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GRANADA consensus on analytical approaches to assess associations with accelerometer-determined physical behaviours (physical activity, sedentary behaviour and sleep) in epidemiological studies

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ABSTRACT

The inter-relationship between physical activity, sedentary behaviour and sleep (collectively defined as physical behaviours) is of interest to researchers from different fields. Each of these physical behaviours has been investigated in epidemiological studies, yet their codependency and interactions need to be further explored and accounted for in data analysis. Modern accelerometers capture continuous movement through the day, which presents the challenge of how to best use the richness of these data. In recent years, analytical approaches first applied in other scientific fields have been applied to physical behaviour epidemiology (eg, isotemporal substitution models, compositional data analysis, multivariate pattern analysis, functional data analysis and machine learning). A comprehensive description, discussion, and consensus on the strengths and limitations of these analytical approaches will help researchers decide which approach to use in different situations. In this context, a scientific workshop and meeting were held in Granada to discuss: (1) analytical approaches currently used in the scientific literature on physical behaviour, highlighting strengths and limitations, providing practical recommendations on their use and including a decision tree for assisting researchers' decision-making; and (2) current gaps and future research directions around the analysis and use of accelerometer data. Advances in analytical approaches to accelerometer-determined physical behaviours in epidemiological studies are expected to influence the interpretation of current and future evidence, and ultimately impact on future physical behaviour guidelines.

INTRODUCTION

Physical activity (PA), sedentary behaviour (SB) and sleep, collectively described as physical behaviours,[1] are of interest to many researchers from previously separate fields. Accounting for the inter-relations of these behaviours is important because: (1) they share the 24 hours of the day (ie, closure), so change in one behaviour results in change in others; and (2) the relation of a specific behaviour with health depends on other behaviours (eg, SB and mortality relation depends on moderate-to-vigorous PA (MVPA)[2 3]). These inter-relations should be considered in modelling their association with health, with attention to collinearity issues potentially leading to spurious findings.

Accelerometers are increasingly being used to estimate different constructs/dimensions of physical behaviours (eg, types (walking, cycling, dancing), intensities (light, moderate, vigorous), and postures (reclining, sitting, standing)). Other constructs focus more on the description of the acceleration signal (eg, time spent within acceleration bands with no energy expenditure interpretation (eg, min/day between 0 and 100 mg), or the acceleration above which the most active 30 min of the day occur). The data-analytical approach usually includes: (1) reduction of the acceleration signal into meaningful behaviours/descriptors; (2) mathematical treatment of the descriptors if needed and (3) selection of the statistical model. Multiple choices are available for each step, and decisions should be adapted to the research question and account for potential collinearity issues arising from behaviours' inter-relationships. However, there are currently no consensus/recommendations to help to choose the most appropriate approach. Online supplemental appendix 1 presents the different choices for descriptors, mathematical treatments and statistical models discussed in the Analytical approaches section.

The 'International Workshop: A focus on statistical methods to analyse accelerometer-measured PA' was held in Granada on 21–22 October 2019. This event brought together a panel of researchers to discuss, reach consensus, and provide recommendations about the most frequently used analytical approaches in the field and about future research directions in physical behaviour epidemiology. The focus was on modelling physical behaviour constructs (mainly related to PA and SB, although we also included sleep to cover the 24-hour continuum) as exposure variables and health indicators as outcomes. We covered *time-use* descriptors as those quantified in time over the day, and *acceleration-based* as those quantified as acceleration magnitude.

Table 1 Description of accelerometer-based descriptors of physical behaviours

Descriptor	Brief description	Examples
Average acceleration or steps per day	Arithmetic average of the processed acceleration throughout the measurement period or per day.	29 36 46–48
Time-use behaviours	Estimates of time spent in physical activity intensities (eg, LPA, MPA, VPA), types (eg, walking, running, cycling), or SB, optionally expressed in bouted and unbouted behaviour. These estimates can be derived with heuristic methods or ML.	29 49–52
Intensity spectrum	The intensity spectrum is an extension of cut-points which attempts to provide a much more detailed description of the physical activity intensity pattern. Instead of using cut-points representative of SB, LPA, MPA or VPA, the cut-points are arbitrarily selected to obtain a wider range of intensity bands.	32 33 53
Intensity gradient	The intensity gradient describes the negative curvilinear relationship between physical activity intensity and the time accumulated at that intensity during the 24-hour day.	36 46
MX metrics	The acceleration above which a person's most active X minutes/time (MX) are accumulated, to focus on a person's most active periods of the day.	54 55
Acceleration functions	Description of the accelerometer data with a function rather than with a scalar. Functions seek a more detailed description of the accelerometer data without making a priori assumptions.	38 39 56
Other indicators	Apart from the descriptors related to energy intensity or acceleration levels, an array of metrics can provide complementary information, such as: physical activity domain, circadian rhythmicity, timing, sleep efficiency, etc.	34 57 58

LPA, light physical activity; ML, machine learning; MPA, moderate physical activity; SB, sedentary behaviour; VPA, vigorous physical activity.

Data collection decisions are outside our focus, although decisions on body attachment site,[4–8] number of days recorded,[9] treatment of weekdays and weekend days,[10 11] seasonality,[12] among others, affect the ability of accelerometer data to identify specific constructs/aspects of physical behaviours. For example, attaching the accelerometer to the hip, wrist or thigh may be considered depending on the constructs of interest (eg, PA intensity,[13–15] postures[16] or sleep patterns,[17 18] among others). A recent consensus report discussed best practices on these decisions.[19]

ANALYTICAL APPROACHES: DISCUSSION AND PRACTICAL CONSIDERATIONS

This section discusses different analytical approaches' applicability in various situations (or research questions). Analytical approaches include the combination of accelerometer descriptors (table 1, online supplemental appendix 1 (Section 1)) and statistical models (table 2, online supplemental appendix 1 (Section 3)) with and without mathematical (compositional) transformation (online supplemental appendix 1 (Section 2)). We provide practical considerations on (1) informativeness of each analytical approach for public health messaging and (2) appropriateness of the analytical approaches for certain research questions. Additionally, table 3 shows the performance of these approaches regarding closure or collinearity, relationship assumptions and interpretation for PA guidelines.

Total PA and linear regression

Average acceleration (or steps per day) provides the simplest estimate of the overall movement and proxy for total daily PA-related energy expenditure. Statistical interpretation of findings using linear regression is straightforward since there is a single variable representing the overall activity volume. Thus, codependence with other explanatory variables is not usually a concern and linear regression models are an option for the analysis. The opinion of the consensus group is that the average acceleration is useful for reducing the confounding effect of PA in a given association analysis (eg, is the association of sugar consumption with body mass index dependent on overall PA?), or as the main exposure in cases where it explains a large proportion of the PA-related energy expenditure in a certain cohort (eg, is PA-related energy expenditure associated with protein intake?). Beyond this, the average acceleration alone is not very informative relative to associations of specific physical behaviours with health outcomes, limiting its applicability for public health messaging. A recent study proposed the minimum clinically informative difference for average acceleration from wrist data,[20] but further studies are needed. Although these descriptors cannot be interpreted in terms of meeting or not meeting the PA guidelines, they may be the best descriptor to test the 'move more' message reported in several guidelines.

Table 2 Brief description of approaches to analyse associations between physical behaviours and health outcomes

Statistical model	Brief description	Examples
Linear regression modelling	Traditional models establishing the relationship between a set of explanatory variables and an outcome (ie, health outcome). Exposure is usually limited to a single time-use behaviour. Interpretation is in terms of increasing time in one behaviour.	59 60
Isotemporal substitution model	Isotemporal substitution models examine the theoretical effects of displacing a fixed duration of time between behaviours. Given the fixed and finite duration of a day, increasing time in one movement behaviour (eg, LPA) will result in a net equal and opposite change in other movement behaviours (eg, SB). Interpretation is in terms of substituting one behaviour for other behaviours.	61 62
Multivariate pattern analysis	A regression approach/analysis that can handle an unlimited number of multicollinear explanatory variables by using latent variable modelling. Models are cross-validated to optimise predictive ability. Interpretation is based on the complete pattern of associations among the explanatory variables in relation to the outcome.	25 63–66
Functional data analysis	Functional data analysis is an extension of scalar regression where the exposure or outcome is defined as a function rather than a scalar variable. The function can describe the full distribution of intensity of acceleration or the time-series of acceleration over the day. The function can be included in linear regression analysis through dimensional reduction techniques. Interpretation is in terms of certain accelerometer trace shapes.	37 38 67–69
Machine learning (ML)	ML entails a broad range of techniques to automate the learning of high-dimensional and/or non-linear patterns in data with predictive ability (supervised ML) or data reduction (unsupervised ML) as its core priority.	41 70 71

LPA, light physical activity; SB, sedentary behaviour.

Table 3 Summary of analytical approaches' (including descriptor, mathematical transformation and statistical model) strengths and limitations in relation to closure, collinearity, relation-shape assumptions and interpretation relative to public health guidelines

Descriptor	CoDA transform	Statistical modelling	Risk of closure?*	Risk of collinearity?	Handles closure?	Handles collinearity?	Relationship assumptions	Allow investigation of longitudinal associations (eg, Cox regression)	Interpretation relative to guidelines? (eg, 150 min/week of MVPA)
Average acceleration	**No**	**Linear**	No	No	NA	NA	Linear	Yes	No
Time-use descriptors	**No**	**Linear**	Yes	Yes	No	No	Linear	Yes	Yes
	Yes	**Linear**	Yes	Yes	Yes	In part†	Log-linear	Yes	Yes
	No	**ISO**	Yes	Yes	Yes	No	Linear	Yes	Yes
	No	**MPA**	Yes	Yes	No	No	Linear	Not at the moment	Yes
	Yes	**MPA**	Yes	Yes	Yes	Yes	Log-linear	Not at the moment	Yes
Intensity spectrum	**No**	**Linear**	Yes	Yes	No	No	Linear	Yes	Yes‡
	Yes	**Linear**	Yes	Yes	Yes	In part†	Log-linear	Yes	Yes‡
	No	**ISO**	Yes	Yes	Yes	No	Linear	Yes	Yes‡
	No	**MPA**	Yes	Yes	No	No	Linear	Not at the moment	Yes‡
	Yes	**MPA**	Yes	Yes	Yes	Yes	Log-linear	Not at the moment	Yes‡
Intensity gradient	**No**	**Linear**	No	No	NA	NA	Linear	Yes	No
	No	**FDA**	No	No	NA	NA	Fewer assumptions than other models	Yes	Yes§
MX metrics	**No**	**Linear**	Yes	Yes	No	No	Linear	Yes	Yes‡
	No	**MPA**	Yes	Yes	No	Yes	Linear	Not at the moment	Yes‡
Other acceleration functions	**No**	**FDA**	No	No	NA	NA	Fewer assumptions than other models	Yes	Yes§

*Closure refers to whether a certain descriptor is a specific part of the daily time constraint (ie, it is measured in time per day).
†Indicates that it solves the collinearity due to the closure, but collinearity can still exist across the CoDA-transformed variables.
‡Indicates that the interpretation is made through a post-hoc application of validated cut-points to identify the PA intensity (eg, MVPA).
§Indicates that more work is needed on the interpretation of functional data analysis, an example can be found elsewhere.[39]
CoDA, compositional data analysis; FDA, functional data analysis; ISO, isotemporal substitution models; MPA, multivariate pattern analysis; MVPA, moderate-to-vigorous PA; MX, acceleration above which a person's most active X minutes/time are spent; NA, not applicable; PA, physical activity.

Time-use behaviours or intensity spectrum and linear regression

Among time-use constructs, time spent in PA intensities is the most frequently used, while PA types and postures have gained momentum recently. These descriptors are often introduced in linear regression models to test the association of time spent in a certain intensity/behaviour with health outcomes. As it is widely used, it is useful for comparing estimates with other cohorts. The intensity spectrum is an extension of PA intensities with higher resolution energy bands. When using such time-use behaviours, requirements for bouts in these behaviours should be considered. We observe a lack of consensus in the literature on how a bout should be calculated, including the definition of both acceptable allowance drop period without terminating the bout and minimum and maximum duration. Bouts of 30 min for SB and 10 min for MVPA, often allowing short time intervals outside the behaviour of interest, are frequently used.[21] It is unclear how much these choices are driven by a desire for harmonisation, by public health guidelines, or by evidence. Although observational data based on 1-minute or longer epoch lengths suggest that any bout duration can produce health benefits, randomised controlled trials investigating the effects of differing bout durations on health outcomes are lacking.[21] Based on the observational studies, the recommendation about accumulating PA in certain bout durations has been excluded from recent guidelines.[22]

Time-use behaviours (or intensity spectrum) include a set of codependent variables, and linear regression does not handle closure and collinearity among explanatory variables. When using these descriptors, linear regression adjusted for all physical behaviour components may be affected by multicollinearity.[23] Variance inflation factors are unable to explain inconsistencies between linear regression models sequentially excluding a behaviour from the explanatory variables[24] and might not be an acceptable diagnostic indicator for the interdependency between time-use descriptors.[24] Additionally, the assumption of linearity of the association between these descriptors and health outcome might not be sufficiently met for analyses to yield valid results. This consensus group recommends moving towards other analytical approaches more suitable for studying the codependencies among time-use behaviours. In this regard, transforming time-use behaviours using the compositional data transformation (isometric log ratio (ILR), online supplemental appendix 1 (Section 2)) represents an option. Using the ILR transformation, each variable indicates the time spent in a given behaviour relative to the time spent in the rest of behaviours of the composition (eg, SB, light PA, MVPA and sleep). In other words, it quantifies the effect of increasing the time in a behaviour while proportionally reducing the time in the rest. Pair-wise reallocations of time can be interpreted from linear regression predictions on specific time compositions arising from hypothetical reallocations of time rather than from regression coefficients (as in isotemporal substitution models, online supplemental appendix 1 (Section 3.2)). By transforming the variables, the codependency among the time-use descriptors relative to their time closure is solved (ie, it accounts for the codependency of time among variables). However, transformed variables can still be collinear, and collinearity should be investigated because linear regression cannot handle collinearity, regardless of its source. This is especially problematic when analysing the intensity spectrum since it provides a wide range of variables (usually more than 10) that are highly correlated, even if using ILR-transformed variables.[25] As such, we recommend testing the correlations and risk of collinearity among the explanatory variables (even when compositionally transformed). In absence of high correlations and collinearity, linear regression can be appropriate.

The opinion of the consensus group is that physical behaviour epidemiology should move to studying the combined effects and interactions of physical behaviours on health, and a feasible option is using ILR-transformed time-use descriptors and linear regression.[24 26] This approach is informative for public health messaging as it provides information on combinations of behaviours (considering every behaviour that occurs in the day) which are beneficial for health. Clustering groups of people based on their behaviours is also an alternative to investigating the interactions between behaviours, although compositional analyses allow the variables to be studied on a continuous scale. With the intensity spectrum, the use of linear regression models is not possible because of collinearity issues in the variables (either transformed or not).[25] The collinearity problem, however, can be solved by using partial least square (PLS) regression. Regression models can be used in different study designs, including longitudinal studies, either with absolute[27–29] or compositional data.[30] Linear regression with compositional data may need appropriate graphical representation of the results to interpret the magnitude of the association.[24]

Time-use behaviours or intensity spectrum and isotemporal substitution models

Isotemporal substitution modelling carries forward the main limitations of linear regression, that is, multicollinearity and assumption of linearity (as the magnitude of the association is derived from regression coefficients). These important limitations preclude us from recommending the use of isotemporal models with time-use descriptors. However, it is notable that this approach provides broadly similar findings to compositional ILR transformation of time-use descriptors and linear regression.[31] Public health messaging can be complemented with information on the effect of reallocating daily time across behaviours (either with isotemporal substitution models or with linear regression with compositional data, the Time-use behaviours or intensity spectrum and linear regression section). The intensity spectrum has not been analysed with isotemporal substitution models thus far. We do not recommend such an analysis since the large number of variables in the intensity spectrum would complicate the interpretation.

Time-use behaviours or intensity spectrum and multivariate pattern analysis

Multivariate pattern analysis fully handles the collinearity among explanatory variables using latent variable modelling. Collinearity is approached as a dimensionality reduction problem in which the variance of the explanatory variables shared with the outcome is retained. Multivariate pattern analysis describes the pattern of associations for the descriptors with the outcome, accounting for the correlated structure of the data. Associations with health are interpreted for each descriptor (each PA intensity or band in the intensity spectrum) considering its codependency with the rest, but without quantifying time exchange between descriptors. A limitation of this analytical approach is that PLS regression models cannot be adjusted as usually done in linear regression. If covariates are included in the PLS model, they will contribute their shared variance with PA and the outcome. Aadland *et al* proposed obtaining residuals for the outcome from a linear regression model including confounders as explanatory variables, prior to entering the outcome variable in the PLS model.[25 32 33] This challenge remains for the analysis of categorical or time-to-event outcomes (eg, mortality).

Likewise, time-use behaviours or the intensity spectrum could be transformed as compositional data before performing multivariate pattern analysis. Since multivariate pattern analysis can handle singular data, the use of ILR coordinates is not necessary. Aadland *et al* recently compared the use of centred log ratio (CLR)-transformed time-use and intensity spectrum descriptors with respect to associations with metabolic health using multivariate pattern analysis.[25] While associations appeared to differ, the interpretation of associations, considering the absolute and relative interpretation, were partly equivalent. The interpretation of CLR-transformed variables may not be very informative for public health messaging as they represent the effect of time exchange from the geometric mean of the time-use descriptors distribution to a specific time-use descriptor (eg, MVPA or any intensity spectrum band).

Other similar alternatives to reduce dimensionality of the data while retaining relevant information by increasing covariance among descriptors (rather than with the outcome) include factor analysis, principal component analysis, or joint and individual variation explained.[34] This consensus group recommends considering these approaches to analyse many explanatory variables (eg, intensity spectrum) in relation to health.[35] There is no clear recommendation on the number of bands (or number of explanatory variables) to generate for this analytical approach, though previous studies have used from 16 (uniaxial data)[32] to 102 (triaxial data)[33] intensity bands. Resolution (number of bands) may influence the relationship with the outcome and depend on the sample characteristics; thus, further research is needed.

Intensity gradient and linear regression

The intensity gradient describes the straight line negative slope of the natural logs of time and acceleration intensity.[36] The intensity gradient was developed to: (1) capture the entire intensity distribution, (2) avoid reliance on population and protocol-specific calibration protocols, and (3) provide information that complements average acceleration. The intensity gradient can be used alongside average acceleration to more fully describe the 24-hour movement profile by capturing both volume and intensity of PA. Using the intensity gradient and average acceleration together in linear regression models allows investigation of independent, additive and interactive associations of volume and intensity of PA with health. More work is needed to interpret the intensity gradient relative to the adherence to PA guidelines.

Intensity gradient or intensity distribution and functional data analysis

The acceleration distribution over time of the day, the acceleration density or the intensity gradient function can be used in functional data analysis. Using scalar-on-function data analysis,[37] these acceleration functions can be used as an explanatory variable in regression models including linear,[38] logistic or Cox regression models. For example, in the case of the acceleration density function as explanatory variable, the association with the event of interest is described along the acceleration range.[38] This shows acceleration sections that are associated with the outcome by accounting for the full acceleration distribution, allowing identification of a cut-point such that proportion of time spent above this acceleration cut-point is associated with the outcome. Once these cut-points are identified, it is possible to estimate differences in the outcome by allocating time below to time above this cut-point.[39]

Functional data analysis has several advantages: (1) it is not affected by multicollinearity since it handles the data continuity; (2) it can test the effects of time reallocation and thus consider closure; and (3) it detects sections of the accelerometer data that are important for a certain health outcome, thus relaxing assumptions of linearity in particular behaviours made by other statistical models. Among its main limitations, acceleration functions usually carry much information that may be irrelevant to the outcome, but is considered in the analysis. Its main drawback is difficulty translating the findings into useful, straightforward public health messages. Investigation of how to make the conclusions of functional data analysis relevant to public health guidelines is highly encouraged by this consensus group (see[39] for an example).

MX metrics and linear regression

MX metrics represent the acceleration above which a person's most active non-consecutive X minutes over the day are spent. An advantage of using MX metrics is that analysis is not affected by cut-point assumptions on energy expenditure, while cut-points may be post-hoc applied to enable public health messaging. For example, if the M60 of a child is 230 mg, this can be compared with an MVPA cut-point, for example, 200 mg, [14] showing that the child meets the 60 min daily MVPA recommendation. However, if compared with a more stringent 250 mg MVPA cut-point, the child does not reach the recommendation. The post-hoc application of cut-points can, therefore, be skipped and keep the interpretation to the descriptive MX values instead. Another advantage of this approach is that the intensity of PA for the specified duration is captured regardless of how inactive a person is. Regarding statistical modelling, the MX metrics usually include a wide range of variables (table 1, online supplemental appendix 1 (Section 1)). These MX metrics are likely to be codependent as they are time-use descriptors, which may increase the multicollinearity risk. Likewise, each MX metric would carry partial and relative information on the pattern, and compositional transformation would also be interesting, although this approach has not been tested yet.

The usefulness of MX metrics with multivariate pattern analysis has not been investigated yet. However, since one of the limitations of MX metrics with linear regression is collinearity among the explanatory variables, multivariate pattern analysis could provide new insights by overcoming collinearity.

Multiple descriptors and machine learning

Machine learning (ML) describes a broad range of techniques to automate finding patterns in data with a focus on predictive ability (supervised ML) or data reduction (unsupervised ML). ML methods have been widely applied to derive accelerometer descriptors,[40] yet rarely applied to study health associations.[41 42] Different ML approaches have different strengths and limitations. In general, strengths include their usefulness for data-driven hypothesis generation, their capacity to handle multidimensional data, their ability to find non-linear patterns, and the possibility of training a model in one dataset and updating it in another. However, it can be difficult to interpret how results are obtained and their significance for public health guidelines. ML methods can also be data hungry and computationally intensive. Overfitting and sensitivity to (potentially unknown) biases in the training data are risks.

In some ways, multivariate pattern analyses and other dimension reduction methods can be considered ML methods. The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) Initiative developed a set of recommendations for reporting of studies developing, validating, or updating ML-based prediction models for diagnostic or prognostic purposes.[43] The TRIPOD statement should be considered when developing or applying ML-based prediction models in physical behaviour epidemiology.

FUTURE RESEARCH DIRECTIONS

The workshop in Granada, as well as the later meeting and the work developed in the following months by this author group, has initiated a discussion on analytical approaches and their usefulness for public health guidelines. Currently, 150 min/week of MVPA in adults and older adults, and 60 min/day of MVPA in children are recommended by different agencies.[22 44] Recent guidelines removed the 10-minute bout requirement for MVPA in adults, and included the importance of replacing SB for PA.[22] The Canadian PA guidelines are the first attempt to promote the combined effects of behaviours on health,[45] although the evidence used was not based on the 24-hour paradigm (and so, appropriateness of statistical approach can be discussed).

We propose future research directions based on the research gaps identified, that is, the uncertainty regarding the accelerometer data descriptors to use and what analytical models are the most appropriate given the research question being addressed. The authors of this consensus article agree that investigations determining associations between physical behaviours and health should be extended to understand the interplay of physical behaviours (PA, SB and sleep) in their relationship with health. Measurement and processing capacity is increasing and offers an opportunity to provide further information on how different intensities and types of PA interact to improve health. At the same time, the focus on translating findings to meaningful information for interpretation in practice cannot be lost when using advanced analytical models. It is notable that most of the information presented comes from the PA and SB fields; thus, the relevance for the sleep research filed can be further discussed. The main implications for the analysis of accelerometer data proposed and agreed by the authors of this consensus manuscript are presented below.

Short-term agenda

- Clear communication on the rationale for the use and limitations of each analytical approach in studies is important for a meaningful interpretation of the findings. Practical recommendations for this are provided in the Analytical approaches section of this document and a decision tree was developed (figure 1) to assist researchers' decision-making.
- Investigation of the associations of physical behaviours with health using different analytical approaches is encouraged. Ideally, physical behaviour epidemiology would draw consistent conclusions independently of analytical approach. To do so, clear reporting on the interpretation of findings derived from each analytical approach is crucial to understand 'a priori' inconsistencies across methods. Triangulation of results from different analytical approaches is currently the best solution to quantify associations of physical behaviours with health. Additionally, using the best-suited analytical approaches for a given research question is crucial (see figure 1).
- Although little explored so far, ML-based approaches for diagnostic/prognostic purposes are worth implementing. We encourage transparent reporting of the resulting tools (TRIPOD initiative checklist).

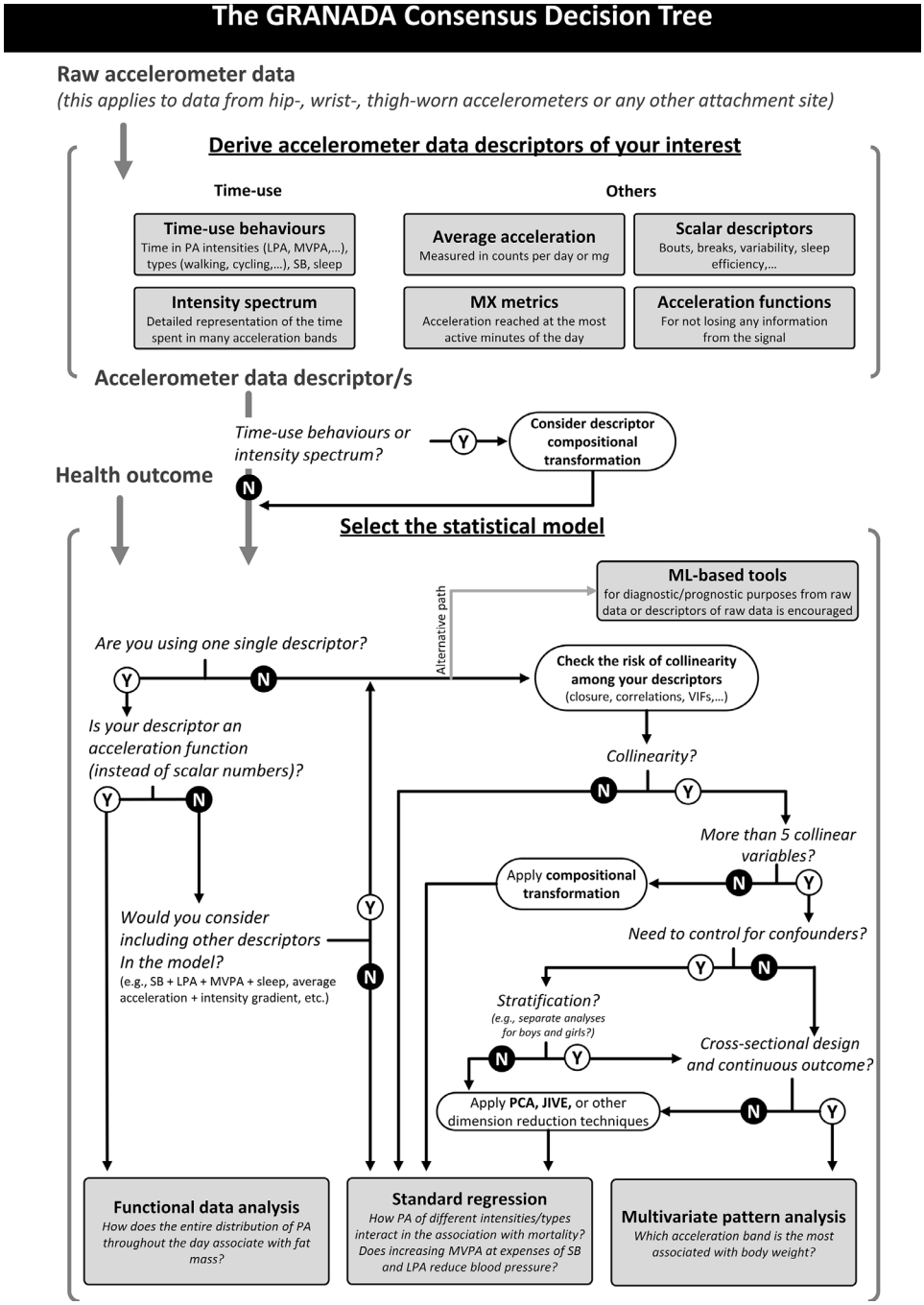

Figure 1 The GRANADA consensus decision tree and research question examples to assist in the selection of an analytical approach in the field of 'physical behaviour epidemiology'. JIVE, joint and individual variance explained; LPA, light physical activity; ML, machine learning; MVPA, moderate-to-vigorous physical activity; PA, physical activity; PCA, principal component analysis; SB, sedentary behaviour; VIFs, variance inflation factors.

- Translating findings to meaningful information for guidelines should be a priority. Accurate reporting of study findings, interpretation and practical implications is highly encouraged.

Long-term agenda

- How to conveniently adjust for confounders in multivariate pattern analysis should be investigated and its application extended to time-dependent outcomes (eg, survival analysis with mortality).
- Further efforts are needed to translate functional data analysis and other advanced analytical approaches' outputs into meaningful information for public health guidelines.
- To evaluate whether the information gathered from the analytical approaches discussed herein can result in complementary information for public health guidelines. Such complementary information may result in more specific recommendations for certain health outcomes or populations, or even in their implementation at population level through movement sensors using evidence-based goals on PA intensity, duration, timing or type, among others.

CONCLUSIONS

This group agreed on several consensus points and research needs for physical behaviour epidemiology (see box 1 and figure 1). This consensus article will increase researchers' understanding

Box 1 Consensus points from the GRANADA report on analytical approaches to assess associations with accelerometer-determined physical behaviours (physical activity (PA), sedentary behaviour (SB) and sleep) in epidemiological studies

1. The study of the association between physical behaviours (ie, PA, SB and sleep) and health should move to a more thorough investigation of the interactions and codependencies between different behaviours (or PA intensities) and health. Several analytical approaches are provided in this consensus document, although none of them is free from limitations.
2. We recommend investigating more detailed PA intensities than the typically studied (ie, SB and moderate-to-vigorous PA). Examples include light PA of different intensities or the more fine-grained intensity bands as described in this document.
3. Public health guidelines on physical behaviours should acknowledge that behaviours are codependent and this may affect the guidelines as traditionally understood.
4. Further investigation in functional data analysis and machine learning is needed concerning the associations of physical behaviours with health.
5. There is not a gold standard able to test which analytical approach is the best for a given research question. Thus, we cannot make a strong recommendation on a single analytical approach. Instead, we provide some practical recommendations to select analytical approaches well suited for a given research question. Triangulation across findings from different analytical approaches is currently the best solution.

of different analytical approaches used in recent epidemiological studies of physical behaviours. This article and the decision tree provided aim to assist researchers in selecting analytical approaches based on their research questions and data. This will ultimately have an impact on the scientific evidence and, therefore, on future public health guidelines on physical behaviours.

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Correction notice This article has been corrected since it published Online First. The co-corresponding author has been added.

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The GRANADA consensus on analytical approaches to assess associations with accelerometer-determined physical behaviours (physical activity, sedentary behaviour, and sleep) in epidemiological studies

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Appendix 1

Contents

Accelerometer data descriptors

Modern accelerometers collect raw accelerations (measured in *G*'s) at sample frequencies typically varying from 20 to 100 Hz. As an example, raw data from a thigh-worn accelerometer is presented in **Figure A1**. This raw signal is usually filtered and aggregated to remove the gravitational acceleration and the noise effects on the signal [1]. Examples of common accelerometer data aggregation metrics are activity counts (brand-specific and proprietary aggregation metrics), Euclidean Norm Minus One with negative values rounded to 0 (ENMO), Mean Amplitude Deviation (MAD), Monitor Independent Motion Summary (MIMS) units, Activity Index (AI_0), or steps, among others (hereinafter we refer collectively to them as 'acceleration metrics'). With regard to MIMS it should be noted that the claim that it is accelerometer brand independent has so far not been demonstrated, only sensor from the Actigraph brand were used in the study by John and colleagues [2]. Further, other metrics like MAD and AI_0 can also be brand independent, although this has not been formally tested yet. MIMS applies a narrow frequency filter by which its potential lack of sensitivity to differences in the monitor comes at the cost of lower sensitivity to movements in the low- and high frequency range. In-depth discussions about the influence that these aggregation metrics on the final estimates have been published elsewhere [1,3–5]; we focus our discussion on the conversion of such acceleration metrics to descriptors at a day or person level. Given the numerous versions of accelerometer data descriptors presented in the literature, we decided to focus on those descriptors representative of physical activity (PA) volume, type, and intensity since they are the most frequently-used in public health guidelines.

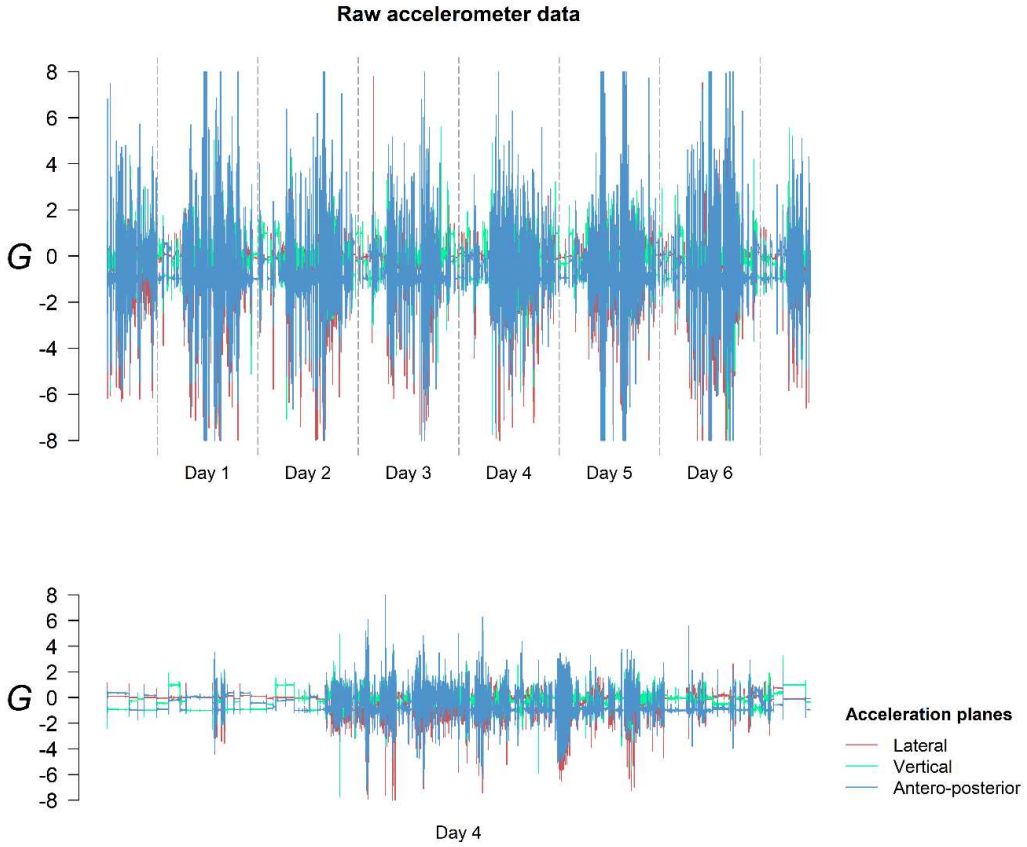

Figure A1. Sample raw accelerometer data recording from a thigh-worn accelerometer. Accelerometer model: Axivity AX3, sampling frequency: 30 Hz, body attachment site: thigh; 24h/day recording protocol.

1.1 Average acceleration or steps per day

Average acceleration over a 24 h period is directly derived from the processed acceleration and can be used as a proxy for total daily PA-related energy expenditure [6]. This single estimate indicates the overall activity level and/or the volume of activity. The same can be obtained from the total number of steps per day, which is also widely used in the field [7,8]. It is usually expressed in m*g* or a manufacturer-provided acceleration metric (usually

counts). Average acceleration usually has a moderate correlation with PA-related energy expenditure (r ~ 0.3-0.5), which can be improved by considering body weight, body composition, and activity type in the models [9,10]. Given that the correlation is not high, it is often used as a direct measure of movement, without making inferences about PA-related energy expenditure.

1.2 Time-use behaviours

Various descriptors quantify the daily time spent in a set of behaviours e.g. time spent in certain activity intensities (e.g., light, moderate or vigorous PA) or types (e.g., sitting, standing, walking). In this regard, cut-points represented one of the first developed and most frequently used methods for assessing the time spent sedentary and in light PA, moderate PA and vigorous PA using the acceleration metric [11]. The identified linear association between acceleration and energy expenditure was used to determine cut-points based on linear absolute metabolic equivalents (METs) thresholds (e.g., sedentary behaviour (SB), ≤1.5; light PA, >1.5 and <3.0; moderate PA, ≥3.0 and <6.0; vigorous PA, ≥6.0 [12]). Thresholds have been also proposed for walking cadence based on the estimation of steps per minute [13,14]. **Figure A2** graphically represents a cut-point-based classification of the acceleration recorded during one day without any definition of bouts. Cut-points can be derived with linear statistical procedures such as linear regression or receiver operating characteristic (ROC) curves, which assume a linear relationship between magnitude of acceleration and METs. However, non-linear approaches have also been used. Otherwise, classification of activity types usually relies on thresholds applied to the device angle variability, usually from thigh- or wrist-placed accelerometers [15,16]. Similarly, thresholds have been applied to acceleration metrics and accelerometer angles to detect

sleep from the accelerometer signal [15,17,18]. More sophisticated models have used the acceleration signal to detect whether the activity performed is locomotion or not, and then applied specific regression models for each activity type (locomotion vs. not locomotion) [19]. Machine learning (ML) methods have gained momentum to classify both activity intensities and types from an accelerometer time series [20]. Classifying behaviours or estimating energy expenditure using a supervised ML approach requires data labelled with 'true' intensity or type (as measured with indirect calorimetry, direct observation, heart rate monitors, among others) [21–25], which is used to iteratively improve classification/estimation. Alternatively, unsupervised ML methods can be used to define "states" in the accelerometer signal pattern that can be interpreted as specific behaviours [26].

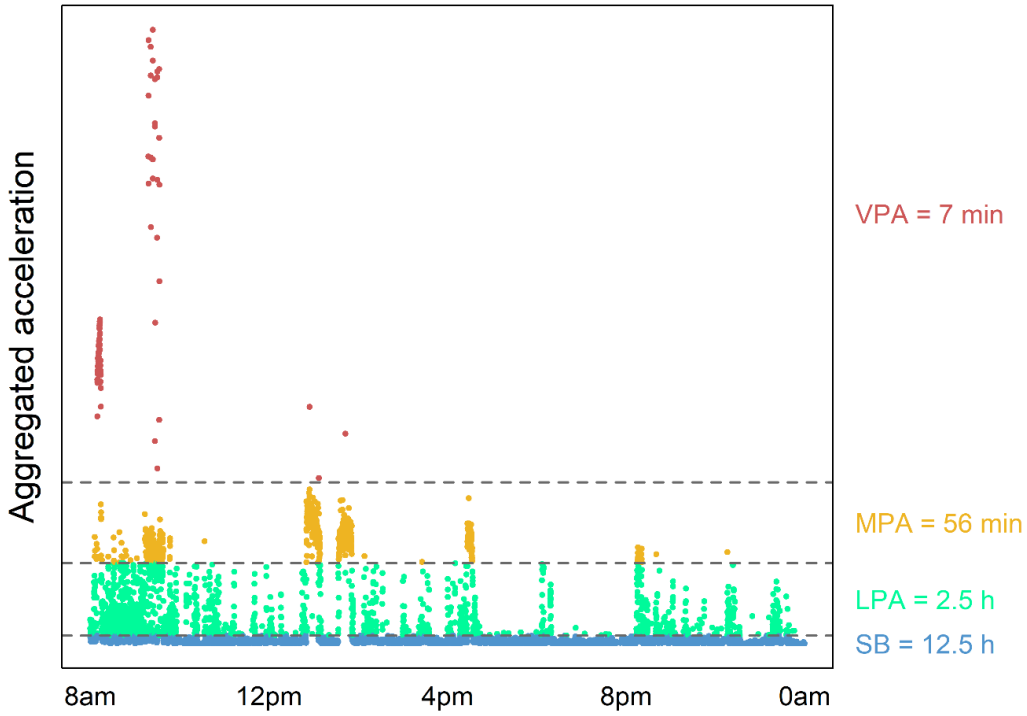

Figure A2. Graphical representation of cut-point-based metrics without bout-specification. Accelerometer model: ActiGraph GT3X+, sampling frequency: 100 Hz, body attachment site: hip; only awake time represented. SB: sedentary behaviour; LPA: light physical activity; MPA: moderate physical activity; VPA: vigorous physical activity.

Independently of the method used to derive these descriptors, they estimate daily time devoted to a specific behaviour. Descriptors of time spent in different PA intensities were first developed to assess objectively the information gained from questionnaire data (the source of most knowledge on the benefits of PA). Use of these time estimates in recent research has confirmed the benefits of PA for health and demonstrated stronger effects of PA than observed with self-report [27].

1.3 Time-use descriptor (intensity spectrum)

The intensity spectrum is also quantified as daily time spent in certain categories, so it is a time-use descriptor. Specifically, time acceleration metric signal over time is classified based on increasing acceleration bands (e.g., time spent from 0-50, 50-100, 100-150, … counts or m*g* or steps per minute). Thus, the intensity spectrum uses a wider range of narrower equally-sized bands for increased resolution of the data [28]. The definition of the bin size is arbitrary, might not directly relate to energy expenditure and does not make any assumption on the behaviour underlying the intensity bin (its purpose is purely descriptive). It can also be regarded as a discretisation of a functional representation of the intensity distribution. The idea behind this approach is to avoid exaggerated aggregation of data (into only 3-4 categories) leading to loss of information. Thus, the number of bands should be large enough to incorporate all essential features in the accelerometer signal.

1.4 Intensity gradient

The intensity gradient describes the negative curvilinear shape of the intensity spectrum (i.e., the higher the intensity the less time spent at this intensity) [29]. The regression coefficient from a linear regression of time spent in an intensity bin on intensity, both on a logarithmic scale, is used as a scalar descriptor of this curvilinear relationship. It is always negative, reflecting the drop-in time accumulated as intensity increases; a more negative (lower) gradient reflects a steeper drop with a large proportion of time accumulated at lower intensities, while a less negative (higher) gradient reflects a shallower drop with time accumulated at higher intensities (**Figure A3**).

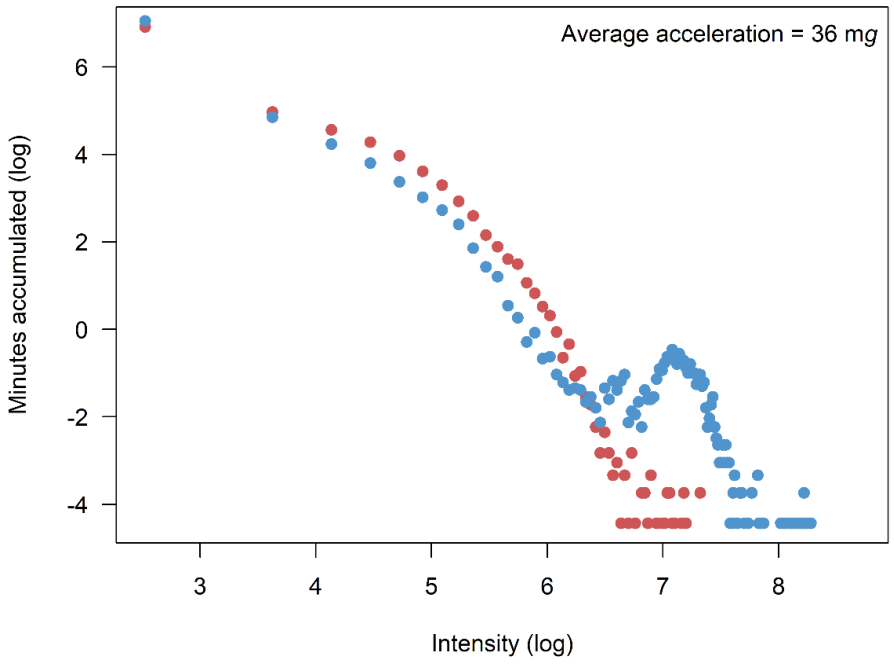

Figure A3. Example of intensity gradients from different participants with a similar average acceleration but discordant intensity distribution (i.e., intensity gradient). Accelerometer model: ActiGraph GT3X+, sampling frequency: 100 Hz, body attachment site: non-dominant wrist.

99

1.5 MX metrics - acceleration values corresponding to a set of percentiles

100 Time-use descriptors were based on the time accumulated in a series of a priori defined
101 behaviours/bands. An alternative is to turn this approach on its head and describe the
102 acceleration intensity distribution in terms of linearized periods of time or fractions of the
103 24 h day (percentiles). The acceleration for each epoch during the day is ranked in
104 descending order to obtain the acceleration above which the person's most active X
105 minutes are accumulated [29]. Therefore, instead of reporting the minutes above a given
106 acceleration threshold, the minimum acceleration achieved for a given duration is reported
107 (the unit of measurement is often m*g* or counts). MX, where X refers to the duration, e.g.
108 M30, refers to the minimum acceleration for the most active 30 min (~percentile 98^{th}) of
109 the day. The MX metrics focus on a person's most active periods of the day, with the active
110 minutes accumulated in any way across the day. For example, if a child had an M60 value
111 of 230 m*g*, the child accumulated 60 min of PA at accelerations (intensity) greater than 230
112 m*g* across the day. Similarly, the periods with the lowest recorded activity can be defined.
113 Similar estimates have been proposed for steps per minute (cadence), being typically
114 referred to as peak-X min (e.g., peak-30 min) [30].

115 A range of MX metrics covering short to long time durations can be used to aid
116 interpretation of the volume and intensity of the 24 h profile of physical activity. Using the
117 MX metrics facilitates interpretation in terms of time spent in indicative activities (e.g.,
118 brisk walking) or above cut-points for different intensities of activity, e.g., moderate-to-
119 vigorous PA (MVPA) or vigorous PA. Plotting a broad range of MX variables on a radar
120 plot illustrates the intensity and volume of the 24h activity profile (**Figure A4**), facilitating

e.g., translation of results from analyses investigating the relative contributions of average acceleration and intensity gradient to markers of health, and/or comparisons between and within groups. For example, the M120, M60, M45, M30, M15, M10, M5 and M2 illustrate the more active periods of the day, while M8h refers to the most active 8 h of the day.

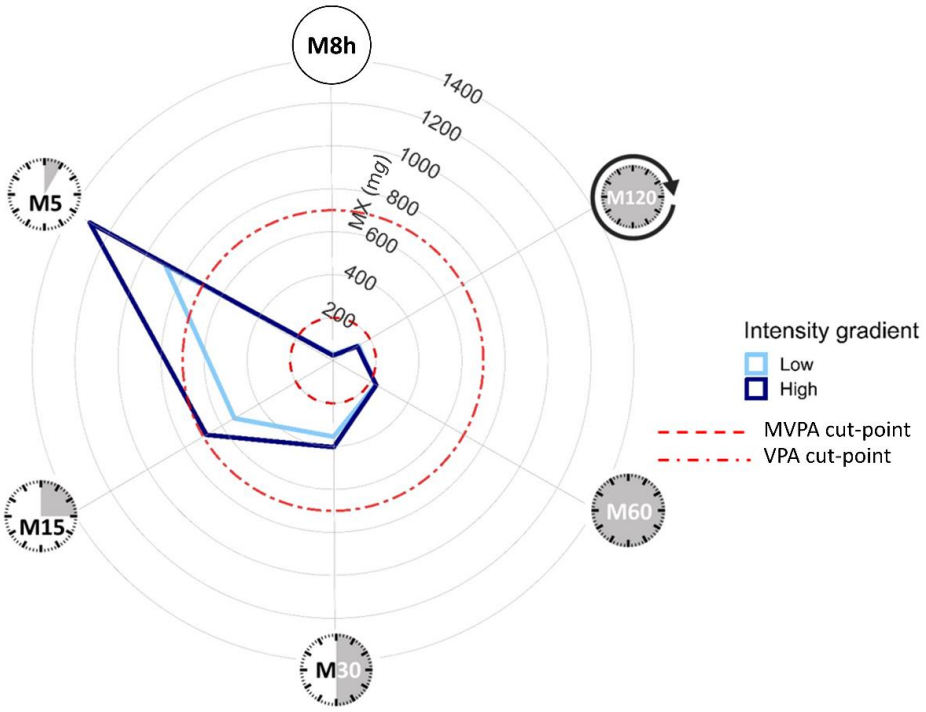

Figure A4. MX metrics example from two participants with similar average acceleration but different intensity gradient. Accelerometer model: ActiGraph GT9X, sampling frequency: 100 Hz, body attachment site: non-dominant wrist. Adapted from Rowlands et al. [31] with the permission from the publisher. IG: intensity gradient; MVPA: moderate-to-vigorous physical activity; VPA: vigorous physical activity.

1.6 Acceleration functions

While the above-mentioned descriptors are represented by scalar numbers, acceleration can also be described using a function. For example, the intensity gradient (described above) can be defined by its function instead of only reporting the beta coefficient. Other functions of interest could be the acceleration over time of the day [32] or the acceleration distribution (**Figure A5**) [33]. Acceleration functions seek a more detailed description of behaviours without making a priori assumptions. For example, while time in light activities assumes that all of the data between two cut-points (e.g., 0.05 to 0.10 *g*) relates similarly to health outcomes, analysis of acceleration functions could detect that a group tend to do more activities at acceleration less than 0.0 m*g* or more activities at acceleration above 0.07 *g*.

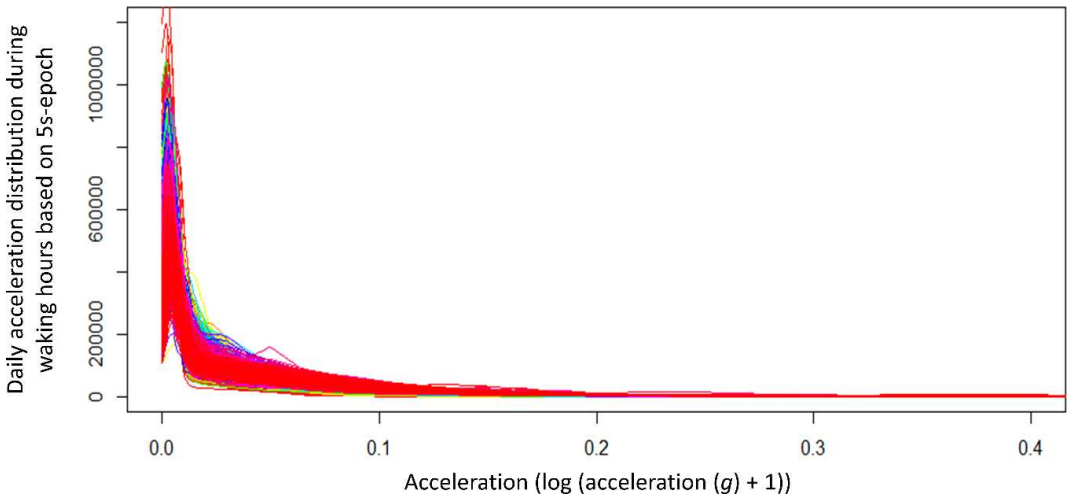

Figure A5. Sample of accelerometer-based distribution as a function of acceleration and time. Accelerometer model: GeneActiv, sampling frequency: 85.7 Hz, body attachment site: non-dominant wrist; 24h/day recording protocol.

1.7 Indicators of movement behaviour patterns and quality

All the above-mentioned descriptors are time-based (time-use behaviours and intensity spectrum) or acceleration-based (average acceleration, MX metrics, acceleration functions) descriptors. That is, they either measure time in a given behaviour or acceleration in a certain time interval. Other descriptors of movement behaviour quality and patterns can be obtained thanks to the time-stamped data derived from accelerometers. Time-stamped accelerometer data can be used to derive certain characteristics of the PA and SB patterns throughout the day, such as the time accumulation in bouts of PA intensities or types. Time-stamped data also provides insight on timing of behaviours, domain (school/work or leisure), and circadian rhythmicity. For example, fragmentation of PA and sleep, sedentary breaks, intradaily variability, interdaily stability, sleep efficiency, or waking periods after sleep onset are frequently used in the field to assess the quality and patterns of PA, SB, and sleep.

Mathematical treatment of descriptors (compositional data analysis)

This section focuses on mathematical treatments to account for the specific singularities of the descriptors presented above. Time-use behaviours and the intensity spectrum consist of a set of components that represent parts of some finite total. This total may be explicit (e.g., complete 24-hour data) or it may arise through interpretation of the data as proportions (e.g., waking day data). Therefore, these descriptors can be considered as compositional data. Each part is called a component and the proportional distribution is called composition. So, for a composition with *i* components:

$$\sum_i Component_i = 1 = 100\% = Whole$$

Compositional data analysis (CoDA) is an approach to analyse compositional data. Its birth is often attributed to Pearson's paper on spurious forms of correlation in ratio data [34]. Arguably the father of CoDA is John Aitchison, who developed comprehensive statistical frameworks to deal with compositional data [35]. CoDA is an established branch of statistics and has been used in many fields of research such as geosciences, nutrition, the study of the microbiome and gene sequencing. In the last five years CoDA has been applied in the field of 'physical behaviour epidemiology' to study the association between daily time use and health (**Figure A6**) [36–38].

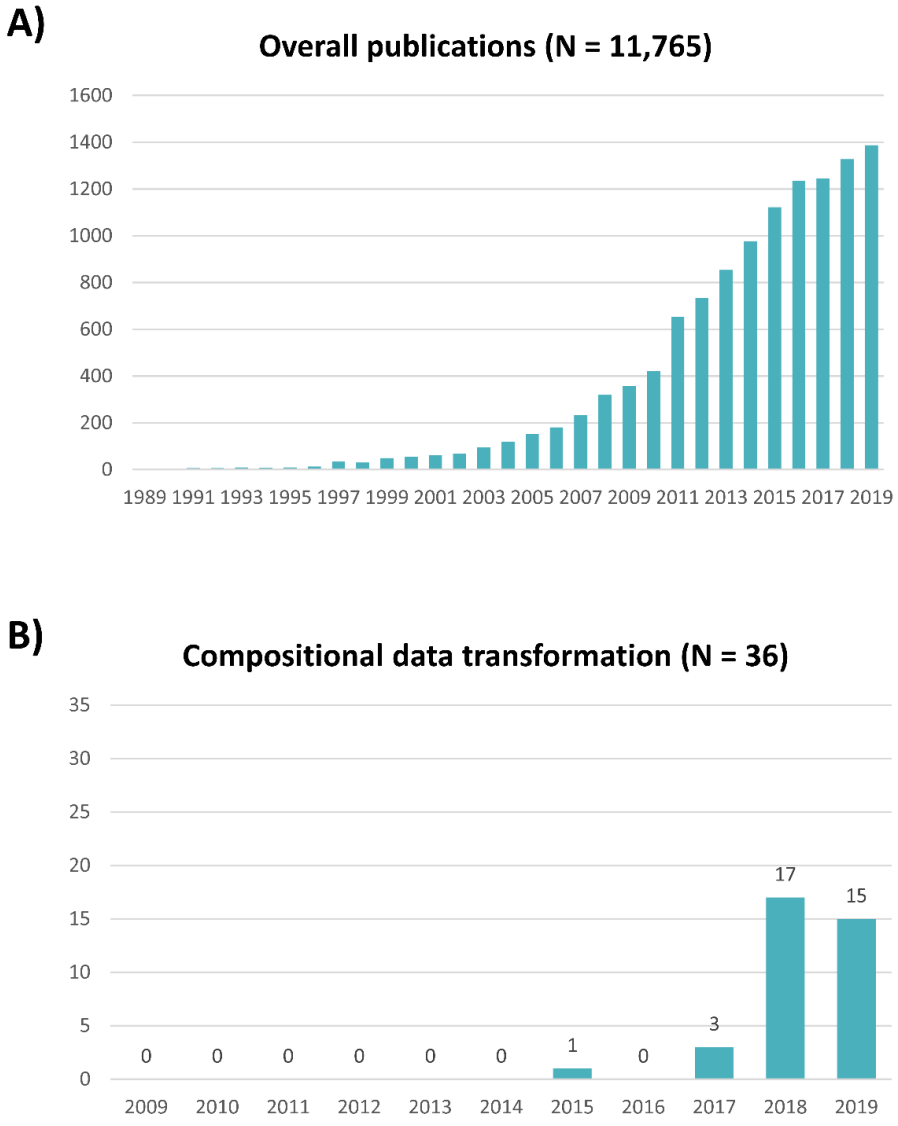

Figure A6. Overall number of publications using accelerometer-determined PA (panel A) and number of publications using compositional data transformations from inception to December 31st, 2019. Search syntax introduced in the Web of Science: Panel A: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*)); Panel B: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("compositional data analysis")).

1.8 Compositional data transformation

Time-use descriptors of physical behaviours are by nature compositional when they describe a time or energy budget (**Figure A7**). Hence the sum of time spent in each behaviour will be the period of interest (24 hours, waking period, week, wear time) and the proportions will sum to 100% of this period. In this example, the composition is made of four components over 24 hours: sleep, SB, light PA and MVPA.

$$t_{sleep} + t_{SB} + t_{LPA} + t_{MVPA} = 24\ hours$$

This is also true if we consider part of the day, such as the composition of movement behaviours during the waking day. Though waking hours are typically not fixed, we can still carry out a compositional data analysis of the proportions.

$$t_{SB} + t_{LPA} + t_{MVPA} = waking\ hours$$

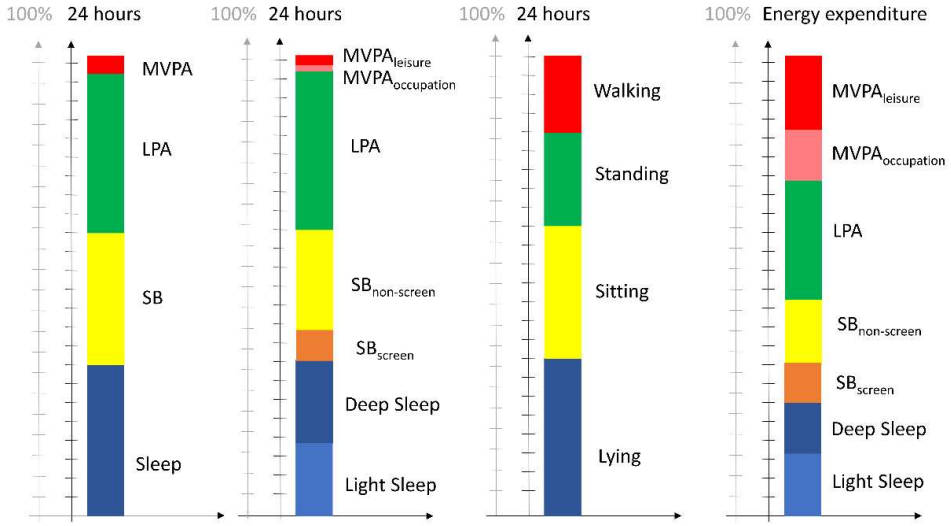

Figure A7. Visualization of the compositional nature of physical behaviour data. SB: sedentary behaviour; LPA: light physical activity; MVPA: moderate-to-vigorous physical activity.

192 A composition can have an unlimited number of parts that can be defined by intensity
193 band,activity type, context information or a combination of those, provided they are
194 mutually exclusive. As a consequence of the fact they describe mutually exclusive
195 components of a time or energy budget, each part only contains relative information rather
196 than an absolute value and, then, the interpretation of compositional data is in terms of
197 relative time spent in the different behaviours. If the data is regarded as a composition;
198 mathematical transformation of the data is required prior to introducing the variables in a
199 statistical model. For some applications, the absolute time may be important, in which case
200 it would not be appropriate to apply the compositional transformation.

201 Compositional data transformations are simple and rely on logarithmic transformations.
202 The purpose of this transformation is to resolve the difficulties around co-dependency and
203 spurious correlation associated with the compositional nature of these descriptors.
204 Statistical models can, therefore, be adjusted for all physical behaviour components without
205 incurring perfect collinearity. Specifically, the data transformations that have been used so
206 far in 'physical behaviour epidemiology' are the centred log ratio (CLR) [39,40] and the
207 isometric-log ratio (ILR) [37,41–43]. Using the CLR method, each component is centred
208 according to the mean logarithm of all the components [35]. The CLR-transformation is
209 mathematically expressed as:

210 $z_i = \ln \frac{t_i}{\sqrt[D]{\prod_{j=1}^{D} t_j}}$ with i indicating each component

211 The sum of the D (number of components) CLR-transformed variables is 0. This fixed sum
212 means they are singular, and cannot be used in regression models. However, we can apply
213 an additional transformation to the CLR components to obtain a D-1 dimensional space

without this constraint. This is referred to as the ILR-transformation when the new space uses an orthonormal basis. There are multiple such bases (and hence ILR transformations) however the most common approach in physical behaviour epidemiology research is shown below (e.g., SB, light PA, MVPA and sleep):

$$z_{SB} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{SB}{(LPA \cdot MVPA \cdot Sleep)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{LPA}{(MVPA \cdot Sleep)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{MVPA}{Sleep} \right) (1)$$

$$z_{LIPA} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{LPA}{(MVPA \cdot Sleep \cdot SB)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{MVPA}{(Sleep \cdot SB)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{Sleep}{SB} \right) (2)$$

$$z_{MVPA} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{MVPA}{(Sleep \cdot SB \cdot LPA)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{Sleep}{(SB \cdot LPA)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{SB}{LPA} \right) (3)$$

$$z_{Sleep} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{Sleep}{(SB \cdot LPA \cdot MVPA)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{SB}{(LPA \cdot MVPA)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{LPA}{MVPA} \right) (4)$$

Thus, the ILR produces a set of coordinates for each component (i.e., z_1, z_2 and z_3 in each component of the example above) that should be introduced together as covariates in any statistical model (see section 2.3 for considerations on the statistical model selection). The main difficulty associated with these transformations is in interpreting the results; this is a problem similar to (for example) in linear regression when a variable is log-transformed. For compositional data, a solution is to find an appropriate graphical representation of the results, keeping in mind the co-dependence of the parts and using model predictions rather than deriving the estimate directly from model coefficients. Another difficulty arising from these mathematical transformations is related to having zeros or values close to zero in any of the components. This can happen in certain populations which may not perform vigorous PA or even MVPA. Considering very low values in a composition could lead to spurious

correlations [44], usually, these values are either ignored in the analysis or imputed to stabilize the models [37].

Statistical modelling

The third and last step of the analytical process relates to the decisions on how to model the associations between the selected descriptor(s) (with or without mathematical transformations) and health. As far back as the 1950's [45,46], many studies have investigated the epidemiological associations of physical behaviours with health outcomes. The use of accelerometers confirmed some of these associations, and allowed a better characterisation of the dose-response curve overcoming the cognitive biases of self-reports. However, most studies have solely focused on basic descriptors of one behaviour in isolation (e.g., MVPA). Out of the 11,765 publications identified in a search in the Web of Science on physical activity and accelerometers (**Figure A6, Panel A**), only 125 studies explored the interdependencies among physical behaviours using isotemporal substitution models, multivariate pattern analysis or functional data analysis (**Figure A8**) [47]. This consensus group believes that now is the right time to move to more detailed and informative studies on the combined effects and interactions across physical behaviours on health outcomes.

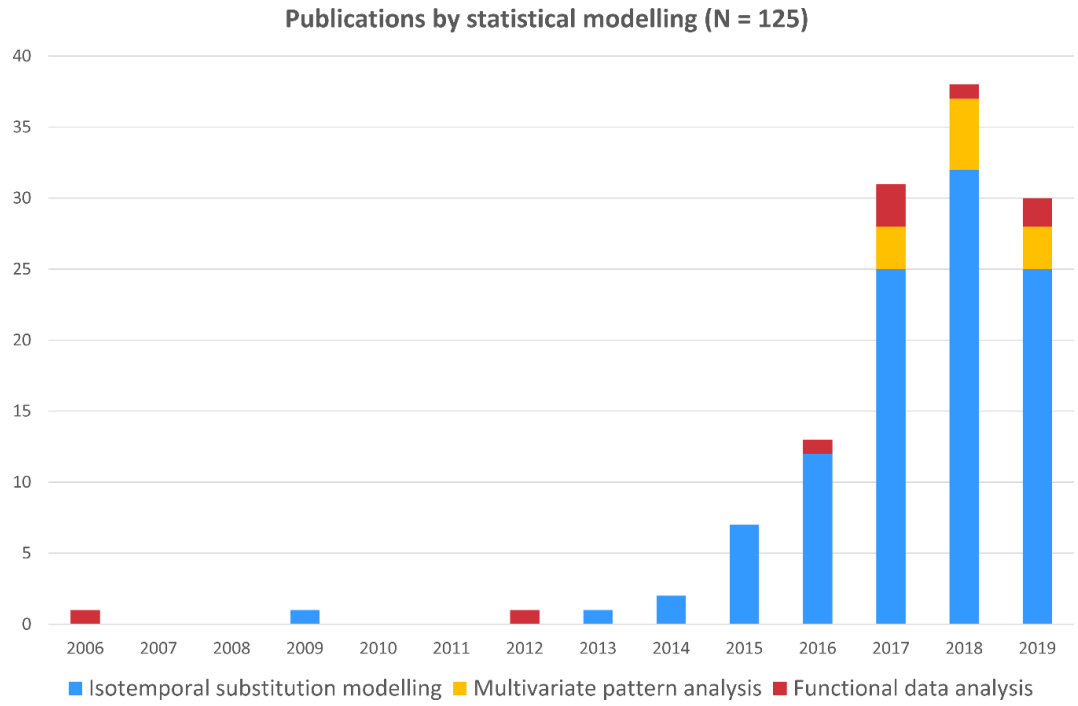

Figure A8. Number of publications using some of the approaches described in the present document from inception to December 31st, 2019. Search syntax introduced in the Web of Science: isotemporal substitution models: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("isotemporal substitution")); multivariate pattern analysis: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("Physical activity signature" OR "multivariate pattern analysis")); functional data analysis: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("Physical activity signature" OR "functional data analysis")).

1.9 Linear regression modelling

Linear regression is the most frequently used statistical model in the field, often including the physical behaviour descriptor as a continuous exposure variable in a linear, logistic or Cox regression (depending on the outcome of interest). Linear regression models are

interpreted in terms of the (theoretical) effect of increasing the explanatory variable on the outcome, under a linear relationship. Standard linear regression models are usually adjusted for the covariates that could influence the association of interest. Highly correlated explanatory variables result in multicollinearity, which is a phenomenon in which redundant information carried by predictors leads to erratic estimation of the models [48].

Linear regression models can also be used with compositional ILR-transformed descriptors, which may eliminate that part of the collinearity which arises from the fixed sum (or closure) constraint [37,38]. In this case, the model coefficients are interpreted in terms of time replacements across behaviours. For example, the estimate for the z_1 coordinate of the z_{SB} equation presented above represents the effect of increasing SB while proportionally reducing the time in light PA, MVPA and sleep. The dose-response association between a specific behaviour and the health outcome is assumed to be logarithmic (curvilinear) using compositionally-transformed descriptors. Likewise, the regression model predictions (using compositional data) can be used to estimate the time replacement between pairs of behaviours (e.g., reallocating time from SB to MVPA). This results in a similar interpretation to the isotemporal substitution models presented in the section 2.3.2. When examining longitudinal associations, advanced regression models (e.g., survival analysis using Cox regression) may be used with either absolute descriptors [27,49,50] or compositional ILR-transformed descriptors [42].

1.10 Isotemporal substitution models

The isotemporal substitution modelling framework considers potential outcomes of increasing one behaviour at the expense of another and whether the strength of the association is dependent on the behaviour being displaced. Isotemporal substitution models

are linear regressions in which all-but-one of the time-use behaviours are introduced as the exposure (together with the pertinent covariates) and the health outcome is the dependent variable. These models examine the estimated effects of replacing time spent in one behaviour (the missing behaviour in the model) with an equal amount of time spent in another, while keeping monitor wear time constant. They do so by dropping the behaviour of interest from the model (otherwise, the model would suffer from perfect collinearity). The linear effects of the pair-wise reallocations are then estimated from the model coefficients. Similar interpretations of time replacement between pairs of behaviours can be obtained from applying linear regression over compositional data (see section 2.3.1).

1.11 Multivariate pattern analysis and other dimension reduction models

Multivariate pattern analysis can handle completely collinear explanatory variables by combining the data into orthogonal latent variables [51]. Thereby, this method tackles collinearity as a dimension reduction problem, rather than a data transformation (as CoDA does). Multivariate pattern analysis is especially well-suited to analyse a wide range of collinear descriptors, such as the intensity spectrum, without requiring any data transformation [28,52], although transformations can be done to make distributions within bands more normal and linearly associated with the outcome. Another important feature is that the models are optimized for predictive ability by Monte-Carlo resampling whereby half of the data are repeatedly used for modelling and half for prediction [53]. In this way, the optimal number of latent variables can be determined and only relevant features in the descriptor retained.

Multivariate pattern analysis uses partial least squares (PLS) regression modelling [51], or other latent-variable regression models [54], to determine the multivariate association

pattern. PLS regression decomposes the explanatory variables into orthogonal linear combinations (PLS components), while simultaneously maximizing the covariance with the outcome variable. Similar procedures to reduce the data can be observed in factor analysis, principal component analysis, or JIVE models. Multivariate pattern analysis differs from these others by creating components that maximize the covariation with the outcome, not internally among the explanatory variables. JIVE models seek to maximize the variance explained across explanatory variables assuming that they come from different dimensions (e.g., PA, sleep, and circadian rhythms) and improving the within and between dimension representation [55]. The procedure for obtaining the multivariate patterns is completely data-driven, with no assumptions on variable distributions or degree of collinearity among variables. Selectivity ratios are calculated to express and rank each single explanatory variables' association with the outcome [56,57]. The selectivity ratio represents each explanatory variable's ratio of explained to residual variance in relation to the outcome (**Figure A9**). By replacing residual variance with total variance in the denominator, a straight-forward measure of explained variance can be obtained [58]. Multivariate pattern analysis has been applied with time-use descriptors and intensity spectrum in both their absolute scale and with the compositional CLR-transformation [39]. Since multivariate pattern analysis can handle singular data (e.g., CLR-transformed data), the ILR-transformation is not necessary if modelling compositional data.

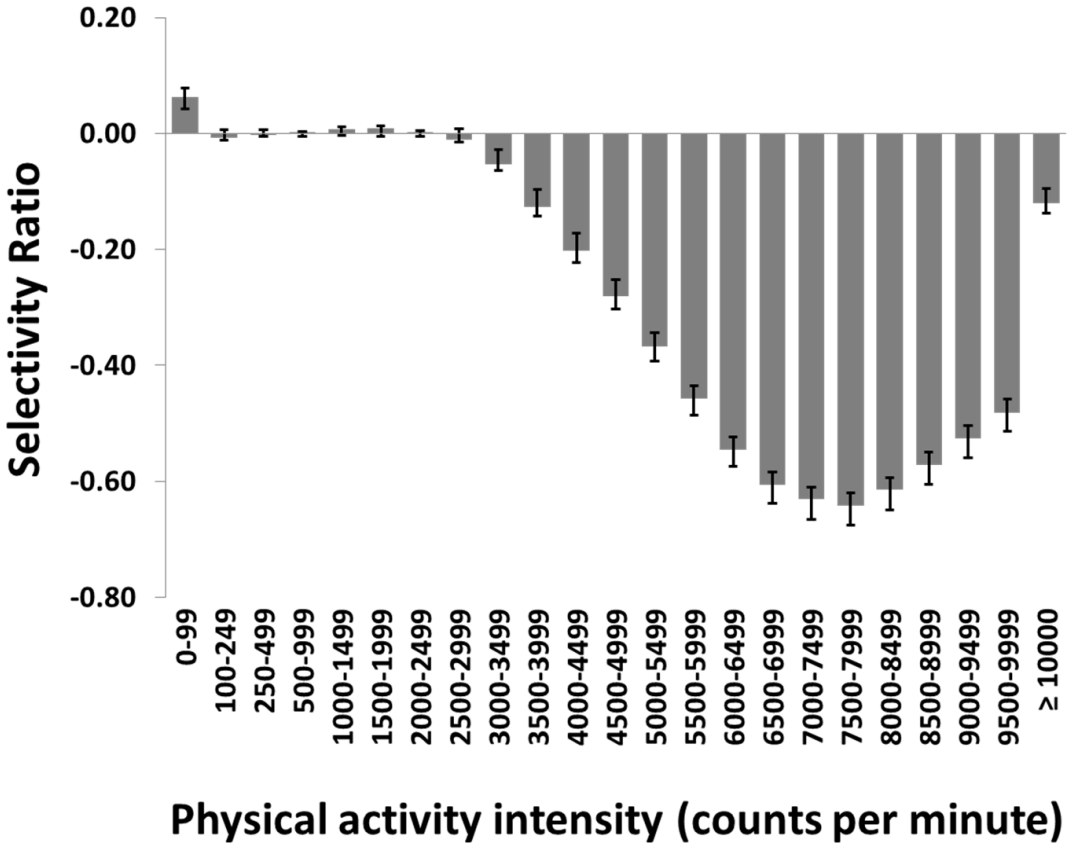

Figure A9. Multivariate pattern analysis example. Accelerometer model: ActiGraph GT3X+, sampling frequency: 30 Hz, body attachment site: right hip; awake time recording protocol. Selectivity ratio represents the explained-to-total outcome variance ratio. Adapted from Aadland et al. [39] with permission from the publisher.

1.12 Functional data analysis

Functional data analysis is an extension of linear regression analysis where the exposure or the outcome (or both) is a function instead of a scalar [59–61]. In physical behaviour epidemiology, the rationale of functional data analysis in the context of accelerometer data comes from the availability of moment-by-moment acceleration data allowing the use of the entire range of accelerations, whatever the aggregated metric used (e.g., counts, ENMO,

MAD) [62,63]. The acceleration functions described in section 2.1.6 can be used in functional data analysis. A first step often consists in smoothing the function of interest so that the smoothed function can then be used in functional data analysis, although some approaches do not smooth the data at subject level and rather pool the data across subjects to avoid the loss of information from the accelerometer signal. For example, when the interest is in the distribution of acceleration over time of the day, one can reduce data into 10 minute epochs as the objective is to assess when individuals are more or less active at each time of the day [64]. When the function of interest is the acceleration density distribution, Gaussian Kernel smoothing methods can be used (**Figure A10**) [65]. In that case, careful attention should be given to the number and place of nodes for acceleration values: a higher number of nodes should be present in the acceleration range where most of the time is spent. Then, the smoothed function of interest can be used for further analysis as an outcome variable (Function-on-scalar analysis), an exposure (Scalar-on-function analysis), or both (Function-on-function analysis) using functional data analysis regression techniques.

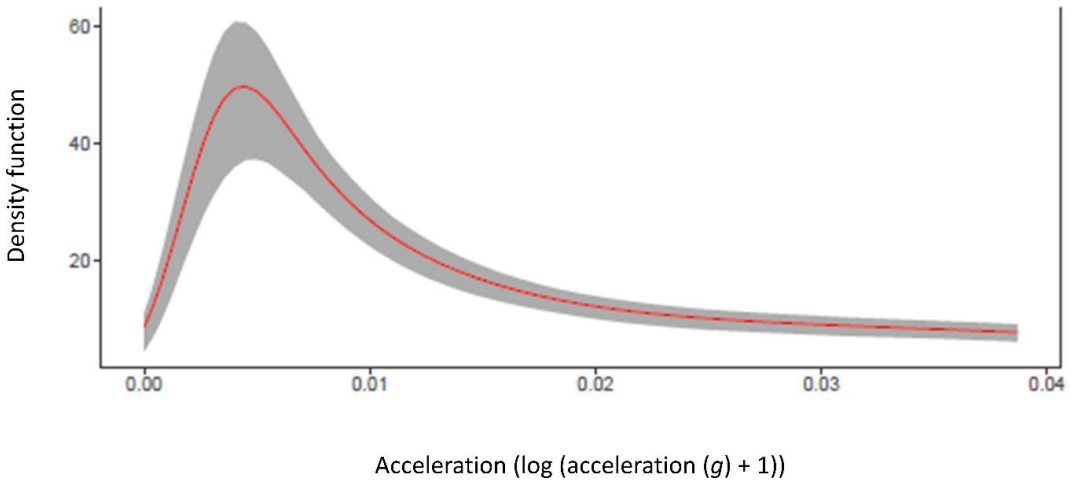

Figure A10. Smooth mean and interquartile acceleration density function. Red curve represents the mean density function of the study population and the grey area the interquartile range.

1.13 Machine learning for epidemiological analysis

ML methods provide a broad range of techniques to identify patterns in data. Although it has been increasingly used to derive descriptors from raw accelerometer data [20], ML has rarely been applied to the study of the associations of accelerometer data descriptors (examples of ML for health association analysis using physical behaviour data include [66,67]). As ML methods typically emphasise prediction or data reduction, they are most often relevant for hypothesis generation and data exploration. While there is no clear distinction between conventional statistical methods and ML, there is typically a different emphasis, and so they can be difficult to apply directly to problems requiring statistical inference. Bi et al. discuss possible epidemiologic applications of a wide range of machine learning methods in detail [68]. Examples of ML methods which could be applied to health association analysis using accelerometer data include Decision Trees/ Random Forests, Support Vector Machines and Neural Networks.

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The GRANADA consensus on analytical approaches to assess associations with accelerometer-determined physical behaviours (physical activity, sedentary behaviour, and sleep) in epidemiological studies

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Appendix 1

Contents

Accelerometer data descriptors

Modern accelerometers collect raw accelerations (measured in *G*'s) at sample frequencies typically varying from 20 to 100 Hz. As an example, raw data from a thigh-worn accelerometer is presented in **Figure A1**. This raw signal is usually filtered and aggregated to remove the gravitational acceleration and the noise effects on the signal [1]. Examples of common accelerometer data aggregation metrics are activity counts (brand-specific and proprietary aggregation metrics), Euclidean Norm Minus One with negative values rounded to 0 (ENMO), Mean Amplitude Deviation (MAD), Monitor Independent Motion Summary (MIMS) units, Activity Index (AI_0), or steps, among others (hereinafter we refer collectively to them as 'acceleration metrics'). With regard to MIMS it should be noted that the claim that it is accelerometer brand independent has so far not been demonstrated, only sensor from the Actigraph brand were used in the study by John and colleagues [2]. Further, other metrics like MAD and AI_0 can also be brand independent, although this has not been formally tested yet. MIMS applies a narrow frequency filter by which its potential lack of sensitivity to differences in the monitor comes at the cost of lower sensitivity to movements in the low- and high frequency range. In-depth discussions about the influence that these aggregation metrics on the final estimates have been published elsewhere [1,3–5]; we focus our discussion on the conversion of such acceleration metrics to descriptors at a day or person level. Given the numerous versions of accelerometer data descriptors presented in the literature, we decided to focus on those descriptors representative of physical activity (PA) volume, type, and intensity since they are the most frequently-used in public health guidelines.

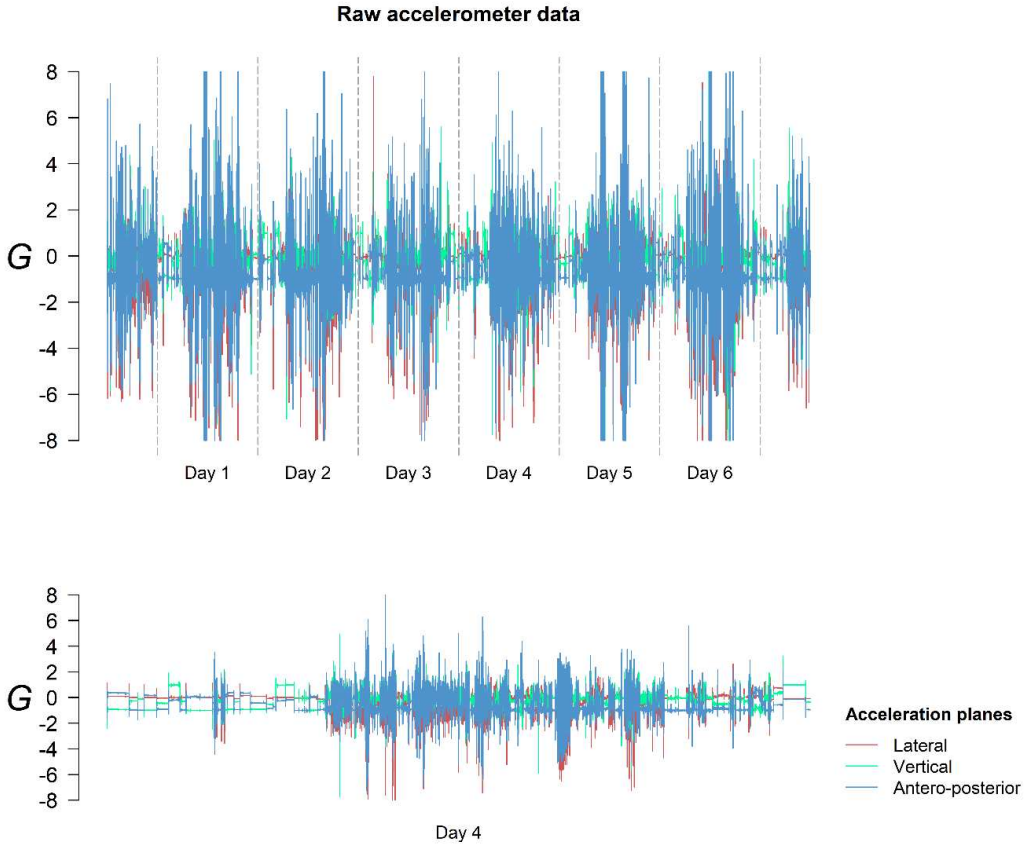

Figure A1. Sample raw accelerometer data recording from a thigh-worn accelerometer. Accelerometer model: Axivity AX3, sampling frequency: 30 Hz, body attachment site: thigh; 24h/day recording protocol.

1.1 Average acceleration or steps per day

Average acceleration over a 24 h period is directly derived from the processed acceleration and can be used as a proxy for total daily PA-related energy expenditure [6]. This single estimate indicates the overall activity level and/or the volume of activity. The same can be obtained from the total number of steps per day, which is also widely used in the field [7,8]. It is usually expressed in m*g* or a manufacturer-provided acceleration metric (usually

counts). Average acceleration usually has a moderate correlation with PA-related energy expenditure (r ~ 0.3-0.5), which can be improved by considering body weight, body composition, and activity type in the models [9,10]. Given that the correlation is not high, it is often used as a direct measure of movement, without making inferences about PA-related energy expenditure.

1.2 Time-use behaviours

Various descriptors quantify the daily time spent in a set of behaviours e.g. time spent in certain activity intensities (e.g., light, moderate or vigorous PA) or types (e.g., sitting, standing, walking). In this regard, cut-points represented one of the first developed and most frequently used methods for assessing the time spent sedentary and in light PA, moderate PA and vigorous PA using the acceleration metric [11]. The identified linear association between acceleration and energy expenditure was used to determine cut-points based on linear absolute metabolic equivalents (METs) thresholds (e.g., sedentary behaviour (SB), ≤1.5; light PA, >1.5 and <3.0; moderate PA, ≥3.0 and <6.0; vigorous PA, ≥6.0 [12]). Thresholds have been also proposed for walking cadence based on the estimation of steps per minute [13,14]. **Figure A2** graphically represents a cut-point-based classification of the acceleration recorded during one day without any definition of bouts. Cut-points can be derived with linear statistical procedures such as linear regression or receiver operating characteristic (ROC) curves, which assume a linear relationship between magnitude of acceleration and METs. However, non-linear approaches have also been used. Otherwise, classification of activity types usually relies on thresholds applied to the device angle variability, usually from thigh- or wrist-placed accelerometers [15,16]. Similarly, thresholds have been applied to acceleration metrics and accelerometer angles to detect

sleep from the accelerometer signal [15,17,18]. More sophisticated models have used the acceleration signal to detect whether the activity performed is locomotion or not, and then applied specific regression models for each activity type (locomotion vs. not locomotion) [19]. Machine learning (ML) methods have gained momentum to classify both activity intensities and types from an accelerometer time series [20]. Classifying behaviours or estimating energy expenditure using a supervised ML approach requires data labelled with 'true' intensity or type (as measured with indirect calorimetry, direct observation, heart rate monitors, among others) [21–25], which is used to iteratively improve classification/estimation. Alternatively, unsupervised ML methods can be used to define "states" in the accelerometer signal pattern that can be interpreted as specific behaviours [26].

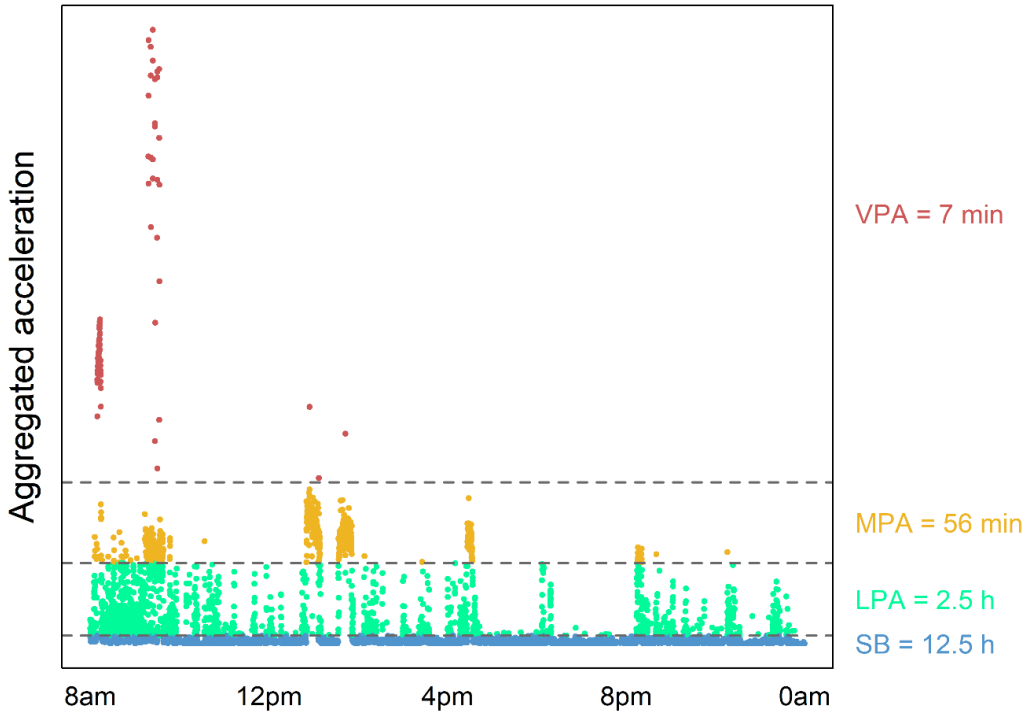

Figure A2. Graphical representation of cut-point-based metrics without bout-specification. Accelerometer model: ActiGraph GT3X+, sampling frequency: 100 Hz, body attachment site: hip; only awake time represented. SB: sedentary behaviour; LPA: light physical activity; MPA: moderate physical activity; VPA: vigorous physical activity.

Independently of the method used to derive these descriptors, they estimate daily time devoted to a specific behaviour. Descriptors of time spent in different PA intensities were first developed to assess objectively the information gained from questionnaire data (the source of most knowledge on the benefits of PA). Use of these time estimates in recent research has confirmed the benefits of PA for health and demonstrated stronger effects of PA than observed with self-report [27].

1.3 Time-use descriptor (intensity spectrum)

The intensity spectrum is also quantified as daily time spent in certain categories, so it is a time-use descriptor. Specifically, time acceleration metric signal over time is classified based on increasing acceleration bands (e.g., time spent from 0-50, 50-100, 100-150, … counts or m*g* or steps per minute). Thus, the intensity spectrum uses a wider range of narrower equally-sized bands for increased resolution of the data [28]. The definition of the bin size is arbitrary, might not directly relate to energy expenditure and does not make any assumption on the behaviour underlying the intensity bin (its purpose is purely descriptive). It can also be regarded as a discretisation of a functional representation of the intensity distribution. The idea behind this approach is to avoid exaggerated aggregation of data (into only 3-4 categories) leading to loss of information. Thus, the number of bands should be large enough to incorporate all essential features in the accelerometer signal.

1.4 Intensity gradient

The intensity gradient describes the negative curvilinear shape of the intensity spectrum (i.e., the higher the intensity the less time spent at this intensity) [29]. The regression coefficient from a linear regression of time spent in an intensity bin on intensity, both on a logarithmic scale, is used as a scalar descriptor of this curvilinear relationship. It is always negative, reflecting the drop-in time accumulated as intensity increases; a more negative (lower) gradient reflects a steeper drop with a large proportion of time accumulated at lower intensities, while a less negative (higher) gradient reflects a shallower drop with time accumulated at higher intensities (**Figure A3**).

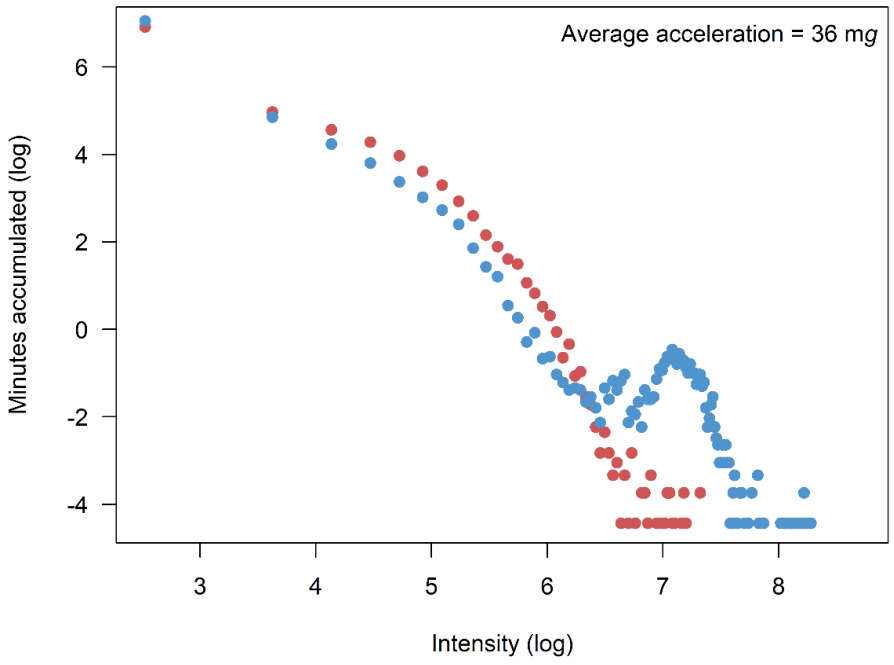

Figure A3. Example of intensity gradients from different participants with a similar average acceleration but discordant intensity distribution (i.e., intensity gradient). Accelerometer model: ActiGraph GT3X+, sampling frequency: 100 Hz, body attachment site: non-dominant wrist.

99

1.5 MX metrics - acceleration values corresponding to a set of percentiles

100 Time-use descriptors were based on the time accumulated in a series of a priori defined
101 behaviours/bands. An alternative is to turn this approach on its head and describe the
102 acceleration intensity distribution in terms of linearized periods of time or fractions of the
103 24 h day (percentiles). The acceleration for each epoch during the day is ranked in
104 descending order to obtain the acceleration above which the person's most active X
105 minutes are accumulated [29]. Therefore, instead of reporting the minutes above a given
106 acceleration threshold, the minimum acceleration achieved for a given duration is reported
107 (the unit of measurement is often m*g* or counts). MX, where X refers to the duration, e.g.
108 M30, refers to the minimum acceleration for the most active 30 min (~percentile 98^{th}) of
109 the day. The MX metrics focus on a person's most active periods of the day, with the active
110 minutes accumulated in any way across the day. For example, if a child had an M60 value
111 of 230 m*g*, the child accumulated 60 min of PA at accelerations (intensity) greater than 230
112 m*g* across the day. Similarly, the periods with the lowest recorded activity can be defined.
113 Similar estimates have been proposed for steps per minute (cadence), being typically
114 referred to as peak-X min (e.g., peak-30 min) [30].

115 A range of MX metrics covering short to long time durations can be used to aid
116 interpretation of the volume and intensity of the 24 h profile of physical activity. Using the
117 MX metrics facilitates interpretation in terms of time spent in indicative activities (e.g.,
118 brisk walking) or above cut-points for different intensities of activity, e.g., moderate-to-
119 vigorous PA (MVPA) or vigorous PA. Plotting a broad range of MX variables on a radar
120 plot illustrates the intensity and volume of the 24h activity profile (**Figure A4**), facilitating

e.g., translation of results from analyses investigating the relative contributions of average acceleration and intensity gradient to markers of health, and/or comparisons between and within groups. For example, the M120, M60, M45, M30, M15, M10, M5 and M2 illustrate the more active periods of the day, while M8h refers to the most active 8 h of the day.

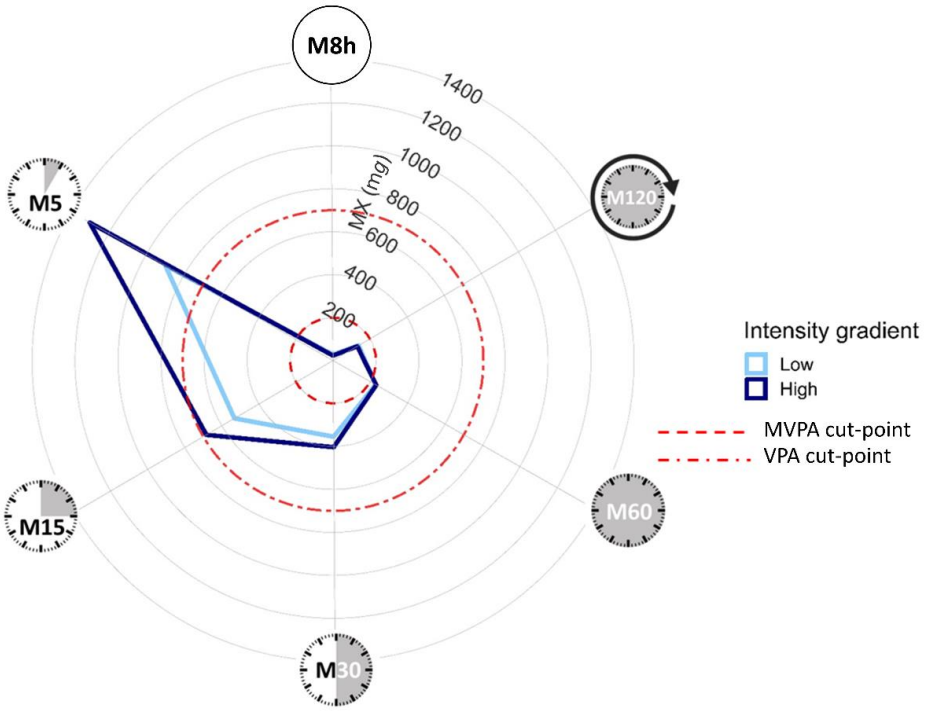

Figure A4. MX metrics example from two participants with similar average acceleration but different intensity gradient. Accelerometer model: ActiGraph GT9X, sampling frequency: 100 Hz, body attachment site: non-dominant wrist. Adapted from Rowlands et al. [31] with the permission from the publisher. IG: intensity gradient; MVPA: moderate-to-vigorous physical activity; VPA: vigorous physical activity.

1.6 Acceleration functions

While the above-mentioned descriptors are represented by scalar numbers, acceleration can also be described using a function. For example, the intensity gradient (described above) can be defined by its function instead of only reporting the beta coefficient. Other functions of interest could be the acceleration over time of the day [32] or the acceleration distribution (**Figure A5**) [33]. Acceleration functions seek a more detailed description of behaviours without making a priori assumptions. For example, while time in light activities assumes that all of the data between two cut-points (e.g., 0.05 to 0.10 *g*) relates similarly to health outcomes, analysis of acceleration functions could detect that a group tend to do more activities at acceleration less than 0.0 m*g* or more activities at acceleration above 0.07 *g*.

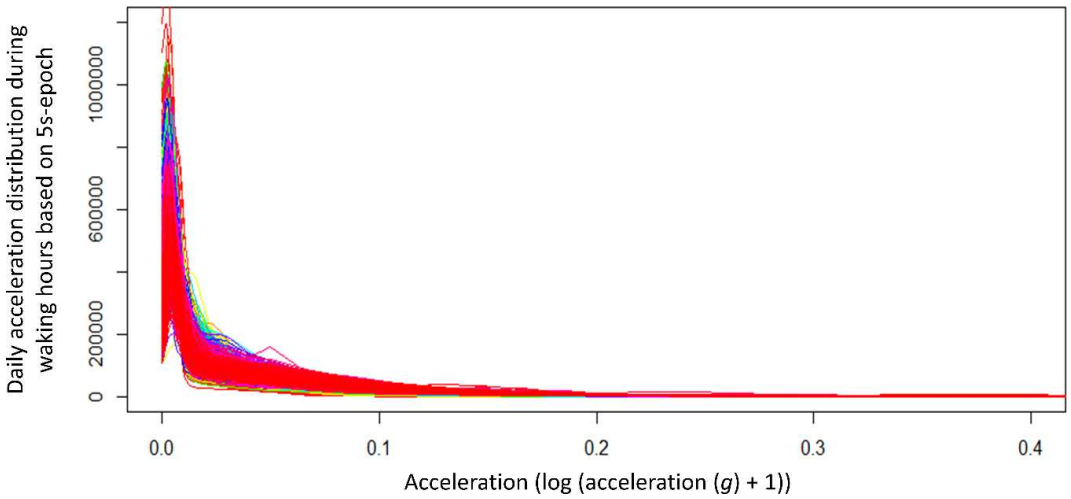

Figure A5. Sample of accelerometer-based distribution as a function of acceleration and time. Accelerometer model: GeneActiv, sampling frequency: 85.7 Hz, body attachment site: non-dominant wrist; 24h/day recording protocol.

1.7 Indicators of movement behaviour patterns and quality

All the above-mentioned descriptors are time-based (time-use behaviours and intensity spectrum) or acceleration-based (average acceleration, MX metrics, acceleration functions) descriptors. That is, they either measure time in a given behaviour or acceleration in a certain time interval. Other descriptors of movement behaviour quality and patterns can be obtained thanks to the time-stamped data derived from accelerometers. Time-stamped accelerometer data can be used to derive certain characteristics of the PA and SB patterns throughout the day, such as the time accumulation in bouts of PA intensities or types. Time-stamped data also provides insight on timing of behaviours, domain (school/work or leisure), and circadian rhythmicity. For example, fragmentation of PA and sleep, sedentary breaks, intradaily variability, interdaily stability, sleep efficiency, or waking periods after sleep onset are frequently used in the field to assess the quality and patterns of PA, SB, and sleep.

Mathematical treatment of descriptors (compositional data analysis)

This section focuses on mathematical treatments to account for the specific singularities of the descriptors presented above. Time-use behaviours and the intensity spectrum consist of a set of components that represent parts of some finite total. This total may be explicit (e.g., complete 24-hour data) or it may arise through interpretation of the data as proportions (e.g., waking day data). Therefore, these descriptors can be considered as compositional data. Each part is called a component and the proportional distribution is called composition. So, for a composition with *i* components:

$$\sum_i Component_i = 1 = 100\% = Whole$$

Compositional data analysis (CoDA) is an approach to analyse compositional data. Its birth is often attributed to Pearson's paper on spurious forms of correlation in ratio data [34]. Arguably the father of CoDA is John Aitchison, who developed comprehensive statistical frameworks to deal with compositional data [35]. CoDA is an established branch of statistics and has been used in many fields of research such as geosciences, nutrition, the study of the microbiome and gene sequencing. In the last five years CoDA has been applied in the field of 'physical behaviour epidemiology' to study the association between daily time use and health (**Figure A6**) [36–38].

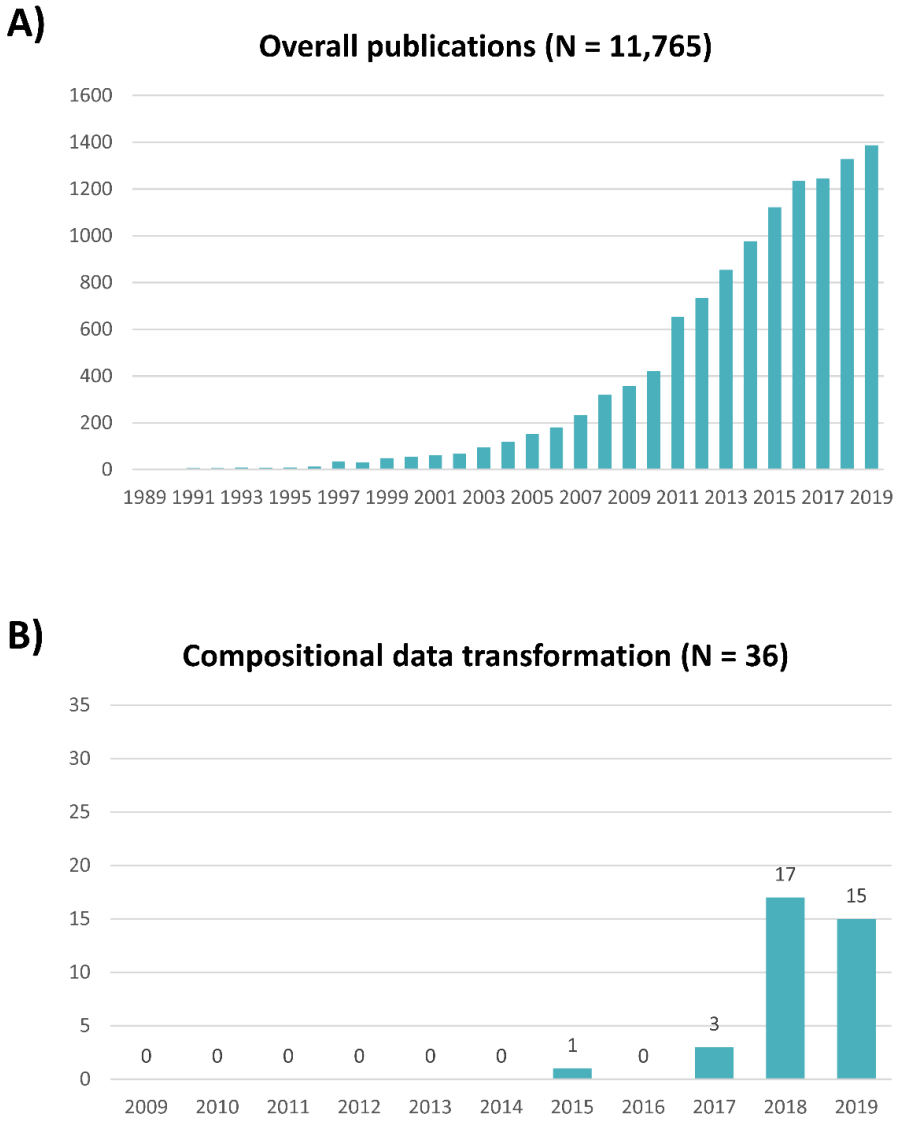

Figure A6. Overall number of publications using accelerometer-determined PA (panel A) and number of publications using compositional data transformations from inception to December 31st, 2019. Search syntax introduced in the Web of Science: Panel A: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*)); Panel B: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("compositional data analysis")).

1.8 Compositional data transformation

Time-use descriptors of physical behaviours are by nature compositional when they describe a time or energy budget (**Figure A7**). Hence the sum of time spent in each behaviour will be the period of interest (24 hours, waking period, week, wear time) and the proportions will sum to 100% of this period. In this example, the composition is made of four components over 24 hours: sleep, SB, light PA and MVPA.

$$t_{sleep} + t_{SB} + t_{LPA} + t_{MVPA} = 24\ hours$$

This is also true if we consider part of the day, such as the composition of movement behaviours during the waking day. Though waking hours are typically not fixed, we can still carry out a compositional data analysis of the proportions.

$$t_{SB} + t_{LPA} + t_{MVPA} = waking\ hours$$

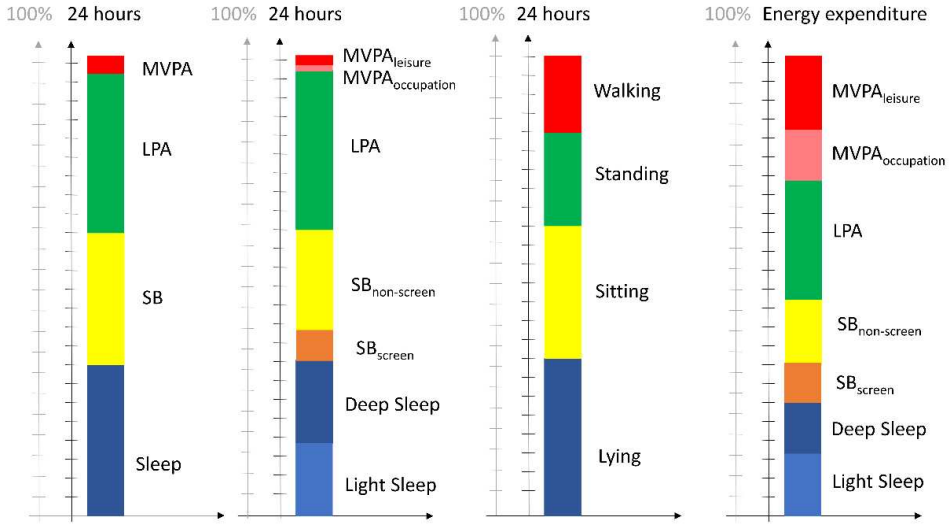

Figure A7. Visualization of the compositional nature of physical behaviour data. SB: sedentary behaviour; LPA: light physical activity; MVPA: moderate-to-vigorous physical activity.

192 A composition can have an unlimited number of parts that can be defined by intensity
193 band,activity type, context information or a combination of those, provided they are
194 mutually exclusive. As a consequence of the fact they describe mutually exclusive
195 components of a time or energy budget, each part only contains relative information rather
196 than an absolute value and, then, the interpretation of compositional data is in terms of
197 relative time spent in the different behaviours. If the data is regarded as a composition;
198 mathematical transformation of the data is required prior to introducing the variables in a
199 statistical model. For some applications, the absolute time may be important, in which case
200 it would not be appropriate to apply the compositional transformation.

201 Compositional data transformations are simple and rely on logarithmic transformations.
202 The purpose of this transformation is to resolve the difficulties around co-dependency and
203 spurious correlation associated with the compositional nature of these descriptors.
204 Statistical models can, therefore, be adjusted for all physical behaviour components without
205 incurring perfect collinearity. Specifically, the data transformations that have been used so
206 far in 'physical behaviour epidemiology' are the centred log ratio (CLR) [39,40] and the
207 isometric-log ratio (ILR) [37,41–43]. Using the CLR method, each component is centred
208 according to the mean logarithm of all the components [35]. The CLR-transformation is
209 mathematically expressed as:

210 $z_i = \ln \frac{t_i}{\sqrt[D]{\prod_{j=1}^{D} t_j}}$ with i indicating each component

211 The sum of the D (number of components) CLR-transformed variables is 0. This fixed sum
212 means they are singular, and cannot be used in regression models. However, we can apply
213 an additional transformation to the CLR components to obtain a D-1 dimensional space

without this constraint. This is referred to as the ILR-transformation when the new space uses an orthonormal basis. There are multiple such bases (and hence ILR transformations) however the most common approach in physical behaviour epidemiology research is shown below (e.g., SB, light PA, MVPA and sleep):

$$z_{SB} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{SB}{(LPA \cdot MVPA \cdot Sleep)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{LPA}{(MVPA \cdot Sleep)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{MVPA}{Sleep} \right) (1)$$

$$z_{LIPA} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{LPA}{(MVPA \cdot Sleep \cdot SB)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{MVPA}{(Sleep \cdot SB)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{Sleep}{SB} \right) (2)$$

$$z_{MVPA} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{MVPA}{(Sleep \cdot SB \cdot LPA)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{Sleep}{(SB \cdot LPA)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{SB}{LPA} \right) (3)$$

$$z_{Sleep} = \left(z_1 : \sqrt{\frac{3}{4}} ln \frac{Sleep}{(SB \cdot LPA \cdot MVPA)^{1/3}}, z_2 : \sqrt{\frac{2}{3}} ln \frac{SB}{(LPA \cdot MVPA)^{1/2}}, z_3 : \sqrt{\frac{1}{2}} ln \frac{LPA}{MVPA} \right) (4)$$

Thus, the ILR produces a set of coordinates for each component (i.e., z_1, z_2 and z_3 in each component of the example above) that should be introduced together as covariates in any statistical model (see section 2.3 for considerations on the statistical model selection). The main difficulty associated with these transformations is in interpreting the results; this is a problem similar to (for example) in linear regression when a variable is log-transformed. For compositional data, a solution is to find an appropriate graphical representation of the results, keeping in mind the co-dependence of the parts and using model predictions rather than deriving the estimate directly from model coefficients. Another difficulty arising from these mathematical transformations is related to having zeros or values close to zero in any of the components. This can happen in certain populations which may not perform vigorous PA or even MVPA. Considering very low values in a composition could lead to spurious

correlations [44], usually, these values are either ignored in the analysis or imputed to stabilize the models [37].

Statistical modelling

The third and last step of the analytical process relates to the decisions on how to model the associations between the selected descriptor(s) (with or without mathematical transformations) and health. As far back as the 1950's [45,46], many studies have investigated the epidemiological associations of physical behaviours with health outcomes. The use of accelerometers confirmed some of these associations, and allowed a better characterisation of the dose-response curve overcoming the cognitive biases of self-reports. However, most studies have solely focused on basic descriptors of one behaviour in isolation (e.g., MVPA). Out of the 11,765 publications identified in a search in the Web of Science on physical activity and accelerometers (**Figure A6, Panel A**), only 125 studies explored the interdependencies among physical behaviours using isotemporal substitution models, multivariate pattern analysis or functional data analysis (**Figure A8**) [47]. This consensus group believes that now is the right time to move to more detailed and informative studies on the combined effects and interactions across physical behaviours on health outcomes.

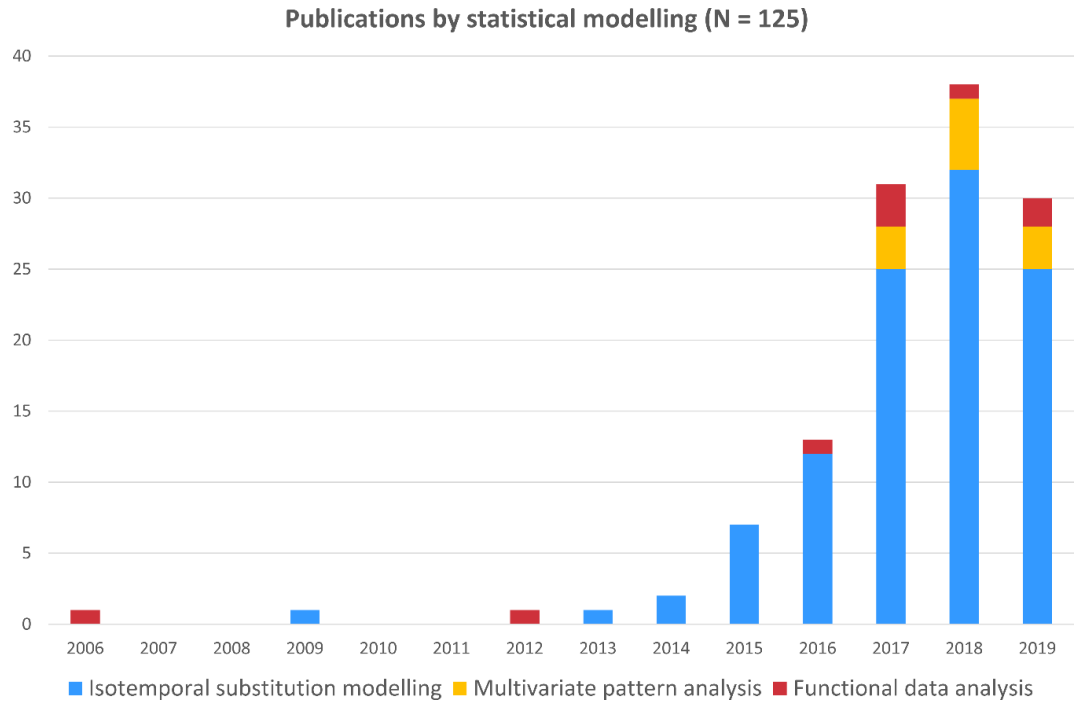

Figure A8. Number of publications using some of the approaches described in the present document from inception to December 31st, 2019. Search syntax introduced in the Web of Science: isotemporal substitution models: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("isotemporal substitution")); multivariate pattern analysis: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("Physical activity signature" OR "multivariate pattern analysis")); functional data analysis: (((((("physical activity")) OR "sedentary")) AND ((acceleromet*) OR actigraph*) AND ("Physical activity signature" OR "functional data analysis")).

1.9 Linear regression modelling

Linear regression is the most frequently used statistical model in the field, often including the physical behaviour descriptor as a continuous exposure variable in a linear, logistic or Cox regression (depending on the outcome of interest). Linear regression models are

interpreted in terms of the (theoretical) effect of increasing the explanatory variable on the outcome, under a linear relationship. Standard linear regression models are usually adjusted for the covariates that could influence the association of interest. Highly correlated explanatory variables result in multicollinearity, which is a phenomenon in which redundant information carried by predictors leads to erratic estimation of the models [48].

Linear regression models can also be used with compositional ILR-transformed descriptors, which may eliminate that part of the collinearity which arises from the fixed sum (or closure) constraint [37,38]. In this case, the model coefficients are interpreted in terms of time replacements across behaviours. For example, the estimate for the z_1 coordinate of the z_{SB} equation presented above represents the effect of increasing SB while proportionally reducing the time in light PA, MVPA and sleep. The dose-response association between a specific behaviour and the health outcome is assumed to be logarithmic (curvilinear) using compositionally-transformed descriptors. Likewise, the regression model predictions (using compositional data) can be used to estimate the time replacement between pairs of behaviours (e.g., reallocating time from SB to MVPA). This results in a similar interpretation to the isotemporal substitution models presented in the section 2.3.2. When examining longitudinal associations, advanced regression models (e.g., survival analysis using Cox regression) may be used with either absolute descriptors [27,49,50] or compositional ILR-transformed descriptors [42].

1.10 Isotemporal substitution models

The isotemporal substitution modelling framework considers potential outcomes of increasing one behaviour at the expense of another and whether the strength of the association is dependent on the behaviour being displaced. Isotemporal substitution models

are linear regressions in which all-but-one of the time-use behaviours are introduced as the exposure (together with the pertinent covariates) and the health outcome is the dependent variable. These models examine the estimated effects of replacing time spent in one behaviour (the missing behaviour in the model) with an equal amount of time spent in another, while keeping monitor wear time constant. They do so by dropping the behaviour of interest from the model (otherwise, the model would suffer from perfect collinearity). The linear effects of the pair-wise reallocations are then estimated from the model coefficients. Similar interpretations of time replacement between pairs of behaviours can be obtained from applying linear regression over compositional data (see section 2.3.1).

1.11 Multivariate pattern analysis and other dimension reduction models

Multivariate pattern analysis can handle completely collinear explanatory variables by combining the data into orthogonal latent variables [51]. Thereby, this method tackles collinearity as a dimension reduction problem, rather than a data transformation (as CoDA does). Multivariate pattern analysis is especially well-suited to analyse a wide range of collinear descriptors, such as the intensity spectrum, without requiring any data transformation [28,52], although transformations can be done to make distributions within bands more normal and linearly associated with the outcome. Another important feature is that the models are optimized for predictive ability by Monte-Carlo resampling whereby half of the data are repeatedly used for modelling and half for prediction [53]. In this way, the optimal number of latent variables can be determined and only relevant features in the descriptor retained.

Multivariate pattern analysis uses partial least squares (PLS) regression modelling [51], or other latent-variable regression models [54], to determine the multivariate association

pattern. PLS regression decomposes the explanatory variables into orthogonal linear combinations (PLS components), while simultaneously maximizing the covariance with the outcome variable. Similar procedures to reduce the data can be observed in factor analysis, principal component analysis, or JIVE models. Multivariate pattern analysis differs from these others by creating components that maximize the covariation with the outcome, not internally among the explanatory variables. JIVE models seek to maximize the variance explained across explanatory variables assuming that they come from different dimensions (e.g., PA, sleep, and circadian rhythms) and improving the within and between dimension representation [55]. The procedure for obtaining the multivariate patterns is completely data-driven, with no assumptions on variable distributions or degree of collinearity among variables. Selectivity ratios are calculated to express and rank each single explanatory variables' association with the outcome [56,57]. The selectivity ratio represents each explanatory variable's ratio of explained to residual variance in relation to the outcome (**Figure A9**). By replacing residual variance with total variance in the denominator, a straight-forward measure of explained variance can be obtained [58]. Multivariate pattern analysis has been applied with time-use descriptors and intensity spectrum in both their absolute scale and with the compositional CLR-transformation [39]. Since multivariate pattern analysis can handle singular data (e.g., CLR-transformed data), the ILR-transformation is not necessary if modelling compositional data.

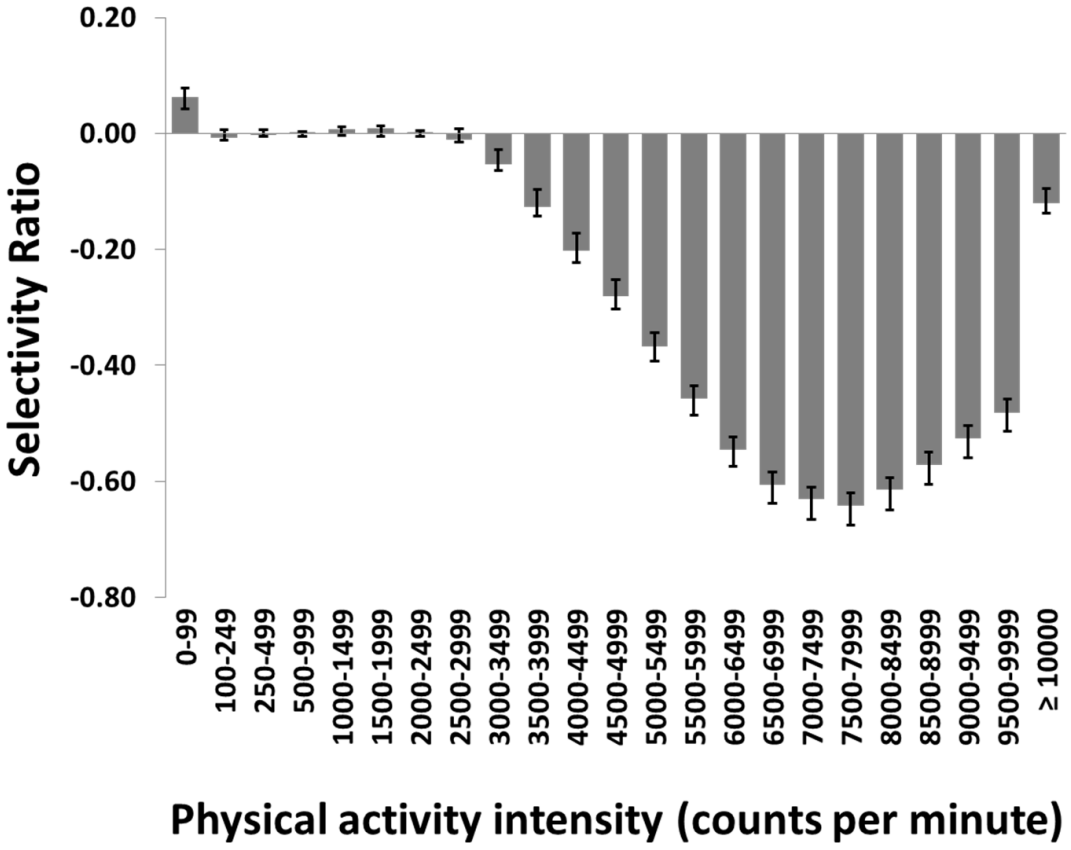

Figure A9. Multivariate pattern analysis example. Accelerometer model: ActiGraph GT3X+, sampling frequency: 30 Hz, body attachment site: right hip; awake time recording protocol. Selectivity ratio represents the explained-to-total outcome variance ratio. Adapted from Aadland et al. [39] with permission from the publisher.

1.12 Functional data analysis

Functional data analysis is an extension of linear regression analysis where the exposure or the outcome (or both) is a function instead of a scalar [59–61]. In physical behaviour epidemiology, the rationale of functional data analysis in the context of accelerometer data comes from the availability of moment-by-moment acceleration data allowing the use of the entire range of accelerations, whatever the aggregated metric used (e.g., counts, ENMO,

MAD) [62,63]. The acceleration functions described in section 2.1.6 can be used in functional data analysis. A first step often consists in smoothing the function of interest so that the smoothed function can then be used in functional data analysis, although some approaches do not smooth the data at subject level and rather pool the data across subjects to avoid the loss of information from the accelerometer signal. For example, when the interest is in the distribution of acceleration over time of the day, one can reduce data into 10 minute epochs as the objective is to assess when individuals are more or less active at each time of the day [64]. When the function of interest is the acceleration density distribution, Gaussian Kernel smoothing methods can be used (**Figure A10**) [65]. In that case, careful attention should be given to the number and place of nodes for acceleration values: a higher number of nodes should be present in the acceleration range where most of the time is spent. Then, the smoothed function of interest can be used for further analysis as an outcome variable (Function-on-scalar analysis), an exposure (Scalar-on-function analysis), or both (Function-on-function analysis) using functional data analysis regression techniques.

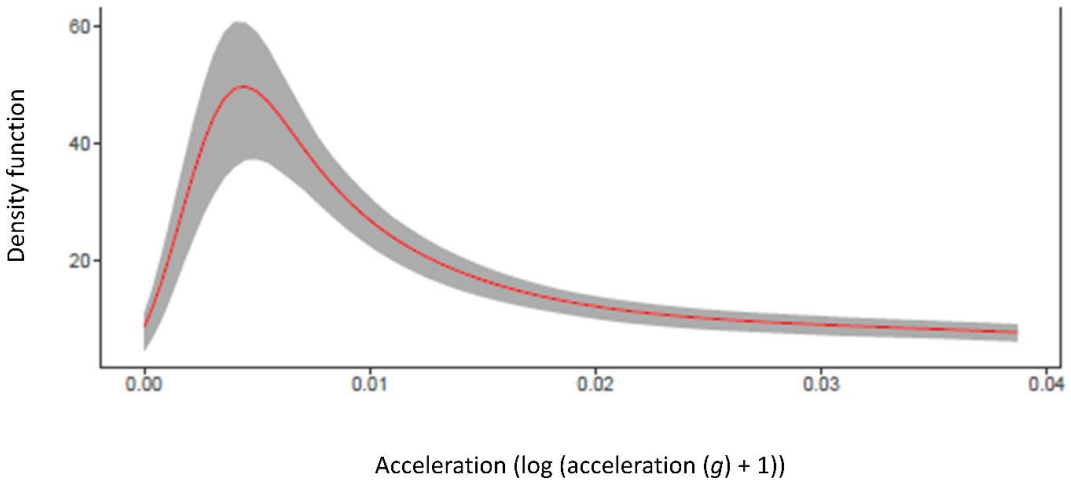

Figure A10. Smooth mean and interquartile acceleration density function. Red curve represents the mean density function of the study population and the grey area the interquartile range.

1.13 Machine learning for epidemiological analysis

ML methods provide a broad range of techniques to identify patterns in data. Although it has been increasingly used to derive descriptors from raw accelerometer data [20], ML has rarely been applied to the study of the associations of accelerometer data descriptors (examples of ML for health association analysis using physical behaviour data include [66,67]). As ML methods typically emphasise prediction or data reduction, they are most often relevant for hypothesis generation and data exploration. While there is no clear distinction between conventional statistical methods and ML, there is typically a different emphasis, and so they can be difficult to apply directly to problems requiring statistical inference. Bi et al. discuss possible epidemiologic applications of a wide range of machine learning methods in detail [68]. Examples of ML methods which could be applied to health association analysis using accelerometer data include Decision Trees/ Random Forests, Support Vector Machines and Neural Networks.

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