandial response during the sitting condition), we repeated the main analysis after further adjusting for the postprandial response to prolonged sitting (categorized as low, medium, or high derived through tertiles).

RESULTS

One hundred twenty-nine participants were included in this analysis. Table, Supplemental Digital Content 3,

TABLE 1. Time-averaged area under the curve values (main effects and 95% CI) and outcome–interaction terms for insulin and glucose responses during each treatment condition.

Variables	Sitting	Standing	Light Physical Activity	Ethnicity–Treatment	Sex–Treatment	Age–Treatment	BMI–Treatment	HOMA-IR–Treatment
Insulin ($mU \cdot L^{-1}$)	69.9 (63.6, 76.3)	75.9 (66.9, 84.9)	56.4 (50.7, 62.0)*	**<0.001**	**0.043**	0.149	**<0.001**	0.240
Glucose ($mmol \cdot L^{-1}$)	5.9 (5.7, 6.1)	5.9 (5.6, 6.1)	5.6 (5.4, 5.8)*	0.354	**0.018**	0.811	**<0.001**	0.549

Covariates to derive the estimated marginal means are fixed at the following values: age = 63.3 yr; HOMA-IR = 2.35; BMI = 27.7 $kg \cdot m^{-2}$. Values displayed as time-averaged response (95% CI).
* P = <0.001 compared with the prolonged sitting condition.

http://links.lww.com/MSS/B868 shows the baseline anthropometric, cardiometabolic and demographic information. There were no significant differences in BMI, age, fasting, or HOMA-IR values between those who dropped out and those who were included in this analysis (see Table, Supplemental Digital Content 3, Metabolic, demographic, and anthropometric characteristics, http://links.lww.com/MSS/B868).

Overall Treatment Effect

Table 1 displays the results for main effects of treatment. After adjustment for HOMA-IR, age, sex, BMI, and ethnicity, the time-averaged insulin responses (reflecting average concentrations over the postprandial period) were 13.6 $mU \cdot L^{-1}$ ((95% CI) 9.5 $mU \cdot L^{-1}$, 17.7 $mU \cdot L^{-1}$) lower during light physical activity breaks compared with prolonged sitting. Similarly, time-averaged glucose responses were 0.3 $mmol \cdot L^{-1}$ (0.2, 0.4 $mmol \cdot L^{-1}$) lower in the light physical activity condition versus prolonged sitting after adjustment for the same variables. There was no treatment effect for standing breaks compared with prolonged sitting for insulin or glucose.

Impact of Demographic (Ethnicity, Age, Sex), Anthropometric (BMI) and Cardiometabolic (HOMA-IR) Variables: Interaction and Stratified Analyses

The results for interactions are presented in Table 1. Figure 2A, B and Table, Supplemental Digital Content 4

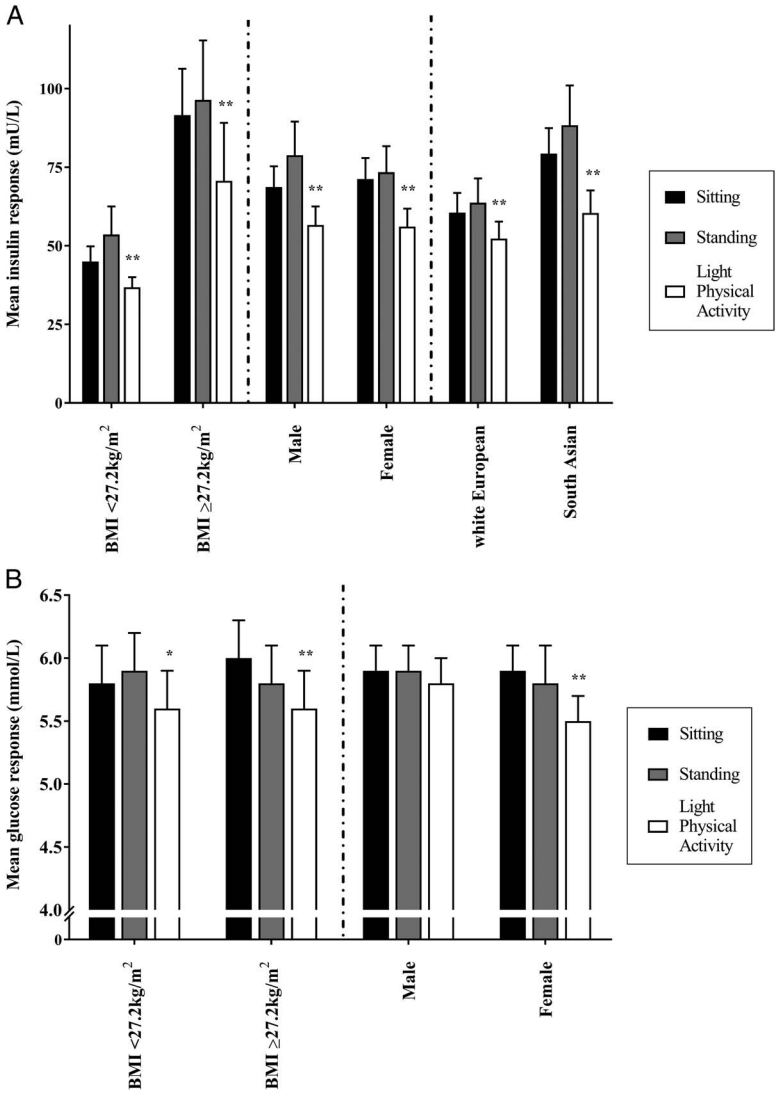

FIGURE 2—Stratified analysis for insulin (A) and glucose (B) responses during each treatment condition. ** P = <0.001, * P = <0.05 compared with the prolonged sitting.

display the stratified analysis for both insulin and glucose (see Table, Supplemental Digital Content 4, stratified analysis for insulin and glucose responses during each treatment condition, http://links.lww.com/MSS/B869).

Ethnicity. There was an ethnicity–treatment interaction for insulin (P = <0.001) but not glucose (P = 0.354). For South Asians, the insulin time-averaged response was 18.9 mU·L^{-1} (13.8, 24.1 mU·L^{-1}) (23.5%) lower during physical activity breaks compared with prolonged sitting, whereas for white Europeans the insulin response was 8.2 mU·L^{-1} (3.5, 13.0 mU·L^{-1}) (9.3%) lower.

BMI. Interactions were seen for both insulin and glucose (both P = <0.001). For those with a BMI above the median split (≥27.2 kg·m^{-2}), the insulin response was reduced by 20.9 mU·L^{-1} (11.7, 30.0 mU·L^{-1}) (22.9%) during physical activity breaks compared with prolonged sitting. Those with a BMI < 27.2 kg·m^{-2} demonstrated an 8.7 mU·L^{-1} (4.7, 12.7 mU·L^{-1}) (18.2%) reduction in insulin. A similar pattern was observed for glucose, where those with a BMI ≥ 27.2 kg·m^{-2} gained a greater metabolic benefit after regular light physical activity breaks (−0.4 mmol·L^{-1} [−0.6, −0.2 mmol·L^{-1}] [−6.7%] vs −0.2 mmol·L^{-1} [−0.4, 0.0 mmol·L^{-1}]; −3.4%).

Sex. A sex–treatment interaction was seen for insulin (P = 0.043) and glucose (P = 0.018). For the insulin response, women reported a greater metabolic benefit when breaking prolonged sitting with light physical activity [−15.0 mU·L^{-1} (−20.0, −10.0 mU·L^{-1}, (−21.2%)], compared with men [−12.1 mU·L^{-1} (−15.9, −8.4 mU·L^{-1}) (−17.6%)]. For glucose, women also displayed a greater reduction than men when breaking up prolonged sitting with light physical activity (−0.4 mmol·L^{-1} [−0.6, −0.2 mmol·L^{-1}], −6.8% vs −0.1 mmol·L^{-1} [−0.3, 1 mmol·L^{-1}], −1.7%).

Age. There was no age–treatment interaction for insulin (P = 0.149) or glucose (P = 0.811).

HOMA-IR. There was no HOMA-IR–treatment interaction for insulin (P = 0.240) or glucose (P = 0.549).

Predicted Response

Figure 3 and Table, Supplemental Digital Content 5, http://links.lww.com/MSS/B870 display how the predicted average difference between conditions for insulin changes as BMI increases for white European and South Asian, men and women, using given values for HOMA-IR (2.0) and age (60 yr) (see Table, Supplemental Digital Content 5, predicted insulin response stratified by sex, ethnic, and BMI categories for a 60-yr-old individual, http://links.lww.com/MSS/B870). The results demonstrate that the average blood insulin response for a 60-yr-old, South Asian woman with a BMI of 35 kg·m^{-2} and HOMA-IR of 2.0, decreased from 90.3 to 58.2 mU·L^{-1} (35.2% reduction) (from prolonged sitting to light physical activity breaks, respectively), whereas average responses for a 60-yr-old, white European man, with a BMI of 25 kg·m^{-2} decreased from 49.5 to 45.1 mU·L^{-1} (8.9% reduction).

Predicted insulin responses were calculated from the following, fully adjusted regression equation, derived from a single GEE model. The light-intensity physical activity condition includes a summation of the beta coefficients for main outcomes and treatment–outcome interactions:

Insulin response during prolonged sitting = −16.327 + (−0.146 × age) + (1.953 × BMI) + (12.871 × HOMA-IR) + (18.789 if South Asian) + (2.457 if female).

Insulin responses during the light-intensity physical activity condition = 12.344 + (−0.111 × age) + (0.547 × BMI) + (12.871 × HOMA-IR) + (8.068 if South Asian) + (−0.414 if female).

Sensitivity Analyses

The significance levels were largely unaffected when the ARMING HEALTH study was removed from the analysis. These results are presented in Table, Supplemental Digital Content 6 [see, Table, Supplemental Digital Content 6, time-averaged area under the curve values (main effects)

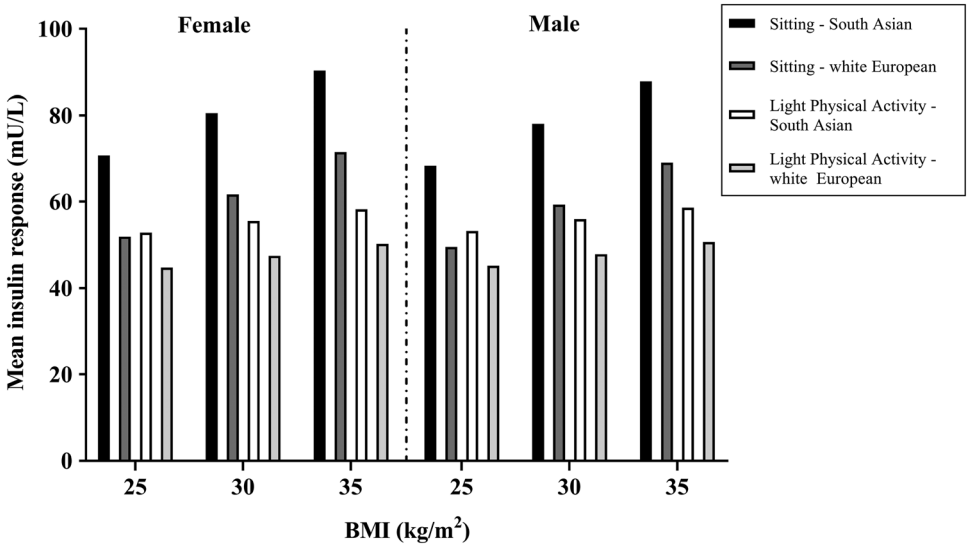

FIGURE 3—Predicted insulin response stratified by sex, ethnic and BMI categories for a 60-yr-old individual.

and outcome–interaction terms for insulin and glucose responses during each treatment condition—with the ARMING HEALTH participants removed (n = 13), http://links.lww.com/MSS/B871]. Furthermore, the pattern of results remained similar when additionally adjusting for the category of postprandial response during prolonged sitting. For insulin, the ethnicity (P = 0.002) and BMI (P = 0.021)–treatment interactions remained. However, the sex–treatment interaction was attenuated (P = 0.124). For glucose, both the BMI (P = 0.002) and sex (P = 0.021)–treatment interactions persisted.

DISCUSSION

This analysis demonstrates that laboratory studies regularly breaking prolonged sitting with light-intensity physical activity lead to acutely lower postprandial insulin and glucose levels. Furthermore, it illustrates that demographic (sex, ethnicity) and anthropometric (BMI) variables modify the insulin and glucose responses, with the results for ethnicity, BMI, and sex (glucose only) being independent of the postprandial response to prolonged sitting. For insulin, being female, South Asian, or having a higher BMI resulted in the greatest metabolic benefit when breaking prolonged sitting. For example, regular light-intensity physical activity breaks for a 60-yr-old South Asian woman, with a BMI of 35 $kg \cdot m^{-2}$ would lower insulin levels by more than a third (35.2%). In contrast, breaking prolonged sitting through regular physical activity breaks in a 60-yr-old white European man with a BMI of 25 $kg \cdot m^{-2}$ would only lower insulin levels by 8.9%.

These data build on previous work reporting potential differences in the postprandial response between white Europeans and South Asians and those with varying levels of underlying glycemia (13). It has been well established that South Asians have a higher risk of cardiometabolic disease than white Europeans (21,22), potentially driven by differences in body composition (23). For example, South Asians develop T2DM up to 12 yr earlier than white Europeans and at lower BMI levels (24). Our results further illustrate that, a 60-yr-old South Asian woman, with a BMI of 25 $kg \cdot m^{-2}$ would have a similar postprandial response during prolonged sitting to that of a 60-yr-old white European woman, with a BMI of 35 $kg \cdot m^{-2}$ (70.7 $mU \cdot L^{-1}$ vs 71.5 $mU \cdot L^{-1}$, respectively). Such findings are also broadly consistent with previous cross-sectional epidemiological data, which demonstrated that South Asians with a BMI of 22.6 $kg \cdot m^{-2}$ have equivalent prevalence of dysglycemia to white Europeans with a BMI of 30 $kg \cdot m^{-2}$ (25). Nevertheless, despite South Asians having greater metabolic dysfunction, the results of our analysis suggest that they are likely to receive the greater absolute benefit per dose of light activity, which is also consistent with previous epidemiological and experimental work (13,26).

In this analysis, women were also shown to derive the greatest metabolic benefit when breaking prolonged sitting with bouts of light physical activity. The sex difference observed in our results are broadly consistent with previous epidemiological work, which has demonstrated that associations between sedentary behavior, total self-reported weekday sitting time, and TV viewing time (a surrogate marker of total sitting time) with markers of cardiometabolic health are stronger in women (27,28).

As all of the significant variables (sex, ethnicity, BMI) are central components to a number of inexpensive and easy to use risk assessment tools (29,30), these variables may be used to further guide the identification of participants for whom breaking prolonged sitting time may yield the greatest benefit. Similar to individualized targets for HbA1c, these findings may also compliment a precision medicine approach, whereby T2DM prevention and treatment take into account individual variability in response to breaking prolonged sitting.

With such a low attainment of current physical activity guidelines (5%–10% achieve 30 $min \cdot d^{-1}$ of at least moderate-intensity physical activity, on at least 5 $d \cdot wk^{-1}$ based on accelerometer data) (31,32), a reasonable goal may be to first break up sitting time with light-intensity physical activity and then eventually progress to higher activity intensities. The intensity of light breaks in this analysis ranged from 1.5 to 4.4 $km \cdot h^{-1}$, with no adverse events, suggesting that the individuals included in this analysis are able to tolerate small activity doses on a regular basis. This also includes the arm ergometry experimental condition, where participants remained in a seated posture throughout, thus offering a potential alternative strategy to breaking sitting time in wheelchair users or those with peripheral neuropathy. In addition, although the beneficial effects of physical activity are generally attributed to intensity (33), evidence from acute, experimental studies demonstrate that higher intensities with increasing frequency in breaks in prolonged sitting are not necessarily a synonym of better postprandial control (15,34). Indeed, high and low intensities and frequencies in breaks, when matched for energy cost, produce similar effects on postprandial concentrations (34,35). The exact timing of the onset of postprandial physical activity to break sitting time may also be important. The first bout of light physical activity in this analysis took place 30 min after the first meal (breakfast), which has been proposed as the optimal timing for post meal exercise as peak post meal values typically occur within 90 min (36). Initiating activity during this time window may blunt peak excursions, even when performed at very light intensities and in small doses (15).

We found no change in the glucose or insulin postprandial values for the standing condition, which is consistent with other acute, experimental studies (37). Nevertheless, replacing sitting with standing may still yield other health benefits. For example, a recent randomized controlled trial demonstrated that a decrease in occupational sitting time (−83 min per workday vs control) at 12 months had a positive impact on multiple subjective outcomes, such as job performance, work engagement, occupational fatigue, sickness presenteeism, musculoskeletal problems, and quality of life (38). Importantly, the time spent sitting was largely displaced with standing, as stepping time remained unchanged.

The current analysis has strengths and limitations. We were able to provide rigorous estimates of the postprandial responses

to breaking prolonged sitting, by using data combined from four laboratory-based, randomized crossover treatments that used the same experimental protocols. For example, meal timing, frequency of blood samples, and duration and frequency of light physical activity breaks were identical across studies (see Figure, Supplemental Digital Content 1, protocols for treatment conditions, http://links.lww.com/MSS/B866). This current analysis also displays a reasonable degree of heterogeneity as it includes both men and women, white Europeans and South Asians, as well as individuals of normal weight and individuals with overweight/obesity, encompassing a broad continuum of postprandial responses. By their nature, the studies were proof of concept experimental studies and utilized protocols that may have limited population generalizability. Future studies should focus on whether the effects observed in this analysis are replicable under free living scenarios over a longer observation period. Furthermore, as there was no formal sample size calculation, *P* values are to be viewed with caution and in relation to the overall pattern of results.

CONCLUSIONS

The present findings suggest that standard demographic and anthropometric outcomes may predict the postprandial response to breaking up prolonged sitting with regular bouts of light-intensity physical activity. Being female, South Asian or having a higher BMI, all predicted greater reductions in postprandial insulin, whereas being female and having a higher BMI predicted greater reduction in postprandial glucose. These results may be used to guide individualized tailored interventions in high-risk participants for whom breaking prolonged sitting time could be a viable and effective prevention strategy.

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