

INPLASY PROTOCOL

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Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest:
None declared.

The effectiveness of physical activities on children with autism spectrum disorder: A systematic review and network meta-analysis

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Review question / Objective: The purpose of this meta-analysis was to evaluate the efficacy of different physical activity interventions and to determine which physical activity interventions are most effective for children with autism spectrum disorder.

Condition being studied: Autism is a set of heterogeneous neurodevelopmental conditions, characterized by early-onset difficulties in social communication and unusually restricted, repetitive behavior and interests. Autism affects more male than female individuals, and comorbidity is common (>70% have concurrent conditions). Exercise has increasingly emerged as one of the promising compensation methods that can positively affect autistic symptoms. The positive effects of various physical activity interventions have been reported, but it is unclear which interventions are most effective at improving symptoms of autism.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 April 2022 and was last updated on 06 April 2022 (registration number INPLASY202240034).

INTRODUCTION

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emerged as one of the promising compensation methods that can positively affect autistic symptoms. The positive effects of various physical activity interventions have been reported, but it is unclear which interventions are most effective at improving symptoms of autism.

METHODS

Search strategy: Search strategy: PubMed: ((ASD[Title/Abstract] OR Autis*[Title/Abstract] OR "Autism Spectrum Disorder"[Title/Abstract] OR Asperger*[Title/Abstract] OR "Asperger* syndrome"[Title/Abstract] OR "Pervasive developmental disorder*" [Title/Abstract] OR PDD[Title/Abstract] OR PDDNOS[Title/Abstract] OR "Rett Syndrome"[Title/Abstract] OR "Rett* disorder"[Title/Abstract] OR "Kanner* Syndrome"[Title/Abstract] OR ("Autistic Disorder"[MeSH] OR "Asperger Syndrome"[MeSH] OR "Autism Spectrum Disorder"[MeSH] OR "Rett Syndrome"[MeSH])) AND ((Sport*[Title/Abstract] OR Exercise*[Title/Abstract] OR Training[Title/Abstract] OR "Locomotor Activit*" [Title/Abstract] OR "Physical* therap*" [Title/Abstract] OR "physical* activit*" [Title/Abstract] OR "motor activit*" [Title/Abstract] OR "Physical Exercise"[Title/Abstract]) OR ("Youth Sports"[MeSH] OR "Sports for Persons with Disabilities"[MeSH] OR Sports[MeSH] OR Exercise[MeSH])) AND ((Child*[Title/Abstract] OR "School-age*" [Title/Abstract] OR "young child*" [Title/Abstract] OR Kid*[Title/Abstract] OR Boy*[Title/Abstract] OR Girl*[Title/Abstract] OR Male*[Title/Abstract] OR Female*[Title/Abstract] OR "Primary-age*" [Title/Abstract] OR Preschool[Title/Abstract]) OR (Child[MeSH] OR "Child,Preschool"[MeSH])) Filters: Clinical Trial, Randomized Controlled Trial Web of Science: #1 TI=(ASD OR Autis* OR "Autism Spectrum Disorder" OR Asperger* OR "Asperger* syndrome" OR "Pervasive developmental disorder*" OR PDD OR PDDNOS OR "Rett Syndrome" OR "Rett* disorder" OR "Kanner* Syndrome") OR AB=(ASD OR Autis* OR "Autism Spectrum Disorder" OR Asperger* OR "Asperger* syndrome" OR "Pervasive developmental

disorder*" OR PDD OR PDDNOS OR "Rett Syndrome" OR "Rett* disorder" OR "Kanner* Syndrome") OR TS=("Autistic Disorder" OR "Asperger Syndrome" OR "Autism Spectrum Disorder" OR "Rett Syndrome")

#2 TI=(Sport* OR Exercise* OR Training OR "Locomotor Activit*" OR "Physical* therap*" OR "physical* activit*" OR "motor activit*" OR "Physical Exercise") OR AB=(Sport* OR Exercise* OR Training OR "Locomotor Activit*" OR "Physical* therap*" OR "physical* activit*" OR "motor activit*" OR "Physical Exercise") OR TS=("Youth Sports" OR "Sports for Persons with Disabilities" OR Sports OR Exercise)

#3 TI=(Child* OR "School-age*" OR "young child*" OR Kid* OR Boy* OR Girl* OR Male* OR Female* OR "Primary-age*" OR Preschool) OR AB=(Child* OR "School-age*" OR "young child*" OR Kid* OR Boy* OR Girl* OR Male* OR Female* OR "Primary-age*" OR Preschool) OR TS=(Child OR "Child,Preschool")

#4 #1 AND #2 AND #3

EBSCO: S1 TI (ASD OR Autis* OR "Autism Spectrum Disorder" OR Asperger* OR "Asperger* syndrome" OR "Pervasive developmental disorder*" OR PDD OR PDDNOS OR "Rett Syndrome" OR "Rett* disorder" OR "Kanner* Syndrome") OR AB (ASD OR Autis* OR "Autism Spectrum Disorder" OR Asperger* OR "Asperger* syndrome" OR "Pervasive developmental disorder*" OR PDD OR PDDNOS OR "Rett Syndrome" OR "Rett* disorder" OR "Kanner* Syndrome") OR SU ("Autistic Disorder" OR "Asperger Syndrome" OR "Autism Spectrum Disorder" OR "Rett Syndrome")

S2 TI (Sport* OR Exercise* OR Training OR "Locomotor Activit*" OR "Physical* therap*" OR "physical* activit*" OR "motor activit*" OR "Physical Exercise") OR AB (Sport* OR Exercise* OR Training OR "Locomotor Activit*" OR "Physical* therap*" OR "physical* activit*" OR "motor activit*" OR "Physical Exercise") OR ("Youth Sports" OR "Sports for Persons with Disabilities" OR Sports OR Exercise)

S3 TI (Child* OR "School-age*" OR "young child*" OR Kid* OR Boy* OR Girl* OR Male* OR Female* OR "Primary-age*" OR Preschool) OR AB (Child* OR "School-

age*" OR "young child*" OR Kid* OR Boy* OR Girl* OR Male* OR Female* OR "Primary-age*" OR Preschool) OR SU (Child OR "Child, Preschool")
S1 AND S2 AND S3

Qualifications: Academic (Peer-Reviewed) Journals

Language: English

Cochrane Library: #1 ASD OR Autis* OR "Autism Spectrum Disorder" OR Asperger* OR "Asperger* syndrome" OR "Pervasive developmental disorder*" OR PDD OR PDDNOS OR "Rett Syndrome" OR "Rett* disorder" OR "Kanner* Syndrome":ti,ab in Trials

#2 [mh "Autistic Disorder"] OR [mh "Asperger Syndrome"] OR [mh "Autism Spectrum Disorder "] OR [mh "Rett Syndrome"] in Trials

#3 "#1 OR #2" in Trials

#4 Sport* OR Exercise* OR Training OR "Locomotor Activit*" OR "Physical* therap*" OR "physical* activit*" OR "motor activit*" OR "Physical Exercise":ti,ab in Trials

#5 [mh "Youth Sports"] OR [mh "Sports for Persons with Disabilities"] OR [mh "Sports"] OR [mh "Exercise"] in Trials

#6 "#4 OR #5" in Trials

#7 Child* OR "School-age*" OR "young child*" OR Kid* OR Boy* OR Girl* OR Male* OR Female* OR "Primary-age*" OR Preschool :ti,ab in Trials

#8 [mh "Child"] OR [mh "Child,Preschool"] in Trials

#9 "#7 OR #8" in Trials

#10 #3 AND #6 AND #9 in Trials.

Participant or population: Children diagnosed with autism spectrum disorder (ASD), including disorders previously known as autism, Asperger's and pervasive developmental disorders not otherwise specified. Individuals over 16 years of age were excluded.

Intervention: Studies that focused on physical activity interventions. Physical activity is planned, structured, repetitive, and purposeful. Of note, studies that employed one or combined two or more types of exercise modalities as an intervention were included. However, we excluded studies if the physical exercise

interventions combined with other non-exercise activities (e.g. behavioral intervention, pharmacotherapy, and video games) and interventions that included unsupervised training sessions.

Comparator: Non-physical activity intervention comparator groups included participants who engaged in no contact, no treatment, waiting list, and usual care for the comparison condition.

Study designs to be included: Types of study designs included randomized controlled trials (RCTs) or non-randomized comparison studies that investigated the effects of physical activity intervention. Studies that did not involve any comparison group or did not report any comparison results between groups were excluded.

Eligibility criteria: For inclusion, studies were required to be published in a peer-reviewed journal, written in English (grey literature, conference abstracts, and registered trials were excluded). All other inclusion criteria followed the Participants, Interventions, Comparators, Outcomes, and Study design framework. The participants of interest were children diagnosed with autism spectrum disorder (ASD), including disorders previously known as autism, Asperger's and pervasive developmental disorders not otherwise specified. Relevant interventions were restricted to studies that focused on physical activity interventions. Non-physical activity intervention comparator groups included participants who engaged in no contact, no treatment, waiting list, and usual care for the comparison condition. Studies were required to include at least one of the outcome measures of primary symptoms of autism: motor function, stereotyped behaviors, social function, and communication. Studies that did not assess autistic symptoms as outcome measures based on change scores between baseline and post-intervention, incomplete data, or unsuccessful contact with the full-text author were also excluded. In terms of study design, those included were

randomized controlled trials (RCTs) or controlled trials (CTs) that investigated the effects of physical activity intervention and reported sufficient statistical detail (e.g., mean, standard deviation, number of participants) available for network meta-analysis. Studies that did not involve any comparison group or did not report any comparison results between groups were excluded.

Information sources: An electronic search of PubMed, Web of Science, EBSCO, and Cochrane Library was conducted from inception through 31 December 2021 to identify all relevant published articles regarding the effect of physical activity interventions on children with ASD. The search was limited to English-language, and peer-reviewed articles. The search strategy was developed, piloted, and refined based on the previously published reviews. The search is carried out using key phrases and Medical Subject Heading (MeSH) terms. In addition to the databases, we manually searched the reference lists of included articles and previously published systematic reviews to identify articles that met the inclusion criteria.

Main outcome(s): Studies were required to include at least one of the outcome measures of primary symptoms of autism: motor function, stereotyped behaviors, social function, and communication. Studies that did not assess autistic symptoms as outcome measures based on change scores between baseline and post-intervention, incomplete data, or unsuccessful contact with the full-text author were also excluded.

Additional outcome(s): None.

Quality assessment / Risk of bias analysis: Risk of bias for each individual study was assessed independently by two reviewers in accordance with the Cochrane Collaboration Risk of Bias Tool, which examined potential selection bias (random sequence generation and allocation concealment), performance bias (blinding of patients and personnel), detection bias (blinding of outcome assessment), attrition

bias (incomplete outcome data), reporting bias (selective outcome reporting) and other bias. For each source of bias, studies were classified as having a low, high or unclear (if reporting was not sufficient to assess a particular domain) risk.

Strategy of data synthesis: The network meta-analyses were conducted using STATA software (Version 16.0, College Station, Texas, USA.) within a frequentist framework in accordance with current PRISMA NMA guidelines. Network geometry was first created to visualize comparative relationships among different interventions. As all of the outcomes of interest were continuous, but could be measured on different scales, standardized mean difference (SMD) with 95% confidence intervals (CI) was used as the effect estimate. The direction of effect size was recoded such that a positive mean difference indicates a greater improvement in the outcome measure in the intervention group relative to the control group. Given the variations in study design and outcome measures, random-effects models were used to address heterogeneity across studies. The I² statistic was used to rate heterogeneity as low (50%). Consistency, whereby the treatment effect estimated from direct comparisons are consistent with those estimated from indirect comparisons, was assessed by fitting both a consistency and inconsistency NMA model. The local inconsistency test evaluates the difference between direct and indirect estimates in all closed loops in the network. Node splitting was used to evaluate the inconsistency of the model. When the p value exceeded 0.05, the consistency model was used to calculate the effect size of different physical activity interventions and evaluate the rank probabilities. The probability ranking for each intervention was carried out using surface under cumulative ranking curve (SUCRA) percentage values as one of the final predictions. SUCRA reports the overall probability, based on the ranking of all interventions that a given intervention is among the best treatments. SUCRAs range from 0% to 100%; larger SUCRAs indicate more effective intervention methods.

Furthermore, to check for the presence of bias due to small scale studies, which may lead to publication bias in NMA, we generated a network funnel plot and visually inspected using the criterion of symmetry.

Subgroup analysis: None.

Sensitivity analysis: None.

Language: Language limited to English.

Country(ies) involved: China.

Keywords: Systematic review; Network meta-analysis; Autism spectrum disorder; Physical activity; Children.

Contributions of each author:

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