

Treatment Intervention Advisory Committee Review and Determination

Date: July 31, 2015

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 25, 2014

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.

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: Aetna considers the use of systemic HBOT experimental and investigational for treatment of autism because there is insufficient evidence in the medical literature establishing that systemic HBOT is more effective than conventional therapies (retrieved April 24, 2014, from Aetna Clinical Policy bulletin, aetna.com).

The FDA cautions against HBOT with the following statements (taken from consumer information publication, retrieved April 24, 2014, from - <http://www.fda.gov/downloads/ForConsumers/>

Date: July 31, 2015

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.
- 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.
- Jepson, 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.

TIAC EBP Literature Review
Article Inclusion Checklist Answers and Rationale

Article Reference:	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. J. Autism Dev Disorder, 42:1127-1132.
IV Description	HBOT (1.5 atmosphere absolute; 100% oxygen) for 1 h., 5 days a week for 8 weeks, followed by a 4 week break, and then another 40 treatments over 8 weeks; totaling 80 treatments over 20 weeks
DV	Cytokine levels, parent reported behavioral changes; clinician reports of CGIS (clinical global impression severity)
# in study	10
Age ranges	3-8 years
Diagnoses	ASD
Design	Pre/post
Study Results	No changes in cytokine levels; CGI-I scale results improved. Inconclusive.
Reviewer Comments	Not rigorous enough. Outcomes inconclusive.

Single-Case Design EBP Inclusion Criteria Checklist

Instructions: Read each item and check the appropriate box. If you check “NO” at any time, the article can be discarded as it will not be included as evidence for a practice.

Item	YES	NO	Rationale
Does the dependent variable align with the research question or purpose of the study?			
Was the dependent variable clearly defined such that another person could identify an occurrence or non-occurrence of the response?			
Does the measurement system align with the dependent variable and produce a quantifiable index?			
Did a secondary observer collect data on the dependent variable for at least 20% of sessions across conditions?			
Was mean interobserver agreement (IOA) 80% or greater OR kappa of .60 or greater?			
Is the independent variable described with enough information to allow for a clear understanding about the critical differences between the baseline and intervention conditions, or were references to other material used if description does not allow for a clear understanding?			
Was the baseline described in a manner that allows for a clear understanding of the differences between the baseline and intervention conditions?			
Are the results displayed in graphical format showing repeated measures for a single case (e.g., behavior, participant, group) across time?			
Do the results demonstrate changes in the dependent variable when the independent variable is manipulated by the experimenter at three different points in time or across three phase repetitions? *Alternating treatment designs require at least 4 repetitions of the alternating sequence.			

Group Design EBP Inclusion Criteria Checklist

Instructions: Read each item and check the appropriate box. If you check “NO” at any time, the article can be discarded as it will not be included as evidence for a practice.

Item	YES	NO	Rationale
Does the study have experimental and control/comparative groups?			
Were appropriate procedures used to increase the likelihood that relevant characteristic of participants in the sample were comparable across conditions?			
Was their evidence for adequate reliability for the key outcome measures? And/or when relevant, was inter-observer reliability assessed and reported to be at an acceptable level?			
Were outcomes for capturing the intervention’s effect measured at appropriate times (at least pre- and post-test)?			
Was the intervention described and specified clearly enough that critical aspects could be understood?			
Was the control/comparison condition(s) described?			
Were data analysis techniques appropriately linked to key research questions and hypotheses?			
Was attrition NOT a significant threat to internal validity?			
Does the research report statistically significant effects of the practice for individuals with ASD for at least one outcome variable?			
Were the measures of effect attributed to the intervention? (no obvious unaccounted confounding factors)			

TIAC EBP Literature Review
Article Inclusion Checklist Answers and Rationale

Article Reference:	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.
IV Description	HBOT
DV	Ratio of regional cerebral blood flow to white matter; CARS scores; ATEC checklist scores
# in study	20
Age ranges	2-9 years
Diagnoses	autism
Design	Pre/post;
Study Results	Improvement in CARS and ATEC scores following HBOT
Reviewer Comments	No control group; not rigorous

Single-Case Design EBP Inclusion Criteria Checklist

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Are the results displayed in graphical format showing repeated measures for a single case (e.g., behavior, participant, group) across time?			
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Article Reference:	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. <i>Research in Autism Spectrum Disorders</i> , 4, 268-275.
IV Description	HBOT (1.3 atmospheric pressure, 24% oxygen).
DV	ASD symptoms as measured by ADOS, ABC, Behavior Rating Inventory of Executive Functioning, Clinical Global Impression Scale, Parent Stress Index, Peabody Picture Vocabulary Test, Repetitive Behavior Scale, Vineland Adaptive Behavior Scales, and others; along with behavioral observations
# in study	18 in IV group; 16 in placebo group
Age ranges	6.8 years mean age
Diagnoses	ASD
Design	Randomized, double-blind, placebo controlled
Study Results	No differences between groups.
Reviewer Comments	Well designed study; showed no results.

Group Design EBP Inclusion Criteria Checklist

Instructions: Read each item and check the appropriate box. If you check “NO” at any time, the article can be discarded as it will not be included as evidence for a practice.

Item	YES	NO	Rationale
Does the study have experimental and control/comparative groups?	X		
Were appropriate procedures used to increase the likelihood that relevant characteristic of participants in the sample were comparable across conditions?	X		
Was their evidence for adequate reliability for the key outcome measures? And/or when relevant, was inter-observer reliability assessed and reported to be at an acceptable level?	X		
Were outcomes for capturing the intervention’s effect measured at appropriate times (at least pre- and post-test)?	X		
Was the intervention described and specified clearly enough that critical aspects could be understood?	X		
Was the control/comparison condition(s) described?	X		
Were data analysis techniques appropriately linked to key research questions and hypotheses?	X		
Was attrition NOT a significant threat to internal validity?	X		
Does the research report statistically significant effects of the practice for individuals with ASD for at least one outcome variable?		X	
Were the measures of effect attributed to the intervention? (no obvious unaccounted confounding factors)			NA

TIAC EBP Literature Review
Article Inclusion Checklist Answers and Rationale

Article Reference:	Hardy, P., et al (2002). Neuropsychological effects of hyperbaric oxygen therapy in cerebral palsy. <i>Developmental Medicine & Child Neurology</i> , 44, 436-446.
IV Description	HBOT (100% oxygen at 1.75 ATA).
DV	Cognitive status
# in study	75
Age ranges	4 – 12 years
Diagnoses	CP
Design	Double-blind placebo study
Study Results	IV and control (sham) group had no statistical differences.
Reviewer Comments	Well designed study; did not support use of HBOT.

Single-Case Design EBP Inclusion Criteria Checklist

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Does the measurement system align with the dependent variable and produce a quantifiable index?			
Did a secondary observer collect data on the dependent variable for at least 20% of sessions across conditions?			
Was mean interobserver agreement (IOA) 80% or greater OR kappa of .60 or greater?			
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Was the baseline described in a manner that allows for a clear understanding of the differences between the baseline and intervention conditions?			
Are the results displayed in graphical format showing repeated measures for a single case (e.g., behavior, participant, group) across time?			
Do the results demonstrate changes in the dependent variable when the independent variable is manipulated by the experimenter at three different points in time or across three phase repetitions? *Alternating treatment designs require at least 4 repetitions of the alternating sequence.			

Group Design EBP Inclusion Criteria Checklist

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Does the research report statistically significant effects of the practice for individuals with ASD for at least one outcome variable?			
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TIAC EBP Literature Review
Article Inclusion Checklist Answers and Rationale

Article Reference:	Jepson, 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. <i>Journal of Autism and Developmental Disorders</i> , 41, 575-588.
IV Description	HBOT at 24% oxygen at 1.3 ATA
DV	Behaviors related to social functioning, verbal functioning and problematic behaviors. Observational data; also Wechsler, and VBAS
# in study	19
Age ranges	2- 10 years
Diagnoses	ASD, PDD NOS or Aspergers
Design	Non-concurrent multiple baseline
Study Results	No impact on behaviors related to autism.
Reviewer Comments	Nicely designed study.

Single-Case Design EBP Inclusion Criteria Checklist

Instructions: Read each item and check the appropriate box. If you check “NO” at any time, the article can be discarded as it will not be included as evidence for a practice.

Item	YES	NO	Rationale
Does the dependent variable align with the research question or purpose of the study?	X		
Was the dependent variable clearly defined such that another person could identify an occurrence or non-occurrence of the response?	X		
Does the measurement system align with the dependent variable and produce a quantifiable index?	X		
Did a secondary observer collect data on the dependent variable for at least 20% of sessions across conditions?	X		
Was mean interobserver agreement (IOA) 80% or greater OR kappa of .60 or greater?	X		
Is the independent variable described with enough information to allow for a clear understanding about the critical differences between the baseline and intervention conditions, or were references to other material used if description does not allow for a clear understanding?	X		
Was the baseline described in a manner that allows for a clear understanding of the differences between the baseline and intervention conditions?	X		
Are the results displayed in graphical format showing repeated measures for a single case (e.g., behavior, participant, group) across time?	X		