Using compositional analysis to explore the relationship between physical activity and cardiovascular health in children and adolescents with and without type 1 diabetes

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Word Count: 4,294
Running Title: PA and cardiovascular health in youth with type I diabetes

Acknowledgements

The authors would like to thank the participants and their parents/guardians for giving their time to support and participate in the research. Additionally, the authors would like to thank Dr Chris Bidder and the clinical teams who facilitated and supported the study.

Contribution Statement

ZM conceived the study, collected the data, performed data and statistical analysis, and drafted the manuscript; MAM conceived the study, aided with physical activity data and statistical analysis and drafting of the manuscript; KM conceived the study, aided physical activity data and statistical analysis and drafting of the manuscript, JWG assisted in the design of the study, supported data collection and drafting of the manuscript. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Declaration of Interest

The authors declare that they have no competing interests

Ethics approval statement

This study was approved by the National Health Service Research Ethics Committee (16/NE/0082 195492), with written informed assent and consent obtained prior to participation from all children and their parents/guardians, respectively.

Abstract

The aim of this study was to use a compositional analysis approach to account for the inherent co-dependencies between behaviours and to explore how daily movement behaviours influence cardiovascular health in children with and without T1D.

Augmentation index, pulse wave velocity (PWV) and heart rate variability were measured in 20 children with (11.9±1.6 years) and 17 children without T1D (11.6±2.2 years). Subsequently, physical activity and sleep were assessed at 20 Hz for 28 consecutive days using a wrist-worn accelerometer. Compositional analyses were utilised to explore the relative effects of each movement behaviour and the overall movement complex on cardiovascular parameters, with predictive modelling used to explore the effects of reallocating 20 mins between behaviours.

Arterial stiffness markers were most influenced by the total movement composition, whereas autonomic function was most influenced by sedentary time and sleep relative to all other behaviours. Reallocation of time from moderate-to-vigorous physical activity (MVPA) to any other behaviour was predicted to negatively affect all cardiovascular measures, independent of disease status, whereas reallocating time to MVPA was consistently predicted to improve all outcome measures. Additionally, the same intensity of physical activity appeared to be more potent for cardiovascular health in T1D children compared to non-diabetic peers.

Intensity, rather than volume, of physical activity may be key in reducing risk of premature adverse changes in cardiovascular health, whereas increasing time in MVPA could potentially the slow progression of cardiovascular aging in ~~diabetic~~ children with diabetes.

Introduction

Physical activity research has predominantly explored the effect of isolated movement behaviours on health in various populations and for various health outcomes, particularly cardiovascular health [1,2]. Specifically, moderate-to-vigorous physical activity (MVPA), one of the most consistently explored movement behaviours, is well established to have a positive effect on cardiovascular health in both healthy [3-5] and clinical populations [6,7], whereas prolonged periods spent in sedentary pursuits exert a negative influence, independent of physical activity [8,9]. However, the concentration of the majority of these studies on a single movement behaviour, which in the case of MVPA typically accounts for less than 4% of the day [10], is not only unlikely to provide a representative insight into habitual physical activity behaviours, and indeed their relationship with health, but also fails to consider the inherent co-dependencies between behaviours [10,11].

Recognising the importance of the inter-relationships between movement behaviours, compositional analyses have been used to explore the combined and relative effects of sedentary time, physical activities and sleep on various cardiometabolic health indicators [10,11]. Compositional analysis utilises log-ratio transformational techniques to determine the relative time spent in each movement behaviour as a proportion of the 24-hour period [10,11]. The use of compositional analysis therefore accounts for the finite and bounded nature of movement behaviours within a day [12], and more appropriately explores the relative associations with health outcomes. Compositional analysis is therefore highly valuable in providing an insight into the relative importance of daily movement behaviours for health. However, the majority of studies using compositional analyses to date have relied on a single week of movement behaviours which does not account for potentially meaningful variations in individual movement behaviours and their impact on health [13],[14,15],[16]. Indeed, the notion that physical activity within an individual may fluctuate around a mean, the ActivityStat hypotheses [17,18], is an important concept that warrants further investigation using compositional analysis methods.

Movement behaviours such as moderate to vigorous physical activity (MVPA) are widely accepted to be crucial factors in the disease management of type 1 diabetes (T1D)[7], not least given its potent role in minimising the risk of cardiovascular disease

(CVD), the most prevalent long-term complication for those with T1D[19]. Pre-clinical markers for CVD risk include arterial stiffening and impaired cardiac autonomic function which may be evident as early as two years post diagnosis in children [20-22]. A greater volume of MVPA is associated with a more favourable central stiffening and cardiac autonomic activity in those with T1D [23,24]. However, children with T1D have been consistently reported to accrue less MVPA than their non-diabetic peers, with many studies finding that this population does not meet the recommended 60 minutes of MVPA per day deemed necessary to achieve these risk-reducing benefits [25-27]. Potentially as a compensation for these lower levels of MVPA, children with T1D demonstrate significantly greater volumes of light intensity physical activity (LPA) than non-diabetic peers [27]. In healthy children, LPA is beneficial for arterial stiffening and autonomic function, albeit to a lesser extent than MVPA [8,28], indicating significantly greater volumes of LPA may be necessary to achieve the same health-associated benefits as 60 minutes of MVPA. However, no study to date has explored the relative effects of these behaviours in children with T1D.

Prolonged periods of sedentary time, increasingly observed in youth, are associated with greater insulin resistance and less favourable lipid profiles [11,29,30], both of which have detrimental effects on glycaemic control and CVD risk in children with T1D [31]. Given that behaviours are known to track from childhood to adolescence, and beyond, the increasing sedentary time in children is especially concerning, potentially further exacerbating the risks of premature, and possibly preventable, deleterious changes in cardiovascular health [32]. Consequently, a much greater understanding of the effects of all movement behaviours in T1D is crucial to identify important targets for intervention, to provide recommendations for clinical teams and, ultimately, to reduce the risk of both short- and long-term complications.

Therefore, the primary aim of this study was to utilise compositional analyses to explore the associations of daily movement behaviours with markers of cardiovascular health in children ~~in~~ with ~~T1D~~ and their ~~non-diabetic~~ peers without diabetes. Furthermore, the secondary aims were to investigate how reallocating time between behaviours is predicted to influence key cardiovascular measures and to ascertain whether the composition of movement behaviours fluctuates across a four-week monitoring period.

Methods

In total, 48 children and adolescents (11.9 ± 2.1 years; 29 T1D; 20 girls) were recruited from paediatric diabetes clinics and local schools in South Wales, with all procedures conducted within local outpatient clinics or the research laboratories at Swansea University. Participants who expressed interest were referred by their paediatric diabetes team to the first author for additional information. Written informed consent and assent were obtained from parents/guardians and participants, respectively, with all assessments and measurements, other than physical activity, collected over a two-hour period. Physical activity was then monitored over 28-consecutive days. Ethics approval was obtained from National Health Service Research Ethics Committee (16/NE/0082 195492), with all procedures conducted in accordance with the Declaration of Helsinki. General exclusion criteria were any cardiovascular conditions, kidney or metabolic disease, or hypertension, with diabetes-specific criteria including a diabetes duration of less than one year or those identified by the respective diabetes team as unsuitable for participation due to complications or currently demonstrating poor glycaemic control (HbA1c ≥80.0 $mmol \cdot mol^{-1}$). Participants above this level were at a significantly increased risk of diabetic ketoacidosis and other complications [33]. Blood glucose control, according to glycated haemoglobin (HbA1c), was obtained from the latest reading present in medical records.

Anthropometrics

Height, sitting height and body mass were measured to the nearest 0.1 cm, 0.1 cm and 0.1 kg, with the use of a calibrated stadiometer (Holtain, Crymych Dyfed, UK), a sitting height stadiometer (Harpenden Sitting Height Table model 607VR, Holtain Ltd, Crymych, Pembrokeshire, UK), and electronic scales (Seca 803, Seca, Chino, CA, USA), respectively. Body mass index (BMI) was subsequently derived. An estimation of maturity was calculated using sex-specific maturity offset equations, which utilise height, sitting height, leg length and age to predict the approximate time in years away from the greatest rate of increase in height during puberty, or peak height velocity (PHV) [34]. The time away from PHV was then employed to classify participants as pre -PHV, peri-PHV or post-PHV [34].

Arterial stiffness

A non-invasive assessment of arterial stiffness was conducted with all participants using an osillometric device (Vicorder, Skidmore Medical, Bristol, UK) and accompanying blood pressure cuffs (D.E.Hokanson Inc, Bellevue, WA, USA). The assessment was conducted after a five-minute resting period in a quiet environment, to ensure a stable heart rate and blood pressure, with the participant in the supine position. Pulse wave analysis (PWA) was conducted with a blood pressure cuff over the brachial artery on the upper left arm. Initially, a stable blood pressure was acquired to inform the inbuilt automated function. Subsequently, pulse pressure (PP) was derived with a transfer function employed to derive augmentation pressure (AP) and augmentation index (AIx), as an estimation of central stiffening. The AP was derived from the systolic waveform as the pressure difference between peaks one and two, whereas AIx was calculated as AP as a percentage of pulse pressure [35]. Aortic pulse wave velocity (aPWV) was assessed with a partial and brachial cuff placed over the carotid and femoral arteries, respectively. The distance between the sternal notch and the centre of the femoral cuff, via the umbilicus, was measured. The time taken for a pulse wave to travel between the two cuffs was recorded according to the carotid and femoral waveforms, giving PWV in $m \cdot s^{-1}$. Both processes were repeated a minimum of three times, or until at least two measures within 5 mmHg, 5% or 0.5 $m \cdot s^{-1}$ were obtained.

Cardiac Autonomic Activity

A three-lead Reynolds CF Holter monitor (Spacelabs Medical Ltd, Hertford, UK), sampling at 1,024 Hz, was used to obtain a short-term, 12-bit electrocardiogram (ECG) recording from which RR intervals were obtained. Electrodes were positioned at three points - the manubrium and the V5 and V5R positions on the anterior of the torso, with placement verified by visually checking each of the three channels prior to recording. A 15-minute rest period in a supine position was followed by a five-minute recording of paced breathing at a rate of six breaths per minute. The ECG recording was processed to identify QRS cycles resulting from sinus node depolarisation, disregarding abnormal cycles, with the normal cardiac (RR) intervals extracted using the Reynolds Pathfinder ECG analysis system (Spacelabs Medical Ltd, Hertford, UK). The extracted RR intervals were then visually inspected to identify and remove any artefacts before being analysed using Kubios-HRV V3.0 (Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland) to derive heart

rate variability (HRV) indices in the time and frequency domains. Specifically, the root mean square of successive differences (RMSSD), and low frequency (LF) and high frequency (HF), both absolute and normalised, were obtained to give an estimation of sympathetic and parasympathetic activation, respectively, at rest [36].

Habitual physical activity

Participants were asked to wear a triaxial accelerometer sampling at 20 Hz (GENEActiv, Activinsights Ltd, Cambridgeshire, UK) on their right wrist for 28-consecutive days, 24-hours a day. The GENEActiv has been validated and reported to provide reliable representations of physical activity behaviours in children [37,38]. Accelerometer data was downloaded from each device utilising the GENEActiv PC software v2.2 (Activinsights Ltd, Cambridgeshire, UK), with the GGIR package (https://cran.rproject.org/web/packages/GGIR/vignettes/GGIR.html), built in R (https://cran.r-project.org), employed for signal processing to convert triaxial data to omnidirectional acceleration. This omnidirectional data was then processed using the Euclidian Norm Minus One ENMO; [39], reduced to five second epochs and converted to milligravity-based acceleration [40]. Wear-time criteria was applied to the processed data with ≥ 16 hours per day over three weekdays and one weekend day required for inclusion in further analysis [41]. Raw acceleration thresholds, derived according to the Hildebrand et al. [42] predictive equations, were applied to classify sedentary time (≤ 23.5 *mg*), LPA (> 23.5-191.6 *mg*) and MVPA (≥ 191.6 *mg*). Sleep was determined according to the Van Hees et al. [43] sleep algorithm as no arm angle change of $> 5^{o}$ for ≥ five minutes.

Data analysis

Compositional analyses were conducted by converting the time spent in each behaviour to a proportion of the overall recorded time, providing the geometric mean for each behaviour and grouping as relative ratios of the overall composition. The pairwise log contrasts between the geometric means of all behaviour combinations was used to produce variation matrices for the total sample and each grouping. Isometric log ratios (ILRs) were produced by converting the overall composition of movement behaviours so all behaviour means added up one. The converted geometric means were then inputted into four sequential linear regression models for each cardiovascular measure, with one behaviour compared to the remaining

behaviours for in each model and covarying for age, sex, maturity and disease status for all models. The p-value for each set of models was obtained as the significance of the model, with the initial coefficient and p-value for each movement behaviour in sequential models taken as an indication of the effect and significance on the outcome measure. Predictive change models, conducted by back-transforming the mean of each behaviour produced in the ILRs to the geometric behavioural composition for each group, were then employed to explore the influence of reallocating 20 minutes from one behaviour to another on cardiovascular measures[10].

Twenty minutes, as opposed to the 10 minutes used in previous studies [10,11], was chosen to explore the impact of meeting physical activity guidelines for children with T1D, as substituting 20 minutes to MVPA would increase time in this behaviour to the recommended 60 minutes per day. Predictive changes were expressed as percentage change for each cardiovascular measure, based on the group mean, then compared to the percentage smallest worthwhile change (SWC%)~~SWC%~~ to identify a meaningful and significant difference.

Statistical analysis

Statistical analyses were performed in IBM SPSS Version 22.0 (IBM SPSS Statistics for Macintosh, IBM, Portsmouth, UK) or the compositions package (V1.40),and its dependencies in R (http://cran.r-project.org). Significance was set as $p \leq 0.05$, with all data expressed as mean ± SD, unless otherwise stated. The minimum clinically important difference (MCID) was identified as more representative of a significant change in cardiovascular measures than the typically employed one SD [44]. Therefore, the MCID for cardiovascular measures was represented by the smallest worthwhile change (SWC) and the percentage SWC (SWC%), calculated according to the mean of cardiovascular outcomes for each group [44]. Potential differences in all measures, according to disease status and sex, were explored with the use of a multivariate ANOVA with Bonferroni correction. The movement composition for both groups was derived for each separate week and for increasing measurement durations (14, 21 and 28 days), with a repeated measures ANOVA with Bonferroni correction subsequently used to explore whether the compositions varied between weeks and/or with increasing measurement duration.

Results

The final sample consisted of 37 participants (20 T1D; 16 girls) following the exclusion of 11 participants (9 T1D and 2 non-diabetes) for monitor failure or failure to meet the weekly wear-time criteria. No significant differences were found between those included and excluded regarding age, anthropometrics, or maturity ($p > 0.05$). Participant anthropometrics, physical activity outcomes and cardiovascular measures are presented in Table 1. Regardless of disease status, girls were more mature than boys (1.32 yrs, $F_{1,33}=6.39$, $p < 0.05$) and engaged in significantly less MVPA (-27.6 min·day^{-1}, $F_{1,33}=4.66$, $p < 0.05$). Furthermore, comparing by sex showed boys engaged in similar volumes of sedentary time and sleep, but more MVPA, relative to girls, regardless of disease status (Figure 1). The HbA1c level for all participants with T1D was above the National Institute for Health and Care Excellence (NICE) recommended levels of 48 mmol·mol^{-1} [45].

Insert Table 1 Here

Insert Table 2 Here

Insert Figure 1 Here

No significant differences were found between the daily average composition of movement behaviours for each week of the monitoring period ($p > 0.05$). Therefore, subsequent analyses were completed using the daily average across all four weeks for all available physical activity data for each participant.

In the full sample, participants spent the majority of waking hours being sedentary or engaged in LPA, with MVPA accounting for less than 4% of waking time and sleep accounting for the greatest percentage of the 24-hour period (Table 3). According to the variation matrices (Table 4), LPA and sleep had the greatest co-dependence, followed by LPA with sedentary time and sedentary time with sleep, whereas MVPA showed the least co-dependence with all other behaviours. Furthermore, overall MVPA was found to account for 85% of the day-to-day variance in an average 24 hours, despite only consisting of 3.5% of the day, further supporting the low co-dependence of this behaviour in comparison to the remaining behaviours.

Insert Table 3 Here

Insert Table 4 Here

Participants with T1D accrued significantly less time in MVPA and slept marginally less but engaged in significantly more LPA when compared to non-diabetic peers (Figure 2).

Insert Figure 2 Here

The average composition of movement behaviours for the whole sample, accounting for sex, age and disease status, was a significant determinant of PP and PWV (Table 5). Additionally, sleep and sedentary time were negatively associated with PP and RMSSD ($p \leq 0.05$), respectively.

Insert Table 5 Here

As shown in Table 6, the reallocation of time from MVPA to any other behaviour was predicted to negatively affect all cardiovascular measures, independent of disease status. In contrast, allocating time to MVPA from other behaviours was consistently predicted to improve all outcome measures. Specifically, ~~T~~the greatest percentage changes, deemed significant according to specific SWC%, were observed with the substitution of 20 minutes from MVPA to the remaining behaviours, which was associated with an increased PP, PWV, and LF, and decreased HF in children with T1D. Increases in PWV were also found with the reallocation of 20 minutes of MVPA to LPA or sleep and in LF with MVPA to sleep, for healthy peers (Table 6).

Insert Table 6 Here

Discussion

The current study is the first to utilise compositional analysis to investigate the combined and individual effect of movement behaviours, relative to one another, on cardiovascular health in children with and without T1D. Overall, arterial stiffness

markers were most influenced by the overall average movement composition, whereas autonomic function was most influenced by sedentary time and sleep, relative to all other behaviours. Reallocation of time from MVPA to any other behaviour was predicted to negatively affect all cardiovascular measures, independent of disease status, whereas allocating time to MVPA was consistently predicted to improve all outcome measures. Additionally, the same intensity of physical activity may be more potent for cardiovascular health in T1D children, compared to non-diabetic peers.

An aim of the present study was to explore how the composition of habitual movement behaviours changed over a month, and to subsequently explore how the postulated fluctuations affected arterial and autonomic health. However, no significant differences in composition were evident between weeks for any habitual behaviour, irrespective of sex or disease status. This lack of significant variation over time may support the ActivityStat hypothesis, which postulates that physical activity behaviours fluctuate around a mean, with extremes above or below this mean followed by reciprocal changes to maintain an overall balance [17]. Conversely, studies have refuted the possible presence of an ActivityStat, with Dale et al. [46] and Saunders et al. [30] finding no compensatory increase in physical activity in children when school-based activities were restricted and sitting time increased. One potential reason for the equivocal findings regarding a compensatory effect in children may be the different time frames over which fluctuation and cycles of movement behaviours occur, both between and within individuals [47]. However, little research has sought to identify a typical time frame for such fluctuations in children and adolescents, likely due to accelerometer monitoring only relatively recently providing high-resolution acceleration data for durations longer than seven days [48]. Future research is therefore warranted to investigate the possible fluctuations and repetitive cycles in behavioural patterns and how these influence key health outcomes.

Research in children with T1D and the general paediatric population has found that, individually, MVPA and LPA may slow the rate of premature stiffening and decline in the ANS function, likely due to the anti-inflammatory effects of physical activity and/or to the stabilisation of glycaemic extremes [24,49]. Conversely, prolonged periods of sedentary time have been shown to increase insulin resistance and to be associated

with a deleterious lipid profile [29,30]. However, compositional analyses indicates that when these behaviours are considered as a proportional whole, they do not necessarily replicate the influences observed on health outcomes when considered in isolation [10,11]. Specifically, the present study found that the average behaviour composition was significantly associated with indicators of arterial stiffening but not HRV indices, highlighting that neither age, sex, disease status or movement behaviours fully explain the variances in autonomic function. Given the potent effect of cardiorespiratory fitness on ANS function [28,50], future studies should consider its mediatory role in the relationship between movement and sleep behaviours and autonomic health.

An increased sedentary time, relative to other behaviours, was associated with lower central stiffening, although it had a significant deleterious effect on parasympathetic activity. This relationship between sedentary time and decreased central stiffening is discordant with previous research assessing the individual effects of sedentary time in children, which were unequivocally negative [8,28,30]. However, using a compositional approach, Carson et al. [11] found sedentary time had a limited influence on cardiometabolic markers, including blood pressure and lipid profile. Comparisons to the earlier studies using an isolated behaviour approach should be limited but the explanation for this unexpected finding is unclear. Whilst the potential role of a small sample size should not be discounted, this relationship may also reflect the complex interaction between activity and arterial health such that high levels of physical activity are not always associated with beneficial changes to arterial stiffness[51-53]. Alternatively, the observed relationship could reflect compensatory behaviours, whereby those who are more active have been found to subsequently compensate with high sedentary time[54], therefore highlighting the need for future research including all movement behaviours. Discordant with previous research [6,55], LPA was associated with an increased central stiffening. Indeed, previous research has shown that LPA in children with T1D is beneficial for health, potentially reducing insulin resistance [6,55]. In the current study, time in MVPA, but not LPA, showed more favourable trends for PP and aortic stiffness, which is in accord with previous research in people with T1D and indicates that intensity of physical activity may be key to preventing premature arterial stiffening [49]. Indeed, in T1D, MVPA is hypothesised to improve insulin sensitivity which is particularly important for adolescents, as puberty is associated with an increase in

insulin resistance, thereby increasing risk of glycaemic extremes and, in turn, stiffening and autonomic decline [6,24,56]. Taken together, these findings highlight the importance of exploring each behaviour as part of the daily movement continuum to identify important associations between daily behaviours and key health outcomes. Overall, this approach can aid future intervention development seeking to reduce disease burden and risk of future complications.

The greatest predicted change was observed when reallocating time to and from MVPA for all cardiovascular measures, with the most significant predicted changes observed in those with T1D. The significant change in cardiovascular measures with changes in MVPA is in line with previous research which found that less time in MVPA was associated with less favourable central stiffening and autonomic function in children with [8,28,57] and without T1D [24,49]. Improvements in cardiovascular measures with increases in MVPA, at the expense of other behaviours, further reinforces the importance of this behaviour for the management of T1D, especially as physical activity levels typically decline with age [32], and are lower in T1D than their non-diabetic peers, irrespective of age [58]. This therefore highlights the importance of meeting the recommended 60 minutes of MVPA per day [25], especially for children with T1D.

Discordant with Farabi et al. [59] and Monzon et al. [60], who found that deprived sleep was associated with poor glucose control and an increased risk of cardiovascular complications, the present study found that reallocating sleep time to other behaviours was predicted to be associated with improvements in central stiffening and vagal modulation. Specifically, the present findings indicate that reallocating 20 minutes of sleep to MVPA may be associated with significant improvement for central stiffening and parasympathetic activity for children with T1D, thereby suggesting MVPA may be of equal, if not greater, importance than sleep. In addition, it is pertinent to note that the smaller changes from the reallocation of 20 minutes to and from LPA indicates that more than 20 minutes is likely necessary to elicit significant changes in cardiovascular health. Indeed, previous research in healthy children demonstrates that LPA can positively effect cardiometabolic and arterial health [61-63], and has been suggested to be an alternative target to MVPA [63]. However, while LPA can positively influence health for children with T1D, the relative time that needs to be displaced is considerably larger than MVPA, and would most likely necessitate a reduction in

sedentary time, given the importance of sleep and MVPA in this population. Furthermore, the difference in findings between LPA and MVPA further emphasise that the intensity, and not total volume, of physical activity may be key to preventing premature increases in arterial stiffening and decline in autonomic function in T1D.

A major strength of the present study was the use of compositional analyses to explore how all daily movement behaviours influence cardiovascular health in a paediatric clinical population, rather than exploring these behaviours in isolation. Additionally, the use of predictive modelling regarding the possible effect of reallocating time from one behaviour to another was a key novelty in those with T1D and could inform targets for future interventions in similar populations. Furthermore, the inclusion of 28 days of habitual movement behaviours allowed us to account for potential behavioural variations and more reliably explore the relationship between physical activity and health. However, this study is not without limitations. Specifically, compositional analyses models may be susceptible to outliers, therefore the relatively small sample size included may limit generalisability. It is also pertinent to note that the analysis was limited to the whole sample, as opposed to each individual group for disease status and sex and therefore is an important area that warrants further investigation when possible. Furthermore, significant differences were evident in the maturity status of the participants, with healthy girls deemed pubertal, whereas all other remaining participants were pre-pubertal. This was statistically accounted for in the present study but future studies should consider the influence of maturity independently. Furthermore, while the predictive models provide valuable insight as to predictive change, they do not indicate whether the changes would be acute or chronic, nor how long the change in behaviour needs to be implemented in order for these changes to occur. It is also pertinent to note that the present subsample of children with T1D could be considered somewhat biased with regards to being more physically active and therefore this may have influenced glycaemic control. This is an important area for future research. Finally, the large variability observed in the cardiovascular measures is likely a consequence of the small sample size, nonetheless the variability of these measures is comparable to that reported elsewhere for those of a similar age[64].

In conclusion, intensity, not just the overall volume, of physical activity may be a key factor in reducing risk of premature negative changes in autonomic and arterial health

for children, with and without T1D. Moreover, increasing time in MVPA, by substituting 20 minutes from any other behaviour, has the potential to slow progression of autonomic decline and central arterial stiffening in children with T1D.

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Table 1. Participant anthropometric characteristics and glycaemic control, according to disease status and sex.

	T1D (n = 20)		Non-Diabetes (n = 17)	
	Girls (n = 10)	Boys (n = 10)	Girls (n = 6)	Boys (n = 11)
Age (yrs)	12.1 ± 1.1	11.7 ± 2.0	11.8 ± 2.3	11.4 ± 2.0
BMI ($kg \cdot m^{-2}$)	21.8 ± 4.3	19.8 ± 3.8	19.0 ± 4.7	19.2 ± 4.2
BMIz	1.2 ± 0.8	0.6 ± 1.1	0.2 ± 1.2	0.5 ±1.3
Maturity offset (yrs)	0.34 ± 1.46*	-1.76 ± 1.69	-0.30 ±1.92*	-2.19 ± 1.75
HbA1c ($mmol \cdot mol^{-1}$)	76.3 ± 13.6	65.4 ± 11.9	-	-
HbA1c (%)	9.1 ± 1.3	8.1 ± 1.1	-	-
Total-c ($mmol \cdot l^{-1}$)	4.3 ± 0.4	4.1 ± 0.3	-	-
LDL-c ($mmol \cdot l^{-1}$)	2.5 ± 0.3	2.2 ± 0.3	-	-
Disease duration (yrs)	4.7 ± 3.5	5.4 ± 3.2	-	-

Data is presented as mean ±SD. Body mass index (BMI), glycated haemoglobin (HbA1c), total cholesterol (total-c), total cholesterol (Total-c), low density lipoprotein (LDL-c). * A significant difference between sexes within a disease group.

701 **Table 2.** Arterial and autonomic outcomes, according to disease status and sex.

	T1D		Non-Diabetes	
	Girls	Boys	Girls	Boys
PP (mmHg)	55 ± 11	59 ± 10	56 ± 16	58 ± 9
AIx (%)	15.1 ± 5.8	12.1 ± 7.1	17.3 ± 6.3	13.3 ± 5.9
MAP (mmHg)	84.3 ± 7.8	80.3 ± 5.2	84.1 ± 6.5	86.1 ± 4.7
PWV ($m \cdot sec^{-1}$)	5.24 ± 0.58	4.96 ± 0.66	4.66 ± 0.90	4.74 ± 0.66
RMSSD (ms)	53.5 ± 26.9	75.69 ± 37.46	76.6 ± 34.7	66.8 ± 53.6
LF (Hz)	6,519 ± 6,882	5,367 ± 2,976	4,860 ± 4,285	5,632 ± 8,503
HF (Hz)	1,349 ± 1545	3,468 ± 4050	1,430 ± 1279	2,577 ± 3,699
LF (nu)	79.2 ± 16.5	69.1 ± 24.9	75.1 ± 16.8	66.2 ± 19.4
HF (nu)	20.7 ± 16.4	30.8 ± 24.9	24.9 ± 16.7	33.8 ± 19.3

Data is presented as mean ±SD. Pulse pressure (PP), augmentation index (AIx), mean arterial pressure (MAP), pulse wave velocity (PWV), root mean square of successive standard deviations of NN intervals (RMSSD), low frequency (LF), high frequency (HF).

702

703 **Table 3.** Time spent in each movement behaviour and asleep according to disease
704 status, calculated as the arithmetic and geometric mean and as a percentage of a
705 given 24-hour period.

		SED	LPA	MVPA	SLEEP
Overall	Mean (min·day^{-1})	435.3	467.2	61.8	475.1
	Geometric Mean (min·day^{-1})	436.0	472.8	50.2	481.0
	Percentage of 24 hours (%)	30.3	32.8	3.5	33.4
T1D	Mean (min·day^{-1})	435.9	486.4	48.0	469.6
	Geometric Mean (min·day^{-1})	434.9	491.6	42.8	470.7
	Percentage of 24 hours (%)	30.2	34.1	3.0	32.7
Non-Diabetes	Mean (min·day^{-1})	434.6	444.6	78.1	481.6
	Geometric Mean (min·day^{-1})	436.5	450.7	60.5	492.4
	Percentage of 24 hours (%)	30.3	31.3	4.2	34.2

706 Sedentary time (ST), light physical activity (LPA), moderate-to-vigorous physical activity (MVPA).

Table 4. Pair-wise log-ratio variation matrix for sedentary time, LPA, MVPA, and sleep for the overall sample and according to disease status.

		SED	LPA	MVPA	SLEEP
Overall	SED	-	0.021	-0.188	0.039
	LPA	0.021	-	-0.067	0.006
	MVPA	-0.188	-0.067	-	-0.103
	SLEEP	0.039	0.006	-0.103	-
T1D	SED	-	0.014	-0.096	-0.004
	LPA	0.014	-	-0.036	-0.003
	MVPA	-0.096	-0.036	-	-0.037
	SLEEP	-0.004	-0.003	-0.037	-
Non-Diabetes	SED	-	0.024	-0.298	0.091
	LPA	0.024	-	-0.082	0.014
	MVPA	-0.298	-0.082	-	-0.182
	SLEEP	0.091	0.014	-0.182	-

Sedentary time (SED), light physical activity (LPA), moderate-to-vigorous physical activity (MVPA).

710 **Table 5.** Compositional linear regression model showing the association of movement
711 and sleep behaviours and each measure of arterial health in the overall sample,
712 adjusted for age, sex, maturity and disease status.

713

	Model p	γ_{SED}	p	γ_{LPA}	p	γ_{MVPA}	p	γ_{SLEEP}	p
PP	0.06	3.31	0.32	6.87	0.11	-3.31	0.09	-6.87*	0.05
AIx	0.52	-0.74	0.74	1.74	0.54	1.08	0.40	-2.08	0.36
MAP	0.28	-1.97	0.35	-2.25	0.41	1.29	0.29	2.94	0.18
PWV	0.06	-0.19	0.34	0.14	0.56	-0.14	0.27	0.17	0.44
RMSSD	0.30	-28.94*	0.05	18.13	0.31	-3.06	0.70	13.87	0.35
LF	0.17	-2.25	0.73	-8.09	0.34	-1.76	0.64	12.10	0.09
HF	0.17	2.24	0.73	8.05	0.34	1.75	0.64	-12.04	0.09

Sequential rotated ILR modelling for each arterial health measure, adjusted for age, sex, maturation and disease status. Beta-coefficient (γ), Sedentary time (SED), light intensity physical activity (LPA), moderate-to-vigorous physical activity (MVPA), pulse pressure (PP), augmentation index (AIx), mean arterial pressure (MAP), pulse wave velocity (PWV), root mean square of successive standard deviations of NN intervals (RMSSD), low frequency (LF), high frequency (HF). Regression coefficients relate to the change in log-ratio for a given behaviour, relative to other behaviours. * A Significant association between movement behaviour and cardiovascular measure.

714

Table 6. Effect on each cardiovascular health outcome of taking 20 minutes of time from the behaviour in the columns and reallocating it to the behaviour in the rows. The values represent the percentage change in the respective health outcome.

		T1D				Non-Diabetes			
		SED	LPA	MVPA	Sleep	SED	LPA	MVPA	Sleep
PP	SED	-	0.24	4.72*	1.67	-	0.19	2.95	1.66
	LPA	-0.30	-	4.46*	1.41	-0.25	-	2.73	1.44
	MVPA	-3.35	-3.08	-	-1.64	-2.48	-2.25	-	-0.78
	Sleep	-1.67	-1.40	3.09	-	-1.66	-1.43	1.32	-
AIx	SED	-	-2.58	2.22	0.86	-	-2.57	0.90	0.76
	LPA	2.53	-	4.72	3.36	2.51	-	3.39	3.24
	MVPA	-1.22	-3.83	-	-0.39	-0.56	-3.16	-	0.18
	Sleep	-0.78	-3.38	1.42	-	-0.69	-3.28	0.19	-
PWV	SED	-	-0.40	4.58*	-0.51	-	-0.46	2.68	-0.55
	LPA	0.40	-	4.97*	-0.12	0.46	-	3.13*	-0.10
	MVPA	-2.89*	-3.29*	-	-3.40*	-2.01	-2.48	-	-2.57
	Sleep	0.50	0.10	5.07*	-	0.55	0.07	3.21*	-
RMSSD	SED	-	-5.54	-6.27	-5.73	-	-5.11	-4.66	-5.10
	LPA	5.65	-	-0.80	-0.26	5.21	-	0.38	-0.06
	MVPA	5.60	-0.12	-	-0.31	4.55	-0.72	-	-0.71
	Sleep	5.83	0.11	-0.62	-	5.20	-0.08	0.37	-
LF	SED	-	-0.06	6.38*	-1.76	-	-0.03	3.68	-1.92
	LPA	0.10	-	6.46*	-1.68	0.07	-	3.73	-1.87
	MVPA	-3.95	-4.04	-	-5.73*	-2.71	-2.76	-	-4.65
	Sleep	1.72	1.64	8.08*	-	1.88	1.83	5.54*	-
HF	SED	-	0.19	-18.19*	4.99	-	0.08	-7.32	3.80
	LPA	-0.29	-	-18.42*	4.76	-0.16	-	-7.43	3.69
	MVPA	11.27	11.52	-	16.32*	5.38	5.50	-	9.23
	Sleep	-4.89	-4.64	-23.02*	-	-3.73	-3.61	-11.01	-

Predicted effects were based on the mean composition. Adjusted for age, sex and maturation. Sedentary time (SED), light intensity physical activity (LPA), moderate-to-vigorous physical activity (MVPA), pulse pressure (PP), augmentation index (AIx), pulse wave velocity (PWV). * A percentage change greater than the SWC % for each arterial measure.