INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease, which causes inflammation of joints and damage to organs of the body [1]. Poor sleep has been identified as a major concern for people with RA, with disturbed sleep and fatigue known to affect up to 70% in this population [2, 3, 4]. This consequently influences their health-related quality of life (HQoL), in addition to their mental and physical health, and may lead to people with RA not being as physically active compared to their more healthier counterparts [5, 6]. Sleep is an important aspect in maintaining the body’s circadian rhythm and is an important factor that influences mood, physical and cognitive performance, and daytime sleepiness [7]. In general getting less than 5 hours sleep per day has been associated with cardiovascular issues, diabetes and obesity and can also be linked to depression, anxiety and poor productivity, with sleep debt representing an ever growing epidemic [8].

It has been well established that being physically active and taking regular exercise are important for those who have been diagnosed with RA [9]. Increases in muscle strength, improvements in cardiovascular fitness and reduction in pain have been shown following participation in exercise and those with increased levels of self-efficacy for physical activity (PA) are more likely to achieve any self-set goals [9, 10]. It is known that in general exercise improves mood state, which can also be an additional factor in improving total sleep time (TST) [11]. Exercise has been identified as an important part of the nonpharmacological management of poor sleep and in improving sleep quality however, in a 2013 Cochrane review that examined exercise and fatigue in RA, it was noted by the authors that sleep quality was yet to be examined in this population [12].

Several studies have investigated the effects of physical activity (PA) and exercise on sleep in other populations [13, 14] and, while results suggest they are beneficial, it is unclear how
large these benefits are. Optimal sleep duration and exercise have been associated with reduced inflammatory bio-markers of cardiovascular disease (CVD) risk [15]. With people who have RA showing a greater than two fold higher risk of myocardial infarction and an almost four times higher number of cardiovascular events [16], there are distinct benefits in investigating both sleep and physical activity, in addition to their relationship with disease related variables, in this population.

While people with RA’s subjective experience of their sleep and activity variables have been reported [3, 4], what has yet to be fully explored or evaluated is the relationship between objectively measured sleep and PA in this population. Newly developed portable instruments provide a less expensive and objective alternative to Polysomnography (PSG) and are a potentially more accurate method of measuring sleep quality in a free-living environment than self-report measures [17]. The SenseWear Pro3 Armband™ (SWA) distinguishes between sedentary activities and sleep and is an accurate measure of TST, which is comparable to existing sleep detection devices [18]. In addition SWA has been shown to have high agreement (85%) with polysomnography (PSQ) in people with lower back pain (LBP), for total sleep time, sleep efficiency and wake after sleep [19]. The device has also been validated to measure moderate to vigorous physical activity (MPVA) [20, 21, 22], and energy expenditure in a number of different populations [23, 24].

Thus, this exploratory study aims to objectively measure total sleep time (TST) and MVPA duration in people with RA; to examine any associations between TST, MVPA duration and related disease variables, in addition to determining what participants were physically active for a minimum of 30+ minutes, 5 times per week.
METHODS

Study Design and Participants

The STROBE reporting guidelines for observational studies were used to guide the reporting of this study [25]. A cross-sectional, two centre, study design was used to recruit people with RA attending rheumatology outpatient clinics. Participants had to have a confirmed diagnosis of RA according to the American College of Rheumatology (ACR) classification criteria. Ethical approval was sought and granted by the University Hospitals Limerick Ethics Review Board (REC Ref: 60/15).

The inclusion criteria were: - participants had to be over 18 years of age, with a diagnosis of RA according to the ACR criteria and mobilising independently or with assistance of one unilateral aid. All procedures performed in studies involving human participants were in accordance with the ethical standards of the University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Potential participants’ healthcare records were screened for RA diagnosis in line with ACR criteria and were approached by a member of their healthcare team to be introduced to the study and to have the inclusion criteria checked. If a potential participant expressed an interest in participating and met the inclusion criteria, an information sheet was provided to them. The researcher arranged a time to follow-up with the participant to allow them time to read the information leaflet. A time was arranged to meet with the researcher to sign consent forms, take baseline measurements and to be given the SWA. Informed consent was obtained from all individual participants included in the study.
Measures

Demographic characteristics were recorded for each participant as follows: age, gender, body mass index (BMI), smoking status, location (urban/rural) and employment. Weight was recoded and classified using the World Health Organisation (WHO) classifications as normal weight (<25 kg/m²), overweight (≥25 and <30 kg/m²) or obese (≥30 kg/m²). Disease activity was assessed using the Disease Activity Score-28 (DAS-28) and the C-reactive protein (CRP) level. Blood samples were drawn by nurses trained in phlebotomy, from sitting, non-fasting individuals on one occasion at the time and location of their initial assessment.

Total sleep time (TST); Moderate to vigorous physical activity (MVPA) duration; and Sedentary behaviour duration (SBD) were recorded in hrs/mins, with Total energy expenditure (TEE) in kcal/day.

Global Health was examined using the Visual Assessment Scale (VAS) [26]. This scale aims to measure a characteristic or attitude that ranges across a continuum of values, in this case the global health of an individual. Participants were provided with a 100mm vertical line with anchors of “Worst imaginable health state” and “Best imaginable health state” on either end.

Disability was measured using the Health Assessment Questionnaire (HAQ), which is a self-report measure of the extent of a patient’s functional ability [27]. HAQ is comprised of 20 questions in eight categories. There are four response options for each question ranging from no difficulty to unable to do, (scored 0 – 3); a higher score indicates greater disability.

As part of the DAS-28, joint tenderness, swelling, VAS score and HAQ score were recorded twice: once on the day of monitor application and again on the day of monitor removal. The
average scores were calculated as the mean of the two days scores and it is this value which is reported.

**Objective measure**

The gold standard for assessing TST and sleep quality is Polysomnography (PSG) however, as this was not a lab-based study it was not feasible. Instead the authors wanted a device that was shown to have a high agreement with PSQ and was validated to measure sleep and MVPA duration, hence the SWA was chosen [18, 19, 20, 21]. The SWA is a multi-sensor PA monitor manufactured by Bodymedia (Bodymedia Inc., Pittsburgh, PA, USA). The SWA continuously records an array of physiological data from the four sensors contained on the armband (skin temperature, galvanic skin response, heat flux, and near-body temperature) as well as by accelerometry [28].

In relation to sleep, the SWA software uses a scoring algorithm to determine if the participant is either asleep or awake for each epoch of 60 seconds by considering the average variations in body movements, differential and proportional changes in heat-flux and skin temperature and the galvanic skin response [18].

**Application protocol**

The detailed SWA application protocol used in this study has been published elsewhere [23]. Participants were encouraged to wear the monitors for 24hrs per day except during water-based activities and were shown how to remove the SWA and accurately re-apply. They were also provided with an information handbook which visually and verbally outlined this process. The handbook was explained at the time of application and any queries were
answered. Participants were also provided with a diary, which they were asked to complete outlining the times the monitor was removed or re-applied.

Monitoring period

Participants were instructed to wear the monitor for eight days. The first day of monitoring was discounted entirely due to behavioural modification caused by the act of being monitored [29] therefore, seven full days of monitoring was utilized. All participants were contacted (with their permission) on three occasions during the week to ensure that they were not experiencing any problems and to remind them to continue to wear the monitor and complete the diary. A PA duration threshold of being active for a minimum of 30 + minutes, 5 days per week was primarily set, with a secondary conservative measurement time frame of at least four valid days with a total of 95% on body time, being determined as the final period for this study [30].

Data analysis

Statistical advice on the analysis was provided by one of the co-authors (AoN). Microsoft Office Excel (2013) was used for descriptive analysis for demographic questions, with further statistical analysis being undertaken with the Statistical Package for Social Sciences for Windows (SPSS Version 22). The Shapiro-Wilk test was used to test the normality of the activity variables. Regarding the final valid sample, other than PA duration, all other variables were found to be normally distributed (p-values = 0.255, 0.005, 0.065, 0.068 for sleep, PA, lying down time, and sedentary time respectively)

Thus, for all cases the mean and SD will be used to describe the centrality and variability, except for PA, where median and IQR are more appropriate measures due to the skewed
nature of the data (table 2). Level of significance was set at p<0.05. P-values were not
text testing [31].
A 2-sample t-test was used to investigate differences in means (sleep, lying down time,
settary time and the log transformed for MVPA), between the groups; gender, location,
 smoking and employment. ANOVA methods were used to test differences between groups
 for age and BMI.

Pearson’s correlation coefficient statistic was used to analyse the strength and direction of
the relationship between SWA’s daily average assessment of sleep, lying down, MVPA and
settary time. Benchmarks for correlations used were r = 0.10 – 0.29 (weak), r = 0.30 –
0.49 (moderate) and r = 0.50 – 1.0 (strong). A sample size of 30 is sufficient to detect a

Pearson’s correlation value of 0.05 as significant and therefore an appropriate statistical
approach for this exploratory study [32].

RESULTS

Participants
Seventy-nine (79) people with RA were recruited. Four (4) participants withdrew from the
study without completing the period of monitoring. Reasons for non-completion were:
illness, family bereavement, family dissatisfaction, and did not provide reason. Of those
who completed the seven days of monitoring (n=75), 51 (68%) met the MVPA duration
 guidelines of 30 + minutes, 5 days per week.
Thirty two (32) participants achieved a valid week of 4 days wear time and 95% on body [19,
30] and recorded a mean TST of 5.7 (SD_1.11) hours per night and a median 1.25
(IQR_1.88) hours of daily MVPA. Further analysis was conducted on the 32 participants
and showed an average sedentary behaviour duration (excluding sleep) of 12.93 (SD = 4.01) hours per day (table 2).

Figure 1 details additional recruitment details and table 1 for descriptive statistics on participants’ demographic details. The total and final percentage of participants included did not differ much across location, gender, age, BMI and employment.

**Sleep and physical activity**

Data for those participants achieving a valid week of measurement time shows a positive and significant relationship with MVPA ($r=0.415; p=0.018$).

Results for those participants recording a valid week of measurement criteria found females had a shorter TST time than men (mean of 5.21hrs compared to 6.21hrs; $p = 0.056$). Results showed a significant difference in MVPA duration between males and females (2.68 hrs for males compared to 0.88 hrs for women; $p = 0.001$). A significant difference was also found for sedentary behaviour duration between age groups ($p = 0.049$), with older adults spending more time in sedentary activities (table 4).

**Physical activity and disease related variables**

MVPA duration demonstrated a negative significant relationship with functional limitation (HAQ) ($r = -0.454; p = 0.009$); physical activity energy expenditure (PAEE) further demonstrated a significant negative correlation with disease activity (DAS-28) ($r = -0.443; p = 0.011$) and low disease activity was strongly correlated with improved global health ($r = 0.638; p < 0.001$).
MVPA duration correlated with lower CRP levels ($r = -0.146; p = 0.426$) and CRP levels had a significant relationship with global health ($r = 0.376; p = 0.034$) (tables 3 and 4).

**DISCUSSION**

This exploratory, and novel study provides an objective profile of total sleep time and MVPA duration in people with RA and indicates that those who are more physically active also have longer TST. This study highlights that TST in people with RA falls below the National Sleep Foundation’s ‘sleep needs spectrum’ of between 7 to 9 hours, with participants reporting an average of 5.7 hours (SD_1.11) sleep per night, which is similar to that reported subjectively [33]. This is concerning as reduced TST may have a profound impact on people with RA’s HQoL and their ability to be physically active [34]. In addition poor sleep quality and disturbances may contribute to feelings of pain and mood disturbances which may further deteriorate functional ability [35]. Recent subjective studies show that sleep is commonly reduced in people with RA, and in those who have lower PA profiles [3, 4], therefore this study provides important objective evidence to support these findings.

Aging and gender are associated with changes in both subjective sleep quality, objective sleep measures and SBD [36]. Epidemiological studies indicate a positive correlation between age and gender, and the prevalence of sleep complaints and increased SBD in the general population [37], with people with RA being no exception. Females complain of more sleep difficulties than males however, PSG indicates men suffer more from sleep fragmentation [38]. While still below the recommended ‘sleep needs spectrum’, from our study males had longer TST and significant longer MVPA duration than females. Gender differences exist in TST and sleep quality in the general population, with research confirming females having a predisposition to insomnia and reporting lower TST [39]. Findings from our
study regarding lower TST in females confirms same in people with RA. Difference in sleep
behavior and sleep disorders may not only be driven by biological factors but also by gender
differences however, significant knowledge gaps in research and lack of awareness of sleep
issues relevant to gender still exist.

With regards to SBD, it is becoming increasingly prevalent in the developed world and is
associated with co-morbidities, including increased cardiovascular disease [36], which is of
particular concern in an inflammatory condition like RA. This study has highlighted that the
average SBD among people with RA was high at almost 13 hours per day, with older adults
spending a significant amount of time in SBD.

In this study disease related factors (DAS, VAS and CRP) and functional variables were also
associated with lower CRP, lower DAS, lower HAQ and increased global health in those with
longer TST and higher MVPA duration. Thus, increased TST and being more physically
active have positive benefits on rheumatoid arthritis’s disease activity and function, which
may in turn have a positive effect on their HQoL.

While pharmacologic interventions have improved the management of RA, with PA and
exercise remaining an important part of overall treatment [40], with health professionals
playing a crucial role in promoting same [41, 42]. Despite PA having significant health
benefits, current PA levels are reported as sub-optimal in this population [6, 43, 44]. While
participants in this study can be considered physically active by meeting the relevant PA
duration guidelines of 30+ minutes, 5 days per week, the volume of lying down time (LDT)
and SBD is concerning.

People with RA have an increased risk of cardiovascular disease due to their chronic
inflammatory disease therefore, improving TST and PA duration should be important options
[45]. There is however, limited evidence on the effect of exercise/increased physical activity
on sleep in RA. A recent systematic review found it difficult to provide any firm conclusions on whether exercise impacts on sleep in people with RA, due to the small number of studies available and a high level of bias within those studies [46]. The authors of the review concluded that there is some indication that exercise may have positive effects with regards to sleep quality and disturbances however, more studies are necessary to confirm these findings with regards to the Frequency, Intensity, Time and Type (FITT) principle. Our study provides evidence that people with RA who are more physically active have higher TST however, the exact mechanisms of how MVPA and TST interact and the directionality of cause is not clear and future research is required.

Future Research

This objective profile adds to the emerging evidence base that people with RA have reduced TST. Continued investigation of the interrelated associations of sleep and PA on health outcomes is needed, given that these behaviours are ultimately derived from the same finite pool of available time, and the potential benefit in improving global health and disease activity in this population from better sleep and greater PA involvement.

While the literature provides evidence for a positive immune response for exercise in chronic diseases, exercise studies are required to specifically investigate the effects of physical activity on sleep and sedentary behaviour, with regards to the FITT principle.

Sleep disturbances and kinesiophobia can be major symptoms in chronic widespread pain (CWP) and it is known that CWP can be together with RA. Until recently the relationship between sleep disturbance and CWP has been unclear however, the available evidence does show that the relationship can be bi-directional [47, 48]. Future researchers should consider
the examination of same in studies looking at sleep and physical activity, with possible
testing for any differential diagnosis.

Consideration should be paid to the physical activity and exercise habits of those participants
prior to any study which may or may not affect any results [49] however, this was not part of
the objectives of this study.

Study Limitations

The final sample size was smaller than expected due to several participants removing the
SWA at night. The device can be worn at night but was still removed hence hindering the
authors’ ability to infer that the participant was asleep. The diary provided only requested
them to record when they removed/attached the SWA and didn’t ask the participant to record
what they were doing when the device was removed. While we have 51 participant’s data for
PA duration and sleep, the final number is 32 using the recommended wear time of 95%
across 4 days.

It was not possible to impute for non-wear time, in line with standard imputation approaches,
as to do so would assume that the person was asleep, which we had no means of verifying.
Hence, while we have supplied data on 51, we erred on having a final smaller sample with
accurate data. We would recommend that future research use a larger sample group to verify
the relationships found in this study.

Polysomnography is the gold standard however, due to its complexity and expense it is
infrequently used in research on sleep in chronic conditions, therefore accelerometry was
used. It is acknowledged accelerometer use is not without its limitations e.g. participant
adherence, correct re-application, cost and how comfortable it is to use, particularly at night
however, it is a more precise objective assessment of PA and is a less biased measure of
habitual physical activity compared to self-reported forms of measurement [50]. The study population was a relatively able bodied one, who used at most one stick. Therefore, it may not be possible to extrapolate the findings to a more disabled population with accuracy. Despite these limitations, this exploratory study provides a novel contribution to the rehabilitation literature and provides insight into sleep and PA in people with RA, which is currently lacking.

CONCLUSIONS

Total sleep time for people with RA is low and falls below the recommended sleep guidelines. When using a valid objective measure to analyse, participants recorded a daily average of 5.7 hours, below the required ‘sleep needs spectrum’ of between 7 to 9 hours per day. Those participants who were more physically active had a longer TST, with males having longer than females. Sedentary behaviour duration was high, with older participants’ spending a significant amount in SBD. Future research is required to confirm the relationship between increased MVPA duration and sleep found in this study and should specifically investigate physical activity’s effect on sleep in terms of the FITT principle.
REFERENCES


36. Fenton SAM, van Zanten JJCSV, Kitas GD, Duda JL, Rouse PC, Yu C-a, Metsios GS. Sedentary behaviour is associated with increased long-term cardiovascular risk in patients with rheumatoid
Sleep and Physical Activity in Rheumatoid Arthritis


