

The challenges of measuring physical activity and sedentary behaviour in people with rheumatoid arthritis

Steultjens, Martijn; Bell, Kirsty; Hendry, Gordon

Published in:
Rheumatology Advances in Practice

DOI:
[10.1093/rap/rkac101](https://doi.org/10.1093/rap/rkac101)

Publication date:
2023

Document Version
Publisher's PDF, also known as Version of record

[Link to publication in ResearchOnline](#)

Citation for published version (Harvard):
Steultjens, M, Bell, K & Hendry, G 2023, 'The challenges of measuring physical activity and sedentary behaviour in people with rheumatoid arthritis', *Rheumatology Advances in Practice*, vol. 7, no. 1, rkac101.
<https://doi.org/10.1093/rap/rkac101>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

If you believe that this document breaches copyright please view our takedown policy at <https://edshare.gcu.ac.uk/id/eprint/5179> for details of how to contact us.



Review

The challenges of measuring physical activity and sedentary behaviour in people with rheumatoid arthritis

Martijn Steultjens^{1*}, Kirsty Bell^{1,2}, Gordon Hendry¹

¹Research Centre for Health (ReaCH), School of Health and Life Sciences, Glasgow Caledonian University, Glasgow, UK

²National Health Service, Tayside, UK

*Correspondence to: Martijn Steultjens, Research Centre for Health (ReaCH), School of Health and Life Sciences, Glasgow Caledonian University, Room A101E, City Campus, Cowcaddens Road, Glasgow G4 0BA, UK. E-mail: martijn.steultjens@gcu.ac.uk

Abstract

The importance of sufficient moderate-to-vigorous physical activity as a key component of a healthy lifestyle is well established, as are the health risks associated with high levels of sedentary behaviour. However, many people with RA do not undertake sufficient physical activity and are highly sedentary. To start addressing this, it is important to be able to carry out an adequate assessment of the physical activity levels of individual people in order that adequate steps can be taken to promote and improve healthy lifestyles. Different methods are available to measure different aspects of physical activity in different settings. In controlled laboratory environments, respiratory gas analysis can measure the energy expenditure of different activities accurately. In free-living environments, the doubly labelled water method is the gold standard for identifying total energy expenditure over a prolonged period of time (>10 days). To assess patterns of physical activity and sedentary behaviour in daily life, objective methods with body-worn activity monitors using accelerometry are superior to self-reported questionnaire- or diary-based methods.

Lay Summary

What does this mean for patients?

Sufficient physical activity and limited time spent being inactive (i.e. sedentary behaviour) are key to a healthy lifestyle for people with RA. Various methods are available to measure physical activity and sedentary behaviour. To show patterns of sedentary behaviour and light, moderate and vigorous physical activity over a period of 5–10 days, body-worn activity monitors provide more useful information than questionnaires. This information can be used to set activity goals for a healthier lifestyle.

Keywords: RA, physical activity, sedentary behaviour

Key messages

- At least 150 min per week of moderate-to-vigorous physical activity leads to clear health benefits in people with RA.
- High levels of sedentary behaviour are a clear health risk.
- Body-worn physical activity monitors are the best method available to establish patterns of physical activity and sedentary behaviour in people with RA.

Introduction

The roles of physical activity and sedentary behaviour in the health outcomes of people with RA or other forms of inflammatory arthritis have been of increasing interest to researchers, clinicians and patients. The benefits of physical activity to people with arthritis have been well established; it is beneficial to quality of life and physical function and has been reported to reduce the risk of RA-induced cardiovascular disease [1, 2]. However, it is also well established that only a minority of RA patients meet existing physical activity guidelines. The current guidelines on physical activity issued by the World Health Organization in 2020 [3] state that older adults and adults living with chronic conditions should engage in a minimum of 150 min of moderate physical activity per week, or a minimum of 75 min of vigorous physical activity, or an

equivalent combination of moderate and vigorous physical activity. A recent study by Bell *et al.* [4] put the proportion of people with RA meeting these guidelines between 2 and 29%, depending on the precise definition used (because some definitions count activity only if it occurs in bouts of ≥ 10 min duration). At the same time, sedentary behaviour is highly prevalent, with the same study reporting an average of 10 h a day of sedentary behaviour. Other studies have reported similar findings [5–7]. In studies of people with inflammatory arthritis, participants reporting high amounts of sedentary behaviour compared with their peers were also more likely to have poor outcomes, including increased pain, inflammation, physical disability and risk of cardiovascular disease, in addition to reduced muscle density (cachexia and sarcopenia) and bone mass (osteopenia and osteoporosis) [8, 9]. As modifiable

Received: 22 December 2021. Accepted: 24 October 2022

© The Author(s) 2023. Published by Oxford University Press on behalf of the British Society for Rheumatology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

protective and risk factors for health outcomes in RA, influencing the amount of time that people with RA spend in physical activity and sedentary behaviour has the potential to improve health and quality-of-life outcomes. However, there are challenges to the accurate measurement of both the duration and the intensity of physical activity and the time spent in sedentary behaviour. Here, we review methods for measuring physical activity and discuss examples of these techniques being used in RA research.

Physical activity is usually banded by intensity levels. This is commonly done by referring to the metabolic equivalent of a task (MET), where 1 MET is equal to energy expenditure at rest (e.g. while sitting quietly). [Table 1](#) provides an overview of commonly used intensity categories of physical activity, with examples of specific activities within that category.

Although these categories provide an easy and intuitive overview of levels of physical activity, there are some issues worthy of discussion. Firstly, the reference MET of activities such as walking has typically been established in healthy young adults [10]. However, studies in people with inflammatory arthritis or OA have shown that the energy cost (and therefore the MET) of walking can differ by age, disability or disease status and can be influenced by surgical and non-surgical treatments [11–13]. It is therefore probably not accurate to assume that an activity such as walking will have a stable and equal energy cost for each patient with RA. Reference MET values for activities might therefore not be valid in people with RA.

Secondly, the question arises, which level of physical activity would generate a health benefit? In exercise physiology, it is assumed that only vigorous exercise leads to improvements in cardiovascular and musculoskeletal systems. However, this is framed in the context of improving sports performance in healthy, and usually younger, adults. For patients with RA, and indeed, for many other long-term conditions, it is clear that both moderate and vigorous physical activity provide health benefits. As a result, in many studies these two categories are lumped together as moderate and vigorous physical activity (MVPA) [4, 14–16]. In the context of measuring health behaviours, it is therefore of particular importance to be able accurately to identify moderate physical activity and above.

Although the science around physical activity and exercise has focused on METs, in popular discourse and in clinical practice, step counts have dominated. The idea that taking 10 000 steps/day comes with tangible health benefits has been widely adopted, although its origin lies in a Japanese commercial marketing ploy rather than in health research [17].

Table 1. Categories of physical activity based on level of energy expenditure

Category	Energy expenditure (MET)	Examples of activity
Inactive	<1.5	Seated desk working, watching TV, driving a car
Light	1.5–3.0	Standing desk working, slow walking
Moderate	3.0–6.0	Normal walking, easy cycling, manual labour
Vigorous	>6.0	Running, swimming and most other forms of exercise

MET: the metabolic equivalent of a task, where 1 MET is equal to energy expenditure at rest (e.g. while sitting quietly).

Subsequent research has established the partial validity of this target number, although it has been suggested that prevention of chronic illness would possibly require daily targets of $\leq 15\,000$ steps [18]. However, regardless of the validity of a specific value as a cut-off between amounts of physical activity that do not and do lead to improved fitness, daily step counts have the potential to be an easily communicable metric for discussing adequate amounts of physical activity if it can be shown that step counts are a valid measure of physical activity.

Measurement of physical activity

Any measurement tool will have to show adequate properties in terms of reproducibility, validity and responsiveness. Reproducibility is the ability to produce consistent results when measurements are repeated in similar conditions. Validity refers to the accuracy of the measurements. A valid measurement tool will not systematically over- or underestimate the characteristic it is measuring and will fully encompass the characteristic it intends to measure. For example, a tool for measurement of physical activity that assesses only vigorous activity would be less valid than a tool that assesses all of low, moderate and vigorous activity. Responsiveness means that the measurement tool is responsive to change; in this case, if there is a clear change in a person's physical activity, a responsive measurement tool should show a significant change in its metrics.

Physical activity measurements can be taken in a variety of settings, with different objectives. However, the vast majority will fit into one of two groups: experimental laboratory settings or daily life. In experimental studies in a controlled environment, the measurement of physical activity is often carried out to establish the difficulty of a specific activity (e.g. the energy cost of walking). This can be highly informative to establish the level of physical (dys)function and disability in people with long-term conditions, such as RA. The measures derived from these experimental studies can also inform the interpretation of data from the second type: real-life studies. In these, physical activity is tracked, usually for a continuous, longer period of time (e.g. 1 week), as the person goes about their daily life. Although both types of studies measure physical activity, the techniques used to establish physical activity are very different.

Laboratory assessment of physical activity

Laboratory measurements for physical activity tend to focus on establishing the energy expenditure or level of exertion associated with a specific activity (i.e. the intensity of a physical activity). Although the intensity of an activity can be expressed in METs, these METs cannot be measured directly and need to be calculated from measurable variables. This is usually done through respiratory gas analysis or calculation of the caloric cost of an activity, hence the term calorimetry as the overarching term for methods of measuring the intensity of a physical activity. Respiratory gas analysis is considered the gold standard for the direct measurement of activity intensity. During quiet sitting, the reference value for oxygen uptake is 3.5 ml/kg body mass/min, which equates to 1 MET. This can also be expressed as 1 kcal/kg body mass/h. However, it must be noted that these are not necessarily exact equivalents of each other, although they are used interchangeably in definitions of MET and energy expenditure. Food

intake [19, 20] and body composition [21] can affect the relationships between the intensity of an activity and the measured oxygen consumption. Also, at high intensities the energy expenditure will be, in part, through anaerobic metabolism, which will affect the validity of oxygen uptake as a measure of exertion.

A disadvantage of respiratory gas analysis is that it requires equipment, including a tight-fitting mask covering the mouth and nose, to be worn by the person being tested. Apart from considerations of complexity of the experimental set-up and discomfort, this might also have implications for the ecological validity of the measurement (i.e. the extent to which the test replicates the usual behaviour and activity performance of the participant).

To overcome these challenges, other measures of exertion have been used. Heart rate (HR) is an obvious candidate, and studies have established that there is a close correlation between HR and MET [22, 23]. Net HR (defined as current HR divided by HR at rest) appears to be slightly superior (i.e. more closely correlated) to MET than other HR measures, such as simply using current HR or metrics where HR at rest is subtracted from current HR. However, the differences in correlations with exertion, as measured by respiratory gas analysis and expressed in MET, between the different HR metrics are small, and all appear valid for use as indicators of current physical activity level.

Another option is to let the person being tested rate their own perceived level of exertion, usually on a numerical rating scale (e.g. 0–10), a visual analogue scale (e.g. 0–100 mm) or a Borg scale [24–26]. In healthy people, good correlations of ratings of perceived exertion with other measures of exertion have been reported [27, 28]. However, a study in people with RA reported only weak associations between the Borg scale of perceived exertion and HR measures during physical activity [29].

Measurement of physical activity in daily life

Measuring physical activity in daily life is markedly different from laboratory-based experimental studies. Rather than identifying the intensity of a single activity, the aim is usually to establish patterns of physical activity and sedentary behaviour over a prolonged period of time. In addition, measures need to be taken in the person's free-living environment rather than in a controlled laboratory setting. Three main types of measures have been used: doubly labelled water (DLW); measures based on body-worn sensors; and self-report through questionnaires and diaries.

The DLW technique uses the measurement in blood, saliva or urine of previously ingested stable isotopes of hydrogen (^2H or deuterium) and oxygen (^{18}O) to establish energy consumption over a prolonged period of time, usually 1–3 weeks. Through these measurements, the production of carbon dioxide over that period can be estimated accurately, which establishes the energy expenditure. It is considered a gold-standard technique for measuring total energy expenditure in living organisms, including humans [30], and does not interfere with the daily living of the participant at all, other than the need for collection of bodily fluid samples. However, there are also considerable limitations. Apart from the cost associated with the technique, the DLW technique does not allow the identification of patterns of physical activity [i.e. time spent in sedentary behaviour, light physical activity (LPA) and MVPA].

Identifying patterns of physical activity is the forte of techniques using body-worn sensors. A commonly used type of sensor is the accelerometer, a device that measures the acceleration of the body, to which it is attached. Uniaxial accelerometers detect any acceleration along the vertical axis. While walking, the centre of mass of the body will transfer a short distance up and down the vertical axis with every step, which is then detected by the accelerometer. Triaxial accelerometers additionally measure acceleration along the sagittal and frontal axes. These accelerometers are theoretically superior to uniaxial accelerometers because they should be able to detect types of physical activities other than walking with higher validity. However, a systematic review of accelerometry-based measurement of physical activity did not report a meaningful difference between uniaxial and triaxial accelerometry in determining total physical activity [31]. Nevertheless, there might be significant differences between the two methods in their ability to distinguish accurately between sedentary behaviour, LPA and MVPA.

The raw data provided by accelerometers identifies acceleration along one or three axes. Data processing then needs to ensure the raw data are translated into meaningful information on time spent in sedentary behaviour, LPA and MVPA. The raw acceleration data will show a periodic signal, with the amplitude and frequency of the signal for a given time interval imparting information on the intensity of the physical activity within that time period. Different methods have been used to identify activity from the duration, amplitude and/or frequency of the acceleration signal. For all commercially available devices, both those aimed at general usage and high-end devices for scientific research, the underlying algorithms for data processing will be proprietary and not available for scrutiny by third parties. An additional issue is that manufacturers might periodically update firmware and algorithms of their devices, or algorithms might be, in part, self-evolving through the use of machine-learning approaches, which potentially leads to systematic differences in sampling rates and signal processing within the same device at different time points.

A relatively accessible method used by various devices is based on cadence. After first establishing minimum thresholds for signal duration and amplitude, this method then uses the frequency of the signal to identify the cadence of the activity (e.g. in walking steps per minute). Accurate cut-off values of 100 steps/min for moderate activity and 130 steps/min for vigorous activity have been reported [32]. Therefore, 100 steps/min appears to be an adequate cadence value to establish MVPA in healthy adults [32]. The cut-off between sedentary behaviour and LPA tends to be put at a cadence of 40 steps/min, with counts <40 steps/min representing incidental or sporadic movement [33]. For physical activities other than walking (e.g. running or cycling), the thresholds for signal duration and amplitude and resulting cadence cut-offs might be different depending on the cyclical nature of the movement pattern of that activity. Studies have specifically established the validity of accelerometry for these other activities [34]. Other methods use algorithms to identify acceleration events from the data, with higher event counts signifying a higher intensity of physical activity, or use the position and movement of a specific body part (e.g. the thigh) to distinguish between sitting, standing and movement. In these methods, cut-off points between sedentary behaviour, LPA and MVPA are device specific and therefore not transferable between

different brands and types of devices. More advanced methods of data processing are also used to identify activity profiles from accelerometer data. These are often based on the comparison of known data shapes for a given activity at a given intensity with the data from a participant; a process known as template matching. With the advance of techniques from big-data analysis (e.g. machine learning), it is likely that these methods will continue to evolve, with the aim of improving the quality of metrics extracted from accelerometry.

There are several brands of accelerometry-based body-worn sensors. In recent years, a number of mass-market devices have become available, whose primary use is to monitor physical activity for the wearer, such as the FitBit, Polar and Apple activity monitors. These tend to have measurement properties that fall short of the required standard for use in scientific research, if the aim is to classify time intervals correctly as sedentary behaviour, LPA or MVPA.

As stated previously, daily step counts potentially offer an easy-to-understand metric that can be used in clinical practice to communicate targets. Most accelerometry devices will generate step counts as a metric. Generally, studies report moderate to strong correlations between daily step counts and total energy expenditure [35, 36]. However, the validity of step counts might differ depending on the intensity of physical activity, with different validity profiles for different devices. Stenbäck *et al.* [37] showed that step count accuracy can be compromised at low walking speeds. This is particularly relevant given the prevalence of walking disability in people with inflammatory arthritis, which reduces self-selected walking speed. Therefore, although step counts are undoubtedly useful to discuss physical activity targets and behaviour between patients and clinicians, their validity is likely to be insufficient for use as a clinical outcome measure.

A third major type of measure of physical activity in daily life is by self-report through standardized questionnaires or diaries. There are a number of questionnaires available that aim to establish the amount of time spent in sedentary behaviour, LPA and/or MVPA. Many different questionnaires for the measurement of physical activity have been developed. A 2010 systematic review of measurement properties of physical activity questionnaires included no fewer than 85 different ones [38]. Its overall conclusion was that there was no single questionnaire that was clearly superior in terms of reproducibility and validity. In general, measures of reproducibility and validity tended to be acceptable but not excellent. However, there were meaningful differences between questionnaires in terms of the populations for which they have been developed and validated (e.g. healthy adults, specific diagnostic groups, children), the setting in which they assess physical activity (e.g. sports, recreational activity, mobility and transport, occupational activity, home) and the metrics that are calculated (e.g. total energy expenditure or time spent in the different physical activity intensity bands).

Other means of collecting real-life physical activity data are potentially available. Online exercise communities habitually log large amounts of exercise data, generally comprising Global Positioning System (GPS) data points. Some providers have started to present analyses based on large amounts of aggregate data (e.g. Strava Labs; <https://labs.strava.com> (6 December 2022, date last accessed)). Although these platforms might provide good insight into time spent in MVPA of their users, the validity of the data is dependent on users logging all activity and on the accuracy of the GPS-based data-

collection systems. Owing to the nature of these communities and platforms, which are almost exclusively aimed at sports and exercise, it is unlikely that these can provide meaningful data on time spent in sedentary behaviour and LPA.

Nevertheless, GPS-based data collection is potentially an exciting new mode of assessing physical activity, because it brings with it the opportunity to incorporate characteristics of the physical environment (e.g. elevation, availability of green space, traffic density) into the activity monitoring. These environmental characteristics might be crucial to determining the physical activity that people engage in, but have so far been described poorly in research. However, issues of privacy and confidentiality will have to be addressed before GPS tracking of research participants is feasible within acceptable ethical boundaries.

Measurement of physical activity in people with RA

A variety of the techniques discussed above have been used to assess physical activity specifically in people with RA. Early studies primarily focused on low physical activity levels in daily life as a potential explanation for the elevated risk of cardiovascular disease in patients with RA. Metsios *et al.* [39] used the international physical activity questionnaire (IPAQ) to classify participants as active, moderately active or inactive. They then established clear differences in risk factors for cardiovascular disease between the three groups, in favour of the active group.

The IPAQ identifies physical activity in the previous 7 days, by self-report, for the domains work, transport, domestic duties, leisure (including sports and exercise) and sedentary behaviour. A short form version (IPAQ-SF) is available in different languages, which condenses the original 31 questions into 7. Although it is a generic rather than disease-specific tool, the IPAQ is currently one of the most commonly used physical activity questionnaires in RA research [40–42]. However, evidence of its reproducibility and validity in this population is scarce. Tierney *et al.* [43] found poor criterion validity of the IPAQ-SF when compared with a previously validated objective measure of physical activity. In other populations similar to the RA population, such as people with OA or people who had undergone total hip or knee replacement, fair to good reproducibility was reported, but poor concurrent validity [44–46].

Other questionnaires have also been used in RA, with similar findings. These include the physical activity frequency questionnaire (PAFQ) [47], the nurses' health study physical activity questionnaire (NHSPAQ) [48] and the global physical activity questionnaire (GPAQ) [49]. In general, questions can be asked about the accuracy with which questionnaires estimate the type, intensity and frequency of physical activity in people with RA. Owing to the systematic bias in estimating time spent in physical activity, and particularly in MVPA, questionnaires are not suitable for establishing whether people with RA meet the guidelines for time spent in physical activity or for accurate calculation of total energy expenditure. For establishing relationships between physical activity and other aspects of health and quality of life, large sample sizes would be needed because of the low statistical power resulting from the use of questionnaires with mediocre reproducibility.

Increasingly, objective methods are being used in RA studies to address these issues with self-reported physical activity.

Paul *et al.* [5] used respiratory gas analysis to identify the energy cost of walking in people with RA compared with healthy controls, in a controlled laboratory environment. This study reported no difference in energy cost between the two groups but did note a lower self-selected walking speed in people with RA compared with healthy controls.

Most other studies have used free-living assessments of physical activity. The DLW technique was used by Roubenoff *et al.* [50], who concluded that total energy expenditure was lower in women with RA compared with healthy controls. A potential issue with the DLW technique in RA or other inflammatory conditions is that the metabolic rate might be affected by RA disease activity. However, it is likely that inflammation increases the metabolic rate [51] and would therefore lead to an overestimation of physical activity when using DLW; the finding that energy expenditure in RA is lower than in healthy controls would therefore only be more pronounced if this effect were to be taken into account. It has also been confirmed by a number of studies using body-worn activity monitors [4, 7]. These studies have consistently reported that only a minority of people with RA spend sufficient time in MVPA to meet guidelines on physical activity, that time spent in MVPA is significantly reduced compared with healthy controls, and that sedentary behaviour is more frequent in people with RA than in healthy controls.

Fortunately, validation studies have been carried out on body-worn sensor techniques for physical activity monitoring in people with RA. The ActivPAL activity monitor was deemed valid for measuring time spent in sedentary behaviour, standing and walking, although it did underestimate the number of steps and transitions when compared with direct observation in a controlled laboratory environment [52]. Another study concluded that the ActivPAL accurately quantifies sedentary, standing and stepping time [53]. This study also included validation of the ActiGraph GT3X+ activity monitor, with similar findings to the ActivPAL. Both devices therefore appear suitable for use in people with RA. Recently, innovative devices, such as the Actiheart, have been used in RA studies [54]. This device combines electrocardiography and accelerometry to obtain both HR and uniaxial acceleration of the trunk to assess physical activity, which might offer further refinement of the accelerometry-based method. Although the results of research using the Actiheart in people with RA are consistent with findings using other devices, it has not been validated specifically for use in RA populations yet.

It must be noted that gait abnormalities are common in RA [55], in particular reduced walking speed and cadence and increased double limb support time (i.e. the phase of the gait when both feet touch the ground). As previously mentioned, accelerometry might be less reliable and valid at lower walking speeds and cadences. It is therefore imperative that devices are validated specifically in RA populations.

Table 2 provides a summary of the methods that were used in studies with RA patients to assess physical activity, including information on their measurement properties, as established in the studies discussed previously, and suitable outcome parameters in this population.

Discussion

The assessment of physical activity levels in people with RA is increasingly seen as important, owing to the established evidence on the increased risk of cardiovascular disease

subsequent to RA and the poor general health and lower quality of life in people with RA who engage in high levels of sedentary behaviour and low levels of physical activity. Studies have shown these behaviours to be highly prevalent in RA, with relatively few patients meeting guidelines on the frequency and intensity of physical activity [4]. However, as this review has shown, the measurement of physical activity in people with RA can be challenging.

In controlled laboratory environments, respiratory gas analysis can establish the energy cost of activity with high validity and precision, but it can be burdensome to participants and might not reflect the behaviour of participants in daily life. In free-living environments, a number of methods are available, each of which has advantages and disadvantages. The DLW technique is the gold standard but is limited to establishing total energy expenditure over time rather than patterns of sedentary behaviour and physical activity. It is also cost prohibitive. Questionnaires can offer a cheaper alternative and the opportunity to estimate time spent in sedentary behaviour, LPA and MVPA, but there are significant questions regarding their validity and reproducibility. Body-worn accelerometers currently offer the best-available solution, with acceptable reproducibility and validity. Innovative devices that incorporate additional information to accelerometry (e.g. HR) might improve the measurement characteristics of these devices further.

Implementation of routine physical activity assessment using body-worn sensors in clinical practice can be challenging. In particular, embedding the logistical process and data processing into clinical practice will require careful consideration. Sensors are usually worn for several days, and although instructions and fitting can conceivably be done after a clinical appointment, returning the device after completion of the wear period will need to be arranged separately or achieved by postal return. Data processing can be done with automated algorithms but does require oversight and for data handling to be compliant with regulations on confidentiality and data security. Nevertheless, it provides the opportunity to make rich behavioural data available, allowing patients and their clinicians to set outcome targets for healthy physical activity.

Interestingly, a recent study has suggested that a decrease in physical activity, as recorded by a body-worn monitor, might serve as an early indicator for an RA flare [56]. This study used machine-learning algorithms to establish patterns in the physical activity data, which could then identify RA disease flares with very high sensitivity and specificity when compared with patient self-report of disease activity flares. This is an excellent example of how machine learning and other big-data techniques might offer a leap forwards in extracting the meaning from the high volumes of data that can be extracted from activity monitors that are worn for a considerable length of time.

The potential relationship between sedentary behaviour and physical activity patterns on the one hand and RA disease activity or symptom severity on the other hand was also highlighted in a study using qualitative methods [57]. Although physical activity research has largely been the domain of quantitative methods, qualitative research can add a unique perspective on behaviour patterns. In particular, qualitative research can elucidate which barriers and facilitators people with RA encounter and perceive when trying to maintain or improve a healthy lifestyle. Currently, only one quantitative study has been published identifying barriers and

Table 2. Methods for assessing physical activity and sedentary behaviour in people with RA

Method	Measurement	Setting	Outcome	Properties	Example of use in RA research
Respiratory gas analysis	Oxygen cost of activity	Controlled laboratory; immediate measurement	Intensity of activity	Good validity and reproducibility; low ecological validity; high participant burden	Paul <i>et al.</i> [5]
Doubly labelled water	Turnover of hydrogen and oxygen isotopes to assess carbon dioxide production	Free-living environment; >5 days	Total energy expenditure	Gold-standard method. High reproducibility and validity; low participant burden	Roubenoff <i>et al.</i> [50]
Questionnaires/diaries	Self-reported activity	Free-living environment; unlimited period	Total energy expenditure; patterns of SB, LPA and MVPA	Fair reproducibility and poor validity; moderate participant burden	Yu <i>et al.</i> [41]
Body-worn activity monitors (accelerometry)	Acceleration of the body or body segment	Free-living environment; 1–10 days	Total energy expenditure; patterns of SB, LPA and MVPA	Good reproducibility and validity; moderate participant burden	Bell <i>et al.</i> [4]

LPA: light physical activity; MVPA: moderate-to-vigorous physical activity; SB: sedentary behaviour.

facilitators to engagement in physical activity in RA [49]. This study identified a number of potential personal and environmental factors that might contribute to people engaging in physical activity or not. High-scoring barriers included lack of affordable and available facilities, low exercise self-efficacy, symptoms such as pain and fatigue limiting the activity that patients can engage in, and lack of suitable exercise offers for people with RA. Qualitative or mixed-methods research should be used to identify these lived experiences of patients with RA in their own words, rather than relying on set items from questionnaires.

The responsiveness of methods to assess physical activity has not featured in this review so far. There have been few intervention trials using physical activity monitoring as an outcome measure. Thomsen *et al.* [58] used ActivPAL accelerometry in a trial with reduction in sedentary behaviour as its primary objective. This study found a statistically significant positive effect of the intervention in reducing sedentary behaviour compared with the control group, which suggests that physical activity monitoring can be a responsive outcome measure in intervention research. A second trial on this topic was published recently [59]. For physical activity to become a key outcome measure in intervention research, the responsiveness of methods for measuring physical activity must be established.

In conclusion, several methods are available to assess physical activity in people with RA. To establish the energy cost of an activity, respiratory gas analysis in a controlled laboratory setting is currently the method of choice. In free-living environments, DLW techniques are the gold standard if the aim is to establish total energy expenditure over an extended period of time. To establish patterns of sedentary behaviour and physical activity, body-worn physical activity monitors based on accelerometry provide the best available method.

Data availability

No original data were used in this paper. All information contained herein is from previously published research.

Funding

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: All three authors previously received a grant from PAL Technologies Ltd for research using the ActivPAL activity monitor.

References

1. Rausch Osthoff AK, Niedermann K, Braun J *et al.* 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. *Ann Rheum Dis* 2018;77:1251–60.
2. Hammam N, Ezeugwu VE, Rumsey DG, Manns PJ, Pritchard-Wiart L. Physical activity, sedentary behavior, and long-term cardiovascular risk in individuals with rheumatoid arthritis. *Phys Sportsmed* 2019;47:463–70.
3. WHO guidelines on physical activity and sedentary behaviour. 2020. <https://www.who.int/publications/i/item/9789240015128> (6 December 2022, date last accessed).
4. Bell K, Hendry G, Steultjens M. Physical activity and sedentary behaviour in people with inflammatory joint disease: a cross-sectional study. *Arthritis Care Res (Hoboken)* 2022;74:493–500.
5. Paul L, Rafferty D, Marshall-McKenna R *et al.* Oxygen cost of walking, physical activity, and sedentary behaviours in rheumatoid arthritis. *Scand J Rheumatol* 2014;43:28–34.
6. O'Brien CM, Ntoumanis N, Duda JL *et al.* Pain and fatigue are longitudinally and bi-directionally associated with more sedentary time and less standing time in rheumatoid arthritis. *Rheumatology (Oxford)* 2021;60:4548–57.
7. Summers G, Booth A, Brooke-Wavell K, Barami T, Clemes S. Physical activity and sedentary behavior in women with rheumatoid arthritis: a comparison of patients with low and high disease activity and healthy controls. *Open Access Rheumatol* 2019;11:133–42.
8. Fenton SAM, Veldhuijzen van Zanten JJCS, Duda JL, Metsios GS, Kitas GD. Sedentary behaviour in rheumatoid arthritis: definition, measurement and implications for health. *Rheumatology (Oxford)* 2018;57:213–26.
9. O'Leary H, Larkin L, Murphy GM, Quinn K. Relationship between pain and sedentary behavior in rheumatoid arthritis

- patients: a cross-sectional study. *Arthritis Care Res (Hoboken)* 2021;73:990–7.
10. Ainsworth BE, Haskell WL, Leon AS. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sport Exerc* 1993;25:71–80.
 11. Waters RL, Perry J, Conaty P, Lunsford B, O'Meara P. The energy cost of walking with arthritis of the hip and knee. *Clin Orthop Relat Res* 1987;214:278–84.
 12. Mattsson E, Broström LA, Linnarsson D. Changes in walking ability after knee replacement. *Int Orthop* 1990;14:277–80.
 13. Takacs J, Kirkham AA, Perry F *et al.* Lateral trunk lean modification increases the energy cost of treadmill walking in those with knee osteoarthritis. *Osteoarthritis Cartil* 2014;22:203–9.
 14. Legge A, Blanchard C, Hanly JG. Physical activity and sedentary behavior in patients with systemic lupus erythematosus and rheumatoid arthritis. *Open access Rheumatol* 2017;9:191–200.
 15. Sobejana M, van den Hoek J, Metsios GS *et al.* Cardiorespiratory fitness and physical activity in people who have rheumatoid arthritis at an increased risk of cardiovascular disease: a cross-sectional study. *Rheumatol Int* 2021;41:2177–83.
 16. Toyoshima Y, Yajima N, Nemoto T, Namiki O, Inagaki K. Relationship between disease activity level and physical activity in rheumatoid arthritis using a triaxial accelerometer and self-reported questionnaire. *BMC Res Notes* 2021;14:242.
 17. Calechman S. 10,000 steps a day — or fewer? <https://www.health.harvard.edu/blog/10000-steps-a-day-or-fewer-2019071117305> (6 December 2022, date last accessed).
 18. Tigbe WW, Granat MH, Sattar N, Lean MEJ. Time spent in sedentary posture is associated with waist circumference and cardiovascular risk. *Int J Obes (Lond)* 2017;41:689–96. doi:10.1038/ijo.2017.30
 19. Ueda C, Hamaoka T, Murase N *et al.* Food intake increases resting muscle oxygen consumption as measured by near-infrared spectroscopy. *Eur J Sport Sci* 2002;2:1–9.
 20. Larsen FJ, Weitzberg E, Lundberg JO, Ekblom B. Effects of dietary nitrate on oxygen cost during exercise. *Acta Physiol (Oxford)* 2007;191:59–66.
 21. McInnis KJ, Balady GJ. Effect of body composition on oxygen uptake during treadmill exercise: body builders versus weight-matched men. *Res Q Exerc Sport* 1999;70:150–6.
 22. Caballero Y, Ando TJ, Nakae S *et al.* Simple prediction of metabolic equivalents of daily activities using heart rate monitor without calibration of individuals. *Int J Environ Res Public Health* 2019;17:216.
 23. Yamamoto S, Ishida T, Misawa K *et al.* The simple method for predicting metabolic equivalents using heart rate in patients with cardiovascular disease. *Int J Cardiol Heart Vasc* 2018;19:88–9.
 24. Melton-Rogers S, Hunter G, Walter J, Harrison P. Cardiorespiratory responses of patients with rheumatoid arthritis during bicycle riding and running in water. *Phys Ther* 1996;76:1058–65.
 25. Hall J, Grant J, Blake D, Taylor G, Garbutt G. Cardiorespiratory responses to aquatic treadmill walking in patients with rheumatoid arthritis. *Physiother Res Int* 2004;9:59–73.
 26. Kim BR, Kim SR, Nam KW *et al.* Effects of body weight support and gait velocity via antigravity treadmill on cardiovascular responses early after total knee arthroplasty. *Medicine (Baltimore)* 2020;99:e19586.
 27. Zinoubi B, Zbidi S, Vandewalle H, Chamari K, Driss T. Relationships between rating of perceived exertion, heart rate and blood lactate during continuous and alternated-intensity cycling exercises. *Biol Sport* 2018;35:29–37.
 28. Alberton CL, Antunes AH, Pinto SS *et al.* Correlation between rating of perceived exertion and physiological variables during the execution of stationary running in water at different cadences. *J Strength Cond Res* 2011;25:155–62.
 29. Brodin N, Bobst N, Opava CH. SAT0732-HPR Rating of perceived exertion in patients with rheumatoid arthritis – which are the correlates? *Ann Rheum Dis* 2018;77(Suppl 2):1827.
 30. Hallal PC, Reichert FF, Clark VL *et al.* Energy expenditure compared to physical activity measured by accelerometry and self-report in adolescents: a validation study. *PLoS One* 2013;8:e77036.
 31. Jeran S, Steinbrecher A, Pischon T. Prediction of activity-related energy expenditure using accelerometer-derived physical activity under free-living conditions: a systematic review. *Int J Obes* 2016;40:1187–1197.
 32. Tudor-Locke C, Aguiar EJ, Han H *et al.* Walking cadence (steps/min) and intensity in 21–40 year olds: CADENCE-adults. *Int J Behav Nutr Phys Act* 2019;16:8.
 33. Webber SC, Strachan SM, Pachu NS. Sedentary behavior, cadence, and physical activity outcomes after knee arthroplasty. *Med Sci Sports Exerc* 2017;49:1057–65.
 34. Bonomi AG, Goris AHC, Yin B, Westerterp KR. Detection of type, duration, and intensity of physical activity using an accelerometer. *Med Sci Sports Exerc* 2009;41:1770–77.
 35. Bassett DRJ, Toth LP, LaMunion SR, Crouter SE. Step counting: a review of measurement considerations and health-related applications. *Sports Med* 2017;47:1303–15.
 36. Montes J, Tandy R, Young J, Lee SP, Navalta JW. Step count reliability and validity of five wearable technology devices while walking and jogging in both a free motion setting and on a treadmill. *Int J Exerc Sci* 2020;13:410–26.
 37. Stenbäck V, Leppäluoto J, Leskelä N *et al.* Step detection and energy expenditure at different speeds by three accelerometers in a controlled environment. *Sci Rep* 2021;11:20005.
 38. van Poppel MNM, Chinapaw MJM, Mokkink LB, van Mechelen W, Terwee CB. Physical activity questionnaires for adults: a systematic review of measurement properties. *Sports Med* 2010;40:565–600.
 39. Metsios GS, Stavropoulos-Kalinoglou A, Panoulas VF *et al.* Association of physical inactivity with increased cardiovascular risk in patients with rheumatoid arthritis. *Eur J Cardiovasc Prev Rehabil* 2009;16:188–94.
 40. Baday-Keskin D, Ekinci B. The relationship between kinesiophobia and health-related quality of life in patients with rheumatoid arthritis: a controlled cross-sectional study. *Joint Bone Spine* 2022;89:105275.
 41. Yu C-a, Rouse PC, Veldhuijzen Van Zanten JJCS *et al.* Subjective and objective levels of physical activity and their association with cardiorespiratory fitness in rheumatoid arthritis patients. *Arthritis Res Ther* 2015;17:59.
 42. Davigrne T, Tekaya R, Sellam J *et al.* Influence of perceived barriers and facilitators for physical activity on physical activity levels in patients with rheumatoid arthritis or spondyloarthritis: a cross-sectional study of 150 patients. *BMC Musculoskelet Disord* 2021;22:915.
 43. Tierney M, Fraser A, Kennedy N. Criterion validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF) for use in patients with rheumatoid arthritis: comparison with the SenseWear Armband. *Physiotherapy* 2015;101:193–7.
 44. Joseph KL, Dagfinrud H, Christie A, Hagen KB, Tveter AT. Criterion validity of The International Physical Activity Questionnaire-Short Form (IPAQ-SF) for use in clinical practice in patients with osteoarthritis. *BMC Musculoskelet Disord* 2021;22:232.
 45. Blikman T, Stevens M, Bulstra SK, Van Den Akker-Scheek I, Reininga IHF. Reliability and validity of the Dutch version of the international physical activity questionnaire in patients after total hip arthroplasty or total knee arthroplasty. *J Orthop Sports Phys Ther* 2013;43:650–9.
 46. Smith RD, McHugh GA, Quicke JG, Dziedzic KS, Healey EL. Comparison of reliability, construct validity and responsiveness of the IPAQ-SF and PASE in adults with osteoarthritis. *Musculoskelet Care* 2021;19:473–483.
 47. Henchoz Y, Bastardot F, Guessous I *et al.* Physical activity and energy expenditure in rheumatoid arthritis patients and matched controls. *Rheumatology (Oxford)* 2012;51:1500–7.

48. Quinn T, Frits M, von Heideken J *et al.* Validity of the Nurses' health study physical activity questionnaire in estimating physical activity in adults with rheumatoid arthritis. *BMC Musculoskelet Disord* 2017;18:234.
49. Tan XL, Pugh G, Humby F, Morrissey D. Factors associated with physical activity engagement among adults with rheumatoid arthritis: a cross-sectional study. *Musculoskelet Care* 2019;17:163–73.
50. Roubenoff R, Walsmith J, Lundgren N *et al.* Low physical activity reduces total energy expenditure in women with rheumatoid arthritis: implications for dietary intake recommendations. *Am J Clin Nutr* 2002;76:774–9.
51. Kominsky DJ, Campbell EL, Colgan SP. Metabolic shifts in immunity and inflammation. *J Immunol* 2010;184:4062–8.
52. Larkin L, Nordgren B, Purtill H *et al.* Criterion validity of the activPAL activity monitor for sedentary and physical activity patterns in people who have rheumatoid arthritis. *Phys Ther* 2016;96:1093–101.
53. O'Brien CM, Duda JL, Kitas GD *et al.* Measurement of sedentary time and physical activity in rheumatoid arthritis: an ActiGraph and activPALTM validation study. *Rheumatol Int* 2020;40:1509–18.
54. Hörnberg K, Pomeroy J, Sandberg C *et al.* Isotemporal substitution of time between sleep and physical activity: associations with cardiovascular risk factors in early rheumatoid arthritis. *ACR Open Rheumatol* 2021;3:138–46.
55. Carroll M, Parmar P, Dalbeth N, Boock M, Rome K. Gait characteristics associated with the foot and ankle in inflammatory arthritis: a systematic review and meta-analysis. *BMC Musculoskelet Disord* 2015;16:134.
56. Gossec L, Guyard F, Leroy D *et al.* Detection of flares by decrease in physical activity, collected using wearable activity trackers in rheumatoid arthritis or axial spondyloarthritis: an application of machine learning analyses in rheumatology. *Arthritis Care Res* 2019;71:1336–43.
57. Thomsen T, Beyer N, Aadahl M *et al.* Sedentary behaviour in patients with rheumatoid arthritis: a qualitative study. *Int J Qual Stud Health Well-being* 2015;10:28578. doi:10.3402/qhw.v10.28578
58. Thomsen T, Aadahl M, Beyer N *et al.* The efficacy of motivational counselling and SMS reminders on daily sitting time in patients with rheumatoid arthritis: a randomised controlled trial. *Ann Rheum Dis* 2017;76:1603–6.
59. Pinto AJ, Peçanha T, Meireles K *et al.* A randomized controlled trial to reduce sedentary time in rheumatoid arthritis: protocol and rationale of the Take a STAND for Health study. *Trials* 2020;21:171.

A 2nd generation, JAK1 preferential inhibitor for moderate to severe RA¹⁻⁶

While 1st generation JAK inhibitors are relatively non-selective,²⁻⁶ JYSELECA has over 5x greater potency for JAK1 over JAK2/3 and TYK2^{1*}

Balancing sustained efficacy⁷⁻¹¹ with acceptable tolerability^{1,12}

Indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs.¹ May be used as monotherapy or in combination with methotrexate.¹

*From biochemical assays, the clinical relevance of which is uncertain. JAK, Janus kinase; RA, rheumatoid arthritis; TYK, tyrosine kinase.

Learn more at
strengthofbalance.co.uk

Refer to Summary of Product Characteristics (SmPC) before prescribing, and for full prescribing information.

JYSELECA[®] filgotinib 100 mg or 200 mg film-coated tablets.

Indication: Jyseleca is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs (DMARDs). Jyseleca may be used as monotherapy or in combination with methotrexate (MTX). **Dosage: Adults:** 200 mg once daily. Taken orally with/without food. It is recommended that tablets are swallowed whole. **Laboratory Monitoring:** Refer to the SmPC for information regarding laboratory monitoring and dose initiation or interruption. **Elderly:** A starting dose of 100 mg once daily is recommended for patients aged 75 years and older as clinical experience is limited. **Renal impairment:** No dose adjustment required in patients with estimated creatinine clearance (CrCl) \geq 60 mL/min. A dose of 100 mg of filgotinib once daily is recommended for patients with moderate or severe renal impairment (CrCl 15 to < 60 mL/min). Not recommended in patients with CrCl < 15 mL/min. **Hepatic impairment:** Mild/moderate hepatic impairment: no dose adjustment required. Severe hepatic impairment: not recommended. **Children (< 18 years):** Safety and efficacy not yet established. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Active tuberculosis (TB) or active serious infections. **Pregnancy/Warnings/Precautions:** See SmPC for full information. **Immunosuppression:** Combination use, with immunosuppressants e.g., ciclosporin, tacrolimus, biologics or other Janus kinase (JAK) inhibitors is not recommended as a risk of additive immunosuppression cannot be excluded. **Infections:** Infections, including serious infections such as pneumonia and opportunistic infections e.g. tuberculosis (TB), oesophageal candidiasis, and cryptococcosis have been reported. Risk benefit should be assessed prior to initiating in patients with risk factors for infections (see SmPC). Patients should be closely monitored for the development of signs and symptoms of infections during and after filgotinib treatment. Treatment should be interrupted if the patient

is not responding to antimicrobial therapy, until infection is controlled. There is a higher incidence of serious infections in the elderly aged 75 years and older, caution should be used when treating this population. **Tuberculosis:** Patients should be screened for TB before initiating filgotinib, and filgotinib should not be administered to patients with active TB. **Viral reactivation:** Cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical studies (see SmPC). If a patient develops herpes zoster filgotinib treatment should be temporarily interrupted until the episode resolves. Screening for viral hepatitis and monitoring for reactivation should be performed. **Malignancy:** Immunomodulatory medicinal products may increase the risk of malignancies. Malignancies were observed in clinical studies (see SmPC). **Fertility:** In animal studies, decreased fertility, impaired spermatogenesis, and histopathological effects on male reproductive organs were observed (see SmPC). The potential effect of filgotinib on sperm production and male fertility in humans is currently unknown. **Haematological abnormalities:** Do not start therapy, or temporarily stop, if Absolute Neutrophil Count (ANC) < 1×10^9 cells/L, ALC < 0.5×10^9 cells/L or haemoglobin < 8 g/dL. Temporarily stop therapy if these values are observed during routine patient management. **Vaccinations:** Use of live vaccines during, or immediately prior to, filgotinib treatment is not recommended. **Lipids:** Treatment with filgotinib was associated with dose dependent increases in lipid parameters, including total cholesterol, and high-density lipoprotein (HDL) levels, while low density lipoprotein (LDL) levels were slightly increased (see SmPC). **Cardiovascular risk:** Rheumatoid arthritis patients have an increased risk for cardiovascular disorders. Patients should have risk factors (e.g., hypertension, hyperlipidaemia) managed as part of usual standard of care. **Venous thromboembolism:** Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving JAK inhibitors including filgotinib. Caution should be used in patients with risk factors for DVT/PE, such as older age, obesity, a medical history of DVT/PE, or patients undergoing surgery, and prolonged

immobilisation. **Lactose content:** Contains lactose; patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take filgotinib. **Pregnancy/Lactation:** Filgotinib is contraindicated in pregnancy. Filgotinib should not be used during breast-feeding. Women of childbearing potential must use effective contraception during and for at least 1 week after cessation of treatment. **Driving/Using machinery:** No or negligible influence, however dizziness has been reported. **Side effects:** See SmPC for full information. **Common (\geq 1/100 to <1/10):** nausea, upper respiratory tract infection, urinary tract infection and dizziness. **Uncommon (\geq 1/1000 to <1/100):** herpes zoster, pneumonia, neutropenia, hypercholesterolaemia and blood creatine phosphokinase increase. **Serious side effects:** See SmPC for full information. **Legal category:** POM. **Pack:** 30 film-coated tablets/bottle. **Price:** UK Basic NHS cost: £863.10. **Marketing authorisation number(s):** Great Britain Jyseleca 100mg film-coated tablets PLGB 42147/0001 Jyseleca 200mg film-coated tablets PLGB 42147/0002 Northern Ireland Jyseleca 100mg film-coated tablets EU/1/20/1480/001 EU/1/20/1480/002 Jyseleca 200mg film-coated tablets EU/1/20/1480/003 EU/1/20/1480/004. **Further information:** Galapagos UK, Belmont House, 148 Belmont Road, Uxbridge UB8 1QS, United Kingdom 00800 7878 1345 medicalinfo@glog.com Jyseleca[®] is a trademark. **Date of Preparation:** January 2022 UK-RA-FIL-202201-00019

∇ Additional monitoring required

Adverse events should be reported.

For Great Britain and Northern Ireland, reporting forms and information can be found at yellowcard.mhra.gov.uk or via the Yellow Card app (download from the Apple App Store or Google Play Store).

Adverse events should also be reported to Galapagos via email to DrugSafety.UK.Ireland@glog.com or 00800 7878 1345

References: 1. JYSELECA SPC. Available at: www.medicines.org.uk. Last accessed: June 2022. 2. Angelini J, et al. *Biomolecules* 2020;10(7):E1002. 3. Banerjee S, et al. *Drugs* 2017;77:521-546. 4. O'Shea JJ, et al. *Nat Rev Rheumatol* 2013;9(3):173-182. 5. Traves PG, et al. *Ann Rheum Dis* 2021;01-11. 6. McInnes IB, et al. *Arthr Res Ther* 2019;21:183. 7. Combe B, et al. *Ann Rheum Dis* 2021;doi:10.1136/annrheumdis-2020-219214. 8. Genovese MC, et al. *JAMA* 2019;322(4):315-325. 9. Westhovens R, et al. *Ann Rheum Dis* 2021;doi:10.1136/annrheumdis-2020-219213. 10. Combe B, et al. *Arthritis Rheumatol* 2021;73(suppl 10). <https://acrabstracts.org/abstract/clinical-outcomes-up-to-week-48-of-filgotinib-treatment-in-an-ongoing-long-term-extension-trial-of-rt-patients-with-inadequate-response-to-mtx-initially-treated-with-filgotinib-or-adalimumab-during-th/>. Last accessed: June 2022. 11. Buch MH, et al. *Arthritis Rheumatol* 2021;73(suppl 10). <https://acrabstracts.org/abstract/clinical-outcomes-up-to-week-48-of-ongoing-filgotinib-ra-long-term-extension-trial-of-biologic-dmard-inadequate-responders-initially-on-filgotinib-or-placebo-in-a-phase-3-trial/>. Last accessed: June 2022. 12. Winthrop K, et al. *Arthritis Rheumatol* 2021;73(suppl 10). Available at: <https://acrabstracts.org/abstract/integrated-safety-analysis-update-for-filgotinib-in-patients-with-moderately-to-severely-active-rheumatoid-arthritis-receiving-treatment-over-a-median-of-2-2-years/>. Last accessed: June 2022.

Galápagos

June 2022 GB-RA-JY-202205-00033

JYSELECA, GALAPAGOS and the JYSELECA and GALAPAGOS logos are registered trademarks of Galapagos NV. © 2022 Galapagos NV. All rights reserved.