

Treatment Intervention Advisory Committee Review and Determination

Date: October 28, 2016

To: DHS/DLTC

From: Wisconsin Department of Health Services, Treatment Intervention Advisory Committee: Lana Collet-Klingenberg, Ph.D. (chairperson) LCK

RE: Determination of Hyperbaric Oxygen Therapy as a proven and effective treatment for individuals with autism spectrum disorder and/or other developmental disabilities

This is an initial review

This is a re-review. The initial review was July 2014. An additional review was completed July 2015.

Section One: Overview and Determination

Please find below a statement of our determination as to whether or not the committee views Hyperbaric Oxygen Therapy as a proven and effective treatment for children with autism spectrum disorder and/or other developmental disabilities. In subsequent sections you will find documentation of our review process including a description of the proposed treatment, a synopsis of review findings, the treatment review evidence checklist, and a listing of the literature considered. In reviewing treatments presented to us by DHS/DLTC, we implement a review process that carefully and fully considers all available information regarding a proposed treatment. Our determination is limited to a statement regarding how established a practice is in regard to quality research. We do not make funding decisions.

Description of proposed treatment

Hyperbaric Oxygen Therapy (HBOT) involves inhaling up to 100% oxygen at a pressure greater than one atmosphere (atm) in a pressurized chamber. Most typical indications for HBOT involve the use of hyperbaric pressures above 2.0 atm. Higher atmospheric pressures are used to treat conditions such as carbon monoxide poisoning and to improve wound healing. In some studies, the use of oxygen appears to enhance neurological function. Because of these outcomes, some investigators have used HBOT to treat certain neurological disorders, including chronic and traumatic brain injury, as well as fetal alcohol syndrome, and clinical improvements in these patients have been observed. Given this background, some physicians have also applied similar lower hyperbaric pressures of 1.3 to 1.5 atm in individuals with autism, with oxygen concentrations ranging from 21% to 100%.

Synopsis of review

In the case of Hyperbaric Oxygen Therapy, please refer to the attached reference listing that details the reviewed research. The committee's conclusions regarding Hyperbaric Oxygen Therapy include that there are several poorly designed or trial studies (e.g., Rossignol et al, 2007) with questionable outcomes supporting the use of HBOT. Interestingly, there were three well designed studies, two double blind, placebo study (i.e., Granpeesheh et al, 2010; and Hardy et al, 2002)) and one multiple baseline study (i.e., Jepson et al, 2011) that clearly demonstrated no positive outcomes associated with the use of the therapy. In addition, there are a number of review articles stating that there is little to no evidence of its

use in effective practices and/or that it is with risk that it is used. Ghanizadeh (2012), in a review of 18 publications regarding the use of HBOT for children with autism, concluded that any promising effects from HBOT were not replicated. McDonagh et al., (2007) reported on studies utilizing HBOT with children with cerebral palsy and made similar conclusions regarding lack of evidence of its effectiveness. In addition, McDonagh et al reported on adverse events associated with the therapy.

A recent review by Xiong, Chen, Lou, and Mu (2016) states that "there is no evidence that hyperbaric oxygen therapy improves core symptoms and associated symptoms of ASD" and that adverse side effects can occur. In addition to poor outcomes, research methodology issues were raised concerning selection bias lack of follow-ups.

Another review by Sampanthavivat, Singkwa, Chaiyakul, Karoonyawanich, and Ajpru (2012) controlled for placebo effects by providing sham air exposure and found "no significant differences in improvement between groups." Problems with rating scales to measure response changes pre- post were noted with parents rating their children as more improved but clinicians finding no significant differences.

In addition, clinicians at Mayo Clinic strongly advise against using HBOT to treat autism (<http://www.mayoclinic.org/tests-procedures/hyperbaric-oxygen-therapy/basics/why-its-done/PRC-20019167>). This position is strengthened by a 2012 FDA report warning consumers to not be misled regarding HBOT efficacy claims (<http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm364687.htm>).

These data indicate that research has not established HBOT as an effective treatment for ASD, a position also taken by the clinical community and the FDA.

In sum, it is the decision of the committee that Hyperbaric Oxygen Therapy has no proven efficacy and, in fact, may be harmful. Therefore we recommend a Level 5 rating – experimental with potential for harm.

Section Two: Rationale for Focus on Research Specific to Comprehensive Treatment Packages (CTP) or Models

In the professional literature, there are two classifications of interventions for individuals with Autism Spectrum Disorder (National Research Council, 2001; Odom et al., 2003; Rogers & Vismara, 2008):

- (a) **Focused intervention techniques** are individual practices or strategies (such as positive reinforcement) designed to produce a specific behavioral or developmental outcome, and
- (b) **Comprehensive treatment models** are “packages” or programs that consist of a set of practices or multiple techniques designed to achieve a broader learning or developmental impact.

To determine whether a treatment package is proven and effective, the Treatment Intervention Advisory Committee (TIAC) will adopt the following perspective as recommended by Odom et al. (2010):

The individual, focused intervention techniques that make up a comprehensive treatment model may be evidence-based. The research supporting the effectiveness of separate, individual components, however, does *not* constitute an evaluation of the comprehensive treatment model or “package.” The TIAC will consider and review only research that has evaluated the efficacy of implementing the comprehensive treatment *as a package*. Such packages are most often identifiable in the literature by a consistently used name or label.

National Research Council. (2001). *Educating children with autism*. Washington, DC: National Academy Press.

Odom, S. L., Brown, W. H., Frey, T., Karusu, N., Smith-Carter, L., & Strain, P. (2003) Evidence-based practices for young children with autism: Evidence from single-subject research design. *Focus on Autism and Other Developmental Disabilities, 18*, 176-181.

Odom, S. L., Boyd, B. A., Hall, L. J., & Hume, K. (2010). Evaluation of comprehensive treatment models for individuals with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders, 40*, 425-436.

Rogers, S., & Vismara, L. (2008). Evidence-based comprehensive treatments for early autism. *Journal of Clinical Child and Adolescent Psychology, 37*, 8-38.

Section Three: DLTC-TIAC Treatment Review Evidence Checklist

Name of Treatment: Hyperbaric Oxygen Therapy

Level 1- Well Established or Strong Evidence (DHS 107 - Proven & Effective Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, National Professional Development Center) have approved of or rated the treatment package as having a strong evidence base; authorities are in agreement about the level of evidence.
- There exist ample high quality studies that demonstrate experimental control and favorable outcomes of treatment package.
 - Minimum of two group studies or five single subject studies or a combination of the two.
 - Studies were conducted across at least two independent research groups.
 - Studies were published in peer reviewed journals.
- There is a published procedures manual for the treatment, or treatment implementation is clearly defined (i.e., replicable) within the studies.
- Participants (i.e., N) are clearly identified as individuals with autism spectrum disorders or developmental disabilities.

Notes: At this level, include ages of participants and disabilities identified in body of research

Level 2 – Established or Moderate Evidence (DHS 107 - Proven & Effective Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have approved of or rated the treatment package as having at least a minimal evidence base; authorities may not be in agreement about the level of evidence.
- There exist at least two high quality studies that demonstrate experimental control and favorable outcomes of treatment package.
 - Minimum of one group study or two single subject studies or a combination of the two.
 - Studies were conducted by someone other than the creator/provider of the treatment.
 - Studies were published in peer reviewed journals.
- Participants (i.e., N) are clearly identified as individuals with autism spectrum disorders or developmental disabilities.

Notes: At this level, include ages of participants and disabilities identified in body of research

Level 3 – Emerging Evidence (DHS 107 – Promising as a Proven & Effective Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have recognized the treatment package as having an emerging evidence base; authorities may not be in agreement about the level of evidence.
- There exists at least one high quality study that demonstrates experimental control and favorable outcomes of treatment package.
 - May be one group study or single subject study.
 - Study was conducted by someone other than the creator/provider of the treatment.
 - Study was published in peer reviewed journal.
- Participants (i.e., N) are clearly identified as individuals with autism spectrum disorders or developmental disabilities.

Notes: At this level, include ages of participants and disabilities identified in body of research

Level 4 – Insufficient Evidence (Experimental Treatment)

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have not recognized the treatment package as having an emerging evidence base; authorities are in agreement about the level of evidence.
- There is not at least one high quality study that demonstrates experimental control and favorable outcomes of treatment package.
 - Study was conducted by the creator/provider of the treatment.
 - Study was not published in a peer reviewed journal.
- Participants (i.e., N) are not clearly identified as individuals with autism spectrum disorders or developmental disabilities.

Notes:

Level 5 – Untested (Experimental Treatment) &/or Potentially Harmful

- Other authoritative bodies that have conducted extensive literature reviews of related treatments (e.g., National Standards Project, NPDC) have not recognized the treatment package as having an emerging evidence base; authorities are in agreement about the level of evidence.
- There are no published studies supporting the proposed treatment package.
- There exists evidence that the treatment package is potentially harmful.**
 - Authoritative bodies have expressed concern regarding safety/outcomes.
 - Professional bodies (i.e., organizations or certifying bodies) have created statements regarding safety/outcomes.

Notes: *No, Hyperbaric Oxygen Therapy (HBOT) has not been clinically proven to cure or be effective in the treatment of cancer, autism, or diabetes. But do a quick search on the Internet, and you'll see all kinds of claims for these and other diseases for which the device has not been cleared or approved by FDA.

*FDA anesthesiologist Nayan Patel reports that persons using HBOT “may experience a lack of improvement and/or worsening of their existing condition(s).”

Date: October 28, 2016

Committee Members Completing Initial Review of Research Base: Lana Collet-Klingenberg, Jeffrey Tiger

Committee Decision on Level of Evidence to Suggest the Proposed Treatment is Proven and Effective:
Level 5 - Untested (Experimental Treatment) &/or Potentially Harmful.

References Supporting Identification of Evidence Levels:

Chambless, D.L., Hollon, S.D. (1998). Defining empirically supported therapies. *Journal of Consulting and Clinical Psychology*, 66(1) 7-18.

Chorpita, B.F. (2003). The frontier of evidence---based practice. In A.E. Kazdin & J.R. Weisz (Eds.). *Evidence-based psychotherapies for children and adolescents* (pp. 42---59). New York: The Guilford Press.

Odom, S. L., Collet-Klingenberg, L., Rogers, S. J., & Hatton, D. (2010). Evidence-based practices in interventions for children and youth with autism spectrum disorders. *Preventing School Failure*, 54(4), 275-282.

Section Four: Literature Review

Bent, S., Bertoglio, K., Ashwood, Nemeth, E. and Hendren, R.L. (2012). Brief report: Hyperbaric oxygen therapy (HBOT) in children with autism spectrum disorder: A Clinical trial. *Journal of Autism and Developmental Disorders*, 42:1127-1132

El-baz, F., Elhossiny, R.M., Azeem, Y.A., and Girgis, M. (2014). Study the effect of hyperbaric oxygen therapy in Egyptian autistic children: A clinical trial. *The Egyptian Journal of Medical Human Genetics*, 15, 155-162.

FDA (2013). Hyperbaric oxygen therapy: don't be misled. Retrieved from <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm364687.htm>

Granpeesheh, D., Tarbox, J., Dixon, D.R., Wilke, A.E., Allen, M.S., and Bradstreet, J.J. (2010). Randomized trial of hyperbaric oxygen therapy for children with autism. *Research in Autism Spectrum Disorders*, 4, 268-275.

Hardy, P., et al (2002). Neuropsychological effects of hyperbaric oxygen therapy in cerebral palsy. *Developmental Medicine & Child Neurology*, 44, 436-446.

Jepgrgson, B., Granpeesheh, D., Tarbox, J., Olive, M.L., Stott, C., Braud, S., Yoo, J.H., Wakefield, A., and Allen M.S. (2011) controlled evaluation of the effects of hyperbaric oxygen therapy on the behavior of 16 children with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 41, 575-588.

Sampanthavivat, M., Singkwa, W., Chaiyakul, T., Karoonyawanich, S., Ajpru, H. (2012). Hyperbaric oxygen in the treatment of childhood autism: a randomised controlled trial. *Diving Hyperbaric Medicine*, 42(3), 128-133. <https://www.ncbi.nlm.nih.gov/pubmed/22987458>

Xiong, T., Chen, H., Luo, R., & Mu, D.(2016). Hyperbaric oxygen therapy for people with autism spectrum disorders. *Cochrane Systems Review*, October 13. <https://www.ncbi.nlm.nih.gov/pubmed/27737490>