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Interventions for Children with Neurocognitive Impairments in Resource-Limited Settings: A Systematic Review

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Abstract

Many children and adolescents around the world suffer from neurocognitive deficits due to chronic disorders, such as Human Immunodeficiency Virus (HIV) and malaria. Resource-limited settings exacerbate the risk of negative cognitive outcomes due to high prevalence of associated disorders, poverty, and limited access to interventions. Current literature does not provide consensus regarding the efficacy of interventions to support children with cognitive impairments in low-resource settings. This research aimed to identify and evaluate interventions for youth with

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None.

neurocognitive deficits in resource-limited settings. A systematic review of peer-reviewed literature was conducted within five databases (PubMed, Web of Science, CINAHL, PsycInfo, and WHO Index Medicus). Cognitive impairment was broadly defined to be inclusive of aspects of intellectual and cognitive functioning (e.g., working memory, attention, executive function). The income status of the country or countries in which each study was located was determined according to World Bank Income Status. Studies conducted in countries classified as low- or middle-income were included. Since low-resource areas exist within high-income countries, the resource availability within study settings in high-income countries was systematically evaluated for inclusion. The search yielded 19 articles that met all inclusion criteria. Interventions included strategies involving caregiver training, computerized and non-computerized cognitive training, physical activity, and nutritional supplementation. Interventions were administered in medical facilities, educational facilities, or the home. The majority of the interventions targeted the domains of memory and attention. Overall, the efficacy of interventions was inconsistent. Further, results indicated that the relationship between cognitive improvement and intervention types was not consistent across cognitive domains. However, when evaluating studies on an individual basis, some strategies demonstrated clinically- and statistically-significant improvement in cognitive function among specific groups of children. The low article yield highlights that few researchers have evaluated pediatric cognitive support interventions in low-resource contexts. This review suggests support strategies that should be considered for future studies as neurocognitive screening capacity improves in resource-limited settings.

Keywords

Neurocognitive Impairment; Youth; Support Strategies; Resource-Limited Setting; Systematic Review

1. Introduction

1.1 Neurocognitive Impairment among Youth

Impaired neurocognitive functioning contributes to decreased educational performance and quality of life among children and adolescents¹. Various mechanisms explain cognitive deficits among pediatric populations, including disease-related mechanisms¹ and treatment-related mechanisms. The relationships between neurocognitive dysfunction in the maturing brain and several chronic disorders and exposures, such as Human Immunodeficiency Virus (HIV), cerebral malaria, brain tumors, and Type 1 diabetes, have been well-documented^{1–5}. The cognitive domains affected vary by disease pathophysiology. For example, perinatal HIV infection commonly impacts working memory, verbal memory, and executive function, whereas brain tumor-related sequelae vary depending on the location of the malignancy⁶.

1.2 Resource-Limited Settings

Children and adolescents in resource-limited settings are particularly vulnerable to neurocognitive deficits due to the higher frequency of chronic illnesses^{7,8} and the concurrent influences of poverty^{9–11}. Targeted research on the development and validation of tools for early identification of neurocognitive challenges among children in several resource-limited settings is currently being pursued¹². Once the assessment tools have been validated and

implemented successfully in these settings, targeted efforts will be needed to provide interventions that provide cognitive support for the children identified as having deficits. Yet, the World Health Organization notes that 75% of affected people in middle- and low-income countries do not have access to services for mental, neurological, and substance use disorders¹³. Therefore, there is a need for effective, scalable interventions in resource-limited settings. However, the evidence to support specific interventions in these settings is limited and conflicting.

1.3 Systematic Review

Current literature does not provide consensus regarding efficacy or feasibility for interventions to support children with cognitive impairments in low-resource settings. To begin with, a great deal of the literature includes studies conducted in high-resource settings^{14,15}. An approach in such settings may include referral to a specialty center with a multidisciplinary team that would facilitate social work, psychological support, family education and participation, and coordination with the child's school^{14–16}. Inadequate staffing in resource-limited settings makes such approaches infeasible^{16,17}. In addition, much of the published literature focuses on specific disease states^{18–20}. However, interventions or strategies to improve function in specific cognitive domains may be relevant regardless of the etiology. Therefore, this study aimed to identify and evaluate support strategies for children and adolescents with neurocognitive impairments in resource-limited settings.

2. Methods

2.1 Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines guided the conduct of this review²¹. The following search string was developed in consultation with a public health research librarian to optimize the identification of relevant published peer-reviewed literature:

*neurocognit * AND (impairment * OR deficit * OR dysfunction * OR delay) AND (therap * OR support OR resource * OR intervention *) AND (low – resource OR developing OR resource – limited) AND (youth OR children OR adolescent * OR pediatric)*

Five databases (PubMed, Web of Science, CINAHL, PsycInfo, and WHO Index Medicus) were selected to capture a broad spectrum of behavioral interventions and supportive measures in both domestic and international settings. However, the search in the WHO Index Medicus database only yielded two non-relevant articles, so the database is not represented in the final dataset.

2.2 Article Screening

Two independent researchers (AEVP, MIL) reviewed the abstracts of all articles found through database searches. Review articles were separated for a secondary review. A secondary review of the references of each included article and the review articles was performed to identify additional studies. The inclusion criteria were applied to all articles

indicated for possible inclusion. Discrepancies were discussed, and a third researcher (EDL) was consulted to resolve any disagreements.

2.2.1 Inclusion and Exclusion Criteria—The following inclusion criteria were applied: peer-reviewed study written in English, youth participants defined according to the World Health Organization as individuals 2–24 years, interventions that target cognitive impairment, and conducted in a resource-limited setting. Cognitive impairment was broadly defined to be inclusive of aspects of intellectual and cognitive functioning (e.g., working memory, attention, executive function). Achievement-specific impairments (e.g., math, spelling, reading) were not included. Articles that were focused on cognitive impairments among children with a specific disease state were not excluded since cognitive domains and consequent interventions could be relevant across diseases. However, disease-specific interventions such as the use of antiretroviral therapy to minimize the cognitive impacts of HIV infection were not included. Articles involving research performed exclusively on animal models or adults were excluded. In addition, interventions that targeted physical impairment rather than cognitive impairment were excluded. Studies performed in high-resource settings were excluded. The search was limited to studies published before July 2019. A post-hoc search for studies published between July 2019–May 2020 was completed.

2.2.2 Determination of Resource-Limited Setting—The income status of the country or countries in which each study was located was determined according to World Bank Income Status²². Studies conducted in countries classified as low- or middle-income were included. Since low-resource areas exist within high-income countries, the resource availability within study settings in high-income countries was systematically evaluated. When authors specifically reported that a setting within a high-income country had limited resources, a multi-step approach was employed to determine whether the study should be included. Available proxy measures for the study participants and setting, such as income, socioeconomic index, poverty, and percentage on free or reduced lunch, were examined on a case-by-case basis. When the socioeconomic status of and resources available to the included population were shown to be comparable to resources available in low- and middle-income countries rather than to resources typically available in high-income countries, those studies were included.

2.3 Data Extraction

Two reviewers independently extracted the data from each of the studies that was chosen for inclusion. Discrepancies were discussed and reconciled through additional review of the full text or consultation with the senior author. The following data were extracted: title, first author, publication year, study location, study design, participants' age range, sample size, participants' disease state(s), additional inclusion criteria, cognitive domain(s) targeted, intervention details, location intervention administered, analysis methods, outcome measure, results, and effectiveness. Decisions on effectiveness were determined based on a critical review of the published data rather than the stated conclusions of the articles' authors. Notes on the justification of the low-resource setting, as described in 2.2.2, were documented. Data that were not relevant to the research question, such as the inclusion of the effectiveness of the intervention in a high-income setting, was not extracted. Further, data that suggested

improvement in cognitive function through a non-generalizable pathway, such as iron supplementation for iron-deficient participants, was not extracted.

2.4 Data Analysis

Each study was evaluated qualitatively, as the heterogeneity of the articles did not allow for pooling of the data across studies (e.g., via meta-analysis). Statistical significance was determined based on a threshold of an alpha of 0.05, when provided. For a more comprehensive evaluation of the data, a thorough review of the clinical significance of each study was performed by a clinical neuropsychologist and a pediatrician. Decisions on clinical effectiveness were made through an assessment of the magnitude of the effect sizes, the consistency of effects across outcome measures assessing similar constructs (e.g., attention), and the relationship of the magnitude of an effect with known benchmarks for clinical significance (e.g., change in standardized score units). Given the heterogeneity of study designs, the quality of the studies and the risk of bias were assessed qualitatively.

3. Results

3.1 Article Yield

The application of the search string to the four databases yielded 645 articles. After removing duplicate articles, 464 articles remained for the first round of screening. The application of the inclusion criteria resulted in two articles to be included in the systematic review, while the remaining articles were excluded due to the following reasons: animal models, no intervention, disease-specific interventions and outcomes, adult participants, high-resource setting, outcomes limited to achievement measures (e.g. math, reading), imaging studies, and non-peer-reviewed literature. The review of the references produced 598 (574 after duplicate deletion) articles for the second round of screening. The application of the inclusion criteria resulted in 16 articles to be included in the systematic review, while the remaining articles were excluded due to the aforementioned reasons as well as the following reasons: statistical software, cognitive test, and manuscript guidelines. A post-hoc search for literature published July 2019-May 2020 resulted in one additional article for inclusion. A total of 19 articles were included in this systematic review. Figure 1 outlines the PRISMA flowchart detailing the article screening process.

3.2 Article Characteristics

Table 1 provides an overview of the article characteristics. The research occurred in five continents: Africa (10), Asia (3), Australia (1), and North America (5). The sample size ranged from 12–409, and participants ranged from 16 months to 19 years. Participants with infectious diseases and chronic diseases were included, and approximately half of the studies enrolled youth with either attention deficit hyperactivity disorder (ADHD) or HIV. The majority of support strategies targeted the cognitive domains of memory (14 studies) and/or attention (13 studies). The studies employed diverse research designs of varying rigor, ranging from quasi-experimental designs to double-blind, placebo-controlled trials.

3.3 Summary of Evidence

Table 2 provides an overview of the type, location of administration, and effectiveness of the interventions in low-resource settings. The support strategies varied from computerized cognitive training to nutritional supplementation that were administered in medical facilities, educational facilities, or the home. The results specific to neurocognitive outcomes are outlined in Table 2. Some of the literature that the search yielded involved studies that occurred in high-income countries but among lower-resourced populations (e.g., low-income). Such studies appeared to be relevant for the current review since they reflected resource limitations. Even though the context differed, these approaches might therefore be adaptable to low- and middle-income countries. Table 3 provides an overview of the type, location of administration, and results of the interventions for the studies conducted in a high-income country. The majority of the studies occurred in the United States.

3.3.1 Caregiver Training—Three studies included training of caregivers or other social support as a strategy to improve cognitive function. Two studies took place in Uganda, and one study took place in the United States. The ages of the participants ranged from 16 months–5 years. The components of the caregiver training included the following: Mediational Interaction for Sensitizing Caregivers (MISC) training²⁸; comparison of the MISC training to the Uganda Community Based Association for Child Welfare program with nutritional support (enriched porridge of millet, soya, sesame, peanuts, rice, and sugar) for both intervention arms³⁰; and combination of the Linking the Interests of Families and Teachers training with non-computerized cognitive training of children³⁵. The caregiver trainings were conducted in the school, home, or research facility. The studies did not target the same cognitive domains, but the trainings resulted in reported improvements in attention, nonverbal IQ, memory, and executive function.

3.3.2 Cognitive Training

Computerized Cognitive Training: Six studies administered computerized cognitive training as a support strategy. These studies occurred in Uganda (5) and the United States. The age of the participants ranged from 6–16 years. The computerized tools for cognitive training included the following: Captain's Log^{24,25,27,29}; Brain Powered Games³³; and Cogmed Working Memory Training³¹. The computerized training was facilitated in a medical facility, home, or school. Overall, the efficacy of the computerized cognitive training was not consistent between studies. Some articles reported improvements in attention, memory, visual-motor processing, executive function, visual-spatial analysis, and mental processing, while other articles described minimal effects in these areas. One study reported a statistically-significant *decline* in working memory.

Non-Computerized Cognitive Training: Three articles discussed non-computerized based cognitive training. These studies occurred in Iran and the United States (2). The age of the participants ranged from 3–19 years. The non-computerized cognitive training involved the following: cognitive-behavioral play therapy²³; a five part program teaching problem-solving skills, behavioral study skills, information processing strategies, compensatory strategies, and collaborative contact with parents and teachers³⁸; and Parents and Children Making Connections- Highlighting Attention³⁵. The trainings were facilitated in a school or

medical facility. Overall, the results on the efficacy of the non-computerized cognitive training on improvements in attention and memory were not consistent, as some studies reported improvement while others reported no improvement or a lack of statistically-significant differences between the control and intervention groups. The cognitive training did reportedly improve nonverbal IQ in one study.

3.3.3 Physical Activity—Three articles examined the effectiveness of physical activity on improving cognitive function. These studies occurred in the United States, South Africa, and Iran. The age of the participants ranged from 5–13 years. Forms of physical activity included the following: one hour of exercise with a minimum of 20 minutes in the target heart rate zone³⁴; cycling⁴⁰; and circuit training⁴¹. The interventions took place in a research facility or school. Overall, physical activity was reported to improve attention and motor skills but not memory.

3.3.4 Nutritional Supplementation—Five articles described nutritional supplementation as a mechanism for improving cognitive function. These studies took place in South Africa (2), Indonesia, Australia, and Mexico. The age of the participants ranged from 3–13 years. Types of nutrition supplementation included the following: fish oil (docosahexanoic acid (DHA) and eicosapentaenoic acid (EPA)) capsules²⁶; bread with fatty acid spread containing fish flour and red palm oil fat³²; drink with fatty acid supplementation (DHA and EPA) or micronutrient supplementation (iron, folate, vitamin B-6, vitamin B-12, zinc, vitamin A, and vitamin C)³⁶; Omega-3 (DHA and EPA) capsules³⁹; and Equazen 'eye q™ polyunsaturated fatty acid capsules³⁷. All of the interventions were administered in a school, except for one study that also provided supplementation for the home. Overall, the efficacy of nutritional supplementation on improvements in memory, executive functioning, and visuomotor function was not consistent. The nutritional supplementation did result in reported improvements in cognitive maturity and processing speed, but supplementation did not improve attention or verbal learning.

3.4 Summary of Clinical Significance of Results

Table 4 provides a summary of the clinical significance for each article. Very few studies discussed clinical significance. The review of clinical significance of the results was limited based on the information provided for each study. Eight articles demonstrated some evidence of clinically-significant improvement in certain aspects of cognitive functioning, while three articles did not suggest clinically-significant improvement post-intervention. Insufficient information (e.g., lack of control group, lack of clinical benchmarks, small sample size, and scales of reporting outcome measures) resulted in an inability to determine clinical significance in eight articles.

3.5 Quality of Study Methodology

Due the heterogeneity of the articles included in this review, the study methodologies were analyzed qualitatively. Broadly, 13 studies were randomized trials, and 6 studies were quasi-experimental designs. Overall, the quality of the studies included in this review were poor due to limitations in the methodological approaches and lack of information provided about the study design, which suggested high risk for bias in the results. Some of the randomized

trials did not report information on blinding^{24,25,27}. One study stated that there was an improvement in cognitive functioning among participants without showing a difference in improvement between the intervention group and the control group³⁴. Further, studies that did not include a control group cannot attribute improvement in cognitive function to intervention effect rather than other potential factors (e.g., practice effects or maturation). The sample sizes in the articles ranged from 12–409. The studies that recruited a small sample size were likely underpowered to detect a significant intervention effect.

4. Discussion

4.1 Discussion of Results

This systematic review aimed to identify and evaluate support strategies for youth with neurocognitive impairment that have been used in resource-limited settings. The systematic review did not yield a high number of articles, and those reviewed did not demonstrate robust or consistent results, which highlights the need for additional research in this area. Overall, the efficacy of different types of intervention was not consistent across studies or cognitive domains. There was very limited evidence for caregiver training or physical activity to be associated with clinically significant improvement in cognitive functioning in the available studies, with mixed results for computerized cognitive training and nutritional supplementation. However, when evaluating studies on an individual basis, some strategies demonstrated significant improvement in cognitive functioning among specific groups of children. Future studies with greater rigor in research design could examine whether such approaches result in greater generalizability of impact.

4.2 Strengths and Limitations

4.2.1 Strengths—This systematic review had multiple strengths. First, two researchers independently completed each step of the data collection and analysis, which increased the rigor of the research. Second, multiple databases across several disciplines were searched to capture published literature of various research designs and foci. Third, studies were included regardless of the participants' disease states, which enabled the collation of a larger body of evidence. Fourth, a comprehensive assessment of both statistically- and clinically-significant improvement was completed.

Most of the articles included in the review reported statistical estimates which allowed for an interpretation of the statistical significance of the results. The statistical significance indicates the probability of the results being due to chance. Thus, many aspects of the study's design, such as sample size, can influence these estimates. To understand an intervention's impact fully, an evaluation of the clinical significance of the results is also necessary. Such an evaluation helps to contextualize the findings by elucidating the intervention's potential impact on measurable function. The holistic approach of assessing both the statistical significance and clinical significance of the data in this systematic review is particularly important since children continue the protracted development of cognitive skills well into their third decade of life, and small changes can be meaningful for long-term cognitive capacity.

4.2.2 Limitations—One limitation of this systematic review is the significant heterogeneity in study designs, which limited comparisons between the results and conclusions across the articles and, consequently, intervention types. Further, heterogeneity in the participants and study settings existed, which limited the generalizability of the strategies described. Some studies assessed the effectiveness of interventions on children with neurocognitive impairment, while other studies included children without neurocognitive impairment. A limitation in all systematic reviews is that the data may have exhibited publication bias, and there was no robust means to test for this bias. None of the studies were conducted in South America, which excludes many low- and middle-income countries that could benefit from the evaluation of support strategies in a low-resource setting. Further, the articles included in this review were peer-reviewed literature, so this approach may have excluded relevant non-peer-reviewed data, such as academic conference abstracts, and biased the data toward positive results. In addition, many of the studies were completed by the same researchers. Since this systematic review summarizes only interventions that were published in peer-reviewed journals, some promising programmatic findings might not be included. Researchers are motivated and funded to publish their work, while individuals working with non-governmental organizations and government programs may have completed unpublished work with promising results in this area. Finally, although an approach to determine the resource status of the participants from a high-income country was developed, the methodology utilized proxy variables that varied by article.

4.3 Implications of Results

Although researchers are developing tools for the detection of neurocognitive deficits among children in resource-limited settings, there are limited evidenced-based interventions for children with neurocognitive deficits in these settings. This systematic review suggests support strategies that could be considered for future studies as neurocognitive screening capacity improves, although none provide consistent evidence at the current time. Future studies of support strategies for resource-limited settings should also consider feasibility and implementation challenges, which may limit the generalizability of these results. For example, strategies that are administered at a medical facility and require frequent visits may not be feasible when accessibility to transportation is limited. Strategies that require a single in-person visit or facilitation in the home or school may be more generalizable to low-resource settings. However, approaches found to be impactful when implemented through longitudinal facility-based approaches might be adaptable for successful implementation in school or community settings.

4.4 Further Research

A primary goal of this systematic review was to provide an evidence base regarding beneficial strategies for improving neurocognitive functioning in children and adolescents in resource-limited settings and to offer recommendations for future research. However, the limited data and poor quality of the published studies included in this systematic review highlight the weak evidence base and a critical need for further research. Important next steps include increasing the quantity and rigor of studies to better determine the efficacy of interventions to improve cognitive function. Additional large-scale research conducted in resource-limited settings would increase the body of evidence.

5. Conclusions

Neurocognitive impairments affect youth around the world. Results of this systematic review highlight that few researchers have effectively evaluated pediatric cognitive support strategies in resource-limited settings. The available evidence indicates that certain strategies may improve cognitive functioning in particular populations, although the efficacy of different intervention types varies substantially across cognitive domains and research studies. This review provides an initial overview of support strategies that should be considered for future studies as neurocognitive screening capacity improves in resource-limited settings.

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Highlights

- 19 articles evaluated cognitive support among youth in resource-limited settings.
- Interventions include caregiver training, cognitive training, exercise, and nutrition.
- The reported efficacy of interventions is not consistent.
- Evidence suggests that some interventions may improve cognitive function.

Figure 1. PRISMA Flowchart of Article Inclusion. The vertical arrows indicate inclusion, while the horizontal arrows indicate exclusion.

TABLE 1

Overview of Articles Included in Systematic Review

Study	Location	Sample Size	Participant Characteristics	Cognitive Domains Targeted	Study Design
Abdollahian et al. (2013) ²³	Iran	30	7–9 years ADHD	Attention	Quasi-experimental
Bangirana et al. (2009) ²⁴	Uganda	65	9.7 years control, 10.1 years intervention [^] Cerebral malaria	Reaction time, spatial working memory and learning, working memory, visual attention, visual learning and memory, and visuomotor processing	Randomized trial
Bangirana et al. (2011) ²⁵	Uganda	61	5–12 years Severe malaria	Attention, learning, reasoning, visual spatial ability, and working memory	Parallel group randomized trial
Baumgartner et al. (2012) ²⁶	South Africa	321	6–11 years Iron deficiency	Long-term memory and retrieval, verbal learning and memory, visuospatial ability, and working memory	2-by-2 factorial
Boivin et al. (2010) ²⁷	Uganda	60	6–16 years HIV	Reaction time, spatial working memory/learning, visual attention/choice reaction time, visual learning and memory, visuomotor processing speed, and working memory	Randomized controlled trial
Boivin et al. (2013) ²⁸	Uganda	120	16 months-5 years HIV	Learning and memory	Randomized controlled trial
Boivin et al. (2016) ²⁹	Uganda	159	6–12 years HIV (Stage I & II)	Mental processing, planning/reasoning, spatial working memory and learning, verbal knowledge, and visuomotor processing speed	Randomized controlled trial
Boivin et al. (2017) ³⁰	Uganda	221	2–3 years HIV-exposed-uninfected	Attention, executive function, memory, visual- spatial processing, sensorimotor, and language	Cluster randomized controlled trial
Chacko et al. (2014) ³¹	United States	85	7–11 years ADHD	Attention and working memory	Randomized clinical trial
Dalton et al. (2009) ³²	South Africa	183	7–9 years	Memory and verbal learning	Randomized control trial
Giordani et al. (2015) ³³	Uganda	33	6–12 years HIV	Attention, detection time, memory, executive functioning/ planning, nonverbal cognitive ability, identification time, memory, visual- motor coordination, and working memory	Pre-test/post-test
McKune et al. (2003) ³⁴	South Africa	19	5–13 years ADHD	Attention, task orientation, and motor skills	Quasi-experimental
Neville et al. (2013) ³⁵	United States	141	3–5 years	Non-verbal IQ and selective attention	Randomized controlled trial
Osendarp et al. (2007) ³⁶	Indonesia	384	6–10 years Well-nourished & malnourished	Verbal learning and memory and visual attention	2-by-2 factorial
Parletta et al. (2013) ³⁷	Australia	409	3–13 years	Cognitive maturity	Randomized controlled trial
Patel et al. (2009) ³⁸	United States	12	7–19 years Cancer survivor	Attention, learning, and memory	Pre-test/post-test
Portillo-Reyes et al. (2014) ³⁹	Mexico	59	8–12 years Mild to moderate malnutrition	Attention, executive functioning, memory, processing speed, and visuomotor coordination	Randomized, doubleblind,

Study	Location	Sample Size	Participant Characteristics	Cognitive Domains Targeted	Study Design
					placebo-controlled trial
Reza and Hamid (2011) ⁴⁰	Iran	20	7–11 years ADHD	Attention	Quasi-experimental
Smith et al. (2013) ⁴¹	United States	17	5.2–8.7 years ADHD	Executive functioning, visual-spatial, processing speed, working memory	Pre-test/post-test

* Estimated based on participants in grades 6–8

^ mean age provided by authors

TABLE 2

Summary of Support Strategies for Studies Conducted in Low-Resource Settings

Study	Intervention Type	Location Intervention Administered	Results
Caregiver Training			
Boivin et al. (2013)	Caregiver training	Home *	Statistically-significant improvement in memory (p=0.02) but not in learning (p=0.10) over time.
Boivin et al. (2017)	Caregiver training and nutritional support	Home and research facility	No statistical tests comparing intervention effects within trial arms. MISC intervention demonstrated better improvement on executive function (p<0.01 immediately post-intervention) than UCOBAC intervention.
Cognitive Training			
Abdollahian et al. (2013)	Cognitive-behavioral play therapy	Medical center	Lower scores for intervention group on ADHD symptom questionnaires (parents (p<0.001) and teachers (p=0.049)) and statistically-significant difference between control and intervention group.
Bangirana et al. (2009)	Computerized cognitive training	Hospital	Statistically-significant difference in reaction time (p=0.04), spatial working memory and learning (p<0.001), and visuomotor processing speed (p<0.001). No statistically-significant difference in working memory (p=0.54), visual attention (0.23), and visual learning and memory (p=0.59).
Bangirana et al. (2011)	Computerized cognitive training	Hospital	Statistically-significant improvement in learning (p=0.04) and decline in working memory (p=0.04). No statistically-significant difference in attention (p=0.64), visual spatial ability (p=0.87), and reasoning (p=0.76).
Boivin et al. (2010)	Computerized cognitive training	Medical office	Statistically-significant improvement in reaction time (p=0.02) and spatial working memory/learning (p<0.001). No statistically-significant improvement in visuomotor processing speed (p=0.06), visual attention/choice reactions time (p=0.19), visual learning and memory (p=0.56), and working memory (p=0.18).
Boivin et al. (2016)	Computerized cognitive training	Home	The full intervention group had statistically- significant improvement in overall mental processing (p<0.01), verbal knowledge (p=0.04), planning/reasoning (p=0.01), visuomotor processing speed (p<0.01), and spatial working memory and learning (p<0.01).
Giordani et al. (2015)	Computerized cognitive training	Medical clinic or home	Statistically-significant improvement in some measures of attention (p<0.01 for percent omission errors and p<0.01 for response time), visual-motor coordination (p<0.01), and executive function/planning (p<0.01). No statistically-significant improvement in some measures of attention (p=0.09 for percent commission error), nonverbal cognitive ability (p=0.91), detection time (p=0.21), identification time (p=0.67), one card learning accuracy (p=0.17), one-back accuracy (p=0.29).
Physical Activity			
McKune et al. (2003)	Physical activity (aerobic exercise)	School	Statistically-significant improvement in attention (p=0.01) and motor skills (p<0.01). No statistically-significant improvement in task orientation. No between-group difference.
Reza and Hamid (2011)	Physical activity (cycling)	Research facility ^	Statistically-significant decrease in ADHD symptoms (p<0.001).
Nutritional Supplementation			
Baumgartner et al. (2012)	Nutritional supplements (fatty acid supplementation)	School	No statistically-significant improvement in working memory, long-term memory and retrieval, short-term memory, or visuospatial cognition.
Dalton et al. (2009)	Nutritional supplementation (bread	School	Statistically-significant improvement in some measures of memory (recognition (p=0.02) and discrimination index

Study	Intervention Type	Location Intervention Administered	Results
	with fatty acid supplementation)		($p=0.01$)). No statistically-significant improvement in verbal learning ($p=0.18$).
Osendarp et al. (2007)	Nutritional supplementation (drink with fatty acid or micronutrient supplementation)	School	No statistically-significant improvement in visual attention or verbal learning and memory.
Portillo-Reyes et al. (2014)	Nutritional supplementation (Omega-3 capsules)	School and home	Statistically-significant improvements in processing speed ($p<0.01$), most measures of visuomotor coordination ($p<0.05$), and some areas of executive function (nonverbal reasoning ($p<0.05$) and response inhibition ($p=0.04$)). No statistically-significant improvement in attention, memory, or some areas of executive function.

When available, estimates reflect adjusted models. Statistical significance is reported at the 0.05 threshold level.

* The caregiver training was conducted at the medical office, but the caregivers facilitated the strategies at home.

^ The location of administration was not clearly stated, so the authors inferred the location.

TABLE 3

Summary of Support Strategies for Studies Conducted with High-Income Countries among Low-Income Populations

Study	Intervention Type	Location Intervention Administered	Results
Caregiver Training			
Neville et al. (2013)	Parent training and cognitive training	School	Statistically-significant improvement in selective attention ($p<0.01$) and nonverbal IQ ($p<0.01$).
Cognitive Training			
Chacko et al. (2014)	Computerized cognitive training	Home	Statistically-significant improvement in working memory ($p<0.05$). No statistically-significant improvement in attention.
Patel et al. (2009)	Cognitive training	Medical center [^]	No statistically-significant improvement in attention or learning and memory.
Physical Activity			
Smith et al. (2013)	Physical activity (circuit training)	Research facility [^]	Statistically-significant improvement in response inhibition ($p<0.05$). No statistically-significant improvement in visual spatial planning ($p=0.40$), spatial working memory ($p=0.80$), verbal working memory ($p=0.45$), working memory ($p=0.25$), processing speed ($p=0.76$), switching (0.11), and inhibition switching ($p=0.18$).
Nutritional Supplementation			
Parletta et al. (2013)	Nutritional supplementation (fish oil capsules)	School	Statistically-significant improvement in cognitive maturity ($p=0.03$).

When available, estimates reflect adjusted models. Statistical significance is reported at the 0.05 threshold level.

[^] The location of administration was not clearly stated, so the authors inferred the location.

TABLE 4

Summary of Clinical Significance of Results

Study	Intervention Type	Clinical Significance of Neurocognitive Results
Abdollahian et al. (2013)	Cognitive-behavioral play therapy	Unable to determine
Bangirana et al. (2009)	Computerized cognitive training	Improvement in visuomotor processing and spatial working memory
Bangirana et al. (2011)	Computerized cognitive training	Unable to determine
Baumgartner et al.(2012)	Nutritional supplementation (iron and fatty acid)	No improvement
Boivin et al. (2010)	Computerized cognitive training	Improvement in spatial working memory and visuomotor processing speed
Boivin et al. (2013)	Caregiver training	Improvement in immediate memory
Boivin et al. (2016)	Computerized cognitive training	Improvement in crystallized intelligence, visual spatial planning, visuomotor processing, and spatial working memory
Boivin et al. (2017)	Caregiver training	No improvement
Chacko et al. (2014)	Computerized cognitive training	Improvement in verbal and non-verbal working memory
Dalton et al. (2009)	Nutritional supplementation (fatty acid)	Unable to determine
Giordani et al. (2015)	Computerized cognitive training	Unable to determine
McKune et al. (2003)	Physical activity (aerobic exercise)	No improvement
Neville et al. (2013)	Parent training and cognitive training	Improvement in nonverbal IQ