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# Complementary and Alternative Treatments for Autism Spectrum Disorders: A Review for Parents and Clinicians

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Complementary and alternative therapy (CAT) methods for children with autism spectrum disorders (ASD) are widespread in European countries and the Russian Federation; however, their efficacy and safety is not routinely considered by parents and clinicians when recommended or used. The current narrative review presents the most widely known CAT interventions for children with ASD synthesizing data from meta-analyses, systematic reviews, and randomized controlled trials obtained from the PubMed database based on the safety-efficacy model. We have found that, of the reviewed CATs, only the melatonin intervention can be considered safe and effective for children with ASD with comorbid sleep problems. The methods that were classified as safe but had inconclusive efficacy are recommended to be implemented only when they do not interfere with front

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line treatment for ASD, Applied Behavior Analysis (ABA). Methods with the lack of current evidence for the efficacy such as auditory integration therapies, bioacoustic correction, sensory integration therapy, micropolarization, animal assisted therapy, and dietary interventions should not be recommended as alternative treatments and can only be used as complimentary to ABA-based interventions. We advise against the use of chelation, hyperbaric oxygen therapy, and holding therapy due their documented harmful psychological and physical effects. When considering CAT for ASD we recommend parents and clinicians use the criteria suggested by Lofthouse and colleagues [59]: only the therapies that are safe, easy, cheap, and sensible can be recommended and used, as opposed to therapies that are risky, unrealistic, difficult, or expensive that should not be recommended or utilized.

**Keywords:** autism spectrum disorders, complimentary treatments, alternative treatments, complementary and alternative therapy, safety-efficacy model.

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## Introduction

Autism spectrum disorders (ASD) is a group of neurodevelopmental disorders characterized by social communication deficits and repetitive and restricted forms of behavior that can be accompanied by difficulties in language, intellectual, and adaptive functioning. Empirically supported treatments for ASD include treatments based on intensive applied behavioral analysis, ABA [35], and pharmacotherapy to address specific comorbid features of the spectrum such as irritability (e.g., risperidone and aripiprazole and self-aggression) [40; 41]. Along with conventional evidence-based treatments, methods of complementary and alternative therapy (CAT) are widespread [37]. Complementary treatment is used together with conventional medicine, while alternative treatment is used instead of conventional medicine [73]. It is assumed that a truly complementary therapy should have empirically demonstrated incremental effects when added to conventional therapy. Likewise, a truly alternative therapeutic approach should have effects comparable to conventional therapy [59]. Applying an efficacy-safety model, described by Kemper and Cohen [48], we have classified the most widely known CAT interventions for ASD. The model helps to evaluate the pros and cons of particular CATs and make a decision about their use. According to this model, CATs with well supported efficacy and safety can be recommended when they do not interfere with conventional interventions. CATs with scientifically proven safety, but with inconclusive, unknown efficacy, or the ones with no demonstrated efficacy, can be accepted and monitored by clinicians as long as they do not prevent families from receiving front line interventions. The use of CATs with little or no efficacy and potentially harmful side effects should be

discouraged. Additionally, expensive and time-consuming CATs should be avoided. The current narrative review integrates results of meta-analyses, systematic reviews, and randomized controlled trials (RCTs) that evaluated efficacy and safety of specific CAT interventions for children with ASD.

## Method

Decisions about efficacy and safety were made after evaluation of the results of identified studies that were searched in PubMed database. The combination of the search terms "autis*" and names of specific CATs were used. The list of the most widely known CATs was derived from the recent meta-analyses and studies of on the prevalence of CATs for the treatment of ASD [85; 86]. The search was performed on articles published in English between the years 2000 and 2020. We report only studies of CAT interventions for children under 18 years old, unless stated otherwise. The identified CATs were assessed using efficacy-safety model described by Kemper and Cohen [48]. The results from meta-analyses and systematic reviews were synthesized to determine efficacy and safety of a given intervention. In the absence of thereof, the results from individual RCTs were included in the assessment of efficacy/safety.

## Results

### *Safe/well-tolerated, effective*

CAT was classified as safe, well-tolerated, and effective if its efficacy and safety for treating ASD or related symptoms was supported by the results of meta-analyses or systematic reviews of RCTs and calculated effect sizes in the identified studies varied from medium to large. Only one intervention was assigned to this category.

*Melatonin.* A number of studies have demonstrated that sleep problems and alterations of circadian rhythms are frequent in ASD across all ages [17]. Melatonin is an endogenous neurohormone released by the pineal gland in response to decreasing levels of light. Decreased levels of melatonin in individuals with ASD were linked to their symptom severity [18]. In the literature, we identified two systematic reviews and meta-analyses [77; 83], six systematic reviews [17; 18; 36; 46; 68; 83], and one meta-synthesis [25]. A meta-analysis of 5 RCTs revealed significant improvements with large effect sizes for sleep duration (73 min compared with baseline ($g$ = 1.97, 95% CI [1.10, 2.84]) and 44 min compared with placebo ($g$ = 1.07, 95% CI [.49, 1.65]) and amount of time it takes to go from being fully awake to sleep, measured by sleep onset latency (66 min compared with baseline ($g$ = -2.42, 95% CI [-1.67, -3.17] and 39 min compared with placebo ($g$ = -2.46, 95% CI [-1.96, -2.98]), but night-time awakenings were unchanged [83]. The dosage varied from 2 to 10 mg. The time of administration was from 10 days to 3 months. The duration of treatment was between 10 days and 12 weeks. Overall side effects of melatonin were minimal (tiredness, dizziness, and diarrhea). A meta-analysis performed by Parker and colleagues found a statistically significant increase in diary-reported total sleep time for melatonin compared with placebo for various disorders (pooled *MD* = 29.6 min, 95% CI [6.9, 52.4], $p$ = .01), with the largest effect for populations with ASD (pooled *MD* = 64.7 min., 95% CI [58.8, 70.7] vs pooled *MD* = 15.9 min., 95% CI [9.2, 22.6] [77]. The dosage was from

.5 to 9 mg. According to a meta-synthesis [25], melatonin had high efficacy for sleep latency, duration, and bedtime resistance. The question about the optimal dosage remains open as the protocols differed across studies. Melatonin is considered a safe and well-tolerated intervention, which can be recommended for children with ASD with comorbid sleep problems. The existing evidence is based on studies of children from 2 to 18 years of age.

***Safe/well-tolerated, inconclusive efficacy***

CAT was classified in this category, if its safety was confirmed in meta-analyses, systematic reviews, or RCTs, while inconclusive results were revealed. Six different groups of intervention comprise this category: music therapy, massage, physical activity interventions, acupuncture, neuromodulation and brain stimulation techniques, and omega-3 supplements.

*Music therapy.* A meta-analysis of music interventions for children and adolescents with ASD that included 9 studies revealed positive effects overall with effect sizes ranging from .09 to 3.36 and an overall effect size of $d$ =.77 [99]. A later systematic review that included 10 studies ($N$ = 156) reported positive effects in the areas of generalized social interaction (standardized mean difference, *SMD* = .71, 95% [CI .18, 1.25], non-verbal communicative skills within the therapy context (*SMD* = .57, 95% CI [.29, .85], verbal communicative skills (*SMD* = .33, 95% CI [.16, .49], initiating behavior (*SMD* = .73, 95% CI [.36, 1.11], and social-emotional reciprocity (*SMD* = 2.28, 95% CI [.73, 3.83]. No side effects were reported in any of the studies [31]. This CAT can be classified as safe, but the evidence is inconclusive, partially due to small sample sizes.

*Massage.* Massage therapy is traditionally used to handle hypo- or hypersensitivity and anxiety of a child with ASD, however, the related evidence is equivocal [98]. Primarily, meta-analytic studies of massage effects are limited to pain treatment [23] and do not focus on the treatment of ASD. According to systematic reviews [15; 54], massage therapy is associated with improvements in parents' and teachers' evaluation of a child's adaptive behavior, compared to control non-conventional intervention or conventional language/special education treatment alone. Moreover, massage seems to have a positive effect on comorbid sleep problems in ASD as revealed by a systematic review of four studies: two of them utilized Qigong massage, one – Thai, and one – traditional massage; the duration of the intervention was in the range of 1–5 months, one or two times a week [69]. Authors of reported studies note the insufficient empirical evidence for firm conclusions regarding efficacy, however, massage therapy is considered to be safe [96]. The studies included in the systematic reviews were conducted with children from 1 to 10 years of age.

*Physical activity interventions.* Physical activity interventions are aimed at managing difficulties with movement control that are common in individuals with ASD (large overlap between the ASD and developmental coordination disorder [94]; poor gross motor skills [62]; reduced bodily awareness [8; 28]; lack of bodily connectedness [78]. Body-oriented treatments are motivated by the bottom-up embodiment approach [27; 30]. Meta-analyses reported that motor activity programs are beneficial for both the physical and mental

health of children with ASD [93; 103]. For example, a meta-analysis by Healy et al. [38] found the overall moderate positive effect of physical activity ($g$ = .62) on manipulative skills, strength, locomotor skills, social functioning, and endurance; however, great heterogeneity in the studies was detected. A more recent meta-analysis by Howells et al. [42] that targeted the physical activity in kindergarten and school-aged children with ASD found no statistically significant effect on communication ($k$ = 4; $g$ = .13, 95% CI [-.12, .38], $p$ = .13) but revealed a moderate effect for social functioning ($k$ = 6; $g$ = .45, 95% CI [.19, .72], $p$ = .001). Overall, the heterogeneity in the studies, utilized intervention programs and measured outcomes make the findings on efficacy inconclusive. If delivered by a qualified specialist, the physical activity interventions are safe. Studies were conducted with children from 3 to 16 years of age.

*Acupuncture.* Acupuncture is a type of traditional Chinese Medicine that uses stimulation of special points of the body (acupoints) by insertion of thin needles to skin to unblock the flow of qi ("energy") [72]. Acupuncture techniques vary from hand to electro- or laser-acupunctures; the sessions usually last for 20-30 minutes (but may vary from 15 seconds to 8 hours), and the duration of treatment ranges from 4 weeks to 9 months [63]. A recent meta-analysis of 17 RCTs revealed that acupuncture complementary to behavioral and educational intervention decreased the overall scores on the Childhood Autism Rating Scale (CARS; *MD* = -8.10, 95% CI [-12.80, -3.40]) and the Autism Behavior Checklist (ABC; *MD* = -8.92, 95% CI [-11.29, -6.54]) in comparison to behavioral and educational monotherapy in children under the age of 18 [54]. Reported side effects varied from none to initial fear or irritability in some children, thus authors cautiously considered acupuncture as a safe method with mild possible adverse effects. Moreover, meta-analytic study of 11 RCTs claims that scalp acupuncture as monotherapy is more effective in lowering both CARS and ABC scores for core ASD symptoms than conventional behavioral and educational interventions [57]. However, the observed studies had methodological issues due to the difference in the onset times of intervention effects that were not taken into account.

*Neuromodulation and brain stimulation techniques.* Neuromodulation techniques are non-invasive methods that use currents of low intensity to stimulate different brain regions in order to change cortical excitability. The most widely applied techniques are transcranial magnetic stimulation, delivered as a single (TMS) or repetitive pulses (rTMS) and transcranial direct current stimulation (tDCS). They are typically delivered in a couple of weekly sessions, but some interventions involve up to 29 days of consecutive therapy [55]. A recent systematic review found that the largest therapeutic effects of TMS and tDCS for a range of neurodevelopmental disorders were observed when treatments were combined with the cognitive training [29]. Another meta-analysis based on 23 studies evaluated the effectiveness of rTMS for the treatment of ASD separately for controlled and non-controlled studies. Findings show that rTMS treatment results have small to moderate effects on stereotyped behaviors ($g$ = -.52, 95% CI [-.72, -.32]), social behaviors ($g$ = -.35, 95% CI [-.67, -.03]) and executive functioning tasks ($g$ = -.38, 95% CI [-.61, -.16]). The observed effects should be considered with caution as authors have identified a risk of reporting bias and no information about the robustness of the gains over time was available [9]. These techniques are considered a safe intervention with minor side effects of physical discomfort such as itching, burning sensations, and headaches, which are not significantly

different from placebo group [16]. A review of 2015 concluded that there is not enough evidence for the use of either tDCS or rTMS in children with ASD due to the lack of understanding of the mechanisms, uncertainty regarding the areas for stimulation, and unclear length of intervention [95]. Most studies were conducted with predominantly male participants in the age range of 9 to 17 years. More research is needed to better understand the demographic and neurophysiological factors that predict the response to stimulation.

*Omega-3.* The rationale for using omega-3 (ω-3) fatty acids in patients with ASD is based on the findings of reduced ω-3 in children with ASD [92]. Four systematic reviews and meta-analyses investigated effects of ω-3 on the symptoms of ASD. While the first of them, synthesized findings from 2 RCTs with the doses from 1.3 to 1.5 mg/day and the duration of supplementation from 6 to 12 months, demonstrated no statistically significant improvements in social interaction, communication, and stereotypical behaviors [44], further meta-analyses, all published in 2017, revealed more positive results. A systematic review and a meta-analysis of 6 RCTs [22] identified significant reductions in hyperactivity (*MD* = -2.69, 95% CI [-5.36, -.02]), lethargy (*MD* = -1.97, 95% CI [-3.57, -.37], and stereotypical behavior (*MD* = -1.07, 95% CI [-2.11, -.03]), while no significant differences between supplementation of ω-3 and placebo were found in the global assessment of functioning or social responsiveness. The dosage varied from .2 to 1.5 g/day and the duration of administration was from 6 to 24 weeks. Another systematic review and meta-analysis of 5 RCTs [41] reported differences in lethargy symptoms (*MD* = 1.98; 95% CI [.32, 3.63]), positive effects for externalizing behavior (*MD* = -6.22; 95% CI [-10.9, -1.59]), social skills (*MD* = -7.0; 95% CI [-13.62, -.38]), and daily-living (*MD* = 6.2; 95% CI [.37, 12.03]). The third meta-analysis of 4 RCTs [67] with dosage from .24 to .84 g/day and administration time from 6 to 16 weeks identified significant improvements in social interaction (*MD* = -1.96, 95% CI [-3.5, -.34]), repetitive and restricted behaviors (*MD* = -1.08, 95% CI [-2.17, -.01]). The age of participants ranged from 3 to 28 years of age. The problem of small sample sizes and the need for further investigation of the ω-3 in complementary treatment of ASD was mentioned in all studies. All described studies characterized ω-3 as a safe and well-tolerated supplement.

### *Safe/well-tolerated, no evidence of efficacy*

This category includes CATs that do not pose any safety concerns, according to meta-analyses, systematic reviews and RCTs; however, there are no efficacy data for the treatment of ASD. Three types of interventions were included in this group: dance therapy, multivitamin/mineral, and prebiotic/probiotic supplements.

*Dance therapy.* Dance therapy and dance movement therapy (DMT) lies at the junction of movement-based therapies, art-therapy and mind-body practices. In DMT, the client follows or leads therapist's motor behaviour (mirroring technique) to achieve mutual attunement; in dance intervention client practices various dance styles [24]. While 2.4% of individuals with ASD use dance and DMT [34], the empirical support for its effectiveness is inconsistent and limited to adult samples [39; 50–52; 66]. The meta-analysis of Koch and colleagues [51] included 41 controlled interventions that implemented dance or DMT for an average of 11 weeks and two sessions per week (range 1–4) that lasted for around one hour (range 40–120 min). The authors reported a medium

effect ($d$ = .60) on mental health outcomes with a highly heterogeneous effect of dance therapy and a more consistent effect of DMT. However, those interventions were implemented in a wide range of clinical populations and age groups, thus results cannot be extrapolated to children with ASD specifically.

*Multivitamin/Mineral Supplements.* The rationale for multivitamin treatment is based on the frequently observed deficiency of vitamins and micronutrients in children with ASD that could result from food selectivity or altered gastrointestinal absorption [15]. Biomarkers of general nutritional status are associated with autism severity [70]. Surveys of 539 physicians found that multivitamin/mineral supplements are widely recommended (by 49% of physicians) [33]; however, the evidence for their efficacy in the treatment of ASD is limited. No systematic reviews and meta-analysis in ASD samples were identified. The only RCT showed significant improvements in hyperactivity, tantruming, and receptive language scores of children with ASD after 3 months of treatment [5]. While more research is needed, micronutrient supplements are safe in prescribed doses and can be recommended for children with restricted or idiosyncratic diets [59].

*Probiotic/Prebiotic Supplements.* An idea of the using of probiotic supplementation in complementary treatment of ASD is based on the evidence about comorbidity of ASD with dysbiosis and gastrointestinal problems, as well as on the assumption that alterations in microbiota composition may contribute to underlying mechanisms of neurodevelopmental disorders [43]. We have identified four systematic reviews investigating effects of pro- and/or prebiotics in treatment of ASD and related problems, meta-analyses have not been found [10; 58; 74; 82]. Despite of the potential positive role of pro- and/or prebiotics in treating ASD, these studies are consistent in the conclusions that there is limited evidence to support this CAT and additional rigorous RCTs are needed. For example, the study by Liu and colleagues identified two RCTs and three non-RCTs indicating trends to improvement in caregiver reported ASD symptoms and gastrointestinal problems. However, both RCTs have revealed flaws in statistical analysis, short trial duration (less than 1 month), small sample and effect sizes, and some additional methodological flaws. Similar concerns were found for non-RCTs. Adverse effects of probiotic therapy are reported to be infrequent and non-severe (in some cases diarrhea, bloating, abdominal cramps, and skin rash were mentioned). While additional studies of side effects are needed in general, pre- and probiotic therapy in prescribed doses is appreciated as safe for the treatment of gastrointestinal problems in ASD. The RCTs listed in this section the age range of children was from 4 to 16 years. Approximately 98% were male and approximately 2% were female. Non-RCT studies included children from 3 to 16 years.

### *Unknown safety, inconclusive or no efficacy*

CATs with unknown or unclear safety and few or no efficacy data were included in this category. Five interventions form this category: sensory-integration therapy, micropolarization, auditory integration therapies, animal assisted interventions, and gluten and/or casein-free diets.

*Sensory Integration Therapy.* Sensory integration therapy is targeting impairments in sensory information processing, associated with ASD. Existing interventions can be grouped into two categories: Ayres Sensory Integration, ASI, and Sensory-based

Interventions, SBIs [97]. ASI therapy sessions are delivered by a certified occupational therapist in the form of guided play in a sensory enriched environment [88]. SBIs primarily occur in the context of everyday life. The procedures include the use of weighted vests and blankets, bouncing balls, brushes, and special moving seating devices [19]. We were unable to identify a meta-analysis on any category of sensory integration therapies. According to the recent systematic reviews, ASI shows promising results for children aged 4-12; the observed effects were positive, effect sizes ranged from $\eta^2 = .23$ to $\eta^2 = 1.2$ [88; 87], while the results for SBIs are less conclusive as most of the studies employed single-subject or case report design [11; 19].

*Micropolarization.* Micropolarization is a variation of tDCS with a current of significantly lower frequency, i.e. up to 100 times smaller than traditional tDCS [26]. The technique was developed in Russia which explains its local popularity in the clinical settings. Clinical trials using this method lack randomization and systematic protocol with regard to current intensity and duration. The evidence described is in favor of its effectiveness points to normalization of EEG patterns and reductions of paroxysmal activity in children 6-16 years [14; 90], but the data can only be seen as preliminary. Importantly, medical service providers in Russia often use the term "micropolarization" to refer to tDCS; therefore, in order to determine the efficacy and safety, current intensity should be considered.

*Auditory integration therapies.* Auditory integration therapies lie at the junction of neuromodulation and sensory integration techniques and include auditory integration training (AIT), Tomatis method, and Samonas sound therapy. The rationale for AIT is to ameliorate auditory processing deficits typical of individuals with ASD. They involve listening to the electronically modulated presentation of voice, classical music, or brain activity which is usually delivered over the headphones. AIT is provided in two 30 minutes intervention blocks a day over the course of 10 days. While no significant side effects were reported, some studies report physical discomfort due to excessive loudness [7; 13]. The outcomes of AIT have questionable clinical significance [91]. We have identified one meta-analysis based on 6 RCTs that reported controversial results. Three studies found no effect over control conditions and the other three showed improvements of ASD symptoms after 3 months of AIT. According to the authors, the validity of the studies is questionable and no effect sizes could be computed [91]. The reported age range was wide from 3 to 39 years. Bioacoustic correction, a type of AIT that is based on listening to computerized transformation of the patient's EEG, suggests that the method allows to ameliorate the sensory deficits by letting the patient "hear his or her brain working" [102]; however, the method has not been systematically studied and lacks evidence for the use with children with ASD.

*Animal Assisted Interventions.* Animal Assisted Interventions (AAI) includes animal assisted therapy that has clear goals and animal assisted activities such as recreational activities with animals [32]. The literature on AAI is rather large, with two meta-analyses and five systematic reviews focusing on its efficacy for different neurodevelopmental disorders. An early meta-analysis, conducted by Nimer and Lundahl [75] and based on 49 studies, found that AAI has a low to moderate effect size in decreasing ASD symptoms in children and adolescents (0-17) and problem behaviors: for well-being ($d = .39$, 95%

CI [.29, .50]), behavioral ($d$ = .51, 95% CI [.38, .65]) and medical indicators respectively ($d$ = .59, 95% CI [.26, .77]). However, the study was later criticized for the lack of specificity for ASD [61]. Another systematic analysis conducted in 2013 demonstrated that children and adolescents (5-19 years of age) in AAI showed increased social interaction, decreased self-absorption, and avoidance that was reported in 9 of 14 studies [76]. However, some studies included interactions with animals as a measure of social communications and language, so the results can be inflated. The most current systematic review and a meta-analysis found support for AAI improving the social skills of individuals with ASD, based on 9 studies that were analyzed [21]. Sample sizes were small, and the effect sizes could not be computed. A review by Kamioka and colleagues [47] that summarized 11 RCTs on the effects of AAI for various mental health problems concluded AAI may be an effective treatment for people who like animals. Though no study has systematically investigated adverse effects of AAI, there are data supporting increased sensory seeking (willingness to touch objects or people), and reduced sensory sensitivity (aversion to jumping or falling) in children exposed to AAI [12; 49]. Some data also points to increased discussion about the animal after the sessions [65], which can be interpreted as promotion of fixations in children with ASD. Currently, both safety and evidence regarding AAI is inconclusive due to heterogeneity of samples and a wide range of animals used in therapy [47; 76].

*Gluten and/or casein-free diets.* Gluten and/or casein-free (GFCF) diets in treatment of ASD are based on the assumption that abnormal metabolism of these two proteins in ASD may lead to excessive opioid activity in the central nervous system, thus altering its functions; this assumption is referred to as “opioid excess theory” [100]. While there is no statistically significant association between ASD and celiac disease [60], GFCF are widely used in ASD treatment with 13% of parents reporting the use of GFCF diets in European countries [85]. Parental reports on GFCF dietary effects found positive rates of symptoms improvement in 41–65% of cases [81]. We identified 3 systematic reviews of GFCF in treatment of ASD [64; 79; 87]. The most recent systematic review that included 6 RCTs (ages 2–16 years) [79] reported that only two trials indicated statistically significant differences in core symptoms of ASD with improvements in communication and social interaction. Included RCTs varied in treatment protocol, duration (from 7 days to 2 years), and outcome measures. No adverse effects were reported (but only 2 RCTs explored this issue). A systematic review of 19 RCTs concluded that there is not enough evidence for the use of dietary treatment in ASD [87]. Taking into account inconclusive efficacy and a risk of deficiency of some nutrients caused by food aversions and selectivity associated with ASD [64; 80], GFCF diets should only be recommended in the cases of diagnosed gluten and/or casein intolerance or allergy.

### Harmful, inconclusive or no efficacy

CATs with questionable efficacy, severe side effects, and/or documented cases of injuries were included in this category. Three interventions (chelation, hyperbaric oxygen, and holding therapy) form this category.

*Chelation*. Chelation is a process of removing heavy metals from the blood. This treatment is based on an unsupported theory that ASD is caused by heavy metal toxicity. One systematic review [45] with only one RCT of a poor quality ($N$ = 82, aged 3–8 years)

compared children who received one versus multiple rounds of oral dimercaptosuccinic acid (DMSA) at doses of 10 mg/kg/d 3 times per day. No significant group differences in ASD symptoms were found. While safety was not examined in this study, other studies have shown that chemicals utilized in chelation treatment have a number of harmful side effects, including gastrointestinal symptoms, fever and vomiting, hypocalcemia, renal impairment, musculoskeletal, hypertension, and cardiac arrest [53]. Reported adverse effects of using pharmaceutical chelating agents for ASD currently outweigh its potential benefits.

*Hyperbaric Oxygen Therapy*. Hyperbaric oxygen therapy, which requires the patient to breath 100% oxygen intermittently, is hypothesized to reduce the biochemical dysfunction and clinical symptoms of ASD [84]. Usually, this therapy is recommended for patients affected by decompression sickness, carbon monoxide poisoning, or infections involving compromised tissue [6]. The most recent systematic review [101] identified only one low quality small RCT ($N$ = 60, age 3–9 years) which showed no improvements in ASD symptoms. Adverse effects included increased occurrence of ear barotrauma. Taking into account the absence of persuasive theory underlying the use of oxygenation, its questionable efficacy, possible barotraumas, and unknown long-term safety, Xiong and colleagues concluded further clinical trials for children with ASD are not appropriate [101].

*Holding Therapy***.** Holding therapy of ASD is based on the unsupported assumption that ASD originates from the disrupted attachment. In a holding therapy session, a caregiver physically restrains a child with ASD in order to force eye contact and repair attachment. The only systematic review [71] identified 8 studies of holding interventions in treatment of ASD. While all of them reported positive effects, the studies were methodologically flawed. Severe side effects, including lethal cases, were documented. In the absence of a scientifically based theory, documented deaths during treatment, and the violent nature of the intervention, this therapy was banned by a number of leading professional organizations. Holding therapy along with other controversial attachment interventions, such as rebirthing, was banned by the American Professional Society on the Abuse of Children [56] and strongly condemned by the ethics code of American Psychological Association [20]. However, in Russia holding therapy is still accepted in academic and clinical settings [1–4], which contradicts international standards of care for individuals with ASD.

### *Presence of CAT among Russian medical services*

To evaluate the popularity of CATs in the treatment of ASD in Russia, we have conducted a small-scale study, analyzing publicly available information from the state and private medical centers of the seven largest cities in Russia. The analysis included website searches and brief surveys broadly asking about the types of services provided for ASD, with regard to CATs specifically. Out of 93 identified clinics, data from 60 clinics were analyzed (Table). Most of the CATs offered in the clinics in Russia are safe but have inconclusive efficacy, which is important considering available resources and the cost of treatment. Alarmingly, 5% of clinics reported the use of holding therapy and another 5% reported the use of hyperbaric oxygen therapy which are classified as harmful CATs with no efficacy.

Table

**Frequency of interventions used by approached clinics (*N* = 60)**

| Group | Intervention | Frequency, n (%) |
|---|---|---|
| Evidence-based treatment | Applied Behavioral Analysis (ABA) | 21 (35%) |
| Safe/well tolerated, inconclusive efficacy | Physical Activity Interventions | 27 (45%) |
| | Massage | 22 (36.7%) |
| | Acupuncture | 11 (18.3%) |
| | Transcranial Direct Current Stimulation (tDCS) | 8 (13.3%) |
| | Music Therapy | 7 (11.7%) |
| | Transcranial Magnetic Stimulation | 5 (8.3%) |
| Safe/well tolerated, no evidence of efficacy | Art Therapy | 20 (33.3%) |
| | Dance and Dance Movement Therapy | 6 (10%) |
| Unknown safety, inconclusive or no efficacy | Sensory Integration Therapy | 23 (38.3%) |
| | Tomatis Method | 10 (16.7%) |
| | Bioacoustic Correction | 10 (16.7%) |
| | Dietary Interventions | 10 (16.7%) |
| | Animal Assisted Interventions | 5 (8.3%) |
| Harmful, inconclusive or no efficacy | Holding Therapy | 3 (5%) |
| | Hyperbaric Oxygen Therapy | 3 (5%) |
| | Chelation | 0 (0%) |
| Unclassified | Speech Therapy | 17 (28.3%) |
| | Speech Therapy Massage | 9 (15%) |
| | Balance Stimulation Activities | 8 (13.3%) |
| | Biofeedback | 6 (10%) |
| | Interactive Metronome | 3 (5%) |

## Conclusion

In this synthesis, we reviewed available complementary and alternative treatments (CAT) for children with ASD based on their efficacy and safety. Oral melatonin is the most investigated complimentary intervention with the most consistent results in favor of its efficacy and safety. Thus, it can be recommended for children with ASD with sleep

disturbances, when ABA-based and cognitive-behavioral therapy alone are not effective. However, further investigations to determine optimal doses and treatment duration, as well as studies on long-term safety of melatonin, are still needed. The methods that were classified as safe but had inconclusive efficacy are recommended to be implemented only when they do not interfere with the front line treatment for ASD, that is ABA-based therapies. Given the lack of current evidence for the efficacy of auditory integration therapies, bioacoustic correction, sensory integration therapy, micropolarization, animal assisted therapy, and dietary interventions, these methods should not be recommended as alternative treatments and can only be used as complimentary to ABA-based interventions. The use of chelation, hyperbaric oxygen therapy, and holding therapy is unethical and unadvised due to harmful psychological and physical effects. In addition to the efficacy/safety model proposed above, we recommend that parents and clinicians use the criteria suggested by Lofthouse et al. [59]: only the therapies that are safe, easy, cheap, and sensible can be recommended, as opposed to therapies that are risky, unrealistic, difficult, or expensive that should not be recommended. Most of the studies reviewed here were conducted with predominantly male samples of children in a wide age range from 1 to 18 years of age. Notably, information on ethnicity and socio-economic characteristics was missing in most studies. Future systematic reviews and meta-analyses should address this shortcoming by including demographic information. Although we have tried to conduct this review as comprehensively as possible and avoid biases associated with the selection of literature, it has a number of limitations. While it was not a systematic review, a number of meta-analyses, systematic reviews, and RCTs may not have been identified. Thus, offered recommendations should be interpreted with caution. It is also worth noting that the paper only focuses on the most popular CATS and does not cover the full spectrum.

In addition to our review, we have also conducted preliminary research of the extent to which alternative interventions for children with ASD are offered in clinical settings in Russia. Obtained information is preliminary and future studies of the prevalence of CATs should be conducted systematically. Additionally, there is a need for dissemination work among parents and professional communities about harmful CATs such as chelation, oxygenation, and holding therapy that are still used in Russia.

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# Дополнительные и альтернативные вмешательства при расстройствах аутистического спектра: обзор для родителей и клиницистов

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Методы дополнительных и альтернативных вмешательств (Complementary and Alternative Therapy, CAT), применяемые в работе с детьми с расстройствами аутистического спектра (РАС), распространены в европейских странах и в Российской Федерации, однако их эффективность и безопасность обычно не рассматриваются клиницистами и родителями составлении рекомендаций и использовании. Данный аналитический обзор посвящен наиболее распространенным дополнительным и альтернативным вмешательствам, применяемым в работе с детьми с РАС. На основе анализа информации, представленной в мета-анализах, систематических обзорах и рандомизированных контролируемых исследованиях в базе данных PubMed, рассматриваются безопасность и эффективность каждого вида вмешательств. Обнаружено, что из всех рассмотренных методов только вмешательства с применением мелатонина можно считать безопасными и эффективными для детей с РАС с сопутствующими нарушениями сна. Методы, которые были классифицированы как безопасные, но не доказавшие свою эффективность, рекомендуется применять только в том случае, если они не противоречат терапии РАС «первой линии» – применению прикладного анализа поведения (Applied Behavioral Analysis, ABA). Методы, доказательств эффективности которых обнаружено не было, такие как терапия слуховой интеграции, биоакустическая коррекция, терапия сенсорной интеграции, микрополяризация, пет-терапия и диета, не должны рекомендоваться в качестве альтернативных методов терапии и могут использоваться только в дополнение к методам лечения на основе АВА-вмешательства. Не рекомендуется использовать хелатирование, гипербарическую кислородную терапию и холдинг- терапию по причине их установленного вредоносного психологического и физического воздействия. При выборе методов дополнительных и альтернативных вмешательств при РАС мы рекомендуем родителям и клиницистам использовать критерии, предложенные Н. Лофтхаусом и коллегами (2012): могут быть рекомендованы только безопасные, простые, экономные и разумные методы вмешательств, тогда как методы лечения, которые являются рискованными, трудно реализуемыми или дорогими, использовать не следует.

**Ключевые слова:** расстройства аутистического спектра, дополнительные вмешательства, альтернативные вмешательства, CAT, модель безопасность-эффективность.

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