Protocol for study entitle: Effectiveness of a structured physiotherapy intervention on psychomotor and quality of life in children with mild to moderate autism spectrum disorder

Project Summary

Children with Autism Spectrum Disorder (ASD) frequently present with motor coordination difficulties, behaviour challenges, reduced physical activity and lower quality of life (QoL). Evidence suggests exercise and motor-based physiotherapy can improve these outcomes. Yet rigorously designed randomized controlled trials (RCTs) in the Malaysian context are limited. This assessor-blinded, parallel-group RCT will evaluate a 12-week structured physiotherapy intervention grounded in the FITT principle versus usual care among children with mild–to–moderate ASD aged 6–10 years.

Sixty-four participants will be recruited from community centres in Terengganu and Klang Valley, hospital rehabilitation units and partner NGOs and randomized 1:1 to intervention or control with concealed allocation. Primary outcome is motor proficiency (Bruininks–Oseretsky Test of Motor Proficiency-2, BOT-2) at 12 weeks. Secondary outcomes include ASD symptom severity (GARS-3), physical activity (parent-report GLTEQ), behaviour problems (CBCL), and QoL (PedsQL). Assessments occur at baseline and post-intervention by blinded assessors. The intervention arm will receive a 12-week structured physiotherapy programme comprising progressive neuromotor, balance, coordination, strength, and aerobic components, delivered by trained physiotherapists in pairs in addition to usual care. “Usual care” refers to services routinely available at participating sites which may include occupational therapy, speech-language therapy and clinical psychology sessions with frequency and duration determined by site clinicians and not standardised by this protocol. Sessions for the study intervention will be held twice weekly for 60 minutes each. The control arm will receive usual care only at their respective sites.

Data will be analysed using intention-to-treat, mixed-effects models for repeated measures with effect sizes and 95% CIs. We expect the intervention to yield clinically meaningful improvements in motor proficiency and secondary domains compared with usual care, informing scalable, context-appropriate physiotherapy for Malaysian children with ASD.

General Information

- **Protocol title:** Development and Evaluation of a Structured Physiotherapy Intervention on Psychomotor and Quality of Life in Children with Mild to Moderate Autism Spectrum Disorder
- **Protocol ID:** ISRCTN pending
- **Sponsor/Funder:** Universiti Kebangsaan Malaysia
  Address: Universiti Kebangsaan Malaysia, Faculty of Health Sciences, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur
- **Principal Investigator:** Dr Asfarina binti Zanudin
  Affiliation & site address: Senior Lecturer, Physiotherapy Programme, Faculty of

Health Sciences, Universiti Kebangsaan Malaysia
Email: asfarina.zanudin@ukm.edu.my
Responsibilities: Overall study oversight, staff training, monitoring, data integrity, adverse event reporting.

- **Co-Investigators:**
    - Nazurah Alwi, Marang Health Clinic — Recruitment, intervention delivery oversight, site coordination.
    - Nor Azizah Mohamad, Hospital Tunku Ampuan Besar Tuanku Aishah Rohani, Children's Specialist Hospital UKM, Jalan Yaacob Latif, Bandar Tun Razak— Recruitment, data collection logistics.
- **Research sites:** Hospital Tunku Ampuan Besar Tuanku Aishah Rohani, Children's Specialist Hospital UKM. Pemulihan dalam Komuniti (PDK) Marang, Bukit Payong,Rawai. Persatuan Autisme Terengganu.
- **Outcome assessment team:** Independent, trained assessors; blinded to allocation.

Rationale & Background

Motor deficits, lower habitual physical activity, behavioural issues and reduced QoL are common in ASD and are linked to poorer participation and family burden. Physiotherapy and structured exercise targeting strength, balance, coordination, and aerobic capacity show promise for improving motor proficiency and related outcomes. However, prior studies often have small samples, heterogeneous protocols, or limited blinding, and there is a scarcity of RCTs tailored to Malaysian service contexts. This trial addresses these gaps by testing a standardized, progression-based physiotherapy program with rigorous methodology and clinically relevant outcomes.

References :

1)Pan CY, Chu CH, Tsai CL, Sung MC, Huang CY, Ma WY.2017. The impacts of physical activity intervention on physical and cognitive outcomes in children with autism spectrum disorder. Autism. 21(2):190-202. doi: 10.1177/1362361316633562. Epub 2016 Jul 9. PMID: 27056845.

2) Yuang Cho ,Lixia Fan & Xiaojin Moa .2023.. The effect of motor interventions on gross motor skills in children with autism: a systematic review and META analysis. 10.21203/rs.3.rs-3802549/v1.

3) Ji YQ, Tian H, Zheng ZY, Ye ZY, Ye Q. 2023. Effectiveness of exercise intervention on improving fundamental motor skills in children with autism spectrum disorder: a systematic review and meta-analysis. Front Psychiatry. Jun 12;14:1132074. doi: 10.3389/fpsyt.2023.1132074. PMID: 37377477; PMCID: PMC10291092.

4)Kaur M, Bhat A. 2019. Creative Yoga Intervention Improves Motor and Imitation Skills of Children With Autism Spectrum Disorder. Phys Ther. 2019 Nov 25;99(11):1520-1534. doi: 10.1093/ptj/pzz115. PMID: 31765484; PMCID: PMC7325451.

5)Djordjevic M, Memisevic H, Potic S, Djuric U. 2022. Exercise-Based Interventions Aimed at Improving Balance in Children with Autism Spectrum Disorder: A Meta-Analysis. *Percept Mot Skills.* Feb;129(1):90-119. doi: 10.1177/00315125211060231. Epub 2021 Dec 22. PMID: 34936828.

6)Dong L, Fan R, Shen B, Bo J, Pang Y, Song Y. 2024. A comparative study on fundamental movement skills among children with autism spectrum disorder and typically developing children aged 7-10. *Front Psychol.* 2024 Mar 28;15:1287752. doi: 10.3389/fpsyg.2024.1287752. PMID: 38605844; PMCID: PMC11007089.

Study Goals and Objectives

Goal: To evaluate the effectiveness of a structured physiotherapy intervention on the psychomotor (motor skills, physical activity, behavior problems) and QoL among children with ASD.

Primary objective:

- To compare change in BOT-2 Total Motor Composite from baseline to 12 weeks between intervention and control.

Secondary objectives:

- To compare changes in GARS-3, GLTEQ (parent-report physical activity), CBCL (behaviour problems), and PedsQL (QoL) from baseline to 12 weeks.
- To evaluate adherence, acceptability, and adverse events associated with the intervention.

Study Design

Design: Assessor-blinded, parallel-group RCT with 1:1 allocation to intervention vs usual care.

Population & setting: Children aged 6–10 years with GARS-3 confirmed AS (mild–moderate) Autism recruited from [PDK centres, hospital rehabilitation units, NGOs/schools] in Terengganu and Kuala Lumpur.

Sample size: N=64 (32 per arm).

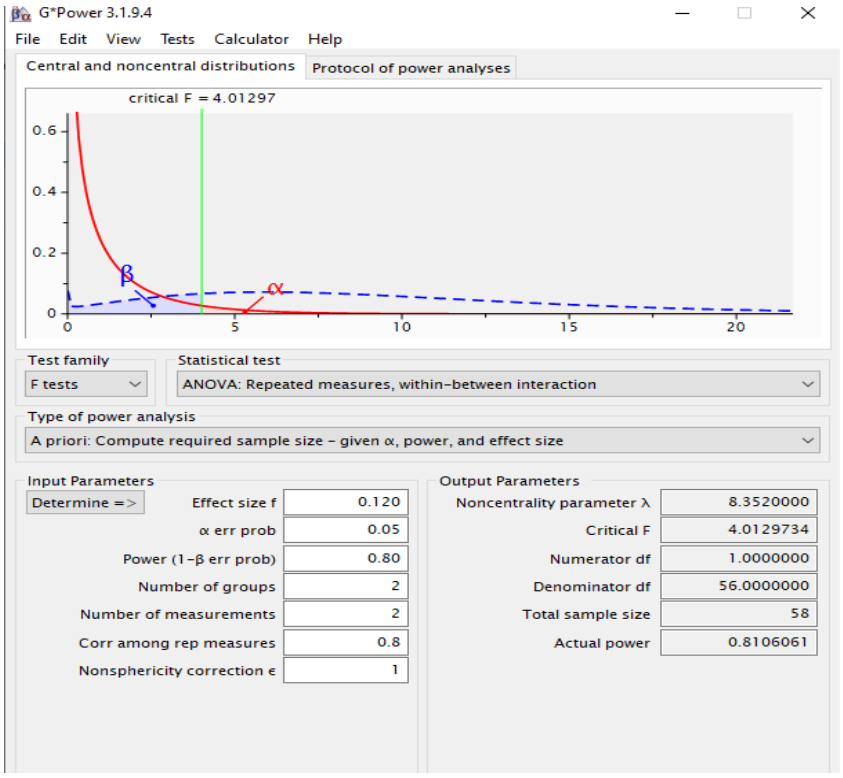

Figure 6. G-Power sample size calculation

G Power software was used to calculate the sample size. To answer the second objective of this study, F-test repeated measure within-between group ANOVA using alpha 0.05, power 0.80 and effect size 0.12. Effect size is determined using reference from previous study Gabriels et al. 2015. The effect size for this study is determined using references from Gabriels et al. (2015). Specifically, the effect size is derived from the motor skills outcomes reported in Gabriels et al. (2019), which also utilized The Bruininks-Oseretsky Test of Motor Proficiency Second Edition (BOT-2), the primary outcome measure for the current study. Cohen's d from Gabriels et al. (2019) was converted to Cohen's f using the escal.site converter. Additionally, based on the recommendations of Cramer et al. (2016), a 10% dropout rate will be factored into this study.Adjusted sample sized considering 10% drop out rate using the calculation below:

N1 = n / (1-d)

N1 = 58/ (1-0.10)

N1 = 64

Total 64 participants will be recruited in this study. A total of 32 participants will be allocate to intervention group and 32 participants in the control group.

Eligibility criteria

- *Inclusion: i)Children diagnosed with ASD ii)Mild to moderate severity based on Gilliam Autism Rating Scale-third edition (GARS-3) iii)Having motor difficulties based on Bruininks-Oseretsky Test of Motor Proficiency Second Edition (BOT-2) iv)Aged 6 to 10 years old v) had no sensory impairments, such as visual or hearing impairments*
- *Exclusion: i)Presence of other neurological or developmental conditions such as epilepsy, Attention-Deficit Hyperactivity Disorder (ADHD) or cerebral palsy ii) Physical disabilities resulting from head injuries or other acquired conditions that interfere with participation in motor-based interventions iii) Currently involved in another clinical trial or intensive motor-based programm iv) Unstable medical condition or recent changes in medical treatment that may affect participation*

Randomization & allocation concealment: Centralized computer-generated sequence with variable block sizes, stratified by site (and ASD severity if feasible). Allocation concealed using opaque, sequentially numbered envelopes or secure REDCap randomization.

Blinding: Outcome assessors and data analysts blinded; therapists and participants unblinded due to intervention nature. Caregivers instructed not to reveal allocation during assessments.

Intervention (12 weeks plus usual care:

- Supervised physiotherapy **2 sessions/week, 60 minutes** per session
- Components: dynamic balance & coordination drills, bilateral integration, task-oriented motor practice, age-appropriate resistance (bands/bodyweight), aerobic play/intervals.
- **Progression (FITT):** Start low-to-moderate intensity, progress volume/complexity weekly; individualized based on baseline motor level and tolerance.
- Therapist training and fidelity checklists used to standardize delivery.

Control (Usual care):

- Continuation of services routinely available at sites (e.g., school/clinic therapy); no structured study physiotherapy.

Assessments & timeframe:

- Baseline (Week 0) and Post-intervention (Week 12). [Optional exploratory follow-up at Week 24 if feasible.]
- Outcomes: BOT-2 (primary); GARS-3, GLTEQ (parent), CBCL, PedsQL (secondary); adherence and adverse events recorded each visit.

Withdrawals/Discontinuation:

- Criteria: medical events contraindicating exercise; inability to attend ≥60% sessions; caregiver request; investigator judgment for safety. Data retained for ITT unless consent withdrawn.

Statistical analysis:

- Intention-to-treat with mixed-effects models (group × time), robust SEs, and multiple imputation if needed. Report adjusted mean differences, 95% CIs, standardized effect sizes, and sensitivity per-protocol analyses.

Methodology

Study design and setting

Assessor-blinded, parallel-group randomized controlled trial (1:1 allocation) comparing a **12-week structured physiotherapy intervention** plus usual care versus **usual care only**. Recruitment will occur at community centres (PDK) in Terengganu and the Klang Valley, hospital rehabilitation units, and partner NGOs. All sites will follow identical SOPs, manuals, and training to ensure standardisation.

Participants

Eligibility (summary):

- *Inclusion:* i)Children diagnosed with ASD ii)Mild to moderate severity based on Gilliam Autism Rating Scale-third edition (GARS-3) iii)Having motor difficulties based on Bruininks-Oseretsky Test of Motor Proficiency Second Edition (BOT-2) iv)Aged 6 to 10 years old v) had no sensory impairments, such as visual or hearing impairments
- *Exclusion:* i)Presence of other neurological or developmental conditions such as epilepsy, Attention-Deficit Hyperactivity Disorder (ADHD) or cerebral palsy ii) Physical disabilities resulting from head injuries or other acquired conditions that interfere with participation in motor-based interventions iii) Currently involved in another clinical trial or intensive motor-based programm iv) Unstable medical condition or recent changes in medical treatment that may affect participation

Interventions

Intervention arm (Physiotherapy + usual care)

- Format & dose: Small groups (2 participants), 2 sessions/week, 60 min/session, for 12 weeks (24 sessions).
- **Content (progressive FITT):**
    - *Neuromotor/coordination:* bilateral integration, sequencing, hand-eye and foot-eye tasks, task-oriented functional drills.
    - *Balance:* static/dynamic balance, obstacle courses, vestibular/proprioceptive challenges.
    - *Strength:* age-appropriate resistance (bodyweight, bands), large muscle groups, 1–3 sets × 8–12 reps, progress load/complexity weekly.
    - *Aerobic:* game-based intervals targeting moderate intensity , 8–15 min accumulated.

    - *Structure:* 5–8 min warm-up → 40–45 min core → 5–7 min cool-down/sensory regulation.

- **Home practice:** 10–15 min/day, 5 days/week; caregiver logbook.
- **Concomitant care:** Usual care permitted, no new intensive motor programmes during the 12 weeks.

Control arm (Usual care only)

"Usual care" denotes services routinely available at sites (e.g., occupational therapy, speech-language therapy, clinical psychology)with frequency/dose determined by site clinicians and not standardised by this protocol. All usual-care utilisation will be recorded.

Therapist training & fidelity

Physiotherapists receive a 1-day competency workshop, manual given for physiotherapist, session checklists used each visit and corrective feedback documented.

Procedures

Screening → enrolment → baseline

- Pre-screen (referral lists), caregiver contact, eligibility verification.
- Medical clearance (where indicated), resting vitals, pre-exercise readiness.
- Written **parent/guardian consent** and **child assent** (age-appropriate).
- Baseline assessments (BOT-2, GARS-3, GLTEQ-parent, CBCL, PedsQL).

Randomization, allocation concealment, and blinding

- **Sequence:** computer-generated using randomization.com, variable blocks, stratified by gender and age.
- **Concealment:** sequentially numbered, opaque, sealed envelopes prepared off-site.
- **Blinding:** outcome assessors blinded. Therapists and participants unblinded. Caregivers instructed not to disclose allocation during assessments.

Visit schedule and timing

- **Intervention period:** Weeks 1–12 (2×/week).
- **Assessments:** Baseline (Week 0) and Post-intervention (Week 12). Optional exploratory follow-up at Week 24 (resources permitting).

Flow diagram (text outline)

Referral/Screen → Eligibility → Consent/Assent → Baseline (T0) → Randomization (1:1)
→ **Intervention + Usual Care** (24 sessions) → **Post-test (T1, Week 12)**
→ **Usual Care Only** → **Post-test (T1, Week 12)**

Outcomes and instruments

- **Primary:** Motor proficiency—**BOT-2 Total Motor Composite** (standardised administration).
- **Secondary:** ASD severity (GARS-3), physical activity (GLTEQ—parent report), behaviour problems (CBCL), QoL (PedsQL).
- **Process/feasibility:** session attendance (%), home-practice adherence, intervention fidelity, acceptability (brief caregiver survey), adverse events (AEs).

Safety considerations

- **Risk level:** minimal to moderate (exercise-related).
- **Pre-session screen:** illness/injury check, vitals; postpone if fever/acute illness, BP or HR outside child-safe parameters or clinician concern.
- **AEs/SAEs:** recorded each visit; **SAEs** reported to PI within 24 hours and to ethics/DSMB within 7 days (fatal/life-threatening within 24–48 hours).
- **Stopping rules (individual):** medical contraindication, SAE judged related to intervention, persistent distress/non-tolerance, caregiver request.
- **Stopping rules (study):** DSMB may pause/stop for excess SAEs or futility based on pre-specified rules.

Follow-up

Participants with AEs are followed until resolution/stabilisation, including after T1 if needed.

Data management and statistical analysis

- **Capture:** audit trails and data entry for key outcomes.
- **Data handling:** de-identified participant IDs; encrypted storage; access role-based; data dictionary maintained; weekly QC reports.
- **Sample size: N=64 (32/arm)** provides 80% power (α=0.05, two-sided) to detect a standardised mean difference.
- **Primary analysis:** intention-to-treat mixed-effects models (group, time, group×time), site as random effect (or fixed if few levels); adjusted mean differences with **95% CIs** and standardised effect sizes.
- **Secondary outcomes:** same framework with distribution-appropriate links; multiplicity handled by hierarchical interpretation (primary first).
- **Missing data:** explored for mechanism; multiple imputation if MAR plausible; sensitivity per-protocol (≥75% session attendance) and complete-case analyses.
- **Interim analyses:** none for efficacy; DSMB safety reviews only.

Quality assurance

- Conduct under ICH-GCP and local regulations; PI oversight; site initiation visits; routine monitoring (source data verification on ≥10% records); calibration of measurement tools; version-controlled SOPs; protocol deviations logged and reported.

Expected outcomes

Demonstrate clinically meaningful gains in BOT-2 and improvements in ASD severity, physical activity, behaviour and QoL, informing scalable, context-appropriate physiotherapy pathways for Malaysian children with ASD.

Dissemination and publication policy

Results shared with caregivers and participating centres (plain-language summary), presented at national/international meetings, and submitted to peer-reviewed journals. **Authorship** per ICMJE; PI leads first manuscript; site leads and key contributors co-author; all contributors acknowledged. Policy briefs prepared for MOH/PDK stakeholders.

Duration and timeline (illustrative, 12 months)

- Months 1–2: Site setup, staff training, pilot fidelity, finalise CRFs.
- Months 3–6: Recruitment and baseline assessments.
- Months 4–9: Intervention delivery (rolling cohorts).
- Months 6–10: Post-tests; data cleaning/QC.
- Months 10–12: Analysis, reporting, dissemination.

Anticipated problems & mitigation

- **Recruitment shortfall:** expand referral networks, add sessions across sites, flexible scheduling.
- **Attrition/attendance:** caregiver engagement, SMS reminders, make-up sessions.
- **Contamination:** clear guidance to avoid new intensive programmes and document all concomitant therapies.
- **Blinding breaches:** assessor re-assignment and reminder scripts to caregivers.
- **Heterogeneous usual care:** detailed recording to adjust in analyses.

Project management

- **PI:** overall leadership, safety oversight, reporting.
- **Co-Is/Site leads:** recruitment, local governance, intervention supervision.
- **Therapists:** deliver sessions, fidelity checklists, AE logs.
- **Blinded assessors:** baseline/post-tests; inter-rater reliability checks.
- **Data manager/Statistician:** analysis plan

Ethics

- Prior approval from JEPUKM.
- **Consent process:** private discussion with caregiver; written consent; child assent (simple language/visuals) for ages 6–10, right to withdraw without penalty.
- **Confidentiality:** coded IDs, secure storage, limited access and reporting in aggregate.
- **Compensation:** reimbursement of transport/parking; no inducements.
- **Risk–benefit:** minor exercise risks vs potential motor/participation benefits.

Informed consent forms (ICFs)

Provide separate ICFs in **English and Malay** for: (1) Parent/Guardian consent; (2) Child assent (age-appropriate); (3) Permission to access routine care records. Each ICF includes: study purpose/procedures, risks/benefits, alternatives, confidentiality, voluntary participation/withdrawal, contacts for questions/complaints, and data use/sharing statements.