Rett syndrome (RTT) is a severe neurodevelopmental disease affecting about 1/10,000 females and a few males, although a higher incidence rate has been reported by some researchers [1–3]. RTT is characterized by a regression of abilities in intellectual functioning, fine and gross motor skills, and communicative ability, which occur after an apparently typical prenatal and perinatal period. Other features include the development of stereotypical hand movements, seizures, disturbed breathing patterns, scoliosis, growth retardation, ataxia, apraxia, and gait disturbances [4]. Gross motor function in RTT is always limited [5]. In the regression phase, patients begin to develop difficulties in coordination and balance that co-occur with uncontrolled movements of body segments and trunk [6–10]. Residual gross motor functions are usually preserved until adulthood, with most patients being able to walk with support and almost half who can walk independently or with minimal support. However, a decrease in motor functioning quality is observed from the age of 13, with a progressive increase in the support needed by the person with RTT [11,12]. Moreover, fluctuation in muscle tone has been reported from early childhood, together with the appearance of compensatory muscle rigidity [13]. Neuromuscular impairment and musculoskeletal abnormalities have been reported in RTT syndrome. Such deformities of the spine and feet are prevalent, although all body joints can be affected [14].

In the framework of such health-related complexities, the primary resource for affected patients is an early and appropriate diagnosis, appropriate care at specialized centers, and the implementation of a multidisciplinary clinical follow-up. Moreover, the complex clinical picture typical of many with RTT requires intensive and specific intervention programs [15]. Parents and family, as primary caregivers, play a vital role in ensuring the health and well-being of children, as the more involved the family is, the more consistent the therapeutic management becomes [16]. A significant trend is a gradual shift of care centeredness from the client to the client’s whole family. The family is perceived as the basic social unit and the primary educator, supporter, and shaper...
of each person [17]. This change of perspective has progressively driven the development of a theoretical framework that supports family enrollment in care service providing, commonly referred to as family-centered care (FCC). FCC can be described as placing the child’s needs, within the context of their family and community, at the center of care and devising an individualized and dynamic model of care in collaboration with the child and family that will best meet these needs [18]. More precisely, the Institute for FCC stated that FCC is an innovative approach to planning, delivering, and evaluating health care grounded in a mutually beneficial partnership among patients, families, and providers. It applies to patients of all ages and may be practiced in any health care setting [19]. FCC puts the intervention emphasis on the needs of the child and family to support the patterns of living and be supported by the family’s strengths and resources [20,21]. Within FCC practice, the family is recognized as the constant in the child’s life and his primary source of strength and support. Family members are involved in their child’s care and learn more about their child and their child’s treatment. In turn, they can share their knowledge with professionals, and this provides a more holistic picture of the child and a way to heighten awareness of the child as part of the family [18]. Families are not referred to or treated as dependent clients, with professionals and policymakers viewing families as equals, citizens with whom they collaborate and empower. Thus, the family plays a fundamental role in the decision-making process concerning services for their child [17]. With the family unit as the primary and principal context for promoting child health and well-being, FCC has been shown to contribute to developmental progress and skill development [22–24]. Therefore, the healthcare professional must involve family members in all areas of assessment, planning, and delivery of health-related services.

Furthermore, as the intervention for individuals with RTT is aimed at compensation and reduction of physical impairments, the therapeutic intervention should not be limited to what is administered in the treatment room or during individually applied sessions (also known as hands-on or direct therapy). Home intervention programs have shown positive effects in improving functionality while at the same time reducing mortality in people with chronic diseases and in reducing the stress expressed by caregivers [25]. A randomized controlled trial proposed an additional home intervention program for children with developmental disorders aimed at skill generalization and family member training. It showed more remarkable cognitive development and behavior changes than children who did not receive additional intervention [26]. A Cochrane review found that home programs seem to be better than classic rehabilitation programs in terms of adherence to the prescribed exercises, especially in the long run [27]. Such findings may be evaluated for specific chronic developmental disabilities such as RTT. As we look at this population, we need first to assess the results of previous intensive and appropriate interventions implemented with these individuals.

In RTT model mice [28] as well as with children with RTT [29,30], an enriched environment and intense intervention program can improve longevity [28], show a significant reduction in coordination deficit, improve locomotor activity, and improve aerobic fitness and function. Moreover, setting proper, intense, and achievable rehabilitation, educational and communicational programs for the individual with RTT is vital [31]. Therefore, to attain a continuous effect, therapists and caring staff should work as a team with the individual’s family to construct a comprehensive intervention program that includes both the educational facility and the individual’s residence.

The significant variations in RTT clinical phenotype necessitate an individually adapted program for each participant, yet, to date, most clinical trials have tested standardized or targeted interventions, leading to generalized guidelines rather than individualized or tailored interventions. Such generalized guidelines can place some difficulty on the therapist when implementing them for the specific client.

The most effective health care interventions for complex chronic medical conditions, such as RTT, necessitate an exchange of information among all people involved in the therapeutic process [32], including the client with RTT and her family. Another important aspect in implementing a physical rehabilitation intervention program is that a specific disorder manifests differently in different individuals, thereby requiring the therapist to suggest different intervention solutions for each client. Moreover, health care providers might more readily adopt evidence-based best practice guidelines if they had more options for tailoring them, thus increasing client satisfaction with treatment and improving clinical outcomes [33]. Recent intervention programs from different therapeutic areas, such as nursing [33], alcoholism support programs [34], programs for older adults [35] as well as others, have begun to see the importance of individually implemented (also termed patient-centered care, in-person, tailored interventions, individualized interventions) interventions. Patient-centered care can thus improve health status and increase the efficiency of an intervention program [32]. Such individual treatment regimens are possible if the therapist/researcher is interested in responding to the unique characteristics of each client rather than automatically supplying a general intervention program. When constructing such individually adapted programs, different factors should guide the therapist/researcher. They should address differences between the clients involving personality factors, goals, needs, preferences, and resources [33].

**Summation**

RTT is a complex and chronic disorder, with clients presenting an array of clinical abilities with significant differentiation from one another. Due to the rarity of RTT, there is no constructed physical program addressing the habilitative needs of these individuals, and few therapists are fully aware of all therapeutic needs presented by this group of clients. Therefore, there is a need to construct a rehabilitation program supported by family members and adapted individually to each participant. There is also a need to oversee and readjust the program to address changes within the pre-administered habilitation program fully.

This study aimed to evaluate the effect of such a home-based family-centered individualized motor rehabilitation program on the motor functioning and musculoskeletal abnormalities of a group of girls and women with RTT.

**Methods**

**Ethical issues**

The study was approved by the Ariel University Ethical Committee and conducted according to the ethical principles of the Helsinki Declaration and local regulation. All details relating to the study procedure were discussed with the participants’ parents or the legal representative, and an informed consent document was signed for all participants. Enrollment was voluntary, with participants not receiving any incentives, financial or otherwise, for participation.
| Patient | Age     | RARS subscales | RESMES subscales | Scoliosis | Mutation |
|---------|---------|----------------|------------------|-----------|----------|
| Patient | Age     | Cognitive | Sensory | Motor | Emotional | Independence | Rett characteristics | Standing | Sitting | Transfer | Walking | Run | Stairs | RESMES total | | |
| 1       | 9 yy 4 mm | 14.5 | 2.5 | 7 | 3.5 | 12 | 20 | 59.5 | 1 | 0 | 14 | 6 | 4 | 8 | 33 |
| 2       | 19 yy 4 mm | 17.5 | 3.5 | 12 | 4.5 | 12 | 28 | 74.5 | 5 | 6 | 22 | 11 | 4 | 8 | 56 |
| 3       | 21 yy 3 mm | 23.5 | 5 | 14 | 5 | 12 | 28 | 87.5 | 0 | 0 | 3 | 0 | 4 | 0 | 7 |
| 4       | 34 yy 4 mm | 8.5 | 2.5 | 7 | 2.5 | 12 | 22 | 54.5 | 3 | 4 | 21 | 8 | 4 | 8 | 60 |
| 5       | 43 yy 3 mm | 12.5 | 4 | 7 | 2 | 12 | 17 | 58.5 | 0 | 0 | 6 | 0 | 4 | 2 | 28 |
| 6       | 43 yy 3 mm | 12.5 | 4 | 7 | 2 | 12 | 20 | 58.5 | 0 | 0 | 6 | 0 | 4 | 2 | 28 |
| 7       | 25 yy 5 mm | 11.5 | 3.5 | 8 | 2 | 12 | 11 | 57.5 | 0 | 0 | 3 | 0 | 4 | 0 | 11 |
| 8       | 10 yy 11 mm | 15 | 3.5 | 14 | 2 | 12 | 21.5 | 68 | 12 | 10 | 25 | 18 | 4 | 8 | 77 |
| 9       | 11 yy 3 mm | 23.5 | 2.5 | 15 | 2.5 | 12 | 25 | 80.5 | 12 | 12 | 25 | 18 | 4 | 8 | 79 |
| 10      | 12 yy 8 mm | 23.5 | 2.5 | 16 | 6.5 | 12 | 24.5 | 86 | 12 | 9 | 25 | 18 | 4 | 8 | 76 |
| 11      | 16 yy 9 mm | 15 | 2 | 13 | 3.5 | 12 | 23.5 | 66 | 12 | 9 | 25 | 18 | 4 | 8 | 75 |
| 12      | 8 yy 11 mm | 15.7 | 3.2 | 10.7 | 3.5 | 11.8 | 22.5 | 61.7 | 5.5 | 4.2 | 16.5 | 9.9 | 4.0 | 6.5 | 46.5 |
| 13      | 17 yy 11 mm | 5.2 | 0.8 | 3.4 | 1.5 | 0.6 | 3.0 | 11.7 | 5.1 | 4.4 | 8.5 | 7.4 | 0.0 | 2.7 | 26.6 |
| Mean    | 17 yy 11 mm | 15.7 | 3.2 | 10.7 | 3.5 | 11.8 | 22.5 | 61.7 | 5.5 | 4.2 | 16.5 | 9.9 | 4.0 | 6.5 | 46.5 |
| SD      | 7 yy 11 mm | 5.2 | 0.8 | 3.4 | 1.5 | 0.6 | 3.0 | 11.7 | 5.1 | 4.4 | 8.5 | 7.4 | 0.0 | 2.7 | 26.6 |
| Range   | 3 yy 4 mm to 34 yy 4 mm | 8–23.5 | 2–5 | 7–16 | 2–6.5 | 10–12 | 17–28 | 54–87 | 0–12 | 0–12 | 3–25 | 0–18 | 4–4 | 0–8 | 7–79 |

SD: standard deviation; yy: years; mm: months; RARS: Rett Assessment Rating Scale; RESMES: Rett Syndrome Motor Evaluation Scale.
Table 2. Consideration of personal characteristics of participants.

| Term                          | Level 0                                                                 | Level 1                                                                 | Level 3                                       | Level 4                                       | Grade |
|-------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------------|----------------------------------------------|-------|
| Body structures/functions      | There are many limitations and little function                         | There are few limitations and some function                            | There are very few limitations and moderate function | There are no limitations                       |       |
| Coping strategies             | Both child and parents negate the presented exercises                  | The child and/or parents present some personal restrictions            | The child and/or parents present few personal restrictions | The family is willing and excited to participate |       |
| Positive mediators – resources | There is no support for the program                                   | Some aspects are supporting the program, and some are negating the implementation of the program | Most aspects support the program, and some negate the implementation of the program | The family's situation highly supports all aspects of the program |       |
| Negative mediators – barriers | Many aspects are preventing this program from happening                 | Some aspects are supporting, and some are negating the implementation of the program | Most aspects support the program, and few negate the implementation of the program | There are no factors negatively influencing the performance of the activity program |       |
| Availability                   | The child and parents have no time to perform the program             | The family has a restricted timetable to implement the program         | The child and parents have a fluent timetable enabling program implementation | Both child and parents have unlimited time to implement the program |       |
| Environmental factors         | The environmental factors do not support the implementation of the program (lives away from appropriate social attractors) | The environmental factors have few advantages and mostly disadvantages in implementing the program | The environmental factors have some advantages and few disadvantages in program implementation | The environmental factors fully support the implementation of the program (live close to appropriate social attractors) |       |
| Motivational factors          | The child does not seem to be interested in anything                   | The child has a limited number of motivational factors                 | The child has some motivational factors       | The child has many motivational factors (food, music, dance, social interaction) |       |

Total sum for participant

RTT (AR and ML) within a specifically designed room in a rehabilitation center in Sicily (Messina Hospital). The room for the evaluations contains a rehabilitation bed and some common rehabilitative equipment for children. Participants’ parents and their physical therapists (when available) participated in the evaluation meetings. Participants’ parents carried out the intervention phase at their houses. Therefore, intervention phase settings and materials were different between subjects.

**Experimental design**

The study design for this investigation was a case series with multiple baselines AABA. Letter “A” represents the evaluation meetings carried out at T1, T2, and T3, while the letter “B” represents the intervention phase conducted between T2 and T3.

**Procedure**

**Evaluation meetings**

Patients’ evaluations were carried out three times (T1–T3), three months apart (±two weeks). Each evaluation session lasted for two hours and 30 min. The first evaluation was three months before the training started. The second assessment (including the construction of the individual intervention program) was carried out the week before the beginning of the intervention phase. The last evaluation session was performed immediately after the end of the treatment. Gross motor abilities were assessed during each evaluation. During the first evaluation meeting, a complete assessment of passive range of motion (PRoM) of all body joints was carried out, relevant information related to participants’ clinical conditions (such as epilepsy, osteoporosis, sleep disturbances, and other conditions typically associated with RTT) and therapeutics interventions in progress (such as physical therapy, hippotherapy, hydrotherapy, and others) were collected, and parents’ expectations and desired motor function improvement for their daughters were discussed together with their reference therapist. At the end of this meeting, a draft of individualized rehabilitation objectives for the intervention phase was compiled in agreement with the parents and therapists. In the second evaluation session, rehabilitation objectives were re-discussed with each family and corrected if needed, then Goal Attainment Scaling (GAS) scores for each goal were set. One or two simple activities to be performed at home were identified to pursue each goal and taught to the parents. In the third evaluation session, the level of achievement of the established objectives was assessed, and a parents’ satisfaction questionnaire was administered. Parents’ considerations related to the intervention phase were also collected.

**Rehabilitation program construction**

From the clinical observation and data collected at T1, three to six specific rehabilitation objectives which can be pursued in the short- and medium-term were identified for each participant. Goals have been grouped into three areas: (a) motor function (gross motor skill and hand function); (b) range of motion (related
to the mobility of joint segments); and (c) general physical fitness (elements of general well-being such as weight, resting HR, respiratory function). Based on the identified objectives, different therapeutic activities that parents can perform at home without specific training and rehabilitation equipment and which can be easily integrated into the family’s daily routine were individuated. Therefore, a weekly activity program was structured for each participant using the activities identified from the individualized rehabilitative objectives. Each program was constructed based on the participant’s and family’s needs and was subsequently refined, discussed, and agreed upon with the parents during the second evaluation meeting (T2).

**Individualizing the program for each participant**

In this research protocol, during the initial evaluation (T1), we evaluated the theoretic availability of the family and participant to be involved in a physical intervention program. Our decision-making process was based on the framework of the Rehab-CYCLE developed by Stucki and Sangha [38], and the "Rehabilitation Problem Solving Form," which is based on the ICF model [39] and is used to identify specific and relevant target problems, discern factors that cause or contribute to these problems, and after that, plan the most appropriate interventions [32]. Under the ICF model, non-problematic aspects of health are summarized under the umbrella term "functioning," whereas "disability" serves as an umbrella term for impairment, activity limitation, or restriction in participation. The ICF model describes ingredients related to human functioning and disability and serves as a framework to organize information. Using such definitions, the health-related states of an individual with RTT and her family are then qualified by numeric codes, specifying the influence of different aspects such as functioning or disability and an environmental factor as facilitators or barriers.

This was done by evaluating the following elements:

- **Body structures/functions** – relates to the health condition of the participants (what are the clinical abilities of the child) and environmental factors (availability of physical as well as surroundings);
- **Coping strategies** – measures the level of child and family’s readiness to participate (reaction of the child and family to the performed exercise – evaluating the child and parent’s response to the child’s behavior during the activities);
- **Mediators** – are elements that influence the client’s condition either directly or indirectly by transmission. They are divided into supportive mediators or resources and adverse mediators defined as barriers:
  - **Resources** (presence of adult children assisting parents; good socio-economic situation; young grandparents living close by);
  - **Barriers** (how many small children are in the family and their ages; the number of jobs held by the parents; presence of any background health limitations of the parents/other children; poor socio-economic situation);
- **Availability** (number of hours the client with RTT is at home every day, number of hours per day other family members are available to perform activities with the person with RTT, who can contribute at home);
- **Environmental factors** – does the family live in a rural area, by the sea, near a mountain, or a forest?
- **Motivational factors/facilitators** – how many motivational factors the child has, and how intense are they for her?

Within the present study, all the elements mentioned above are coded on a four-points scale for each item following the coding structure of the ICF model (see Table 2). To be included in the present study, researchers established that candidate families and participants had to achieve an overall minimum score of 14.

Although personal factors or resources are crucial in the rehabilitation process [40], they are not classified within the ICF model due to the significant social and cultural variance associated with them [39]. Yet, in our opinion, this is a crucial part affecting adherence to the program by most girls with RTT. Therefore, personal factors relevant to each participant were included within the final scoring, which led to the suggestion of a specific, individually tailored intervention program.

The researchers would like to emphasize that this was not a one-sided decision making by the researchers, but an ongoing discussion between the researchers and the parents (for instance, showing the parents some motivational factors they overlooked/suggesting simple use of household appliances to replace missing rehabilitation equipment). This process improved communication between the researchers and the participating families and enabled the construction of an intervention program specifically tailored to each participant and her family.

The researchers and others [32] believe that a rehabilitation management program for complex medical conditions such as RTT warrants a routine check of program adherence and goal attainment. Therefore, during the Skype calls, the researchers used the Rehab-CYCLE model [38] to revise the program and adapt it to problems or successes mentioned by the family members concerning program implementation. Such decisions were taken to meet the patient’s expectations or needs while always considering the researchers’ practical, clinical, and evidence-based knowledge regarding RTT.

**Intervention phase**

Participants’ parents carried out the individualized programs at their homes for three months. Each family could organize the activities as they prefer during the week, according to their household routine and habits. The rehabilitation activities included in the programs comprised but were not limited to maintenance passive positions to prevent the worsening of the secondary musculoskeletal problems related to RTT, maintenance of active asymmetrical postures to balance the trunk muscles and improve balance, the exercise of residual functional abilities (e.g., sitting position, standing position, walking, postural change, and climbing/descent of stairs), and functional use of the hands. The objectives and activities identified were considerably different among the participants in content, difficulty, and intensity to adapt to each client by considering the high clinical variability of patients with RTT. The programs included a maximum of one non-consecutive hour of activity a day for five days a week for the duration of the intervention. During the intervention phase, two remote supervisions of the implementation of the programs were performed through a videoconference call with each family at one and two months after the start of the interventions, respectively. The supervisions lasted for one hour each and were aimed to support the execution of the program, answering parents’ questions, adapting it to the emerged needs, solving problems, rearranging time tables, adapting the suggested exercises, evaluating achievement of the goals and, if needed, setting new goals.

**Outcome measures**

**Severity level.** The severity of clinical manifestation was assessed with the RARS. This is a 31-items RTT-specific severity scale standardized for the Italian population on a sample of 195 subjects with RTT [36]. Each item concerns a specific phenotypic
characteristic and describes four increasing levels of its severity. A total score between 31 and 124 is computed by summing the individual ratings. The total score allows the evaluator to identify the level of severity of RTT, conceptualized as a continuum ranging from mild symptoms (lower score) to heavy deficits (higher score) [41]. The RARS was established by a standardization procedure involving a sample of 220 Italian patients with RTT. Skewness and kurtosis values, calculated for the total score distribution, were 0.110 and 0.352, respectively. The distribution was found to be normal. Internal consistency was found at 0.912, and the internal consistency of the subscales was also high (0.811–0.934) [36,41,42].

Goal Attainment Scaling. The GAS was administered to assess the degree of achievement of the rehabilitation objectives identified for each participant. This scaling system represents a mathematical technique used to quantify the identified objectives’ achievement (or not) and can be used in rehabilitation [43]. The GAS represents a sensitive measure of patient achievements due to the intervention in relation to a specific therapeutic objective. It has been identified as the most sensitive tool to reflect and measure small changes in patients’ functioning and conditions that otherwise would not be found using standardized or physiological measures [44]. Objectives set should follow the SMART principle: Specific, Measurable, Attainable, Realistic, and Timely [45]. Each identified rehabilitation goal received weight from 1 (a mild) to 3 (substantial) to consider the relative importance of the goal to the individual and the difficulty that the rehabilitation team anticipates in achieving it. Higher weight represents higher importance and/or difficulty of goal achievement [46]. The degree of achievement of each objective is assessed on a five-points scale: a score of 1 represents the pre-intervention situation, a score of 2 represents worsening compared to pre-intervention assessment. If the patient reaches the expected level, this is assigned the value 0. If obtained results are better than expected, these are given the values +1 (a little more than expected) or +2 (much more than expected). Each level of each goal is defined by the team or the experimenter and should be as objective and observable as possible. To obtain one numerical score for each patient regarding the rehabilitation goal achievement, the goals of each participant were averaged together, giving an overall score between −2 and +2 for the goals as a whole [47,48].

Rett Syndrome Motor Evaluation Scale. RESMES was used to assess the gross motor functioning of all participants at each evaluation meeting. This tool is a 25-item RTT-specific scale investigating subjects’ gross motor performance across six sections: (i) standing, (ii) sitting, (iii) transitions, (iv) walking, (v) running, and (vi) walking up/downstairs. Sixteen items are rated on a 0–4 discrete scale, where 0 indicates null or very mild impairment and 4 indicates severe impairment for a total maximum score of 82 points. Nine items related to walking abilities are rated on a 0–2 discrete scale; 0 indicates that the subject could always complete a task and 2 indicates that the task could not be completed. RESMES was recently validated on a sample of 60 female subjects with RTT (mean age: 12y 5mo, SD 8y 9mo; range: 3 – 40y) showing optimal inter-rater agreement among clinicians (s* statistic values always >0.70) and strong internal consistency (split-half reliability coefficient = 0.96 SD 0.18; Cronbach’s alpha coefficient for the entire scale = 0.95 CI 0.93–0.97) [42,49].

Passive range of motion. Joint mobility was manually assessed through goniometric measurement as described by Norkin and White [50]. A mobility evaluation of all body joints was performed at the first evaluation meeting (T1). Joints that showed PROM limitations were assessed again at T2 and T3. The PROMs were collected to evaluate the level of goal achievement in the area of range of motion and will be presented within GAS results.

Parents’ satisfaction questionnaire. A 10-items questionnaire was created to investigate parents’ satisfaction related to program implementation. Each item scored parents’ feelings between 0 and 5 in the areas of adherence and workload (three items), perceived usefulness of the intervention (two items), adherence/compliance with the rehabilitation team (three items), and general satisfaction (two items). The average score was obtained for each area from related items scores. A higher score corresponded to better feeling in the field of the investigated area. The questionnaire was received from families by e-mail within two weeks from the end of the post-intervention evaluation meeting (T3).

Statistical analysis

Friedman’s test was run to compare the RESMES average total scores and RESMES subscale scores at the three evaluation points. The Friedman test is the non-parametric alternative to the one-way ANOVA with repeated measures. It is used for data that has violated the assumptions necessary to run the one-way ANOVA with repeated measures (e.g., the dependent variable measured is ordinal). Post hoc analysis with Wilcoxon’s signed-rank tests was conducted for pairwise comparisons. The threshold for significance for the comparisons above has been assumed as α = 0.05. No correction for multiple comparisons was applied [51]. The effects size for the above reported repeated measures comparison was conducted with Kendall’s W coefficient, while for the pairwise comparisons, the matched-pairs rank-biserial correlation was used [52,53]. The effect size was considered small if between 0.140 and 0.310, medium if between 0.310 and 0.610, and large if above 0.610 [54].

Results

The influence of different aspects such as functioning or disability and environmental factors as facilitators or barriers was assessed for each candidate family with the criteria presented in Table 2. All candidates reached the minimum score to be included (mean: 19.1 ± 2.2; range: 16–24). Among the 13 families who completed the protocol, no critical limitations (score: 1) for participation in the research were found in any criteria except “Body structures/functions” and “Motivational factors.” Most participants had numerous functional limitations (mean score: 2.1 ± 0.9; range: 1–3). However, all families were highly motivated to participate (mean score: 3.6 ± 0.5; range: 3–4), and positive mediators well supported their participation (mean score: 3.0 ± 0.3; range: 3–4) and little influenced by negative mediators (mean score: 2.9 ± 0.6; range: 2–4). Furthermore, all the families involved had sufficient time to carry out the planned activities despite some limitations (mean score: 2.9 ± 0.3; range: 2–3). Environmental factors only partially supported the program’s implementation (mean score: 2.6 ± 0.5; range: 2–3). Finally, on average, the participants were interested in few motivational factors (mean score: 1.8 ± 0.7; range: 1–3).

Participants’ stated goals, pre- and post-intervention situation descriptions, obtained GAS scores, goals weight, and average GAS scores are available as Supplementary materials (Online Resource 1). One participant received two goals. Three goals were identified
for six participants. Four participants received four objectives, and for two participants, five and six goals were set, respectively. The numbers of goals for each goal area and respective GAS scores are summarized in Table 3. For six participants (46.1%), the identified goals were adequate for the intervention (average GAS score between 0 and 1). For six participants (46.1%), the goals set overall underestimated the treatment potential (average GAS score >1). Only in one participant (7.7%) were the overall goals overestimated for the potential of the intervention (average GAS score <0). On average, the intervention proposed to the whole group slightly underestimated the potential of the treatment (mean averaged GAS score = 0.85 ± 0.79).

The changes in the participants' PRoM due to the treatment were available in the Online Resource 1 in the referred goals. Descriptive statistics of the REMES scores obtained by participants at each evaluation session are shown in Table 4. Differences between the REMES scores at the three evaluation meetings were analyzed, and the effect size of occurred changes was calculated (Table 5). The average total REMES score showed a significant decrease across the evaluation meetings (p < 0.001) with an effect size of 0.714. Pairwise comparison showed a significant decrease between total REMES score measured at T2 and T3 (p = 0.043) with an effect size of 0.604 and at T1 and T3 (p = 0.002) with an effect size of 0.604. The average motor functional level increased between T1 and T2 and between T2 and T3 but at a different velocity. The total REMES score of five participants (38.5%) improved between T1 and T2 with an average change of −0.4 ± 0.5 points while, between T2 and T3, 10 participants (76.9%) have improved their total REMES score with an average difference of −3.6 ± 3.1 points. The total REMES score of three participants did not change at any evaluation point. These three subjects had the first and third-lowest and the highest severity RARS score of our sample, respectively. The REMES subscale scores change significantly across the evaluation meeting. A slightly descending trend (that represents an improvement in motor functioning) was observed for the standing (p = 0.002; effect size = 0.462), sitting (p = 0.009; effect size = 0.365), postural change (p = 0.022; effect size = 0.292), and walking (p = 0.004; effect size = 0.431) subscales. Walking subscales showed a statistically significant improvement between T1 and T3 (p = 0.050) with an effect size of 0.231. Clinically, between T2 and T3, six participants elongated the endurance of their standing ability (three independently, two with single support, one with bilateral support) with an effect size of 0.231. At the same time, five subjects improved their stability in sitting position (four without feet and back support, one without back support, and with feet on the floor) with an effect size of 0.165. As for postural changes, two subjects reduced the assistance needed to perform the transfer from supine to sit on the floor between T1 and T2 with an effect size of 0.033. Between T2 and T3, two participants reduced the support required to stand up from a chair and from the floor. For one of them, these transfers became independent with an effect size of 0.066. After the intervention phase (at T3), six subjects increased the number of steps they can walk (three for independent walking, two with single support, and one with bilateral support). During the baseline (between T1 and T2), two girls improved their ability to overcome an obstacle with a single support. One of them could not do it at all at T1 with an effect size of 0.033. On the other hand, between T2 and T3, six subjects improved this ability, and four of them learned it during the treatment with an effect size of 0.231. Moreover, two girls reduced the support needed for stair climbing and descending with an effect size of 0.033. One of them learned to go up and down stairs without physical help.

The parents’ answers to the satisfaction questionnaire were analyzed. On average, the families reported an elevated level of satisfaction concerning the areas of perceived usefulness (mean = 4.4/5), compliance with the rehabilitation team (mean = 4.4/5), and general satisfaction (mean = 4.5/5). Overall satisfaction related to workload was moderate to high (mean = 3.7/5).

### Discussion

This article describes the results of a remotely supervised, home-based, individualized-centered motor rehabilitation program for individuals with RTT, performed in the South of Italy (Sicily). The authors found motor rehabilitation objectives for all participants in this group of individuals and constructed successful individualized, motor home-based rehabilitation programs which yielded significant positive outcomes. The findings highlight that an individualized motor rehabilitation intervention is effective for individuals with RTT when support is provided to participants, their family members, and professionals, positively affecting achieving the rehabilitation goals. Participation in the proposed intervention allowed the participants to improve their motor functioning. Positive effects with small to medium effect sizes were seen in the outcomes obtained at T3 for standing (0.231) and walking (0.231) REMES subscales and total REMES (0.604) scores. These improvements reflect an increased level of independence in motor skill performance. Comparable results were found in other populations when relying on family members’ involvement and healthcare professionals’ attitudes [55]. Our findings support Kerr’s statement [56] that a constant set of repeated exercises performed by caregivers is highly recommended for the quality of life of the individual with RTT. Our findings also support her notion that regular activity is essential for the long-term health of this population [56]. The results of the present research are extremely important when considering the age of the participants. Our sample includes a wide age range. The implemented programs lead to an improvement in participants at different ages, ranging from childhood to adulthood, suggesting that people with RTT across all ages can benefit from such a remotely supervised, home-based intervention even for those in the so-called IV stage of the disorder (late motor deterioration). The average age of the participants within the present intervention was close to 19 years. According to existing literature, at that point, deterioration in health and function is expected by individuals with RTT [4], yet, despite such decline, paradoxically, at the same time, a reduction in health services is registered for this population [57]. Our findings suggest that the typical path (stage IV of

| Goal area                | Amount (%) | -2  | -1  | 0   | +1  | +2  | Average GAS score |
|-------------------------|------------|-----|-----|-----|-----|-----|-------------------|
| Motor function          | 28 (59.6%) | 0   | 4   | 2   | 9   | 13  | 1.26              |
| Range of motion         | 10 (21.3%) | 1   | 3   | 2   | 2   | 2   | 0.31              |
| General physical fitness| 9 (19.1%)  | 1   | 1   | 4   | 1   | 2   | 0.13              |
| Total                   | 47 (100%)  | 2   | 8   | 8   | 12  | 17  | 0.85              |

GAS: Goal Attainment Scaling.
RTT) described in the literature is not mandatory and that if such a program had been implemented at a younger age, it might have yielded even better outcomes. Furthermore, the participants in our group improved their motor function despite their many initial functional limitations and the small number of motivational factors available, suggesting that these two elements do not represent a limitation to the implementation of this type of program. Our intervention assumptions that indicated that such a program’s focus should be on daily living activity have been confirmed. The findings highlight the fact that, for individuals at a high-moderate level of motor activity, the focus of the program for the parents should be on improving function within daily functional activities while, for those with high functional severity, the emphasis for parents intervention should be on the adoption of postural hygiene strategies to counter the development of musculoskeletal abnormalities. Moreover, our results suggest that, on average, the intervention potential was underestimated (led to better than expected results) for goals related to functional abilities (average GAS score for goals in the area of motor functioning = 1.26) such as walking, ascending, and descending stairs, and sitting without support. This underlines the high potential of the presented intervention for improving the functional abilities of people in this population. On the other hand, the identified goals within the other goal areas such as improving joint range of motion (average GAS score for goals in the area of range of motion = 0.31) and general physical fitness (average GAS score for goals in the area of general physical fitness = 0.13), were found adequate for the intervention potential. It is authors opinion that when caregivers/parents are recruited as program managers, the importance of functional goals is better understood than other/non-functional goals. Therefore, these goals are less actively pursued by the parents. As such, when constructing such a program in the future, functional goals should be the responsibility of the parent/caregiver while other less obvious or less functional outcomes (such as range of motion) which complement and support the achievement of the functional goals should be pursued by therapists.

**Parental satisfaction**

The participants’ parents reported a high level of satisfaction and a good level of adherence to the proposed activities suggesting that the creation and supervision of a home-based, remotely supervised, individualized motor rehabilitation program, focused on the person and adapted to his and family needs, is motivating for family members. The identification of functional activities that could lead to visible results in everyday life led to better adherence to the program by the family, contributing to a good level of parental satisfaction and positive functional outcomes. This information suggests that when building such programs, the researcher/therapist should consider family members’ motivation to carry out the activities and the possibility of integrating them into the family’s daily routine. Comparable results have also been found in other populations suggesting the importance of building this type of program [58,59].

The participants’ parents reported a high level of satisfaction regarding the habilitation program suggested by the researchers (this relates to the evaluation of the objectives and for the drafting and supervising of the therapeutic programs) compared to their previous habilitation experience. This result is attributed to the relationship of trust that the rehabilitation team established with families by following them remotely via Skype and addressing their concerns and suggestions. Therefore, the authors suggest the need for remote supervision for similar programs in regular and frequent intervals to support the family in overcoming obstacles and maintaining a positive attitude towards the proposed activities. Such long-distance supervision is in high demand for families living in rural areas or with limited access to specialized care.

### Table 4. Descriptive statistics of RESMES subscales and total scores across three evaluation session.

|        | Standing (max = 12) | Sitting (max = 12) | Postural change (max = 28) | Walking (max = 18) | Run (max = 4) | Stairs (max = 8) | Total (max = 82) |
|--------|---------------------|-------------------|-----------------------------|-------------------|---------------|-----------------|-----------------|
| **T0** | Mean (SD) 5.5 (5.1) | 4.2 (4.4)         | 16.5 (8.5)                  | 9.9 (7.4)         | 4.0 (0.0)     | 6.5 (2.7)       | 46.5 (26.6)     |
|        | Median 4            | 4                 | 20                           | 11                | 4             | 8               | 48              |
|        | Min–max 0–12        | 0–12              | 3–25                         | 0–18              | 4–4           | 0–8             | 7–79            |
| **T1** | Mean (SD) 5.5 (5.1) | 4.1 (4.3)         | 16.3 (8.5)                  | 9.8 (7.4)         | 4.0 (0.0)     | 6.5 (2.7)       | 46.1 (26.6)     |
|        | Median 4            | 4                 | 19                           | 11                | 4             | 8               | 48              |
|        | Min–max 0–12        | 0–12              | 3–25                         | 0–18              | 4–4           | 0–8             | 7–79            |
| **T2** | Mean (SD) 4.8 (5.4) | 3.2 (3.5)         | 15.8 (8.4)                  | 8.7 (7.7)         | 4.0 (0.0)     | 6.0 (2.9)       | 42.4 (26.6)     |
|        | Median 3            | 4                 | 18                           | 9                 | 4             | 8               | 39              |
|        | Min–max 0–12        | 0–12              | 3–25                         | 0–18              | 4–4           | 0–8             | 7–79            |

RESMES: Rett Syndrome Motor Evaluation Scale; SD: standard deviation; T1: baseline; T2: pre-intervention; T3: post-intervention.

### Table 5. Results of RESMES subscales and total scores comparisons between the three evaluation sessions and related effect sizes.

|                       | Standing | Sitting | Postural change | Walking | Run | Stairs | Total |
|-----------------------|----------|---------|-----------------|---------|-----|--------|-------|
| Repeated measure p value | 0.002*   | 0.009*  | 0.022*          | 0.004*  | 1.000         | 0.135 | <0.001* |
| Repeated measure effect size | 0.462        | 0.365  | 0.292           | 0.431    | 0.000 | 0.154  | 0.714 |
| Pairwise comparisons p value | T1 vs. T2 1.000 | 0.845 | 0.556           | 0.695    | –   | –      | 0.980 |
|                        | T1 vs. T3 0.078 | 0.117 | 0.141           | 0.050*   | –   | –      | 0.002* |
|                        | T2 vs. T3 0.078 | 0.170 | 0.377           | 0.117    | –   | –      | 0.043* |
| Pairwise comparisons effect size | T1 vs. T2 0.000 | 0.011 | 0.033           | 0.033    | 0.000 | 0.000  | 0.165 |
|                        | T1 vs. T3 0.231 | 0.165 | 0.165           | 0.231    | 0.000 | 0.033  | 0.604 |
|                        | T2 vs. T3 0.231 | 0.165 | 0.066           | 0.231    | 0.000 | 0.033  | 0.604 |

RESMES: Rett Syndrome Motor Evaluation Scale.

*p value < 0.05.
at present when many are under lockdown due to the Covid-19 outbreak. Similar positive results were received by physical therapists of the research participants involved in the therapeutic program suggested for their clients with RTT.

The results suggest that a remotely supervised, individually adapted, client-centered, home-based motor exercise program could support program satisfaction and enhance exercise adherence while, at the same time, leading to the understanding of the prescribed exercise by the parents. We assume that parental satisfaction might have promoted their involvement, resulting in the continuation of the prescribed exercises, integrating the exercise program as a part of their daily activities. As several activities in the programs (walking, stair climbing, sitting, standing) were functional exercises that could facilitate visible outcomes, their execution was easily integrated into the daily routine of the participants/families who began to use the suggested exercises during everyday activities regularly. We can affirm that identifying the functional activities that concern the parents of children with RTT and prescribing those specific activities as part of the home exercise program caused improved adherence to the program and increased both parental satisfaction and achievements of positive functional outcomes.

Planning an individuality adapted physical therapy program

Due to phenotypic variability, there are various individual clinical expressions of RTT and a variety of functional conditions and family needs in this population. Thus, the program’s effectiveness may depend on the personal characteristics of each patient and their family. For a heterogenic population like people with RTT, no “one type fits all” therapy can be defined as more effective than another. Therefore, the therapist should be highly knowledgeable regarding his clients with RTT and competent in adapting proper intervention techniques to each individual and family, focusing on their specific needs. When evaluating the child and family’s abilities and needs, the therapist should work within the ICF model suggested by Steiner et al. [32] and take into account all elements which might have negative (barriers) and positive (resources) effect on the proposed program including the client and family physical and emotional capabilities and limitations. In the words of Yalom [60]: "inspire yourself to create a new treatment for each client."

Implementation of the program

When a program is initiated, it should be implemented as any exercise or training program. Initially, the activities should involve a reduced effort implemented for short durations, and these parameters should then progressively increase over time. The activities should always include a good motivational factor that supports the program’s execution (e.g., see a favorite cartoon or receive the compliments and cheering of the parents). The program should be flexible to adapt to any sudden change in medical conditions, sleep habits, or changes in medication, including changes in dose. The activities should be carried out daily to create a stable regular structure that is easy to follow. The program should also take advantage of the moments in which the girls carry out activities similar to those of the program (e.g., take advantage of the times when they have to go out and return home to go up and down the stairs, walk during indoor transitions instead of using a wheelchair). Moreover, as discussed above, the attitudes of parents and therapists can positively or negatively affect the program outcomes. Therefore, the therapist in charge must oversee the participants’ attitudes and, through remote rehabilitation (in this project, the technology platform was Skype) to adapt the program and maintain adherence of all involved. The remote supervisions have proved extremely useful. This program element is suggested here as an integral part of any habilitation program, supporting family members and therapists in carrying it out, intercepting needs/difficulties as soon as they arise, and addressing them.

Settings

The geographical area where the present investigation took place suggests but little support to adults with disabilities. Therefore, many family members are yearning for a program for their daughter with RTT. Due to these circumstances, the setting was highly favorable to this type of intervention, and the parents embraced it wholeheartedly. In a different environment, a slightly changed program might be required, yet it is the responsibility of the therapist to adapt the program to factors that will positively influence the acceptance of the program and the adherence to it, to maximize the positive effects. Individual happenings can influence intervention outcomes as well. It is challenging to master personal events, but some can be predicted and prevented. For instance, if the family is planning to move to a new apartment, the program’s initiation should be postponed as the involvement of the parents in the event will be an obstacle for them to start the program. Moreover, the new house might be built differently from the old one, presenting new difficulties, thereby needing the program’s reconstruction. In the present investigation, one of the families had a new baby, and the mother’s pregnancy prevented the full implementation of the program, which led to less than optimal results for their daughter with RTT participating in the exercise program.

Limitation

This study presents some limitations. First, we did not carry out a follow-up evaluation to measure the program’s effects after a wash-out period. Second, we did not include a control group to compare the outcomes of participants who implemented the program with those who followed a common rehabilitation intervention. However, while the versatility of influencing factors is diverse enough to prevent the comparison of different individuals with RTT, we used a research design that allowed us to assess spontaneous advances/regressions in the participating group in the pre-intervention period. Third, we did not suggest spinal X-rays to be taken, yet this was due to extremely poor radiologic services where the research intervention took place. Therefore, although many activities could have had a positive effect on the mobility of the spine (scoliosis and kyphosis), we cannot comment on the program’s impact on these aspects. Moreover, we did not collect any data on the fidelity with which parents implemented the intervention. Lastly, although 13 subjects completed our research protocol, and it is one of the most extensive physical intervention programs ever implemented for this population, the number of participants is still too small to generalize the results. Therefore, replications of this project are needed to confirm our results. All these limitations should be considered in planning future studies about implementing home intervention programs for people with RTT.
Conclusions

The present investigation focused on the effect of a remotely supervised, home-based, motor individualized rehabilitation functional program on the motor functioning and musculoskeletal abnormalities of a group of girls and women with RTT. The involved researchers were able to identify effective activities that significantly improved the participants’ motor function and musculoskeletal conditions. Remote supervision was found to improve adherence to the program and is highly recommended for this type of intervention. Using highly trained therapists with substantial knowledge in RTT in conjunction with family members of the participants in constructing an appropriate program and program implementation was a valuable and potent tool. However, this observation is mostly accurate, but not exclusively in areas where such services are scarce. The presented findings strongly support the implementation of such programs for this population to support their motor functioning, postural position during hygiene procedures, physical activity, and therapeutic goals. Moreover, the authors highlight the need for adequate and specific motor rehabilitation for this population which can be effectively supported remotely by experienced professionals through a low-cost device such as video calls. Implementing such a tool (remote rehabilitation) within the widespread Covid-19 lockdown would have prevented ill effects and functional regressions, resulting from such a prolonged duration where therapeutic services are denied to people with disabilities in general and individuals with RTT specifically.

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Disclosure statement

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