Objective measurement of sedentary time and physical activity in people with rheumatoid arthritis: protocol for an accelerometer and activPALTM validation study

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ABSTRACT

Background: The accurate measurement of sedentary time and physical activity in Rheumatoid Arthritis (RA) is critical to identify important health consequences and determinants of these behaviours in this patient group. However, objective methods have not been well-validated for measurement of sedentary time and physical activity in RA. Aims: Specific objectives are to: 1) validate the ActiGraph GT3X+ accelerometer and activPAL3μTM against indirect calorimetry and direct observation respectively, and define RA-specific accelerometer cut-points, for measurement of sedentary time and physical activity in RA; 2) validate the RA-specific sedentary time accelerometer cut-points against the activPAL3μTM; 3) compare sedentary time and physical activity estimates in RA, using RA-specific vs. widely-used non-RA accelerometer cut-points.

Methods: Objective 1: People with RA will wear an ActiGraph GT3X+, activPAL3μTM, heart rate monitor and indirect calorimeter, whilst being video-recorded undertaking 11 activities representative of sedentary behaviour, and light and moderate intensity physical activity. Objectives 2 and 3: People with RA will wear an ActiGraph GT3X+ and activPAL3μTM for 7 days to measure free-living sedentary time and physical activity.

Discussion: This will be the first study to define RA-specific accelerometer cut-points, and represents the first validation of the ActiGraph accelerometer and activPALTM, for measurement of sedentary time and physical activity in RA. Findings will inform future RA studies employing these devices, ensuring more valid assessment of sedentary time and physical activity in this patient group.

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ABBREVIATIONS
ADLs: Activities of daily living
AUC: Area under the curve
BMI: Body-mass index
cpm: Counts per minute
DAS-28: Disease Activity Score-28
METs: Metabolic equivalents
NHANES: National Health and Nutrition Examination Survey
RA: Rheumatoid Arthritis
ROC: Receiver Operating Characteristic
VM: Vector magnitude

INTRODUCTION
There exists a wealth of research documenting levels of physical activity participation in diverse populations, and
reporting the health benefits of engagement in light (1.6-2.9 metabolic equivalents [METs]) and moderate-to-vigorous (≥3 METs) intensity physical activity for specific groups. More recently, research has begun to examine the levels of engagement in sedentary behaviour (waking behaviour expending ≤1.5 METs whilst sitting/reclining/lying), in order to understand implications for health. Indeed, there is evidence to suggest that sedentary behaviour is an independent risk factor for heightened inflammation, incidence diabetes, and all-cause, cardiovascular disease and cancer mortality in adults.

For people living with Rheumatoid Arthritis (RA), the positive effects of physical activity for pertinent RA outcomes are well-established. For example, evidence suggests that physical activity is beneficially linked to disease activity, systemic inflammation, physical function, pain, fatigue, rheumatoid cachexia outcomes, psychological wellbeing and markers of cardiovascular disease. Furthermore, new evidence suggests that sedentary behaviour may be adversely linked to disease activity, physical function and cardiovascular risk in this patient group. However, available data indicate that people with RA typically do not engage in sufficient levels of physical activity to yield positive health outcomes, and spend long periods of the day sedentary.

Until recently, our understanding of the levels and health consequences of sedentary behaviour and physical activity in RA has largely been based on studies employing self-report methods to quantify engagement in these behaviours. The selection of self-report instruments introduces issues around measurement validity and reliability, such as social desirability bias and errors in participant recall, limiting the accuracy of such measures in sedentary behaviour and physical activity research. However, objective devices, such as accelerometers and posture sensors, are now more readily employed to quantify levels of free-living sedentary behaviour and physical activity in the general population. As such, there now exists significant opportunity to employ such instruments to the surveillance of sedentary time and physical activity in the RA population. That is, to understand dose-response relationships between sedentary time and physical activity with RA outcomes, identify salient determinants of such behaviours to be targeted in interventions, and subsequently evaluate the efficacy of such interventions for improving RA outcomes.

Accelerometers

Accelerometers are typically small and lightweight devices, usually worn on the hip or wrist, that afford the ability to continuously monitor free-living sedentary time and physical activity. The ActiGraph accelerometer (ActiGraph, LLC., Pensacola, Florida, USA) is the most frequently employed accelerometer in field-based research. This device can capture human movement (accelerations) on the vertical (Y), horizontal right-left (X) and horizontal front-back (Z) axes, and these data can be used to determine the vector magnitude (VM) of these accelerations (VM = \sqrt{(axisY^2 + axisX^2 + axisZ^2)}). Accelerations are recorded over user-defined time intervals (epochs), which are converted by the manufacturer’s software (Actilife) into ‘activity counts’. Researcher-developed algorithms (referred to as ‘cut-points’) are then applied to the accelerometer activity counts, in order to quantify time spent in different intensities of activity (sedentary behaviour, and light, moderate and vigorous intensity physical activity).

The most common accelerometer cut-point employed to assess sedentary time is ≤99 counts per minute [cpm]. This is a uniaxial (single axis) cut-point, which originates from a validation study of the ActiGraph accelerometer, conducted among adolescent girls. Following publication, the ≤99 cpm cut-point was subsequently employed in the National Health and Nutrition Examination Survey (NHANES) to estimate population prevalence of sedentary time among American adults. In conjunction, uniaxial accelerometer cut-points were employed to the NHANES data to estimate frequency and duration of light, moderate and vigorous intensity physical activity among children and adults. These physical activity cut-points were defined by Troiano et al., on the basis of weighted averages of criteria from 4 calibration studies, and have since been frequently employed in studies of sedentary behaviour and physical activity in RA.

However, more recently, researchers have started to move away from the assumption that ‘one size fits all’, and there has been an increase in the number of population-specific accelerometer cut-points developed. Still, researchers employing accelerometry in RA studies are heavily reliant on algorithms developed in validation studies of ‘healthy adults’, since no RA-specific accelerometer cut-points have been derived. This is particularly problematic when we consider that the physiology and associated activity patterns of people living with RA are likely to differ substantially to those among ‘healthy adults’ in the general population (eg, a relatively higher basal metabolic rate is characteristic of RA). As such, there is an urgent requirement for validation studies to develop RA-specific accelerometer cut-points to permit more accurate measurement of accelerometer-assessed sedentary time and physical activity in RA. Further, to ensure progress in this field, it is essential that the validity of these accelerometer cut-points for the measurement of free-living behaviour is established.

Despite several advantages relative to self-report, accelerometers are still limited in their ability to measure posture – an important facet of the characterisation of
sedentary behaviour. That is, the established definition of sedentary behaviour stipulates a consideration of both low energy expenditure (≤1.5 METs) and a sitting/ reclining/lying posture. Indeed, whilst cut-points can be applied to accelerometer data to provide an (indirect) measure of energy expenditure, accelerometers are less able to detect the posture at which low-energy behaviours are undertaken. In this way, the activPAL™ posture sensor (PAL Technologies Ltd., Glasgow, UK) offers an advance over accelerometers for free-living assessment of sedentary time, and is currently considered the ‘gold standard’ to measure sedentary time in field-based research.

**ActivPAL™ posture sensor**

The activPAL™ is a small, lightweight device, worn attached to the front of the right thigh, in a mid-anterior position. The activPAL™ has increasingly been used to measure free-living sedentary time, due to its ability to distinguish between sitting/lying and standing postures. Certainly, the activPAL™ has demonstrated high validity for the measurement of sedentary time in different populations, when compared against the criterion of direct observation. Less frequently, the activPAL™ is used to measure time spent stepping as an estimate of physical activity. However, the activPAL™ is limited to the extent at which these data can be accurately interpreted to determine physical activity intensity, which is currently estimated based on step cadence. To date, only 1 study has validated the activPAL™ against direct observation in the RA population. In this study, participants wore an activPAL™ whilst lying, sitting, standing, walking on a treadmill, and undertaking 10 activities of daily living (ADLs [eg, reading a newspaper, washing and drying dishes, placing bed linens on pillows and duvet]). In analysis, t-tests indicated overall estimates of time spent sedentary, standing and stepping (seconds [mean ± standard deviation]) from the activPAL™ vs. direct observation did not significantly differ. Linear regression also demonstrated a strong relationship between time spent sedentary (r = .74), standing (r = .86) and stepping (r = .93) derived from the activPAL™ vs. direct observation. However, Bland and Altman explained that regressions indicating the strength of a relationship, does not provide scope to determine the degree of agreement between 2 methods. Indeed, it would be surprising to find non-significant comparability of 2 methods that measure the same variables.

**Study aims**

To address these critical knowledge gaps, this study will validate the ActiGraph GT3X+ accelerometer and activPAL3™ posture sensor for the measurement of free-living sedentary time and physical activity in the RA population. Specific objectives are as follows:

**Objective 1: Laboratory-based validation**

- Validate the ActiGraph GT3X+ and activPAL3™ against criterion standards (indirect calorimetry and direct observation, respectively), for the measurement of sedentary time and physical activity in RA. Using the criterion of indirect calorimetry, calibrate the ActiGraph GT3X+ to define RA-specific accelerometer cut-points for sedentary time, and light and moderate intensity physical activity.

**Objective 2: Field-based validation of RA-specific sedentary time accelerometer cut-points against the activPAL™**

- Establish the validity of the new RA-specific sedentary time accelerometer cut-points for free-living assessment of sedentary time in RA. Estimates of sedentary time computed using RA-specific accelerometer cut-points, will be compared against the criterion of activPAL3™-assessed sedentary time (minutes/day).

**Objective 3: Accelerometer cut-point comparison (RA-specific vs. non-RA accelerometer cut-points)**

- To compare estimates of time spent sedentary, and engaged in light and moderate intensity physical activity – specifically, to compare:
  1. Sedentary time estimates derived from widely-used ‘healthy adult’ (non-RA) accelerometer cut-points, against the criterion of activPAL3™-assessed sedentary time (minutes/day) in people living with RA.
  2. Estimates of free-living sedentary time, and light and moderate intensity physical activity (minutes/day) in people living with RA, derived using: a) the new RA-specific accelerometer cut-points vs. b) widely-used ‘healthy adult’ (non-RA) accelerometer cut-points.

**METHODOLOGY**

**Participants and recruitment**

This study has been approved by the local National Health Service Research Ethics Committee (West Midlands – Black Country Research Ethics Committee 16/ WM/0371). People with RA will be recruited from Rheumatology outpatient clinics at a hospital in Dudley, England. Eligibility criteria for this study will be: a clinical diagnosis of RA according to the American College of Rheumatology-European League Against Rheumatism Classification Criteria, aged ≥18 years old and the ability to ambulate independently without (Objective 1) with (Objectives 2 and 3) the use of an assistive device. All participants will give informed consent, prior to initiating data collection.

**Protocol**

**Objective 1: Laboratory-based validation**

Participants (target n = 20) will be asked to report to
a temperature-controlled laboratory (22°C) in a fasted state (12 hours prior), having refrained from exercise for 48 hours before data collection. One hour prior to participant arrival, the indirect calorimeter (Cortex Metalyzer® 3B [Cortex Biophysik, Leipzig, Germany]) will be calibrated using Cortex Metalyzer® 3B software (MetaSoft®), in accordance with the manufacturer's instructions (criterion standard for ActiGraph GT3X+). A video camera will be set up on a tripod overlooking the laboratory for direct observation of behaviour (criterion standard for activPAL3™).

Upon arrival, participants will undertake physical assessments, including height (cm), weight (kg), body composition (body-mass index [BMI], body fat [%], fat-free mass [kg]) and Disease Activity Score-28 (DAS-28 [Erythrocyte Sedimentation Rate plus 28 swollen-and-tender joint count]). Participants will then be fitted with the ActiGraph GT3X+, activPAL3™, Polar heart rate monitor (Polar Electro Oy Ltd., Kempele, Finland) and Cortex Metalyzer® 3B (via face mask) for the duration of the laboratory study (approximately 2 hours).

Whilst wearing this equipment, each participant will be instructed to carry out a total of 11 activities (Table 1), comprising a standardised testing component of 6 activities and 5 ADLs. These activities have been selected to represent various energy expenditures (METs), ranging from sedentary behaviour to light and moderate intensity physical activity. The selected ADLs have been used in previous studies aiming to replicate a free-living environment in a laboratory setting, in order to validate

| Table 1. Activities undertaken during the laboratory-based validation study (Objective 1). |
|---------------------------------------------|---------------------|
| **Standardised testing component 1**        | **Energy expenditure (METs)** |
| Reclining                                   | 1.3                 |
| Reclining on a hospital bed                 |                     |
| Sitting                                     | 1.3                 |
| Sitting on a still chair with uncrossed legs|                     |
| Standing                                    | 1.3                 |
| Standing on the floor with feet flat and arms by side |                     |
| **Activities of daily living**              | **Energy expenditure (METs)** |
| Reading a newspaper                         | 1.3                 |
| Sitting on a chair without a desk/table     |                     |
| Washing and drying dishes                   | 1.8                 |
| Standing whilst washing up and drying up bowls, small plates and large plates |         |
| Ironing and folding clothes                 | 2.0                 |
| Standing whilst taking clothes out of a laundry bag, and ironing them using an iron and mini ironing board | |
| Folding the ironed clothes                 |                     |
| Placing bed linens on pillows and duvet     | 2.5                 |
| Standing whilst placing a bed sheet on a single hospital bed, pillow cases on 2 pillows and a duvet cover on a single duvet | |
| Sweeping the floor                         | 3.3                 |
| Using a broom to sweep up a pile of debris into a cardboard box, emptying the cardboard box and continuing cycle | |
| **Standardised testing component 2**        | **Energy expenditure (METs)** |
| Walking at 3.2 km/h                         | 2.8                 |
| On a treadmill, no incline                  |                     |
| Walking at 4 km/h                           | 3.0                 |
| On a treadmill, no incline                  |                     |
| Walking at 4.8 km/h                         | 3.5                 |
| On a treadmill, no incline                  |                     |

MET, metabolic equivalent of task; km/h, kilometres per hour
All MET values are based on the Compendium of Physical Activities
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ActiGraph accelerometers and the activPAL™ in different populations. Recalling, sitting and standing (standardised testing component 1) will be completed prior to the ADLs. Participants will then perform the ADLs in a random order to avoid ordering effects. In Microsoft Excel [Microsoft Corporation, Redmond, USA] will be used to randomly sort ADLs, prior to participant arrival, and will be permitted to use their upper limbs during sit-stand transitions. Furthermore, participants will be given general, non-specific advice about how to carry out each activity, to ensure that their movement patterns during the ADLs are representative of a free-living environment. Treadmill walking (standardised testing component 2) will be completed after the ADLs. Each activity will be undertaken repeatedly for 6 minutes. Resting heart rate (beats per minute), VO2 (mL/min/kg) and METs will be measured during the 6-minute period of sitting (standardised testing component 1), and used to establish a baseline for each participant. Five-minute rest periods will be implemented to separate each of the ADLs, in order to allow heart rate and VO2 (mL/min/kg) to return to resting levels. Consecutive 1-minute rest periods will be added if these values do not return to resting levels after 5 minutes.

All equipment will be synced to ensure recording at the same time of day (MetaSoft®, video camera, ActiLife and activPAL3™ software [PAL Connect]). The start and finish time of the protocol, individual activities and rest periods, will be recorded by the researcher using the time displayed on the computer interface (MetaSoft®). These times will be used to ensure accurate comparison between time-stamped raw data collected via the ActiGraph GT3X+ and activPAL3™, with criterions (VO2 [mL/min/kg] and METs [indirect calorimetry], and direct observation [video camera recordings]).

Objective 2: Field-based validation of RA-specific accelerometer cut-points
The protocol for Objective 2 of this study has been described elsewhere. Briefly, participants (target n = 100) will undertake physical measures (height [cm], weight [kg], BMI, body fat [%], fat-free mass [kg] and DAS-28). Following which, they will be asked to wear the ActiGraph GT3X+ and activPAL3™ for 7 days, for assessment of free-living sedentary time and physical activity.

Objective 3: Accelerometer cut-point comparison
The same protocols employed in Objective 2 will be employed to achieve Objective 3 of this study.

Measures
Indirect calorimetry
The Cortex Metalyzer® 3B uses a breath-by-breath system to directly measure an individual’s concentration of inspired oxygen (O2) and expired carbon dioxide (CO2). These data are transferred to MetaSoft® in real-time, and the individual’s VO2 (mL/min/kg) and METs are calculated and displayed in real-time on the computer interface. Participant details, such as biological sex, date of birth, height (cm), weight (kg) and the size of the face mask will be entered into MetaSoft®. After answering any questions, the researcher will fit the participant with the Polar heart rate monitor and face mask; the face mask will be attached to a head net and a mouthpiece turbine. The gas sensor will be fitted to the mouthpiece turbine once the participant confirms they are comfortable in the face mask.

Once the participant assumes a lying position (standardised testing component 1), they will rest for 5 minutes. Following this, once heart rate has reached steady state for 1 minute, the researcher will start data collection with MetaSoft®. The participant will be instructed to refrain from speaking at this point, but to give agreed hand signals (e.g., thumbs up/down) for the duration of data collection. At the end of the testing period (after all activities have been completed), the researcher will stop the MetaSoft® recording, and data will be exported to Microsoft Excel for further analysis.

Direct observation
Direct observation is commonly used when validating devices such as the activPAL3™ in different populations. In this study, participants will be video-recorded (at standard recording speed, 25 frames/second) throughout the laboratory testing procedure, in order to observe their time spent sedentary, standing, stepping (seconds), as well as number of steps and sit-stand transitions. The video camera will start recording when the participant is lying on the bed, ready to begin the first activity. The recording will be stopped when the participant has finished the last activity.

ActiGraph accelerometer and activPAL3™ posture sensor
The ActiGraph GT3X+ is a triaxial accelerometer (19g; 4.6cm x 3.3cm x 1.5cm) that records accelerations on 3 axes (Y, X, Z), which are used to compute VM (VM = V(2axis2 + axisX2 + axisZ2)). The device can be configured to record accelerations at a sample rate of 30-100 Hertz (Hz). During data reduction, raw accelerations stored in the ActiGraph GT3X+ are processed through a digital filter using ActiLife, which limits the range of frequency to 0.25-2.5 Hz. Each sample is then summed over user-defined epochs (range 1-60 seconds), which are converted (by ActiLife) to activity counts. In this study, the ActiGraph GT3X+ will be configured to record accelerations in 1-second epochs, at a rate of 30 Hz. The ActiGraph GT3X+ will be vertically positioned on the right
The actiPAL3™ posture sensor (9g; 2.35cm x 4.3cm x 0.5cm) uses proprietary algorithms to detect the inclination of the thigh, categorising behaviour during daily time spent sitting/lying (sedentary), standing and stepping, as well as the number of steps and sit-stand transitions. In this study, the actiPAL3™ will be initialised using the manufacturer’s software, PAL Connect. The actiPAL3™ will be attached with a waterproof, adhesive Tegaderm dressing to the right thigh of each participant, in a mid-anterior position.

The positioning of both devices will be checked throughout the laboratory-based validation procedure (Objective 1). For Objectives 2 and 3, the researcher will instruct participants to remove the ActiGraph GT3X+ only during water-based activities (eg, bathing), and wear the actiPAL3™ continuously. Participants will be asked to record dates and times of any device removal and replacement in logbooks.

**Data reduction and statistical analysis**

Objective 1: Laboratory-based validation

ActiGraph GT3X+ (criterion standard = indirect calorimetry). Time-stamped raw data from the ActiGraph GT3X+ will be downloaded and exported into Microsoft Excel using Actilife, which will display the activity counts for each axis (Y, X, Z) and the VM, recorded per 1-second epoch. Each participant’s VO2 (mL•min•kg) data from indirect calorimetry will be graphed for each of the 11 activities, and the time period at which steady state VO2 is reached will be identified, allowing for variation ± .50 mL•min•kg (a total margin of 1.0 mL•min•kg). Once steady state VO2 periods have been identified, (eg, minutes 4-6), ActiGraph GT3X+ activity count data (Y-axis and VM) and METs (from indirect calorimetry), recorded during these steady state periods, will be extracted for statistical analysis.

Where participants do not reach steady state VO2 during a specific activity, their data recorded during that activity will be excluded from statistical analysis. ActiGraph GT3X+ activity counts (Y-axis and VM) and METs from each participant, per activity, will be averaged across the identified steady state VO2 time period for use in Receiver Operating Characteristic (ROC) curve analysis. This statistical test will be used to define both uniaxial (based on Y-axis activity counts) and triaxial (based on VM activity counts) accelerometer cut-points for sedentary time, and light and moderate intensity physical activity. The independent variable will be the average ActiGraph GT3X+ activity counts recorded during steady state VO2. Binary indicators (0 or 1) will classify the intensity of activities (as sedentary or moderate intensity physical activity), on the basis of average MET values recorded during steady state VO2 (dependent variable [Table 2]). ROC curve analysis will be conducted using SPSS (IBM Corporation, Armonk, NY [version 24]). Each point on the ROC curve generated, will correspond to an activity count. Then, the activity count that maximises sensitivity (y-axis) and specificity (x-axis) will be identified using this curve. ROC curves will be generated for sedentary time and moderate intensity physical activity, on the Y-axis and VM. The activity counts representative of sedentary time and moderate intensity physical activity will correspond to the lower and upper threshold values for light intensity physical activity, respectively. Furthermore, the value corresponding to the area under the curve (AUC) will represent the accuracy, or ‘fit’, of the analysis, whereby 0.90-1.00 = excellent, 0.80-0.89 = good, 0.70-0.79 = fair, 0.60-0.69 = poor, and <0.60 = failure.

ActiPAL3™ (criterion standard = direct observation). Time-stamped raw data recorded by the actiPAL3™ during the laboratory protocol, will be downloaded and exported to Microsoft Excel using PAL Connect. Epoch data will be generated, to show time spent sedentary, standing or stepping every 15 seconds during the laboratory testing procedure, and the total number of steps and sit-stand transitions occurring during this period. The researcher will observe the video camera recordings of each participant, and record behaviour during 15-second time intervals which correspond to the actiPAL3™ 15-second epoch data generated by PAL Connect. Specifically, the researcher will record whether the participant was sitting/lying (sedentary), standing or stepping at every 15-second epoch, during each activity (standardised testing components and ADLs). These data will then be summed to determine total directly observed time spent sedentary, standing and stepping (minutes). The total number of steps and sit-stand transitions occurring throughout each activity (standardised testing components and ADLs) will be converted to METs, using actiPAL3™ cut-points. The independent variable will be the total number of steps and sit-stand transitions occurring throughout each activity (standardised testing components and ADLs). The dependent variable will be the total number of steps and sit-stand transitions occurring throughout each activity (standardised testing components and ADLs).

### Table 2. The binary indicators that will be created in ROC curve analysis, using energy expenditure (METs) to classify the intensity of each activity for each participant.

| Energy expenditure (METs) | Intensity of activity | Binary indicator |
|---------------------------|-----------------------|-----------------|
| ≤1.5                      | Sedentary             | 1               |
| >1.5                      | >Sedentary            | 0               |
| ≥3                        | Moderate intensity physical activity | 1               |
| <3                        | <Moderate intensity physical activity | 0               |

**MET, metabolic equivalent of task**

All MET values are based on the Sedentary Behaviour Research Network, and American College of Sports Medicine and the American Heart Association.

### Table 2.

| Energy expenditure (METs) | Intensity of activity | Binary indicator |
|---------------------------|-----------------------|-----------------|
| ≤1.5                      | Sedentary             | 1               |
| >1.5                      | >Sedentary            | 0               |
| ≥3                        | Moderate intensity physical activity | 1               |
| <3                        | <Moderate intensity physical activity | 0               |
components and ADLs) will also be recorded. Observed behaviours will be defined as: sitting – the participant’s back in an upright position, supporting their bodyweight through their buttocks; lying – the participant being horizontal on a surface; standing – the participant is upright with their feet supporting their body weight; step (singular) – the participant is in an upright position, and their foot has left the ground before making complete contact with the ground; stepping – continuous movement whilst in an upright posture.32,33

Using SPSS, means and standard deviations will be generated from activPAL3TM and direct observation data, to enable comparison between activPAL3TM-assessed and directly observed time spent: 1) sedentary; 2) standing; 3) stepping (minutes), as well as the total number of steps and sit-stand transitions during the testing period. Bland-Altman plots will then be generated using SPSS, to evaluate the agreement between activPAL3TM estimates and direct observation of behaviours. Finally, misclassification by the activPAL3TM of time spent sedentary, standing and stepping, as well as the number of steps and sit-stand transitions, will be calculated and reported as the percentage difference between activPAL3TM-assessment and direct observation of behaviours.

Objective 2: Field-based validation of RA-specific accelerometer cut-points

Raw ActiGraph GT3X+ data will be downloaded and exported into Microsoft Excel using Actilife, which will display the activity counts for each axis (Y, X, Z) and the VM, recorded per 1-second epoch. To identify periods of non-wear, ≥60 and ≥90 minutes of consecutive ‘0’ counts, with a spike tolerance = 2 minutes, will be applied to the ActiGraph GT3X+ data. Data will be considered as valid for inclusion in subsequent statistical analysis, where participants have worn the accelerometer for ≥10 hours each day, for ≥4 weekdays, including ≥1 weekend day. The RA-specific sedentary time accelerometer cut-points derived during the laboratory-based validation (Objective 1) will then be applied to the free-living (7-day) ActiGraph GT3X+ data, to estimate time spent in sedentary behaviour (minutes/day [mean ± standard deviation]).

PAL Connect will be used to download and export activPAL3TM data, in 15-second epochs, to Microsoft Excel. Sleep time will be removed manually using information from wear-time logbooks, self-reported waking and sleeping time, and non-wear periods identified by Actilife (computed according to the aforementioned non-wear criteria). ActivPAL3TM-assessed sedentary time will then be calculated (minutes/day [mean ± standard deviation]). Bland-Altman plots will be used to determine agreement between estimates of sedentary time assessed by the ActiGraph GT3X+ and activPAL3TM, and bias and 95% limits of agreement will be calculated.

Objective 3: Accelerometer cut-point comparison

For Objective 3, estimates of sedentary time, and light and moderate intensity physical activity (minutes/day [mean ± standard deviation]), will be generated using the novel RA-specific accelerometer cut-points (Objective 1) and existing widely-used non-RA (uniaxial) accelerometer cut-points (Y-axis: sedentary time, ≤99 cpm; light intensity physical activity, 100-2019 cpm; moderate intensity physical activity, 2020-5998 cpm).45,47 Then, using the criterion of the activPAL3TM, the validity of applying the non-RA accelerometer cut-point for measuring free-living sedentary time in RA, will be evaluated using Bland-Altman plots.

Using t-test analysis, estimates of sedentary time, and light and moderate intensity physical activity (minutes/day [mean ± standard deviation]), computed using RA-specific vs. non-RA accelerometer cut-points, will be compared within this sample of RA participants.

DISCUSSION

The accurate assessment of sedentary time and physical activity among people living with RA is critical in order to understand the dose-response relationships between sedentary time and physical activity with RA outcomes. Numerous studies in non-RA populations have validated accelerometers against indirect calorimetry, developing population-specific accelerometer cut-points (eg, for children, adults and older adults), to provide a more valid means of quantifying sedentary behaviour and physical activity.45,49,76 More recently, the activPALTM has been reported to demonstrate high validity when compared against direct observation in several populations,58,61,64,65 and is considered the ‘gold standard’ measure of sedentary time.37,59,60 The current study will take the first steps to establish analytical procedures, that ensure widely-used objective devices can be employed to accurately measure sedentary time and physical activity in RA.

Future research directions

Findings from this comprehensive validation study will therefore serve to direct future research employing activity count-based accelerometers (eg, ActiGraph) and the activPALTM, to measure sedentary time and physical activity in RA. Specifically, this study’s results will provide guidelines for researchers when analysing these data. As such, results from this study will provide great potential for future research to more conclusively determine important relationships between sedentary time and physical activity, with pertinent RA outcomes and modifiable determinants of these behaviours, as well as evaluating the efficacy of interventions targeting sedentariness and physical activity in this patient group.

CONFLICT OF INTEREST

The authors have declared no conflicts of interest.
Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06. Eur Heart J 2011;32(5):590-7. [https://doi.org/10.1093/eurheartj/ehq451] [PMID: 21224291] [PMCID: PMC3634159]

13. Henson J, Yates T, Edwardson CL, Khunti K, Talbot D, Gray LJ, et al. Sedentary time and markers of chronic low-grade inflammation in a high risk population. PLoS One 2013;8(10):e78350. [https://doi.org/10.1371/journal.pone.0078350] [PMID: 24205208] [PMCID: PMC3812126]

14. Patterson R, McNamaera E, Tarino M, de Sa TH, Smith AD, Sharp SJ, et al. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur J Epidemiol 2018;33(9):811-29. [https://doi.org/10.1007/s10654-018-0380-1] [PMID: 29580922] [PMCID: PMC6133009]

15. Cooney JK, Law RJ, Matsuichi V, Lennmy AB, Moore JP, Ahmad Y, et al. Benefits of exercise in rheumatoid arthritis. J Aging Res 2011;2011:681640. [https://doi.org/10.4061/2011/681640] [PMID: 21403833] [PMCID: PMC3042669]

16. Cramp F, Hewlett S, Almeida C, Kirwan JR, Choy EH, Chalder T, et al. Non-pharmacological interventions for fatigue in rheumatoid arthritis. Cochrane Database Syst Rev 2013;8:CD008322. [https://doi.org/10.1002/14651858.CD008322.pub2] [PMID: 23975674]

17. Metsios GS, Stavropoulos-Kalinoglou A, Sandoo A, van Zanten JJ, Toms TE, John H, et al. Vascular function and inflammation in rheumatoid arthritis: the role of physical activity. Open Cardiovasc J 2010;4:99-96. [https://doi.org/10.2174/18741924010040020098] [PMID: 20361002] [PMCID: PMC2847820]

18. Metsios GS, Stavropoulos-Kalinoglou A, Veldhuizen van Zanten JJ, Trehearn GJ, Panoulias VF, Douglas KM, et al. Rheumatoid arthritis, cardiovascular disease and physical exercise: a systematic review. Rheumatology (Oxford) 2008;47(3):239-48. [https://doi.org/10.1093/rheumatology/kem260] [PMID: 18045810]

19. Stavropoulos-Kalinoglou A, Metsios GS, Veldhuizen van Zanten JJ, Nightingale P, Kitsa GD, Koutedakis Y. Individualised aerobic and resistance exercise training improves cardiorespiratory fitness and reduces cardiovascular risk in patients with rheumatoid arthritis. Ann Rheum Dis 2013;72(11):1819-25. [https://doi.org/10.1136/annrheumdis-2012-202075] [PMID: 23155222]

20. Summers GD, Metsios GS, Stavropoulos-Kalinoglou A, Kitsa GD, Rheumatoid cachexia and cardiovascular disease. Nat Rev Rheumatol 2010;6(8):445-51. [https://doi.org/10.1038/nrrheum.2010.105] [PMID: 20647995]

21. Metsios GS, Stavropoulos-Kalinoglou A, Veldhuizen van Zanten JJ, Nightingale P, Sandoo A, Dimitroulas T, et al. Individualised exercise improves endothelial function in patients with rheumatoid arthritis. Ann Rheum Dis 2014;73(9):748-51. [https://doi.org/10.1136/annrheumdis-2013-203291] [PMID: 23904472]

22. Tan XL, Pugh G, Hurnby F, Morrissey D. Factors associated with physical activity engagement among adults with rheumatoid arthritis: A cross-sectional study. Musculoskeletal Care 2019. [https://doi.org/10.1016/j.msc.1385] [PMID: 30728653]

23. Khoja SS, Almeida GJ, Chester Wasko M, Terhorst L, flaton SV. Association of Light-Intensity Physical Activity With Lower Cardiovascular Disease Risk Burden in Rheumatoid Arthritis. Arthritis Care Res (Hoboken) 2016;68(4):424-31. [https://doi.org/10.1002/aacr.22771] [PMID: 26314595] [PMCID: PMC6217964]

24. Metsios GS, Stavropoulos-Kalinoglou A, Panoulias VF, Wilson M, Neville AM, Koutedakis Y, et al. Association of physical inactivity with increased cardiovascular risk in patients with rheumatoid arthritis. Eur J Cardiovasc Prev Rehabil 2009;16(2):188-94. [https://doi.org/10.1097/HJR.0b013e3283271ceb] [PMID: 19238083]

25. Piascik G. The role of physical activity in rheumatoid arthritis. Physiol Behav 2008;94(2):270-5. [https://doi.org/10.1016/j.physbeh.2007.12.012] [PMID: 18234247]

26. Tummonson C, Matteson EL. Cardiovascular risk factors, fitness and physical activity in rheumatic diseases. Curr Opin Rheumatol 2007;19(2):190-6. [https://doi.org/10.1097/BOR.0b013e3280147107] [PMID: 17278937]
Indeed, there is evidence to suggest that sedentary behaviour is an independent risk factor for heightened periods of the day sedentary. RA typically do not engage in sufficient levels of physical instruments to the surveillance of sedentary time and behaviour expending the levels of engagement in sedentary behaviour (waking (ActiGraph, LLC., Pensacola, Florida, USA) is the most recall, limiting the accuracy of such measures in such as social desirability bias and errors in participant produces issues around measurement validity and reliability, self-report methods to quantify engagement in these be-
dynamics. The selection of self-report instruments intro-
2.9 metabolic equivalents [METs]) and moderate-to-vig-
intensity physical activity). Accelerometers are typically small and lightweight de-
41. Tudor-Locke CE, Myers AM. Challenges and opportunities for measuring physical activity in sedentary adults. Sports Med 2001;31(2):91-100. [https://doi.org/10.2165/0000322-2001310200-00002] [PMID: 11227981]
42. Cain KL, Conway TL, Adarme MA, Husak LE, Sallis JF. Comparison of older and newer generations of ActiGraph accelerometers with the normative filter and the low frequency extension. Int J Behav Nutr Phys Act 2013;10:51. [https://doi.org/10.1186/1479-5868-10-51] [PMID: 23681461] [PMCID: PMC3641979]
43. John D, Tyo B, Bassett DR. Comparison of four ActiGraph accelerometers during walking and running. Med Sci Sports Exerc 2014;46(2):369-74. [https://doi.org/10.1249/ MSS.0b013e318e1b3a4f] [PMID: 19927022] [PMCID: PMC8209132]
44. Gorman E, Hanson HM, Yang PH, Khan KM, Liu-Ambrose T, Ashe MC. Accelerometry analysis of physical activity and sedentary behavior in older adults: a systematic review and data analysis. Eur Rev Aging Phys Act 2014;11:35-49. [https://doi.org/10.1007/s11556-013-0392-x] [PMID: 24765212] [PMCID: PMC9990855]
45. Treuth MS, Schmitz K, Catellier DJ, McMurray RG, Murray DM, Almeida MJ, et al. Defining accelerometer thresholds for activity intensities in adolescent girls. Med Sci Sports Exerc 2004;36(7):1259-66. [PMID: 15235535] [PMCID: PMC2423321]
46. Matthews CE, Chen KF, Freedson PS, Buchowski MS, Beech BM, Pate RR, et al. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol 2008;167(7):857-81. [https://doi.org/10.1093/aje/kwn390] [PMID: 18303006] [PMCID: PMC3537832]
47. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. Med Sci Sports Exerc 2008;40(1):181-8. [https://doi.org/10.1249/ msb.0b013e31815a1b3] [PMID: 18091006]
48. Brage S, Wedderkopp N, Franks PW, Andersen LB, Froberg K. Reexamination of validity and reliability of the CSA monitor in walking and running. Med Sci Sports Exerc 2003;35(8):1447-54. [https://doi.org/10.1249/01.MSS.0000079078.62035.EC] [PMID: 12900703]
49. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. Med Sci Sports Exerc 1998;30(5):777-81. [PMID: 9588623]
50. Leenders NY, Sherman WM, Nagaraja HK, Kien CL. Evaluation of methods to assess physical activity in free-living conditions. Med Sci Sports Exerc 2001;33(7):1233-40. [PMID: 11445774]
51. Yngve A, Nilsson A, Spjöström M, Ekelund U. Effect of monitor placement and of activity setting on the MTI accelerometer output. Med Sci Sports Exerc 2003;35(2):320-6. [https://doi.org/10.1249/01.MSS.0000048829.75758.AQ] [PMID: 12569223]
52. Fenton SAM, Veldhuijzen van Zanten J, Kitas GD, Duda JL, Rouse DM, Almeida MJ, et al. Defining accelerometer thresholds for identifying sedentary behaviour in older adults in free-living environments. J Sci Med Sport 2014;17(3):293-9. [https://doi.org/10.1016/j.jsams.2013.07.002] [PMID: 2392994]
53. Copeland JL, Estiger DW. Accelerometer assessment of physical activity in active, healthy older adults. J Aging Phys Act 2009;17(1):17-30. [PMID: 19299836]
54. Sandroff BM, Riskin BJ, Agiovlasitis S, Mott RW. Accelerometer cut-points derived during over-ground walking in persons with mild, moderate, and severe multiple sclerosis. J Neurol Sci 2014;340(1-2):50-7. [https://doi.org/10.1016/j.jns.2014.02.024] [PMID: 24635890]
55. Metsios GS, Stavropoulos-Kalinoglou A, Panouss VS, Koutedakis Y, Nevill AM, Douglas KM, et al. New resting energy expenditure prediction equations for patients with rheumatoid arthritis. Rheumatology (Oxford) 2008;47(4):500-6. [https://doi.org/10.1093/rheumatology/kep088] [PMID: 18237090] [PMCID: PMC3527832]
59. Pfister T, Matthews CE, Wang Q, Kopciuk KA, Courneya K, Friedenreich C. Comparison of accelerometers for measuring physical activity and sedentary behaviour. BMJ Open Sport Exerc Med 2017;3(1):e000227. [https://doi.org/10.1136/bmjsports-2017-000227] [PMID: 28761711] [PMCID: PMC5530107]

60. Chastin SF, Granat MH. Methods for objective measurement, quantification and analysis of sedentary behaviour and inactivity. Gait Posture 2010;31(1):82-6. [https://doi.org/10.1016/j.gaitpost.2009.09.002] [PMID: 19854651]

61. Grant PM, Ryan CG, Tighe WW, Granat MH. The validation of a novel activity monitor in the measurement of posture and motion during everyday activities. Br J Sports Med 2006;40(12):992-7. [https://doi.org/10.1136/bjsm.2006.030262] [PMID: 16980531] [PMCID: PMC2577473]

62. Sellers C, Dall P, Grant M, Stansfield B. Validity and reliability of the activPAL3 for measuring posture and stepping in adults and young people. Gait Posture 2016;43:42-7. [https://doi.org/10.1016/j.gaitpost.2015.10.020] [PMID: 26669690]

63. Baumgartner TA, Jackson AS, Mahar MT, Rowe DA. Measurement for Evaluation in Kinesiology, 6th Edition. [157-8].

64. Bassett DR, Jr., John D, Conger SA, Rider BC, Passmore RM, Clark JM. Detection of lying down, sitting, standing, and stepping using two activPAL monitors. Med Sci Sports Exerc 2014;46(10):2025-9. [https://doi.org/10.1249/MSS.0000000000000326] [PMID: 24596998]

65. Lyden K, Kozezy Keadle SL, Staudehnayer JW, Freedson PS. Validity of two wearable monitors to estimate breaks from sedentary time. Med Sci Sports Exerc 2012;44(11):2243-52. [https://doi.org/10.1249/MSS.0b013e3182600477] [PMID: 22648343] [PMCID: PMC3475778]

66. Montoye AHK, Favarnik JM, Mudd LM, Biswas S, Pfeiffer KA. Evaluation of the activPAL accelerometer for physical activity and energy expenditure estimation in a semi-structured setting. J Sci Med Sport 2017;20(11):1003-7. [https://doi.org/10.1016/j.jsams.2017.04.011] [PMID: 28483558]

67. Steeves JA, Bowles HR, McClain JJ, Dodd KW, Brychta RJ, Wang J, et al. Ability of thigh-worn Actigraph and activPAL monitors to classify postural and motion. Med Sci Sports Exerc 2015;47(9):952-9. [https://doi.org/10.1249/MSS.0000000000000497]

68. Larkin L, Nordgren B, Purtill H, Brand C, Fraser A, Kennedy N. Criterion Validity of the activPAL Activity Monitor for Sedentary and Physical Activity Patterns in People Who Have Rheumatoid Arthritis. Phys Ther 2016;96(7):1093-101. [https://doi.org/10.2522/ptj.20150281] [PMID: 26637646]

69. Romanzini M, Petroski EL, Ohara D, Dourado AC, Reichert FF. Calibration of Actigraph GT3X, Actical and RT3 accelerometers in adolescents. Eur J Sport Sci 2014;14(1):91-9. [https://doi.org/10.1080/17461391.2012.732614] [PMID: 24533499]

70. Esliger DW, Rowlands AV, Hurst TL, Catt M, Murray P, Eston RG. Validation of the GENEA Accelerometer. Med Sci Sports Exerc 2011;43(6):1085-93. [https://doi.org/10.1249/MSS.0b013e31820513be] [PMID: 21088626]

71. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, 3rd, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010;62(9):2569-81. [https://doi.org/10.1002/art.27584] [PMID: 20872595]

72. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR, Jr., Tudor-Locke C, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. Med Sci Sports Exerc 2011;43(8):1755-81. [https://doi.org/10.1249/ MSS.0b013e31821eac12] [PMID: 21681120]

73. Dowd KP, Harrington DM, Donnelly AE. Criterion and concurrent validity of the activPAL professional physical activity monitor in adolescent females. PLoS One 2012;7(10):e47633. [https://doi.org/10.1371/journal.pone.0047633] [PMID: 23094069] [PMCID: PMC3477132]

74. Kim Y, Welk GJ. Criterion Validity of Competing Accelerometry-Based Activity Monitoring Devices. Med Sci Sports Exerc 2015;47(11):2456-63. [https://doi.org/10.1249/MSS.0000000000000691] [PMID: 25910051]