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ABSTRACT

Introduction: Higher levels of physical activity are associated with lower cardio-metabolic risk. However, the relative contribution of overall activity and the intensity of activity is unclear. Our aim was to determine the relative contribution of overall activity and intensity distribution of activity to cardio-metabolic risk in in a cross-sectional analysis of apparently healthy office workers and in people with one or more chronic disease. **Methods:** Clustered cardio-metabolic risk score was calculated from mean arterial pressure, HDL cholesterol, triglycerides and HbA1c. Open-source software (GGIR) was used to generate average acceleration and intensity gradient from wrist-worn accelerometer data for two datasets: office-workers who did not have a self-reported medical condition (N=399, 70% women) and adults with ≥1 chronic disease (N=1,137, 34% women). Multiple linear regression analyses were used to assess the relative contribution of overall activity and intensity of activity to cardio-metabolic risk. **Results:** When mutually adjusted, both overall activity and intensity of activity were independently associated with cardio-metabolic risk in the healthy group ($p<0.05$). However, for the chronic disease group, while mutually adjusted associations for average acceleration were significantly associated with cardio-metabolic risk ($p<0.001$), intensity was not. In healthy individuals, cardio-metabolic risk was lower in those with high overall activity and/or intensity of activity, and who also undertook at least 10 minutes brisk walking. In those with a chronic disease, risk was lower in those who undertook at least 60 minutes slow walking. **Conclusions:** These findings suggest interventions aiming to optimise cardio-metabolic health in healthy adults could focus on increasing both intensity and amount of physical activity. However, in those with chronic disease increasing the amount of activity undertaken, regardless of intensity, may be more appropriate.

Key Words: ACCELEROMETRY, GGIR, CARDIOMETABOLIC RISK, CHRONIC DISEASE, INTENSITY GRADIENT

INTRODUCTION

Non-communicable diseases such as cancers, cardiovascular diseases, diabetes and non-infectious respiratory disorders are responsible for approximately 70% of deaths globally(1). This indicates a shift in the causes of mortality from communicable to non-communicable disease(2), contiguous with the increase in ageing populations globally(3). Consequently, understanding the mechanisms behind these conditions is important. Physical activity is widely accepted as being beneficial for health and has been shown to reduce the risk of cardiovascular disease, diabetes, hypertension, dyslipidaemia and multimorbidity(4-6), with cardio-metabolic disease outcomes inversely associated with level of physical activity(7, 8). Even a modest increase from a low activity level over time has been shown to reduce the incidence of cardio-metabolic risk factors(9). Consequently, it is increasingly recognised that physical activity of all intensities across the 24 h day should be considered for population health benefits, not only time spent in moderate-to-vigorous physical activity (MVPA)(10).

Two metrics that facilitate analysis of the 24 h activity profile from raw accelerometer data are average acceleration and intensity gradient(11). The average acceleration reflects the overall physical activity, or the total amount of physical activity; the intensity gradient reflects the distribution of activity intensity across the day, with a higher value reflecting a greater proportion of activity at higher intensities. Crucially, these two metrics are only moderately correlated(12), thus can be used to glean insights into the relative importance of the amount of activity or the intensity for health(12). For example, application of these methods has suggested that the intensity of activity is key for bone mineral density in adults(13), adiposity in children(11), cardiovascular risk in children(14), and physical function in adults(11). However, both amount and intensity of

activity are additively associated with adiposity in adults(11), and high amounts of lower intensity activity during adolescence may be beneficial for hip structural geometry in young adults(13).

To our knowledge, these metrics have not been used to investigate associations between physical activity and cardio-metabolic risk in adults. An understanding of the relative importance of the amount of activity and the intensity of activity for cardio-metabolic risk could provide insight into mechanisms underlying associations and inform the development of interventions tailored to different populations. This stems from the most recent World Health Organisation (WHO) physical activity guidelines which for the first time provided guidance specific to those with a chronic disease(15). As such it is important to assess health outcomes in relation to physical activity in a similar manner in order to meet the needs of specific populations.

Thus, this study aims to determine the relative contribution of the overall activity and intensity of physical activity to cardio-metabolic risk in apparently healthy office workers and people with one or more chronic disease.

MATERIAL AND METHODS

Data source and study populations

Data were taken from four cross-sectional studies, within the Leicester Diabetes Centre, all of which assessed physical activity using wrist-worn accelerometers: healthy office workers (Healthy); adults with multi-morbidity, adults with type 2 diabetes, and adults 12 to 24 months post cardiac event diagnosis. All extracted measures were collected in line with the published protocols for each of the studies(16-18). Methodologies used in these studies were all very similar.

The Stand More at (SMART) Work and Life data (healthy) has been previously described by Edwardson et al.(16). In brief, participants were adult office workers aged ≥18 years within local Councils in the Leicester, Manchester, and Liverpool areas (N = 723). For the current study, participants who had a self-reported medical condition (N = 275) were excluded to form an ostensibly healthy sample.

Chronotype of Patients with Type 2 Diabetes and Effect on Glycaemic Control (CODEC) has been previously described by Brady et al.(19). In brief, it is an ongoing study at the involving people with type 2 diabetes aiming to recruit ~2,000 participants. Data were obtained from adult participants aged 18-75 years (N = 712) currently enrolled in the study.

Movement through Active Personalised engagement (MAP) has been previously described by Dalosso et al.(17). In brief, it is a study involving people with two or more long term conditions aged 40-85 years recruited from primary care as. Data were extracted for those with accelerometer data available at baseline (N = 346).

Physical Activity after Cardiac EventS (PACES) has been previously described by Herring et al.(18). In brief, it is a study involving adults aged ≥18years, 12 to 48 months post diagnosis of a coronary heart disease related cardiac event as. Data were extracted for those with accelerometer data available at baseline (N = 285).

All studies received ethical approval from the local NHS research ethics committee and participants provided written informed consent. Where a study had multiple time-points, baseline data were used.

For this study, the three chronic disease groups (CODEC, MAP and PACES) were combined into a single chronic disease group (CD). These three groups contained people with similar characteristics as well as the chronic conditions sharing common mechanisms. This newly merged group pooled data from participants with one or more chronic disease (N = 1,343). Descriptive characteristics for each of these groups is presented in Supplemental Table S1 (see Supplemental Digital Content, Descriptive characteristics and physical activity by chronic disease sub-groups, http://links.lww.com/MSS/C573).

Demographics

The following data were extracted from the relevant cohorts: age, sex, ethnicity, socioeconomic status, smoking status and whether lipid lowering, or blood pressure medications were prescribed. Self-reported ethnicity was collapsed into categories of white, South Asian, or other, in view of the small number of people from other ethnic groups. Socioeconomic status was estimated from the index of multiple deprivation (IMD) which was determined from self-reported postcode (20). Smoking status was categorised as never smoked, former smoker and current smoker.

Anthropometric and biomedical characteristics

Height, body mass, waist circumference, blood pressure, resting heart rate, and body fat percentage (assessed using bioelectrical impedance (Tanita SC-330ST, Tanita Europe BV, Middlesex, UK)),

and biomedical markers (HbA1c, fasted blood glucose and lipid profile), were extracted from each dataset. BMI was calculated as Body mass (kg) / Height $(m)^2$. A clustered cardio-metabolic risk score was calculated from mean arterial pressure, HDL cholesterol, triglycerides and HbA1c, as has previously been used to assess associations between physical activity and cardio-metabolic risk in healthy and at risk populations (21,22,23). Triglycerides, HDL cholesterol and HbA1c were not normally distributed and were log transformed. Variables were standardised within group, and the standardised score for HDL cholesterol inverted. The individual z-scores were summed, and the cardio-metabolic risk score was calculated as the mean of the standardised scores. Thus, the cardiometabolic risk scores were group specific which is appropriate for investigation of associations within each of the groups (23). An additional cardio-metabolic risk score was calculated including waist circumference a measure of adiposity.

Physical Activity

Participants were requested to wear accelerometers on their non-dominant wrist 24 h a day for up to 8-days. In the CD groups the participants wore the GENEActiv (ActivInsights Ltd, Cambridgeshire, UK), while the healthy group wore the Axivity AX3 (Axivity, Newcastle, UK). Accelerometers were initialised to record accelerations at 100 Hz with a dynamic range of +/- 8*g*. Available evidence suggests that physical activity outcomes from the GENEActiv and Axivity devices worn on the non-dominant wrist can be considered largely equivalent(24).

Accelerometer data processing

All devices were initialised and downloaded using their specific software prior to receipt into this study. GENEActivs were initialised and data downloaded in binary format using GENEActiv PC

(version 3.1). Axivity devices were initialised and data downloaded in .cwa format using OmGui open-source software (OmGui Version 1.0.0.30, Open Movement, Newcastle, UK).

All accelerometer files were processed and analysed identically with R-package GGIR version 1.9-0 (http://cran.r-project.org)(25). Signal processing in GGIR included auto-calibration using local gravity as a reference(26), detection of sustained abnormally high values, detection of non-wear, calculation of the average magnitude of dynamic acceleration (i.e., the vector magnitude of acceleration corrected for gravity (Euclidean Norm minus 1 *g*)) in milli-gravitational units (m*g*) averaged over 5 s epochs. Participants were excluded if their accelerometer files showed: post-calibration error greater than 0.01 *g* (10 m*g*), fewer than three days of valid wear (defined as >16 h per day)(27), or wear data not present for each 15 minute period of the 24 h cycle. The default setting was used for the detection of non-wear as described previously(26).

The following outcomes were generated and averaged across all valid days ('AD' variables in GGIR): average acceleration (m*g*) (overall activity); intensity gradient (intensity); acceleration (intensity) above which a person's most active X minutes (MX metrics, where X is the number of minutes) are accumulated (m*g*): M$_{1/3\mathrm{DAY}}$; M120; M60; M30, M15; M10; M5; M2. These metrics have been described in full previously (28) and are detailed in the supplemental material (Table S2, see Supplemental Digital Content, Physical activity metrics, http://links.lww.com/MSS/C573).

Analysis

Pearson's correlation coefficients were used to investigate the correlations between the average acceleration and the intensity gradient within each sample to confirm they contained independent information on the physical activity profile.

A series of multiple linear regression analyses were used to explore the relative contributions of overall activity and intensity of activity on cardio-metabolic risk score and for each of the risk factors individually (waist circumference, mean arterial pressure, HbA1c, triglycerides and HDL cholesterol). In each case, Model 1 was unadjusted, and Model 2 was adjusted for the potential co-variates (age, sex, ethnicity, smoking status, IMD and lipid lowering or blood pressure medication). Models 1 and 2 were run for average acceleration and the intensity gradient. Model 3 was also adjusted for potential co-variates, but both average acceleration and the intensity gradient were entered together to test whether associations were independent, and the product term of average acceleration and the intensity gradient entered to determine whether there was an interactive effect of the amount and intensity of physical activity. Results were deemed significant at $p<0.05$. Continuous variables were centred before entry into the analyses. Centring involves subtracting the mean from each individual score; therefore, the mean of the centred variable was zero. The product term of average acceleration and the intensity gradient was calculated from the centred scores. The variance inflation factor (VIF) was calculated to check for multicollinearity with a value >5 indicating the effects of the predictors could not be reliably estimated (29).

To elucidate the form of significant independent, additive and interactive effects, the relationship between overall activity and cardio-metabolic risk when the intensity gradient was medium (at its mean), high (1 SD above the mean), and low (1 SD below the mean) were graphed, as described elsewhere(30). These illustrate the predicted cardio-metabolic risk for a male participant with mean values for all the co-variates. By entering both overall activity and intensity of activity metrics and their product term into regression analyses (as described above) it is possible to determine whether: only intensity or overall activity is important (main effect of one independent of the other, but no additive or interactive effect); there are additive effects of overall activity and intensity (main effects of intensity and overall activity independent of each other, but no interaction); or the effect of overall activity differs by intensity, e.g. at high intensities there is little added benefit from increasing overall activity, but at low intensities adding activity is beneficial (interactive effect)(11).

As the overall activity and intensity metrics may not be immediately interpretable, in order to visualise the physical activity profiles in relation to typical activities, group means for the MX values were plotted on radar plots as previously described(31). Dotted/ dashed circles show approximate values for slow walking (100 m*g*), brisk walking (250 m*g*) and vigorous physical activity (400 m*g*) taken from laboratory calibration studies(32) as previously described(28,33). Walking values are included in the translation of the data to provide a user friendly measure of physical activity. To clearly illustrate relative differences between groups for each of the MX metrics a standardised plot is also presented. The MX metrics were standardised within metric relative to the mean and standard deviation (SD) of the healthy reference group. The *z* scores were plotted on the standardised radar plot, illustrating how each metric differs from the healthy group

in terms of SDs. These plots illustrate the intensity profile across which the amount of activity is accumulated.

Linear regressions were run using Stata 16 (StataCorp LP, Texas, USA) and the radar plots were generated using a ggplot2 in R. Alpha was set at 0.05. Interactions were considered significant at $p<0.1$.

RESULTS

Data were available for 2,066 participants, of which 530 were excluded from this study (detailed in Figure 1), resulting in 1,536 participants being included in the final analysis. Descriptive statistics are presented in Table 1. Mean (SD) age for participants in the healthy group was 43 (10.5) years, approximately 20 years younger than the CD group. The healthy group had better markers for health than the CD group. Proportionally more people had never smoked in the healthy group (67.9%) compared to the CD group (48.7%) and the healthy group had a higher proportion of women in its sample (70.4%) compared with the CD group (33.5%). White participants made up the largest proportion of both groups, but the proportion was higher in the CD group (90.2%) compared to the healthy group (74.4%). Healthy office workers who were excluded based on an incomplete co-variate profile were similar to those included, but less likely to have never smoked. Those excluded from the chronic disease group did not differ on demographics but were less likely to be on blood pressure medication, had more favourable HbA1c and triglycerides, and poorer overall activity and HDL cholesterol (Supplemental Table S3, see Supplemental Digital Content, Participant characteristics by inclusion/exclusion, http://links.lww.com/MSS/C573).

The correlations between the average acceleration and the intensity gradient were moderate at 0.56 and 0.63, shared variance 31% and 40%, for the healthy group and CD group, respectively, indicating the two metrics provided complementary information. The R^2 for the intensity gradient was >91% in both groups indicating it was a good fit for the intensity distribution(12).

Association between physical activity and cardio-metabolic risk

The results of the analyses of all models are presented in table 2. The modelled cardiometabolic risk associated with +/- 1 SD difference in average acceleration and/or intensity gradient of a male participant with mean values for all the co-variates is illustrated in Figures 2a and 3a, and the physical activity profiles associated with different levels of risk are illustrated in in Figures 2b and 3b.

Healthy group

Both higher overall activity and higher activity intensity were associated with lower cardio-metabolic risk (Model 1), with the associations maintained after accounting for co-variates (Model 2). Both average acceleration and the intensity gradient were associated independently of each other, with intensity adding a further 1% ($p<0.05$) to the variance explained (Model 3). The associations between physical activity and cardio-metabolic risk score did not differ whether cardio-metabolic risk score was calculated with or without a measure of adiposity (waist circumference).

When looking at risk factors individually, both higher overall activity and higher intensity were beneficially associated with waist circumference, HbA1C, and HDL cholesterol independent

of co-variates, but only the intensity with mean arterial pressure (model 2). When both activity metrics were entered (Model 3), the association with intensity remained significant for waist circumference, mean arterial pressure and HDL cholesterol, while for HbA1c the association with overall activity remained significant. Triglycerides were not associated with either physical activity metric in any model. There were no significant interactions between overall activity and intensity for cardio-metabolic risk or individual risk factors. The VIF was <1.8 in all cases.

Chronic disease group

Both higher overall activity and higher activity intensity were associated with lower cardio-metabolic risk (Model 1). These associations were maintained after adjusting for co-variates (Model 2); however, only overall activity was independently associated with cardio-metabolic risk, with intensity not adding significantly to the model (R^2 change = 0.1%, $p>0.05$) (Model 3). This suggests that there is not an association between cardiometabolic risk and physical activity intensity over and above that accounted for by overall physical activity. The associations between physical activity and cardio-metabolic risk score did not differ whether cardio-metabolic risk score was calculated with or without a measure of adiposity (waist circumference). Associations between physical activity and cardiometabolic risk for the chronic disease sub-groups are shown in Supplemental Table S4 (see Supplemental Digital Content, Associations between physical activity and cardiometabolic risk in the chronic disease sub-groups, http://links.lww.com/MSS/C573).

When looking at risk factors individually, both higher overall activity and higher intensity were beneficially associated with waist circumference, HbA1c, triglycerides, and HDL cholesterol independent of co-variates, but only intensity for mean arterial pressure (model 2). When both

activity metrics were entered (Model 3), only the association with overall activity remained beneficially associated for waist circumference, HbA1c, triglycerides and HDL cholesterol. There were no significant interactions between overall activity and intensity for cardio-metabolic risk or individual risk factors. The VIF was <1.9 in all cases.

Illustration of the associations between physical activity and cardio-metabolic risk

The significant associations between physical activity (overall and intensity) and cardio-metabolic risk are presented in Figures 2a (healthy, additive association of overall activity and intensity) and 3a (CD, independent association with overall activity). The physical activity patterns indicative of the intensity gradient/average acceleration combinations associated with poorer and better cardiometabolic risk are illustrated in Figure 2b (healthy), and Figures 3b (CD). The colour of the lines for the activity profiles in Figure 2b and 3b correspond with the colour of the bar borders in Figures 2a and 3a to link the average acceleration/intensity gradient combination with the associated cardiometabolic risk.

In the healthy group, those with the lowest cardio-metabolic risk within this group had high amounts of overall activity and intensity of activity (Figure 2a, green bar border), while those with the highest cardio-metabolic risk had low overall activity and intensity (Figure 2a, red bar border). However, the cardiovascular risk was similar for those with high overall activity at low intensity (Figure 2a, purple bar border) and those with low overall activity at high intensity (Figure 2a, blue bar border).

Those with the lowest cardiovascular risk (Figure 2b, green line) had 30 minutes of brisk walking compared with only 2 minutes of brisk walking in those with the highest risk (Figure 2b, red line). The two groups with similar risk (Figure 2b, blue and purple lines) both had 10 minutes of brisk walking, but very different patterns of low and high intensity physical activity.

For the CD group, cardio-metabolic risk within this group was lowest in those with high overall activity (Figure 3a, green bar border) and cardiometabolic risk highest in those with low overall activity (Figure 3a, red bar border), irrespective of the intensity. Figure 3b shows those with the lowest risk (Figure 3b, green line) had 5 minutes of brisk walking, compared to 2 minutes of brisk walking for those with the highest risk (Figure 3b, red line). Only the group with the highest risk did not achieve 60 minutes of slow walking (Figure 3b, red, line).

DISCUSSION

Physical activity was associated with lower cardio-metabolic risk in healthy people and those with chronic diseases; however, the relative importance of the amount and intensity of physical activity was not consistent across different groups. For those who have a chronic disease, higher levels of overall physical activity, regardless of the intensity of that activity, was associated with lower cardio-metabolic risk. Whereas, for apparently healthy office workers, cardiovascular risk was lowest in those with high overall activity and high activity intensity. Notably, high levels of overall activity at low intensity, or low levels of overall activity but at high intensity, were also favourably associated with cardiovascular risk.

The finding that higher physical activity is associated with better cardio-metabolic health is consistent with previous literature(4, 5, 7, 9), as are similar results regardless whether or not adiposity is included in the risk score(21). However, assessing physical activity using these metrics provides novel insight into the relative contributions of overall activity and its intensity with health(28). Whilst this method has been implemented previously this is the first time it has been used to assess cardio-metabolic risk in adults and to assess how these associations differ in those with and without a chronic disease. As shown, the associations differ based on the health status of the participant, thus it is likely to be important to apply the findings to people relative to this. This also aligns with the most recent WHO guidelines (2020) which for the first time included guidance specific to those with a chronic disease, and allows the needs of this specific population to be considered(15).

Importantly, these methods could facilitate the development of evidence-based tailored recommendations. Translating these findings into more meaningful health messages is important for improving the potential impact of the message. For example, for those with chronic disease, increasing overall activity can be explained as simply moving more and more often; this may be achieved through replacing inactivity with light activity such as slow walking. For those without chronic disease, an increase in the overall activity and its intensity is warranted; here more of an emphasis should be placed on increasing work rate, for example when walking, walk briskly. These recommendations align with research demonstrating brisk walking is associated with reduced mortality and longer life expectancy(33, 34), and that replacing sedentary or inactive time with standing or walking benefits cardio-metabolic health in inactive populations(35-37). In the current study, in people free from chronic disease, brisk walking was key with a more favourable

cardio-metabolic risk profile seen in those who achieved 10 minutes of brisk walking, alongside either 1-2 hours of slow walking or brief periods (~2 min) of vigorous intensity activity. However, for those with a chronic disease, those who undertook at least 60 minutes of walking, albeit at a slow pace, had better cardio-metabolic risk than those who did not.

Assessing the components of the cardio-metabolic risk score provides further insight into the associations of physical activity and health markers. For example, waist circumference was significantly associated with activity intensity in the healthy group but overall activity in the CD group. In practice this translated to a person in the CD group having a 4.7 cm smaller waist circumference when overall activity was 1 SD higher and a person in the healthy group having 3.8 cm smaller waist circumference when activity intensity was 1 SD higher. Similar differences in waist circumference were seen in both groups, in relation to a 1 SD difference, but importantly this was for overall activity in the chronic disease group, while it was for intensity of activity in the healthy group. This indicates that higher amounts of activity regardless of intensity may improve these factors for individuals with a chronic disease, however for those free from a chronic disease ensuring some higher intensity activity is undertaken may be needed to gain the same benefit. Assessing these individual components of cardio-metabolic health, may allow possible prescriptions to be made when it is identified that an individual factor is elevated, rather than waiting for co-morbidities to develop and the combined score being elevated, before implementing change.

It is possible that the lack of importance of intensity of activity for the chronic disease group reflects a lower physiological capacity, resulting in little activity of a higher absolute

intensity in their profile and thus a narrower intensity distribution. The translation of accelerometer data to slow and brisk walking used the same absolute cut-points for both groups. While it is likely that walking at a given pace represents a higher relative physiological intensity for the people in the chronic disease group, this does not impact on the overall message for the chronic disease group - to move more, i.e., focus on volume rather than intensity.

This study has some limitations. Firstly, the analysis is cross-sectional and as such there is potential for reverse causality and residual confounding due to unmeasured factors and/or error in measured variables. As such the findings should be conferred by future prospective interventional studies. It should also be noted that our translation of results into slow and brisk walking used the same accelerometer values to represent slow and brisk walking for the healthy and chronic disease groups. Further, the group sizes were unbalanced with the chronic disease group larger than the healthy group, and gender and age balances differed between groups. These factors may have impacted on our findings. Despite the sample being slightly unbalanced, the study benefits from a large sample size, using accelerometers assessed physical activity across a 24-hour day.

Finally, while the volume and intensity of physical activity are inherently related, the shared variance between the average acceleration and intensity gradient metrics was low at under 40%, indicating the two metrics provided complementary information. This facilitated investigation of the relative importance of intensity and volume of physical activity, adding insight into how physical activity is associated with cardio-metabolic health in those who are both healthy and those who have a chronic disease. Thus, this approach to analysing accelerometer-assessed physical activity data has potential to inform individualised tailored interventions as part of

precision medicine. Furthermore, the accelerometer data were processed in the open-source software GGIR, ensuring transparent and replicable methods. Biomarkers were used to assess cardiometabolic risk; future research should use direct health outcomes to build on the findings of this study.

CONCLUSIONS

In conclusion, this study demonstrates how the intensity gradient and average acceleration can be used together to facilitate a simple investigation into the relative importance of intensity and volume of activity for cardiometabolic health. Results from this cross-sectional study suggest that lower cardio-metabolic risk was associated with higher amounts of overall physical activity in both people who are healthy and those with chronic disease. However, while the healthy group had more favourable cardio-metabolic risk if this activity was higher intensity, the intensity did not matter for the chronic disease group. In those who are free from chronic disease lower cardio-metabolic risk was seen in those with high levels of overall activity and/or intensity of activity, while also undertaking at least 10 minutes of brisk walking. In those with chronic disease, lower risk was seen in those who undertook at least 60 minutes of slow walking. These findings are cross-sectional but support physical activity recommendations emphasising that if low-active 'every minute counts' and 'some is better than none', with an increasing focus on moderate and vigorous intensity for those who are more active / free from chronic conditions(15). Longitudinal studies are needed to confirm the findings of this study.

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The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the presented study do not constitute endorsement by the American College of Sports Medicine.

Conflict of interest

The authors report no conflict of interest.

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FIGURE LEGENDS

Figure 1. Participant flow chart.

Figure 2. Translation of the additive effect of average acceleration and intensity gradient on cardiometabolic risk in in ostensibly healthy office workers. The colour of the lines in Figure 2c correspond with the colour of the column borders in Figure 2b.

a) The relationship between intensity gradient and cardiometabolic risk when overall activity was low (1 SD below the mean), medium (at its mean) and high (1 SD above the mean). Root mean square error = 0.49.

b) Illustration of the physical activity profile (MX metrics) associated with low intensity and low overall activity, low intensity and high overall activity, high intensity and low overall activity and high overall activity and high intensity for raw MX metrics (left) and standardised MX metrics (right). Each plot shows (clockwise) the most active 8 h of the day (M⅓DAY), 120 minutes (M120), 60 minutes (M60), 30 minutes (M30), 15 minutes (M15), 10 minutes (M10), 5 minutes (M5) and 2 minutes (M2).

Figure 3. Translation of the main effect of average acceleration on cardiometabolic risk in those with one or more chronic disease. The colour of the lines in Figure 3c correspond with the colour of the column borders in Figure 3b.

a) The relationship between intensity gradient and cardiometabolic risk when average acceleration was low (1 SD below the mean), medium (at its mean) and high (1 SD above the mean). Root mean square error = 0.54.

b) Illustration of the physical activity profile (MX metrics) associated with low, medium and high amount of activity but similar intensity for raw MX metrics (left) and standardised MX metrics (right). Each plot shows (clockwise) the most active 8 h of the day (M⅓DAY), 120 minutes (M120), 60 minutes (M60), 30 minutes (M30), 15 minutes (M15), 10 minutes (M10), 5 minutes (M5) and 2 minutes (M2).

SUPPLEMENTAL DIGITAL CONTENT

SDC 1: SA P2 – MSSE_suppl_tables_R1.docx

Supplemental Table S1. Descriptive characteristics and physical activity by chronic disease sub-groups.

Supplemental Table S2: Physical activity metrics

Supplemental Table S3: Participant characteristics by inclusion / exclusion

Supplemental Table S4. Associations between physical activity and cardiometabolic risk in the chronic disease sub-groups.

Figure 1

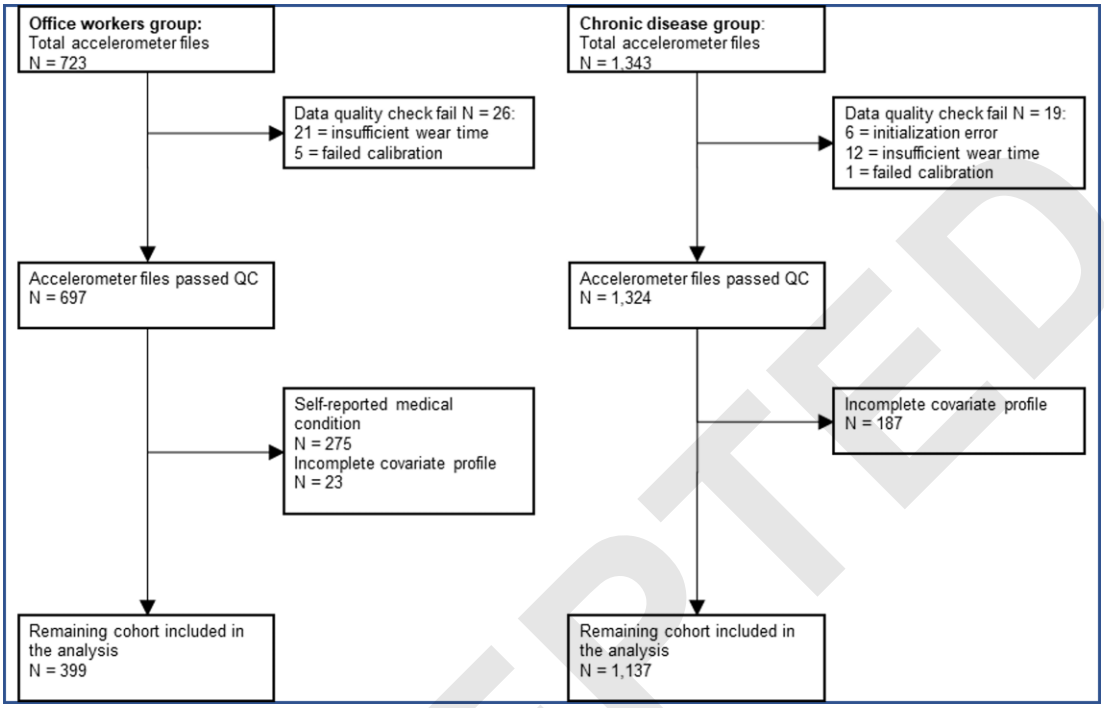

Figure 2

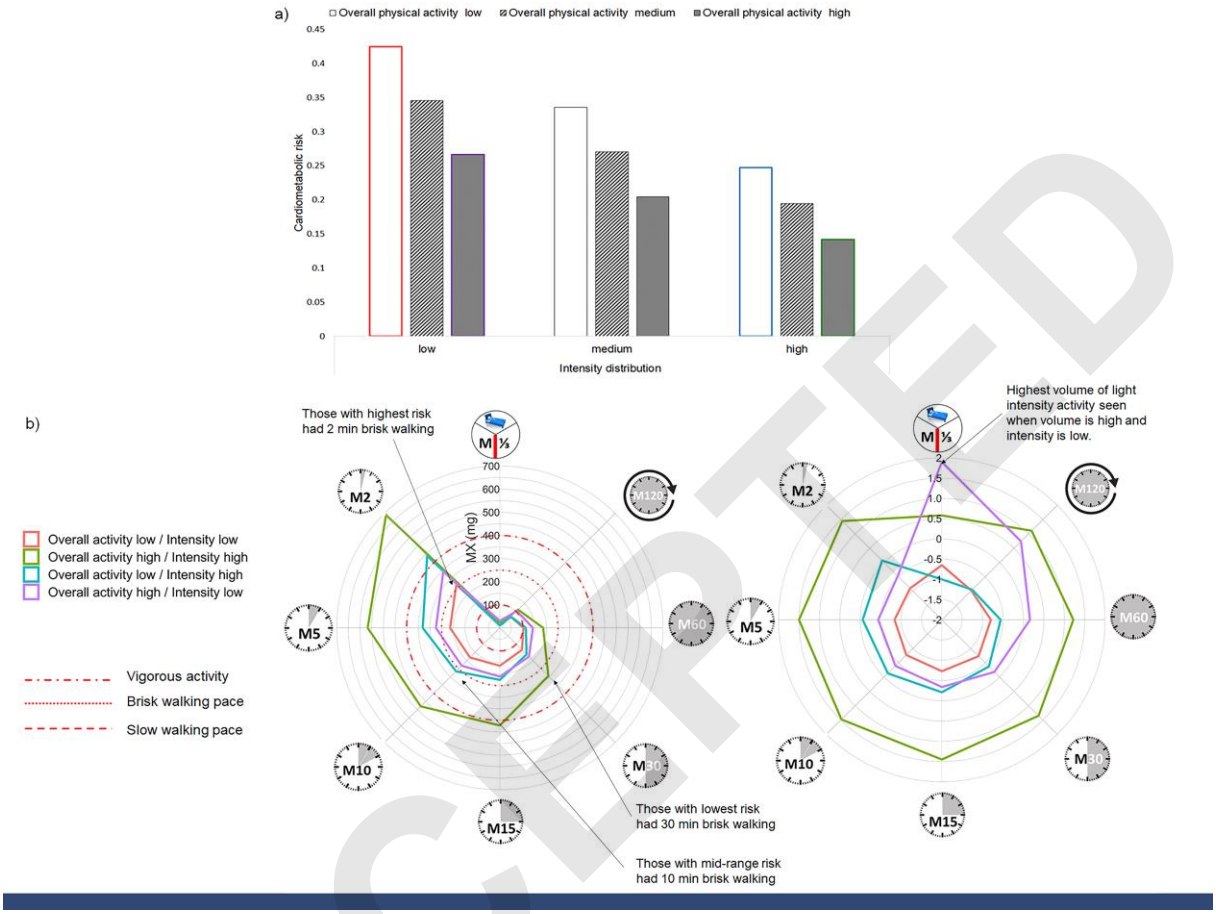

Figure 3

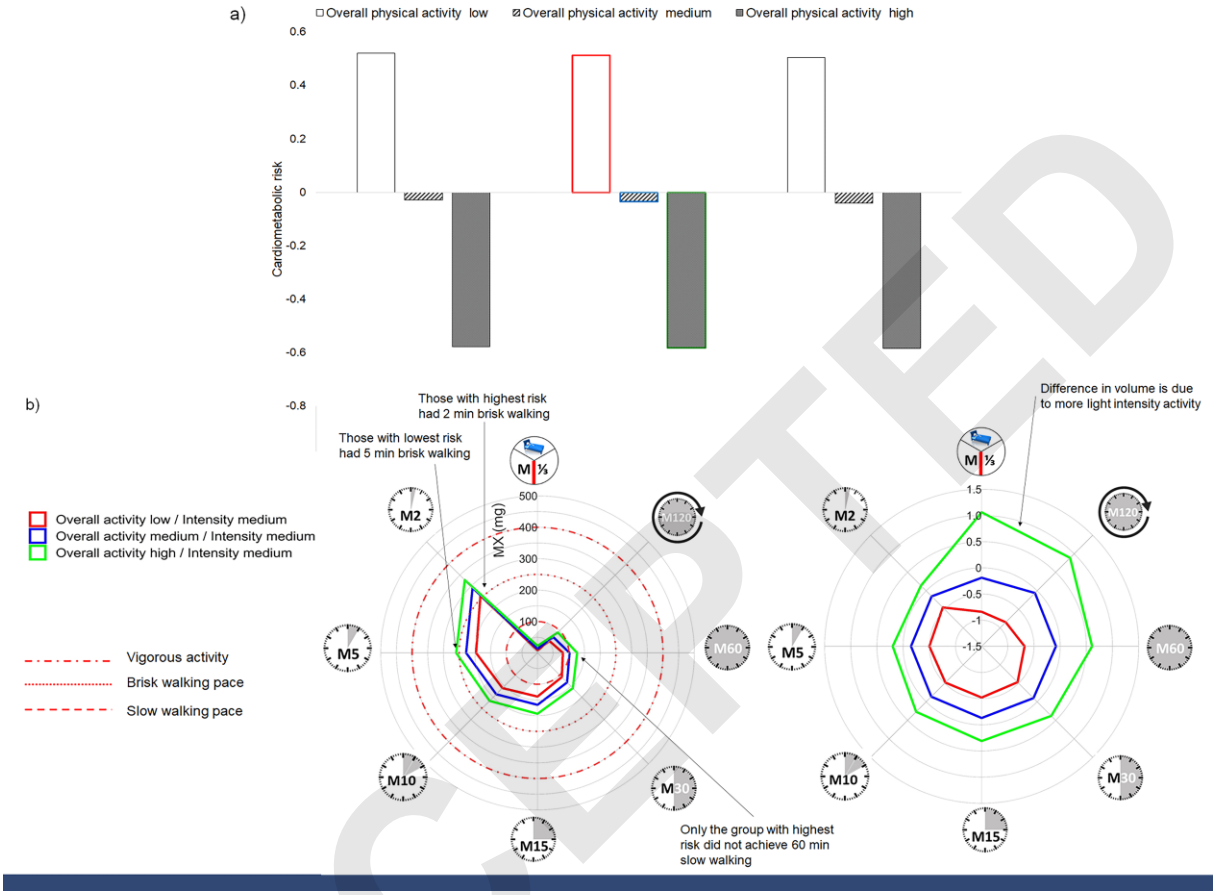

Table 1. Descriptive characteristics and physical activity by group. Values are presented as mean (standard deviation) or N [%].

	Healthy office workers (N = 399)	Chronic disease (N = 1,137)
Continuous variables		
Age (y)	43.0 (10.5)	65.2 (9.2)
Height (cm)	166.9 (9.3)	168.9 (9.3)
Mass (kg)	71.0 (15.5)	86.6 (17.3)
BMI (kg/m^2)	25.4 (4.8)	30.3 (5.1)
Mean arterial pressure	90.7 (10.9)	98.0 (12.3)
HbA1c (mmol/mol)	33.0 (3.5)	49.5 (13.9)
HbA1c (%)	5.2 (0.3)	6.68 (1.27)
Triglycerides (mmol)	1.17 (0.62)	1.72 (0.97)
HDL cholesterol (mmol)	1.45 (0.42)	1.34 (0.41)
Waist circumference (cm)	85.7 (13.7)	104.6 (14.3)
IMD rank	18,308.0 (9290.4)	20,546.2 (8744.7)
IMD decile	6.08 (2.81)	6.75 (2.67)
Categoric variables		
Ethnicity (white)	297 [74.4]	1,024 [90.2]
Sex (Female)	281 [70.4]	381 [33.5]
Smoking (Never)	271 [67.9]	554 [48.7]
Lipid medication (No)	397 [99.5]	331 [29.1]
Blood pressure medication (No)	397 [99.5]	285 [25.1]
Physical activity variables		
Average acceleration (m*g*)	27.9 (7.3)	22.4 (7.0)
Intensity gradient	-2.53 (0.20)	-2.73 (0.21)

BMI: body mass index
IMD: index of multiple deprivation

Table 2. Associations between physical activity (average acceleration and intensity gradient) and cardiometabolic risk and the individual variables in office workers and people with one or more chronic disease(s).

		Model 1		Model 2			Model 3		
		Coefficient	95% CI	R^2 (%)	Coefficient	95% CI	R^2 change with intensity (%)	Coefficient	95% CI
Healthy group (office workers without a self-reported medical condition)									
Cardiometabolic risk	Average acceleration (m*g*)	**-0.015**	**-0.022, -0.007**	**24.3**	**-0.013**	**-0.019, -0.007**	**+1.0**	**-0.009**	**-0.017, -0.001**
	Intensity gradient	**-0.486**	**-0.743, -0.229**	**24.5**	**-0.524**	**-0.779, -0.270**		**-0.382**	**-0.708, -0.057**
Cardiometabolic risk (with WC)	Average acceleration (m*g*)	**-0.016**	**-0.023, -0.008**	**28.0**	**-0.014**	**-0.020, -0.008**	**+1.5**	**-0.009**	**-0.017, -0.000**
	Intensity gradient	**-0.551**	**-0.810, -0.292**	**28.9**	**-0.604**	**-0.852, -0.356**		**-0.475**	**-0.793, -0.156**
Waist circumference	Average acceleration (m*g*)	**-0.296**	**-0.478, -0.114**	**21.9**	**-0.258**	**-0.421, -0.094**	**+2.0**	-0.099	-0.307, 0.110
	Intensity gradient	**-12.064**	**-18.205, -5.922**	**23.7**	**-13.848**	**-19.738, -7.959**		**-12.572**	**-19.836, -5.309**
Mean arterial pressure	Average acceleration (m*g*)	-0.085	-0.222, 0.052	11.7	-0.063	-0.196, 0.070	**+0.9**	0.020	-0.148, 0.188
	Intensity gradient	-4.743	-10.107, 0.620	**12.5**	**-5.751**	**-11.274, -0.228**		**-6.649**	**-13.183, -0.116**
HbA1c	Average acceleration (m*g*)	**-0.066**	**-0.108, -0.024**	**16.2**	**-0.056**	**-0.096, -0.017**	+0.3	**-0.056**	**-0.103, -0.005**
	Intensity gradient	**-2.442**	**-4.050, -0.833**	**15.7**	**-1.723**	**-3.301, -0.146**		-1.001	-2.954, 0.952
Triglycerides	Average acceleration (m*g*)	**-0.008**	**-0.015, -0.001**	**6.1**	-0.007	-0.014, 0.001	+0.1	-0.006	-0.017, 0.005
	Intensity gradient	**-0.278**	**-0.546, -0.009**	**5.9**	-0.211	-0.501, 0.080		-0.126	-0.534, 0.282
HDL cholesterol	Average acceleration (m*g*)	**0.009**	**0.003, 0.015**	**20.9**	**0.011**	**0.005, 0.017**	**+1.2**	0.006	-0.001, 0.012
	Intensity gradient	**0.261**	**0.063, 0.458**	**21.1**	**0.426**	**0.241, 0.610**		**0.255**	**0.035, 0.475**

Chronic disease group									
Cardiometabolic risk	Average acceleration (m*g*)	**-0.018**	**-0.023, -0.014**	**13.2**	**-0.026**	**-0.031, -0.022**	+0.1	**-0.025**	**-0.031, -0.019**
	Intensity gradient	**-0.288**	**-0.445, -0.131**	**7.9**	**-0.564**	**-0.735, -0.393**		-0.078	-0.276, 0.119
Cardiometabolic risk (with WC)	Average acceleration (m*g*)	**-0.022**	**-0.026, -0.018**	**17.1**	**-0.030**	**-0.034, -0.026**	+0.1	**-0.029**	**-0.035, -0.024**
	Intensity gradient	**-0.350**	**-0.503, -0.198**	**9.8**	**-0.639**	**-0.803, -0.747**		-0.081	-0.268, 0.107
Waist circumference	Average acceleration (m*g*)	**-0.515**	**-0.620, -0.409**	**13.0**	**-0.650**	**-0.763, -0.537**	+0.2	**-0.665**	**-0.808, -0.522**
	Intensity gradient	**-8.658**	**-12.318, -4.997**	**7.4**	**-13.489**	**-17.375, -9.602**		-1.365	-5.919, 3.189
Mean arterial pressure	Average acceleration (m*g*)	-0.031	-0.127, 0.066	**4.7**	-0.085	-0.186, 0.017	+0.2	-0.018	-0.149, 0.114
	Intensity gradient	-2.034	-5.338, 1.270	**4.9**	**-3.688**	**-7.279, -0.096**		-2.874	-7.321, 1.574
HbA1c	Average acceleration (m*g*)	**-0.022**	**-0.032, -0.012**	**7.4**	**-0.034**	**-0.045, -0.023**	+0.3	**-0.032**	**-0.045, -0.019**
	Intensity gradient	**-0.403**	**-0.728, -0.077**	**6.0**	**-0.855**	**-1.226, -0.484**		-0.305	-0.719, 0.109
Triglycerides	Average acceleration (m*g*)	**-0.018**	**-0.027, -0.009**	**5.9**	**-0.026**	**-0.036, -0.016**	+0.2	**-0.024**	**-0.035, -0.012**
	Intensity gradient	**-0.382**	**-0.661, 0.103**	**4.5**	**-0.664**	**-0.983, -0.345**		-0.237	-0.576, 0.103
HDL cholesterol	Average acceleration (m*g*)	**0.011**	**0.007, 0.014**	**15.3**	**0.014**	**0.011, 0.018**	**+0.3**	**0.016**	**0.012, 0.021**
	Intensity gradient	0.594	-0.060, 0.179	**10.8**	**0.194**	**0.073, 0.315**		**-0.134**	**-0.257, -0.011**

Model 1: unadjusted. **Model 2:** adjusted for sex, age, height, body mass, ethnicity, SES, lipid lower and blood pressure altering medication status. **Model 3:** further adjusted for alternate physical activity metric and the product term (average acceleration X intensity gradient) entered to investigate interactive effects.

WC = Waist circumference, 95% CI = 95% confidence interval, significant associations are denoted in bold.

Continuous variables were centered before entry into the analysis. Physical activity interaction terms were calculated from the centered scores.

Supplementary Table S1. Descriptive characteristics and physical activity by chronic disease sub-groups. Values are presented as mean (standard deviation) or N [%].

	CODEC (N = 590)	MAP (N = 291)	PACES (N = 256)
Continuous variables			
Age (y)	63.7 (8.5)	67.4 (9.5)	65.8 (9.9)
Height (cm)	169.4 (9.8)	167.1 (9.2)	169.6 (7.9)
Mass (kg)	89.0 (17.1)	84.4 (19.0)	83.6 (14.8)
BMI (kg/m^2)	30.9 (5.0)	30.1 (5.7)	29.0 (4.3)
Mean arterial pressure	99.4 (11.3)	102.7 (12.0)	89.6 (11.1)
HbA1c (%)	7.2 (1.1)	6.2 (1.2)	6.0 (0.9)
Triglycerides (mmol)	1.76 (0.98)	1.77 (1.05)	1.55 (0.79)
HDL cholesterol (mmol)	1.30 (0.38)	1.49 (0.48)	1.27 (0.32)
Waist circumference (cm)	107.4 (13.3)	102.6 (15.9)	100.3 (13.5)
IMD rank	19,625.6 (9309.1)	22,359.1 (7379.3)	20,600.0 (8546.1)
IMD decile	6.47 (2.84)	7.27 (2.29)	6.79 (2.61)
Categoric variables			
Ethnicity (white)	488 [82.7]	280 [96.6]	280 [96.6]
Sex (Female)	207 [35.1]	136 [46.9]	136 [46.9]
Smoking (Never)	289 [49.0]	149 [51.4]	149 [51.4]
Lipid medication (No)	168 [28.5]	146 [50.3]	146 [50.3]
Blood pressure medication (No)	188 [31.9]	79 [27.2]	79 [27.2]
Physical activity variables			
Average acceleration (m*g*)	22.0 (7.0)	21.8 (6.3)	23.9 (7.6)
Intensity gradient	-2.74 (0.20)	-2.76 (0.21)	-2.69 (0.22)

CODEC: Chronotype of Patients with Type 2 Diabetes and Effect on Glycaemic Control
MAP: Movement through Active Personalised engagement
PACES: Physical Activity after Cardiac EventS
BMI: body mass index
IMD: index of multiple deprivation

Supplementary Table S2. Physical activity metrics.

Metric	Unit	Abbreviation	Interpretation
Average acceleration	m*g*	Overall physical activity	Proxy for total physical activity
Intensity gradient	N/A	Intensity distribution	Reflects the distribution of acceleration intensity across the 24 h day. It is always negative; a lower (more negative) value indicates time is mainly spent inactive and at lower intensities, while a higher (less negative) value indicates people are also accumulating time at higher intensities [2, 3].
MX	m*g*	M(time period) e.g. 30 minutes = M30	The acceleration above which a person's most active X minutes are accumulated, where X = time. The activity can be accumulated at any point across the day, i.e., it does not need to be continuous or in bouts. For example, M30 would be the acceleration which corresponds with the top 30 minutes of accelerations and shows the intensity that a person exceeded for a total of 30 minutes across the day. This is calculated for each day and then the mean across valid days calculated.

Supplementary Table S3. Participant characteristics by inclusion / exclusion (based on incomplete co-variate profile)

	Healthy office workers		Chronic disease	
	Included (N = 399)	Excluded (N = 12 – 23)	Included (N = 1,137)	Excluded (N = 60 to 187)
Continuous variables				
Age (y)	43.0 (10.5)	41.4 (10.5)	65.2 (9.2)	65.9 (7.9)
Height (cm)	166.9 (9.3)	163.8 (7.0)	168.9 (9.3)	169.1 (9.9)
Mass (kg)	71.0 (15.5)	67.7 (3.1)	86.6 (17.3)	88.5 (19.5)
BMI (kg/m^2)	25.4 (4.8)	25.4 (5.9)	30.3 (5.1)	30.9 (5.7)
Mean arterial pressure	90.7 (10.9)	88.6 (9.5)	98.0 (12.3)	98.8 (13.8)
HbA1c (mmol/mol)	33.0 (3.5)	34.8 (2.9)	**49.5 (13.9)**	**30.1 (44.0)**
HbA1c (%)	5.2 (0.3)	5.3 (0.3)	**6.68 (1.27)**	**4.91 (4.03)**
Triglycerides (mmol)	1.17 (0.62)	1.09 (0.43)	**1.72 (0.97)**	**1.05 (2.61)**
HDL cholesterol (mmol)	1.45 (0.42)	1.52 (0.39)	**1.34 (0.41)**	**0.58 (2.46)**
Waist circumference (cm)	85.7 (13.7)	84.9 (15.2)	104.6 (14.3)	106.0 (14.9)
IMD rank	18,308.0 (9290.4)	16,950.5 (9432.1)	20,546.2 (8744.7)	19,752.6 (9912.4)
IMD decile	6.08 (2.81)	5.53 (2.85)	6.75 (2.67)	6.48 (3.01)
Categoric variables				
Ethnicity (white)	297 [74.4]	14 [60.9]	1,024 [90.2]	149 [94.9]
Sex (Female)	281 [70.4]	18 [78.3]	381 [33.5]	54 [32.1]
Smoking (Never)	**271 [67.9]**	**15[65.2]**	554 [48.7]	74 [49.0]
Lipid medication (No)	397 [99.5]	23 [100]	331 [29.1]	56 [33.3]
Blood pressure medication (No)	397 [99.5]	22 [95.7]	**285 [25.1]**	**57 [33.9]**
Physical activity variables				
Average acceleration (m*g*)	27.9 (7.3)	28.6 (7.1)	**22.4 (7.0)**	**21.0 (6.8)**
Intensity gradient	-2.53 (0.20)	-2.50 (0.24)	-2.73 (0.21)	-2.76 (0.21)

BMI: body mass index
IMD: index of multiple deprivation

Significant differences ($p<0.05$) denoted in bold (continuous variables: t-tests, categorical variables: chi square)

Supplementary Table S4. Associations between physical activity (average acceleration and intensity gradient) and cardiometabolic risk in the chronic disease sub-groups.

		Model 1		Model 2			Model 3		
		Coefficient	95% CI	R^2 (%)	Coefficient	95% CI	R^2 change with intensity (%)	Coefficient	95% CI
CODEC (Chronotype of Patients with Type 2 Diabetes and Effect on Glycaemic Control)									
Cardiometabolic risk	Average acceleration (m*g*)	**-0.014**	**-0.020, -0.008**	**13.0**	**-0.018**	**-0.023, -0.012**	+0.1	**-0.017**	**-0.025, -0.009**
	Intensity gradient	**-0.217**	**-0.422, -0.131**	**10.4**	**-0.422**	**-0.646, -0.198**		-0.103	-0.367, -0.164
Cardiometabolic risk	Average acceleration (m*g*)	**-0.018**	**-0.023, -0.013**	**20.0**	**-0.022**	**-0.027, -0.017**	+0.4	**-0.020**	**-0.027, -0.013**
(with WC)	Intensity gradient	**-0.326**	**-0.521, -0.131**	**16.2**	**-0.560**	**-0.769, -0.351**		-0.182	-0.424, -0.060
MAP (Movement through Active Personalised engagement)									
Cardiometabolic risk	Average acceleration (m*g*)	**-0.023**	**-0.033, -0.013**	**19.9**	**-0.029**	**-0.039, -0.019**	+0.1	**-0.028**	**-0.041, -0.015**
	Intensity gradient	-0.182	-0.495, 0.131	**14.5**	**-0.523**	**-0.830, -0.215**		-0.040	-0.396, 0.315
Cardiometabolic risk	Average acceleration (m*g*)	**-0.030**	**-0.041, -0.020**	**27.3**	**-0.036**	**-0.046, -0.027**	+0.0	**-0.037**	**-0.049, -0.025**
(with WC)	Intensity gradient	-0.259	-0.572, 0.054	**18.7**	**-0.603**	**-0.901, -0.305**		0.024	-0.313, 0.361
PACES (Physical Activity after Cardiac EventS)									
Cardiometabolic risk	Average acceleration (m*g*)	**-0.014**	**-0.020, -0.008**	**18.1**	**-0.024**	**-0.031, -0.016**	+0.5	**-0.020**	**-0.030, -0.011**
	Intensity gradient	**-0.284**	**-0.555, -0.013**	**13.5**	**-0.639**	**-0.970, -0.308**		-0.223	-0.618, 0.173
Cardiometabolic risk	Average acceleration (m*g*)	**-0.014**	**-0.020, -0.008**	**20.3**	**-0.025**	**-0.031, -0.018**	+0.3	**-0.021**	**-0.030, -0.013**
(with WC)	Intensity gradient	-0.255	-0.516, 0.007	**14.6**	**-0.623**	**-0.942, -0.304**		-0.162	-0.538, 0.215

Model 1: unadjusted. **Model 2:** adjusted for sex, age, height, body mass, ethnicity, SES, lipid lower and blood pressure altering medication status. **Model 3:** further adjusted for alternate physical activity metric and the product term (average acceleration X intensity gradient) entered to investigate interactive effects.

WC = Waist circumference, 95% CI = 95% confidence interval, significant associations are denoted in bold.

Continuous variables were centered before entry into the analysis. Physical activity interaction terms were calculated from the centered scores.