

# BMJ Open Implementing telehealth support to increase physical activity in girls and women with Rett syndrome – ActivRett: protocol for a waitlist randomised controlled trial

Jenny Downs <sup>1,2</sup>, Meir Lotan,<sup>3</sup> Cochavit Elefant,<sup>4</sup> Helen Leonard <sup>1</sup>, Kingsley Wong,<sup>1</sup> Nicholas Buckley,<sup>1,2</sup> Michelle Stahlhut<sup>5</sup>

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For numbered affiliations see end of article.

## Correspondence to

Dr Jenny Downs;  
Jenny.Downs@telethonkids.org.au

## ABSTRACT

**Introduction** Individuals with Rett syndrome (RTT) experience impaired gross motor skills, limiting their capacity to engage in physical activities and participation in activities. There is limited evidence of the effectiveness of supported physical activity interventions. This study aims to evaluate the effects of a telehealth-delivered physical activity programme on physical activity, sedentary behaviour and quality of life in RTT.

**Methods and analysis** This is a multicentre study, conducted in Australia, Denmark and Israel. It is a randomised waitlist-controlled trial comparing an intervention to support physical activity with usual care. Participants are children and adults with RTT, recruited from the Australian Rett Syndrome Database, the Danish Center for Rett Syndrome and the Rett Syndrome Association of Israel. The intervention duration is 12 weeks, including fortnightly telephone contact to plan, monitor and develop individual activity programmes. Outcomes are measured at baseline, at 13 weeks and then at 25 weeks. The primary outcomes are sedentary behaviour assessed with an activPAL accelerometer and the number of daily steps measured with a StepWatch Activity Monitor. Secondary outcomes include sleep, behaviour and quality of life. Caregiver experiences will be assessed immediately after the intervention using a satisfaction questionnaire. Group differences for each outcome will be evaluated with analysis of covariance, adjusting for baseline values on an intention-to-treat basis.

**Ethics and dissemination** Ethics approval has been obtained in Western Australia from the Child and Adolescent Health Services (RGS3371), in Denmark from the Capital Region Ethics Committee (H-19040514) and in Israel from the Ariel University Institutional Review Board (AU-HEA-ML-20190331). Manuscripts on the development of the intervention from pilot work and the results of the intervention will be submitted to peer-reviewed journals. Results will be presented at conferences and consumer forums. We will develop an online resource documenting the physical activity programme and available supporting evidence.

**Trial registration number** NCT04167059; Pre-results.

## Strengths and limitations of this study

- This study will use clinical trial methods to evaluate an intervention delivered via telehealth to increase objectively measured physical activity in individuals with Rett syndrome (RTT).
- Activities will be determined by goals that are set, modified and developed in collaboration with caregivers,<sup>42</sup> and based on contemporary models for participation<sup>37</sup> and quality of life.<sup>20 38</sup>
- Recruitment will be non-probabilistic, and the sample may not be representative of the population of RTT with some walking skills.
- We acknowledge that our findings will not inform how to increase activity in individuals who are unable to walk.
- The waitlist control condition may bias the study in favour of the intervention group because the control group could be less likely to initiate changes in lifestyle.

## INTRODUCTION

Rett syndrome (RTT, MIM:312750) is a rare neurodevelopmental disorder affecting approximately 1 in 9000 live female births.<sup>1</sup> It is characterised by largely normal early development followed by loss of acquired hand and communication skills. There are four main criteria: loss of hand skills, loss of communication skills, hand stereotypies and gait abnormalities.<sup>2</sup> RTT is caused by a mutation in the X-linked *MECP2* gene,<sup>3</sup> it is a severe neurodevelopmental disorder<sup>4</sup> impacting multiple body systems<sup>5–7</sup> and associated with severe functional impairments. The clinical spectrum is broad and varied and closely linked to the type of genetic mutation.<sup>8–10</sup> The clinical presentation is severe for some children who are unable to walk or go on to require enteral feeding, whereas it is

milder for others who can walk, negotiate stairs and self-feed. Communication is most often non-verbal, although a range of abilities is seen. Across the literature, findings are consistent that much of the clinical spectrum relates to the type of genetic mutation. For example, the Arg270\*, Arg255\* and Arg168\* mutations are associated with more severe symptoms, whereas the Arg133Cys, Arg294\* and C-terminal deletions are associated with less severe symptoms.<sup>11–14</sup>

Specifically, early gross motor impairments may include delay in the acquisition of gross motor skills prior to regression,<sup>15</sup> loss of balance during the regression period<sup>16</sup> and difficulty in walking.<sup>2</sup> Gross motor skills are variable<sup>12</sup>; the majority of individuals are able to sit, fewer than half learn to walk independently and less than one quarter can transfer from sitting to standing independently.<sup>17</sup> Recent systematic reviews of physical therapy interventions for individuals with RTT have reported mostly positive effects on gross motor skills, motor endurance and fitness within therapy settings.<sup>18–20</sup> Opportunities for training have been observed as enjoyable for the child when accompanied with a microswitch that delivered a light and sound sensory response to walking.<sup>21</sup> We note that the majority of studies were case studies, case series and single-case design studies, and only one study used randomisation in a stepped wedge design.<sup>22</sup>

Use of gross motor skills as physical activity during everyday living is also an important component of health<sup>23</sup> and quality of life.<sup>24</sup> We have previously investigated sedentary time and physical activity in RTT.<sup>25–28</sup> Girls and women recruited from the Australian Rett Syndrome Database (ARSD, n=64)<sup>25 26</sup> wore a StepWatch Activity Monitor (SAM) during waking hours. An average of 62% (SD 19%) of time was sedentary and approximately 20% (SD 8%) of time was spent in light-intensity walking, with the volume of activity influenced by whether walking was independent or required assistance or even close supervision, older age and the presence of comorbidities such as epilepsy and scoliosis.<sup>27</sup> We found similar results in Denmark, again using the activPAL to measure sedentary time and the SAM to count steps.<sup>28</sup> On average, 83% of waking hours were sedentary (n=48), the median daily step count was 5127 (n=28) and older age and lower levels of gross motor skill were strong predictors of reduced activity levels.<sup>28</sup>

Individuals with RTT are mostly dependent on others for support in daily activities.<sup>29 30</sup> Providing support for the individual to engage in additional activities could reduce sedentary time and increase physical activity. Reducing sedentary time by increasing the number and duration of episodes of standing and walking, especially in individuals with more severe mobility limitations, has been suggested.<sup>31</sup> Providing support for more light activities in RTT could be an important focus for intervention. More recently, we evaluated the feasibility and effectiveness of an individualised 12-week intervention using a pretest–posttest design that aimed to increase standing and walking activity in 14 girls and women with RTT.<sup>32</sup> The intervention involved working

with caregivers and service providers to identify standing and walking activities using strategies developed to meet activity goals<sup>33</sup> and that were consistent with the concept of participation in home, school and community settings.<sup>34</sup> An important focus was the collaborative efforts with families in selecting meaningful and engaging goals and in implementing and evaluating the individual intervention plan. It was well received and considered feasible by caregivers and therapists. Some positive effects were found including reduced sedentary time, increased daily step count and a small but significant increase in quality of life.<sup>32</sup>

In sum, individuals with RTT live sedentary lives and engage in low levels of physical activity relative to the general population, which has shown to reduce functional abilities throughout adulthood in people with disabilities.<sup>35</sup> Programmes of support for increasing participation in meaningful activities are feasible and have been proven to increase function,<sup>36</sup> but the level of evidence is low. As RTT is a rare condition, individuals are geographically dispersed but telehealth methods are being used increasingly across distances for the delivery of rehabilitation services such as for individuals diagnosed with cerebral palsy and traumatic brain injury<sup>37</sup> and across a range of domains to improve adaptive skills in those with multiple disabilities.<sup>38</sup> To build on previous research and inform practice, we designed this *ActivRett* clinical trial protocol.

The primary aim is to evaluate the effects of a telehealth-delivered physical activity programme on sedentary behaviour and physical activity in RTT. Our secondary aims are to evaluate the effects of the programme on quality of life, sleep and behaviour. We will also seek to evaluate the acceptability of the physical activity programme for caregivers and to explore the characteristics of individuals who are more responsive to the programme and the adaptability of activities in accordance with family resources. Following trial completion, we aim to provide the study manual as an attractive and freely available online resource for physical activity support in RTT, for use by families, caregivers and therapists wherever they live.

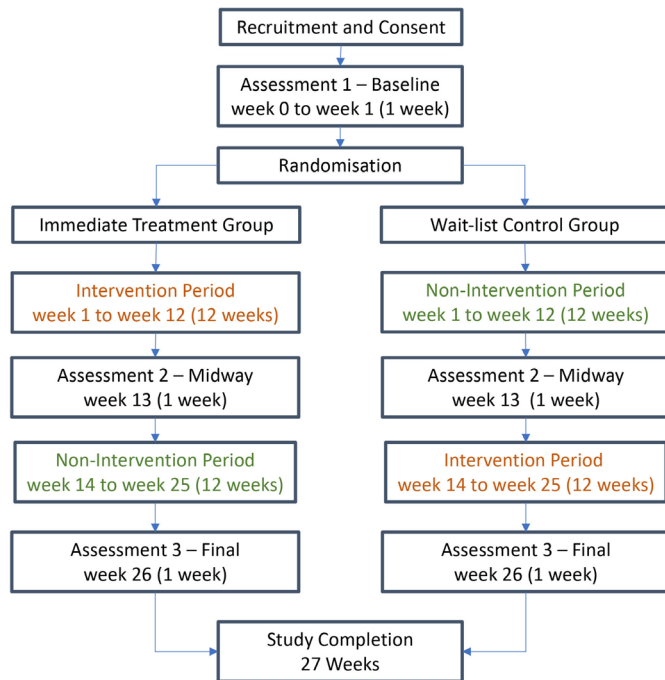
## METHODS AND ANALYSIS

### Study design

A randomised waitlist-controlled trial will be implemented. Participants who are randomised to control conditions during the first time period will receive the intervention during the second time period. Outcomes will be assessed at baseline, immediately following a 12-week intervention period and then 12 weeks after the second intervention period. An overview of the study design is shown in [figure 1](#). The trial is registered with ClinicalTrials.gov and summary data are presented in [table 1](#).

### Participant and public involvement

This study is funded by the peak international patient advocacy organisation for RTT ([Rettsyndrome.org](http://Rettsyndrome.org)) and



**Figure 1** Participant flow through the study.

our proposal has been subject to scientific and consumer review. Prior to our previous feasibility study,<sup>32</sup> we held a teleconference with Australian parents who shared their experiences of enjoyable physical activities for their daughters. When developing our manual for the current study, we conducted an international survey of caregivers and professionals who support individuals with RTT about how they supported their daughter to be physically active and what they would want in a physical activity programme. These ideas and perspectives informed the study intervention manual. Insights from the survey will be published to share with parents and therapists key insights on facilitators and barriers to individuals with RTT being physically active. The dissemination plan will include presentations to families at consumer and community forums for their feedback.

### Participants and settings

Individuals aged 5 years and older with genetically confirmed RTT and who live in either Australia, Denmark or Israel will be recruited to the study, commencing the beginning of 2020. Some will be able to walk independently, and others will need assistance. We will exclude individuals who are unable to walk because our intervention will be provided remotely, and we are unable to organise or provide participants with the necessary equipment such as a standing frame within the time frame of this study. We will also exclude participants who have had a spinal fusion over the previous 12 months or lower extremity orthopaedic surgery over the previous 6 months.

For this study, we will recruit from three sources:

1. The ARSD is an ongoing population-based longitudinal study of RTT which was established in 1993 and

**Table 1** Summary of the WHO Trial Registration Data Set for the ActivRett trial

Data category	
Primary registry and trial identifying number	ClinicalTrials.gov (NCT04167059)
Protocol version	V.4, 3 October 2019
Date of registration in primary registry	18 November 2019
Source of monetary or material support	Rettsyndrome.org
Primary sponsor	Rettsyndrome.org
Contact for public queries	JD, email address
Contact for scientific queries	JD, email address
Public title	<i>ActivRett</i>
Scientific title	Implementing telehealth support to increase physical activity in girls and women with Rett syndrome
Countries of recruitment	Australia, Denmark, Israel
Problem being studied	Low levels of physical activity in individuals with Rett syndrome
Intervention	Active comparator: participation-based activity programme aiming to increase standing and walking activities  Control comparator: usual activity
Key inclusion and exclusion criteria	Ages eligible for study: 5 years and older; genetically confirmed Rett syndrome; female because Rett syndrome mostly affects females  Inclusion criteria: able to walk independently or with assistance  Exclusion criteria: spinal fusion over the previous 12 months; lower extremity orthopaedic surgery over the previous 6 months
Study type	Interventional  Randomised waitlist-controlled trial  Primary purpose: prevention  Phase III
Date of first enrolment	7 January 2020
Target sample size	60
Recruitment status	Recruiting
Primary outcomes	Number of steps per day; per cent of sedentary time
Key secondary outcomes	Quality of life; sleep; behaviour

includes individuals with genetically confirmed and clinical RTT born since 1976.<sup>26 39</sup> Clinical and multiple waves of family-reported data are stored in the database.

2. The Danish Center for Rett syndrome was established in 2007 and offers counselling and annual follow-up across the lifespan of all individuals diagnosed with RTT.<sup>30</sup> Clinical and medical data are stored in the Danish Rett syndrome database.
3. The Rett Syndrome Association of Israel was established in 2001 and is in contact with approximately 200 individuals diagnosed with RTT.

Families will be contacted by telephone by the site investigator for initial discussion of the study and invited to participate if it is established that they are eligible. Individuals with RTT are presumed to have cognitive impairment and are unable to provide informed consent to participate in the study. As is usual in the population, informed consent will be collected from the parents/legal guardians of the individual (see online supplemental file 1).

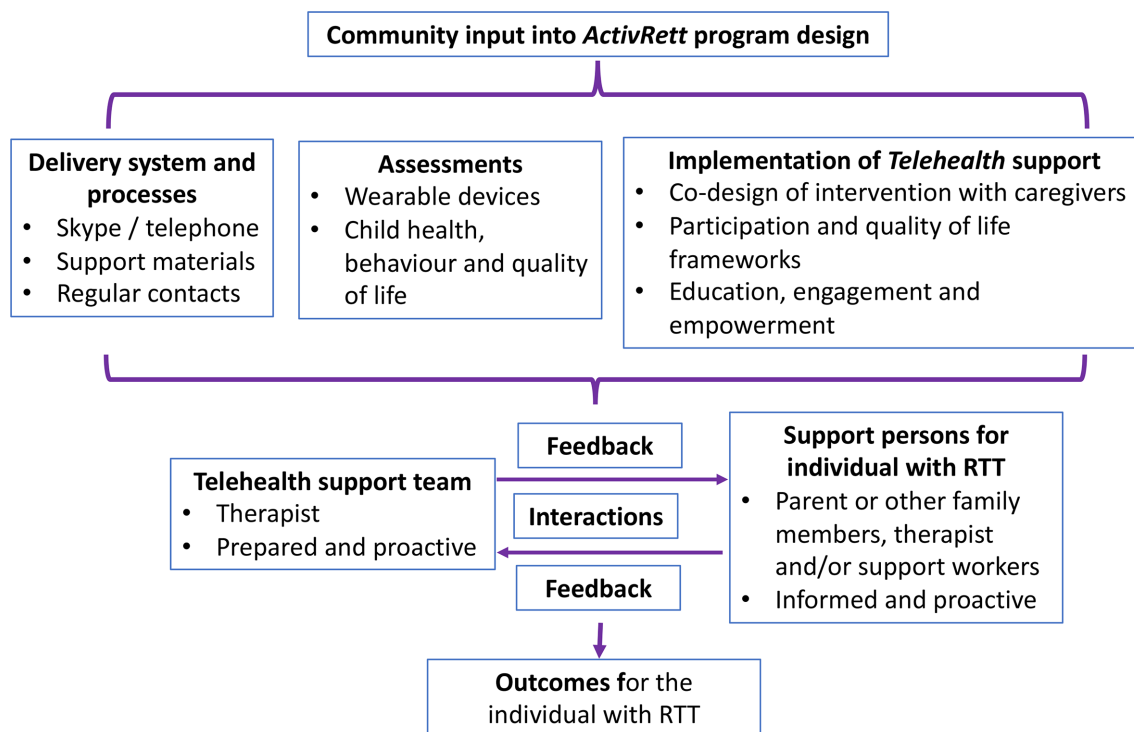
### Randomisation

Allocation concealment will be ensured by performing allocation after completing baseline assessments (figure 1). At each site, individuals will be stratified by walking ability (independent or assisted) and then randomised using computer-generated randomisation (V.14.1, StataCorp, College Station, Texas, USA) to the immediate treatment group or waitlist control group. A statistician independent to other study processes is responsible for group allocation and communicating this to the site investigators.

### Intervention procedures

Contact for the intervention sessions will be made using the telephone and Skype or Zoom platforms (figure 2). The initial intervention session will involve review of the gross motor skills, care routines, participation activities as well as physical surrounding opportunities of the individual with RTT and discussion of the activity patterns with the caregiver and other service providers as appropriate. If several caregivers are involved, we will aim for a joint meeting at the beginning of the intervention with subsequent contacts separately or together, as is feasible.

The intervention aims to increase the quantity of standing and walking activities, collectively termed ‘uptime’,<sup>40</sup> for girls and women with RTT. The increased ‘uptime’ activities will be codesigned with the caregivers and service providers for use in their own environments (home, school, community) and supported by the usual caregivers and service providers in those environments. These will primarily be parents, but may also include others such as siblings, carers and service providers. The intervention will be delivered over a 12-week period, supported by fortnightly telehealth video/telephone calls with a physiotherapist (the site investigators) who will consult and provide recommendations for strategies to increase the quantity and frequency of ‘uptime’ activities. The activity recommendations will be formed into goals and evaluated at the next session using Goal Attainment Scaling.<sup>41</sup> The research therapists will also be available between scheduled fortnightly video calls for



**Figure 2** Summary of the components of the assessment and telehealth delivered intervention, and iterative feedback processes over the intervention period.

support via email, phone call or video call. Throughout, the investigators and carers will discuss physical activity needs, determine and adapt relevant activities, modify the programme as necessary and plan additional goals. For example, goals will articulate what the activity is (eg, increased opportunities for standing or walking as suitable for the individual's ability), where (eg, in the home, garden, at school or in the community) and when the activity will happen (eg, the new activity could be scheduled at particular times in the day to suit routines) and with whom (eg, parent, sibling, carer) and why the goal is meaningful and of value. At any time during the intervention period, an individual will have two to four goals which could change, as more suitable and challenging goals are identified. The interactive nature of the delivery of the programme is illustrated in [figure 2](#).

The intervention strategies will be consistent with contemporary participation,<sup>42</sup> quality of life<sup>24 43</sup> and goal setting frameworks for disability.

1. Optimal participation in recreational activities involves an interaction and balance between the dimensions and determinants of participation.<sup>42</sup> Dimensions of participation include: (1) physical engagement—doing the activity. Being actively involved underlies participation and has positive impacts on fitness and physical health; (2) social engagement—interactions and feeling included. A sense of belonging defines successful and meaningful participation; and (3) self-engagement—enjoyment and choice-making. Enjoyment is paramount to engagement in activities and through choice people can identify preferred activities.<sup>42</sup> Determinants of participation include: (1) child-related attributes—combination of body function and personal factors, (2) family-related and caregiver-related attributes—socioeconomic status and family functioning, and (3) environmental attributes—supportive of the physical, social, attitudinal and service environments.<sup>42</sup>
2. Quality of life domains identified as important for individuals with RTT include aspects of physical and mental well-being and social and recreational functioning. More specifically, the quality of life factors include 'physical health', 'positive emotions', 'negative emotions', 'social interaction', 'leisure and the outdoors' and 'independence'<sup>43</sup> and are consistent with the International Classification of Functioning, Disability and Health (ICF) structure.<sup>44</sup>
3. Achievement of goals will guide the development of ongoing programme activities. Meaningful activity goals will be identified with carers at the baseline assessment, informed by participation<sup>45</sup> and quality of life<sup>43</sup> models and measured using Goal Attainment Scaling.<sup>46</sup> The setting and review of goals is recognised as supporting the learning of new routines and health behaviours.<sup>47</sup>

Usual care comprising medical care and therapy activities will continue during the intervention and control periods.

### Intervention consistency

Each site investigator participated in the development of the study manual and was familiar with the delivery of the assessment and intervention protocols. The site investigators meet regularly to discuss implementation of the protocol and any problems that arise. This is to ensure intervention consistency within and across sites.

### Adverse event reporting

At each contact, investigators delivering the intervention will check with the caregiver as to the well-being of the individual with RTT and how the intervention activities have progressed. The intervention aims to increase the volume of everyday activities under the supervision of primary caregivers and there is the risk of a fall. Any adverse events will be reported to the study data safety monitor, a paediatric orthopaedic surgeon and the ethics committee. The data safety monitor will use clinical judgement as to the circumstances around any adverse events and will advise whether the individual can continue in the trial or not. Participants who have an adverse event will be followed up by the site investigator as required to ensure they are receiving appropriate medical care.

RTT is associated with increased risk of fracture and we have previously determined that the incidence of any fracture episode was 43.3 episodes per 1000 years.<sup>48</sup> We will be observing 60 individuals with RTT over a period of 6 months per individual, and this would equate to 30 person years. We would expect that up to two episodes of fracture could occur during the study period, associated with either activity or a pathological fracture. The stopping rule for this study will be the occurrence of two episodes of fracture that are associated with a study activity-related fall. The risk of adverse events is low and a data monitoring committee is not needed, additional to the data safety monitor, for this study.

### Data collection

Data will be provided to Telethon Kids Institute using REDCap which is maintained and administered by the biostatistics team at Telethon Kids Institute, who are Good Clinical Practice compliant. The system runs on secure (password-protected), encrypted servers located at Telethon Kids with offsite backup. For analysis, data will be downloaded from REDCap to Excel and thereafter to STATA statistical analysis software. Participant's information and outcome measures are summarised in the schedule of assessments ([table 2](#)). Data will be checked regularly for outliers and missing data. If an outlier is found, the site investigator will attempt to check whether the value is likely or not. It will be included unless it is identified as very unlikely. If missing data are found, the Investigator will attempt to collect the missing value.

### Participant characteristics

At the beginning of the study, parents will be asked about their child's gross motor abilities, which will inform the completion of the Rett Syndrome Gross Motor Scale<sup>12</sup> by

**Table 2** SPIRIT schedule of enrolment, interventions and assessment

Timepoint		Study period				
		Enrolment	Allocation	Post allocation		
		-t	0	Baseline	Midway	Final
Enrolment	Eligibility screen	x				
	Informed consent	x				
	Allocation		x			
Baseline variables	Demographic data		x			
	Rett Syndrome Gross Motor Scale		x			
	Presence of comorbidities		x			
	Daily care regimens		x			
Intervention	Intervention, then waitlist control			↔		
	Waitlist control, then intervention			↔		
Primary outcomes	activPAL			x	x	x
	StepWatch Activity Monitor			x	x	x
Secondary outcomes	Quality of Life Inventory-Disability			x	x	x
	Sleep Disturbance Scale for Children					
	Rett Syndrome Behaviour Questionnaire			x	x	x
Process evaluation	Satisfaction survey				x*	x*

\*Satisfaction survey is administered post intervention, which will be either at the midway or final assessment, depending on randomisation to the intervention or non-intervention group for the first 12-week block.

the investigators. Daily care regimens and activities will be documented and participation will be measured using the Participation and Environment Measure for Children and Youth,<sup>49</sup> to guide the design of the intervention. To describe other aspects of health and well-being, diagnosed comorbidities will be described.

#### Primary outcome measures

Suitable outcome measures with validation data for RTT were selected.<sup>50</sup>

1. The primary outcome of sedentary time will be measured using the activPAL. The activPAL (PAL Technologies, Glasgow, UK) is a small (53×35×7 mm, 20 g) uniaxial accelerometer which is attached to the skin on the anterior thigh with an adhesive pad. It contains an inclinometer which determines the position of the thigh and estimates the time spent in a sitting/lying or standing position in 15 s epochs. We have validated its use as a measure of sedentary time in RTT.<sup>51</sup> Four valid days of data including 1 weekend day will be required for analysis. For each day and guided by diary data indicating awake hours out of bed, we will calculate the per cent of time in uptime activities, that is, upright activities of standing and/or walking, of the total awake hours out of bed. Mean values across each of the valid days will be calculated.<sup>51</sup> This will be calculated using data collected for a 1-week period at the baseline, mid and final assessment.

2. Daily steps will be measured using the SAM. The SAM (Modus Health LLC, Washington, DC) is a small (70×50×20 mm, 38 g) accelerometer-type device that records the number of steps taken every minute. It is attached to the ankle using an elastic Velcro strap. We have validated the SAM as a measure of daily steps in individuals with RTT.<sup>52</sup> Four valid days of data including 1 weekend day will be required for analysis. These assessments have also been validated against a proxy-report measure of 'uptime' (total time standing and walking) and 'downtime' (lying and sleeping) using the modified Bouchard activity record.<sup>40 51</sup> For each day and guided by diary data indicating hours out of bed, we will calculate the number of steps for total awake time. Mean values across each of the valid days will be calculated. This will be calculated using data collected for a 1-week period at the baseline, mid and final assessment.

#### Secondary outcome measures

The secondary outcome of quality of life will be measured using the Quality of Life Inventory for Disability,<sup>43</sup> sleep will be measured with the Disorders of Initiating and Maintaining Sleep and the Disorders of Excessive Somnolence subscales of the Sleep Disturbance Scale for Children<sup>53</sup> and behaviour will be measured with the Mood and the Fear and Anxiety subscales of the Rett Syndrome Behavior Questionnaire.<sup>54</sup>

### Caregiver satisfaction

Carers and parents will complete a study-specific satisfaction questionnaire immediately following the intervention to document how the programme was received, enablers and barriers when implementing the programme and other impacts on daily life.

### Data analysis

#### Hypothesis testing

Data related to sedentary behaviour, step counts, sleep, behaviour and quality of life at each assessment will be described and visualised to illustrate levels and trends.  $\chi^2$  test and Student's t-test will be used for categorical and continuous variables, respectively, to detect differences in baseline characteristics between the immediate treatment and waitlist control groups. Difference in values of each outcome variable by intervention status at assessment 2 will be analysed using analysis of covariance, adjusted for baseline values, age, walking status and country. Analyses will be on an intention-to-treat basis with the last known value carried forward in the event of missing data. Further within-group analyses on treatment effect will be conducted by combining data collected immediately pre intervention and immediately post intervention from both groups. In this analysis, the independent variables will be factors that could influence the magnitude of change, such as age and walking ability, and the dependent variables will be the change scores of the primary outcomes (ie, sedentary time and step counts). Univariate and multivariate linear regression models will be conducted. For the group which receives the intervention in the first time period, we will evaluate change in outcomes between assessment 2 and assessment 3 using a paired t-test. The analyst will be blind to treatment allocation.

### Sample size

In preliminary Danish data,<sup>32</sup> the response of individuals to the physical activity programme (per cent of sedentary behaviour) in a repeated measures design was normally distributed with an SD of 11%. If the true reduction, following the intervention, in the mean per cent of sedentary time is 5% and assuming a pairwise correlation of 0.5, we will need to study 50 individuals in a two-sample trial to be able to reject the null hypothesis that this response difference is 0, with probability (power) 0.8. The type I error probability associated with this test of the null hypothesis is 0.05. We will recruit 60 families, allowing for some dropout. A total of 26 individuals will be recruited from Australia, 14 from Denmark and 20 from Israel.

### Caregiver satisfaction

Satisfaction survey questions are rated on a 1–10 Visual Analogue Scale and will be described and graphed to illustrate frequency distributions to identify positive and negative aspects of the study processes.

## ETHICS AND DISSEMINATION

### Ethics approval

Ethics approval has been obtained from the Child and Adolescent Health Services (RGS3371) in Australia, the Capital Region Ethics Committee in Denmark (H-19040514) and the Ariel University Institutional Review Board (AU-HEA-ML-20190331) in Israel. Protocol amendments will be submitted to each ethics committee.

### Dissemination

We plan to submit a manuscript on the development of the intervention and a manuscript of the trial results to a peer-reviewed journal. Results will be presented at conferences and consumer forums. Following the conclusion of the study, a website will be developed that presents strategies of how to evaluate and support individuals with RTT to live physically active lives. It will contain introductory information about how the current project was conducted, the participation and quality of life frameworks that inform how to address physical activity needs and the findings from the current proposal. Information will be suitable for families, caregivers and therapists, and will also be suitable for a wide range of disabilities in addition to RTT. Strategies will be illustrated with line drawings. Draft content will be presented to the Consumer Reference Groups of the Australian Rett Syndrome Study and InterRett, open also to Danish and Israeli families, for review prior to being finalised and translated. In the first instance, we will produce the website in English, Danish and Hebrew. The database infrastructures, family advocacy associations and the institutions and networks of the investigators will support us with dissemination strategies.

## DISCUSSION

Many individuals with a developmental disability including those with RTT experience low levels of physical activity in their daily lives, threatening both their health and quality of life. There is a need for scalable, flexible and accessible interventions to promote activity programmes in RTT. Yet, the current level of evidence for interventions that guide how to achieve this is low. This study will be the first clinical trial investigating strategies to increase physical activity in RTT. Participants will be children and adults. The literature over the years has suggested the need to develop management plans that can translate from research designs to the daily life of the participants and across their life span.<sup>55–57</sup> Our proposal represents affirmative action in this regard.

Telehealth is being used in many fields of medicine and rehabilitation and our proposal will be one of the first to apply this method in RTT. This is a particularly attractive modality because RTT is rare, families live in widespread geographic locations and telehealth can bring specialist skills to the affected individual in her own environment. Particularly, in light of the social isolation and disruption to traditional therapy delivery caused by the ongoing COVID-19 pandemic, telehealth represents an attractive

method to provide therapy to populations that are likely to be disproportionately negatively affected, such as individuals with RTT and their caregivers. Families, carers and therapists will guide the setting of goals and be responsible for implementing activities that they have had a role in determining. Their grass roots involvement will facilitate the continuation of programmes beyond the immediate study period. Our proposal will be build on available resources and strengths, respond to locally identified needs and empower those working in local communities to improve physical activities and participation of the individuals with RTT under their care.

The intervention is in alignment with participation<sup>58</sup> and quality of life<sup>24</sup> frameworks, developed by our team of international investigators, to enable the intervention to be applicable across diverse settings. As follow-up to the proposed evaluation, there is also a critical need to develop mechanisms by which evidence-based practice can be readily available to the community. We also propose the translation of available strategies including those tested in the current study and their level of evidence into an online resource, in order that physical activity strategies are available to those in need wherever they live. There is potential for the findings of our study to provide evidence of how individuals with RTT can live more active lives, in order that they may gain health and well-being benefits from greater levels of meaningful activities, within their home, school and community environments.

#### Author affiliations

<sup>1</sup>Telethon Kids Institute, The University of Western Australia, Nedlands, Western Australia, Australia

<sup>2</sup>School of Physiotherapy and Exercise Science, Curtin University, Perth, Western Australia, Australia

<sup>3</sup>Department of Physiotherapy, Ariel University, Ariel, Israel

<sup>4</sup>School of Creative Arts Therapies, University of Haifa, Haifa, Israel

<sup>5</sup>Department of Paediatrics and Adolescent Medicine, Center for Rett Syndrome, Copenhagen, Denmark

**Twitter** Jenny Downs @drjennydowns

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**Contributors** JD led the study conceptualisation and the first draft of the proposal and development of intervention, and is leading the study. ML, CE, HL and MS contributed to study conceptualisation, development of intervention content and edited the protocol. KW designed the analysis plan and edited the protocol. NB contributed to the development of intervention content and edited the protocol. All authors edited and approved the final manuscript.

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**Competing interests** JD is employed at Telethon Kids Institute where she is program head of Child Disability. The protocol for this study was developed for this

grant received from Rettsyndrome.org. The authors do not have competing interests to declare in relation to this study.

**Patient consent for publication** Not required.

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#### ORCID iDs

Jenny Downs <http://orcid.org/0000-0001-7358-9037>

Helen Leonard <http://orcid.org/0000-0001-6405-5834>

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