HEALTH EVIDENCE REVIEW COMMISSION (HERC)

# EVALUATION OF EVIDENCE: APPLIED BEHAVIOR ANALYSIS FOR AUTISM SPECTRUM DISORDERS

**HERC reviewed 8/14/2014**

## BACKGROUND

Oregon Senate Bill 365 was passed by the Oregon legislature in the 2013 regular session. That bill directs the Health Evidence Review Commission to evaluate applied behavior analysis (ABA) as a treatment for autism spectrum disorder (ASD) for the purposes of updating the prioritized list of health services. The bill also establishes requirements for state-regulated health plans to approve and manage autism treatment, including ABA therapy and any other medical or mental health services identified in an individualized treatment plan. The law applies to patients who seek care before age nine, covering up to 25 hours of ABA per week, and continuing as long as medically necessary. Health plans that provide coverage to OEBB and PEBB are required to begin coverage in 2015, and all other health plans are required to begin coverage in 2016. Applied behavior analysis is defined in the bill as the following:

The design, implementation and evaluation of environmental modifications, using behavioral stimuli and consequences, to produce significant improvement in human social behavior, including the use of direct observation, measurement and functional analysis of the relationship between environment and behavior and that is provided by:

> (i) A licensed health care professional registered under section 3 of this 2013 Act;
>
> (ii) A behavior analyst or an assistant behavior analyst licensed under section 3 of this 2013 Act; or
>
> (iii) A behavior analysis interventionist registered under section 3 of this 2013 Act.

"Applied behavior analysis" excludes psychological testing, neuropsychology, psychotherapy, cognitive therapy, sex therapy, psychoanalysis, hypnotherapy and long-term counseling as treatment modalities.

For details of the public process used to develop this evaluation of evidence, see http://www.oregon.gov/oha/herc/Pages/blog-ABA.aspx

DRAFT

EVIDENCE SOURCES

Warren, Z., Veenstra-VanderWeele, J., Stone, W., Bruzek, J.L., Nahmias, A.S., Foss-Feig, J.H., et al. (2011). *Therapies for children with autism spectrum disorders. Comparative effectiveness review no. 26.* (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2007-10065-I). AHRQ Publication No. 11-EHC029-EF. Rockville, MD: Agency for Healthcare Research and Quality. April 2011. Retrieved from http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=651

*Update of Warren 2011 in draft form:*

*Therapies for children with autism spectrum disorder – Behavioral interventions update. Draft Comparative Effectiveness Review*. Rockville, MD: Agency for Healthcare Research and Quality. Retrieved January 27, 2014, from http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayProduct&productID=1845

Lounds Taylor, J., Dove, D., Veenstra-VanderWeele, J., Sathe, N.A., McPheeters, M.L., Jerome, R.N., et al. (2012). *Interventions for adolescents and young adults with Autism Spectrum Disorders. Comparative Effectiveness Review No. 65.* (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2007-10065-I.) AHRQ Publication No. 12-EHC063-EF. Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=1197&pageaction=displayproduct

Maglione, M., Motala, A., Shanman, R., Newberry, S., Schneider Chafen, J., & Shekelle, P. (2012). *AHRQ Comparative Effectiveness Review Surveillance Program: Therapies for Children with Autism Spectrum Disorders, 2nd Assessment.* Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1536

Oono, I.P., Honey, E.J., & McConachie, H. (2013). Parent-mediated early intervention for young children with autism spectrum disorders (ASD). *Cochrane Database of Systematic Reviews*, Issue 4. Retrieved from http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009774.pub2/abstract

- *List of included studies in Oono 2013 provided in Appendix D*

DRAFT

*Glossary Sources*

Agency for Healthcare Research and Quality (AHRQ) Effective Health Care Program. (n.d.). Glossary of terms. Retrieved from http://effectivehealthcare.ahrq.gov/index.cfm/glossary-of-terms/

National Cancer Institute (NCI) at the National Institutes of Health (NIH). (n.d.). NCI dictionary of cancer terms. Retrieved from http://www.cancer.gov/dictionary

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

## SUMMARY OF EVIDENCE

### Clinical Background

The following clinical background summary is extracted from the update to the Warren 2011 report (AHRQ draft, 2014).

> Autism spectrum disorder (ASD) is a neurodevelopmental disorder marked by impaired social communication and social interaction accompanied by atypical patterns of behavior and interest. ASD is differentiated from other developmental disorders by significant impairments in social interaction and communication, along with restrictive, repetitive, and stereotypical behaviors and activities. Social communication and social interaction features include deficits in social-emotional reciprocity (e.g., deficits in joint attention, atypical social approach and response, conversational challenges, reduced sharing of interest, emotions, and affect), deficits in nonverbal communication (e.g., atypical eye contact, reduced gesture use, limited use of facial expressions in social interactions, challenges understanding nonverbal communication), and deficits in forming and maintaining relationships (e.g., diminished peer interest, challenges joining in play, difficulties adjusting behavior to social context). ASD features of restricted, repetitive patterns of behavior, interests, or activities may include stereotyped motor mannerisms, use of objects, or speech (e.g., simple motor stereotypies, repetitive play, echolalia, and formal or idiosyncratic speech); insistence on sameness, inflexible adherence to routines, or ritualized patterns of behavior (e.g., distress at small changes, rigid patterns of thought and behavior, performance of everyday activities in ritualistic manner); intense preoccupation with specific interests (e.g., strong attachment to objects, circumscribed or perseverative topics of interest); and sensory sensitivities or interests (e.g., hyper- or hypo-reactivity to pain and sensory input, sensitivity to noise, visual fascination with objects or movement). These symptoms cause impairment across many areas of functioning and are present early in life. However, impairments may not be fully evident until environmental demands exceed children's capacity. They also may

> be masked by learned compensatory strategies later in life. Many children with ASD may also have intellectual impairment or language impairment, and the disorder may be associated with known medical, genetic, or environmental factors. (p. ES-1)
>
> The prevalence of ASD in the United States is 11.3 cases per 1,000 (or 1 in 88) children living in the communities surveyed, with rate estimates varying widely by region of the country, sex, and race/ethnicity. Considerably more males (1 in 54) than females (1 in 252) are affected. For some individuals, the core symptoms of ASD (impairments in communication and social interaction and restricted/repetitive behaviors and interests) may improve with intervention and maturation; however, core deficits typically translate into varying developmental presentations that remain throughout the lifespan. Longitudinal studies indicate that adults with ASD struggle to obtain adaptive independence. (p. 1)
>
> Treatments for ASD include behavioral, educational, medical, allied health, and complementary approaches. Individual goals for treatment vary for different children and may include combinations of therapies. For many individuals, core symptoms of ASD (impairments in communication and social interaction and restricted/repetitive behaviors and interests) may improve with intervention and over time5-8; however, deficits typically remain throughout the lifespan. Chronic management—often using multiple treatment approaches—may be required to maximize ultimate functional independence and quality of life. (p. ES-1)

This review of the evidence addresses only behavioral interventions for ASDs that utilize principles of applied behavior analysis (ABA).

> ABA is an umbrella term describing principles and techniques used in the assessment, treatment and prevention of challenging behaviors and the promotion of new desired behaviors. The goal of ABA is to teach new skills, promote generalization of these skills, and reduce challenging behaviors with systematic reinforcement. The principles and techniques of ABA existed for decades prior to specific application and study within ASDs. (AHRQ draft, 2014, p. 5)

Interventions that utilize the principles of ABA include comprehensive treatments referred to as Early Intensive Behavioral and Developmental Interventions (EIBI). Two of these intensive treatments have been manualized (i.e., have published treatment manuals to facilitate replication): the UCLA/Lovaas model and the Early Start Denver Model (ESDM). There are other treatment approaches that also incorporate ABA principles, and may be intensive in nature, but have not been manualized. A third particular set of interventions include those using the principles of ABA to focus on key

pivotal behaviors rather than global improvements. These approaches emphasize parent training as a modality for treatment delivery (e.g., Pivotal Response Training, Hanen More than Words, social pragmatic intervention, etc.) and may focus on specific behaviors such as initiating or organizing activity or on core social communication skills.

Play-/interaction-based interventions may employ ABA principles and are included in this review. These interventions use interactions between children and adults (either parents or researchers) to improve outcomes such as imitation or joint attention skills or the ability of the child to engage in symbolic play. They include teaching parents how to interact differently with their children within daily routines and interactions, often using standard behavior management strategies.

## Evidence Review

### Children Ages Two to Twelve

*EIBI and Other ABA Interventions*

Warren (2011)

The Warren (2011) AHRQ review included all study designs as long as there were at least 10 participants. A total of 30 discrete studies were included, with the largest study population being 78 participants. The longest duration of treatment in any included study was three years. The mean age of children at intake in the included studies ranged from 21 to 66 months for EIBI interventions and from 42 months to 10.8 years for other ABA interventions. Authors reach the following conclusions:

> The evidence suggests that early intensive behavioral and developmental intervention (EIBI) may improve core areas of deficit for individuals with ASDs; however, randomized controlled trials (RCTs) are few and include small numbers of participants. In addition, there are no direct comparison trials. “Within this category, studies of UCLA/Lovaas-based interventions report greater improvements in cognitive performance, language skills, and adaptive behavior skills than broadly defined eclectic treatments available in the community. However, strength of evidence is currently low” (Warren, 2011, p. ES-7). In addition, the consistency of benefit is lacking, in that “not all children demonstrate rapid gains, and many children continue to display substantial impairment” (Warren, 2011, p. ES-7). Although positive results are reported for the effects of intensive interventions that use a developmental framework, such as ESDM, evidence for this type of intervention is currently insufficient because few studies have been published to date.

DRAFT

Less intensive interventions focusing on providing parent training for bolstering social communication skills and managing challenging behaviors have also been studied. Some interventions have shown short-term gains in social communication and language use, but the current evidence base for such treatment remains insufficient. Strength of evidence is also considered insufficient for play- and interaction-based approaches.

Only one study was identified that directly addressed whether there are any modifiers of outcomes for different ABA-based behavioral approaches. It examined the impact of which provider (parent vs. professional) delivered the UCLA/Lovaas protocol-based interventions. There was no significant difference in outcomes for children receiving the intervention in a clinical setting vs. at home from highly trained parents.

Other potential correlates that warrant further study because of conflicting data include pretreatment IQ and language skills, and age of initiation of treatment (with earlier age potentially associated with better outcomes). "Social responsiveness and imitation skills have been suggested as skills that may correlate with improved treatment response in UCLA/Lovaas treatment, whereas 'aloof' subtypes of ASDs may be associated with less robust changes in IQ. Other studies have seen specific improvement in children with PDD-NOS vs. Autistic Disorder diagnoses, which may be indicative of baseline symptom differences. However, many other studies have failed to find a relationship between autism symptoms and treatment response" (Warren, 2011, p. ES-8).

"Research on very young children is preliminary, with four studies identified. One good-quality RCT suggested benefit from the use of ESDM in young children, with improvements in adaptive behavior, language, and cognitive outcomes. Diagnostic shifts within the autism spectrum were reported in close to 30 percent of children but were not associated with clinically significant improvements in Autism Diagnostic Observation Schedule severity scores or other measures" (Warren, 2011, p. ES-9).

There was no evidence identified in the Warren review that addressed treatment effectiveness in specific subgroups such as race, ethnicity, gender or socioeconomic status, other than age. Details of all comparative studies that reported comparative statistics are provided in the table below.

**Table 1. Comparative Studies included in Warren 2011**

| Author | Study Design | Intervention Intensity | Intervention Duration | Summary of Outcome |
|---|---|---|---|---|
| **Smith 2000** | RCT, intensive vs. parent training | Intensive: 30 hrs/wk with therapist, 5 | intensive: 2-3 yrs | Intensive group had improved IQ, developmental |

| Author | Study Design | Intervention Intensity | Intervention Duration | Summary of Outcome |
|---|---|---|---|---|
| | | hrs/wk with parents X 3 months<br>Parent: taught techniques from Lovaas manual 2 sessions/wk | parent: 3-9 mos | scores compared to parent training, as well as in 1 communication score, but not in 3 others, and no sig diff in adaptive function<br>MIXED |
| **Drew 2002** | RCT, parent training vs. local services (ST, OT, ABA, home worker) | Parent: 6.3 hrs/wk<br>Local: 3.5 hrs/wk | Not specified; follow up at 1 year | No sig diff between groups in cognitive[1] outcomes. parent group had some better communication outcomes<br>MIXED |
| **Aldred 2004** | RCT, social communication intervention vs. routine care (not described) | Intervention: monthly treatment sessions X 6 months (time not specified), then less frequent for another 6 months<br>Control: routine care | 1 year | Intervention group had better language scores, parent synchrony. No diff in shared attention<br>MIXED |
| **Eikeseth 2002/ 2007** | Non-randomized CT, Lovaas behavioral treatment vs. eclectic (TEACCH, sensory-motor therapies, ABA) | Lovaas: 28 hrs/wk<br>Eclectic: 29 hrs/wk | Not specified; first follow up at 1 year | Lovaas group had sig more improvement than eclectic in IQ, communication, adaptive behavior at both 1 and 8 year follow up for most measures<br>POSITIVE |
| **Reed 2007** | Non-randomized CT, high intensity ABA vs. low intensity ABA | High: mean 30 hrs/wk<br>Low: mean 13 hrs/wk | Not specified | No diff in autism severity, adaptive behavior. Mixed result for cognitive, with high intensity scoring better on one measure but not another<br>MIXED |
| **Howard 2005** | Prospective cohort, intensive ABA vs. intensive eclectic (delivered in school) vs. non-intensive public early intervention | ABA: 25-30 hrs/wk for age <3, 35-40 for age >3 plus parent training<br>Intensive eclectic: not specified<br>Public EI: not specified | Follow up at 14 mos | ABA group had sig higher scores than mean of the other two groups for all outcome measures except motor skills<br>POSITIVE |
| **Remington** | Prospective cohort, | EI: mean 26 hrs/wk | 2 years | EI group had sig higher |

[1] Educational, cognitive, and academic outcomes are reported together and noted as "cognitive" unless specified otherwise.

DRAFT

| Author | Study Design | Intervention Intensity | Intervention Duration | Summary of Outcome |
|---|---|---|---|---|
| **2007** | home-based early intervention (parent delivered with tutors) vs. local education standard treatment | Control: not specified | | scores for most outcomes, including social skills, communication, adaptive behavior, cognitive function POSITIVE |
| **Cohen 2006** | Prospective cohort, EIBI (Lovaas) vs. services from public school (parent choice) | Intervention: 35-40 hrs/wk, 47 wks/yr Control: not specified | 3 years | Intervention group had higher IQ, were more likely in regular classroom and had higher adaptive scores; no sig diff in communication POSITIVE |
| **Stahmer 2001** | Prospective cohort, parent information support group and education course on PRT vs. education course only (control) | 2 hrs/week for intervention group vs 1 hr/wk for control | 12 weeks | Sig more parents in the intervention group correctly used PRT techniques, and their children had improved communication POSITIVE |
| **Zachor 2007 (appears to be a subset of Itzchak 2009)** | Prospective cohort, behavioral vs. eclectic | Behavioral: 1 to 1 35 hrs/wk Eclectic: special ed teacher, various therapists (OT, ST), parent training, at least 16 hrs/wk | Not specified | Sig improved overall severity, communication behavioral group compared to eclectic, no sig diff in social skills POSITIVE |
| **Hayward 2009/ Eikeseth 2009** | Prospective cohort, clinic based vs. parent managed | Clinic: 37 hrs/week Parent: 34 hrs/week (mean supervision hrs/mo = 5) | 1 year | No differences between groups in communication, adaptive behavior, cognitive/academic NEGATIVE |
| **Eldevik 2006** | Retrospective cohort, low intensity behavioral (Lovaas) vs. eclectic (alternative communication, TEACCH, sensory-motor, ABA | Behavioral: 12 hrs/wk Eclectic: not specified | Behavioral: 20 mos Eclectic: 21 mos | Behavior group had mixed outcomes on cognitive measures (better on some measures, no diff on others), better communication scores, fewer problem behaviors. no diff in adaptive scores MIXED |
| **Reed 2007** | Retrospective cohort, ABA vs. special nursery vs. portage (parent training) | ABA: mean 30 hrs/wk Special nursery: mean 12 hrs/wk Portage: mean 8 hrs/wk | Not specified | 27 diff outcomes measures reported on, no sig diffs on 18. ABA group had better scores than one or the other of the comparators for the following measures: 2 of 3 overall ratings, 4 of 8 communication scores, 3 of |

DRAFT

| Author | Study Design | Intervention Intensity | Intervention Duration | Summary of Outcome |
|---|---|---|---|---|
| | | | | 7 behavior scores. There were no diffs in motor skills scores, cognitive scores, comorbidities<br>MIXED |

In summary, the intensity of experimental interventions ranged from less than two hours per week to 40 hours per week. For the control interventions, intensity was often not specified, but was as high as 34 hours per week. Of those studies showing a mostly positive outcome for the intervention, intensity ranged from 26 to 40 hours per week, with the exception of the Stahmer study, which was a very narrowly focused intervention aimed at teaching parents a specific skill.

With regard to duration, five studies did not specify the length of the intervention period. The shortest study was 12 weeks, while the longest was 3 years. Of those studies showing a mostly positive outcome for the intervention, duration ranged from no more than a year to three years, with the exception of the Stahmer study.

The following limitations of the evidence were noted by the report authors:

> A high proportion of studies in this review (36 percent) fail to use a comparison group, and while substantial strides have been made in the analysis of single-subject designs, these are not ideal for assessing effectiveness at a population level, nor are they appropriate for comparative effectiveness research. They are, however, used frequently in the behavioral literature, and so we address our decisions regarding them here. Because there is no separate comparison group in these studies they would be considered case reports (if only one child included) or case series (multiple children) under the rubric of the EPC study designs. Case reports and case series can have rigorous evaluation of pre- and post-measures, as well as strong characterization of the study participants.
>
> Studies using this design that included at least 10 children were included in the review. Studies of this type can be helpful in assessing response to treatment in very short time frames and under very tightly controlled circumstances, but they typically do not provide information on longer term or functional outcomes. They are useful in serving as demonstration projects, yielding initial evidence that an intervention merits further study, and, in the clinical environment, they can be useful in identifying whether a particular approach to treatment is likely to be helpful for a specific child. Our goal was to identify and review the best evidence for assessing the efficacy and effectiveness of therapies for children with ASD, with an eye toward their utility in the clinical setting, and for the larger population

DRAFT

of children with ASD. By definition, “populations” in single-subject design studies are likely to be idiosyncratic and therefore not to provide information that is generalizable.

Nonetheless, even in studies with a comparison group, sample size is frequently insufficient to draw conclusions, and larger, multisite trials are needed across all treatment types. Furthermore, the choice of comparison groups in the studies that employed a group design was uneven. A number of studies used comparison groups that were inappropriate for observing group differences in treatment effect (e.g., comparing treatment in children with autism to the effects of the treatment in typically developing peers or to children with a different developmental disorder), and for those studies we could only use the pre-post case series data available in the group with autism, limiting the ability to comment on effectiveness.

We encourage investigators to provide adequate detail as they describe their interventions to allow for replicable research. In ideal circumstances, investigators publish and reference treatment manuals, but many studies made general references to their use of an underlying approach (e.g., ABA) without specifying the ways in which they used the technique or modifications they made to the original, published use of it. Lack of detail about the intervention makes it difficult to assess the applicability of individual studies, to synthesize groups of studies or to replicate studies.

Characterization of the study population was often inadequate, with 125 of 159 studies failing to use or report “gold standard” diagnostic measures (clinical DSM-IV-based diagnosis plus ADI-R and/or ADOS) for the participants. Because ASDs are spectrum disorders, it is difficult to assess the applicability of interventions when the population in which they were studied is poorly defined or described. Authors often do not consider diagnostic criteria in selecting participants for their studies; nor do they fully describe the children who do participate. We recommend that investigators fully describe participants in their study, both diagnostically and otherwise. In addition, because the myriad causes of ASDs are unknown, even children with the same diagnosis may have distinct genetic or other “causes” that could affect treatment effectiveness. Ideally, future research will better characterize participants genotypically and phenotypically.

We identified more than 100 distinct outcome measures used in this literature base, not accounting for subscales. The use of so many and such disparate outcome measures makes it nearly impossible to synthesize the effectiveness of the interventions, and we recommend a consistent set of rigorously evaluated outcome measures specific to each intended target of treatment to move

DRAFT

comparative effectiveness research forward and to provide a sense of expected outcomes of the interventions. At the same time, the means for assessing outcomes should include increased focus on use of observers or reporters masked to the intervention status of the participant, and where some outcomes are measured in a masked fashion but others not, more emphasis should be placed on those that are.

There also was a strong tendency for authors to present data on numerous outcomes without adjusting for multiple comparisons, and to fail to report the outcome that was the primary outcome of *a priori* interest and on which sample size calculations were based (when they were present). This may suggest a level of selective reporting bias in which results are published on a select group of outcomes that show the most effect. We attempted, but were unable, to identify a clear primary intended outcome in almost all of the papers.

Duration of treatment and follow up was generally short, with few studies providing data on long-term outcomes after cessation of treatment. Future studies should extend the follow up period and assess the degree to which outcomes are durable. Few studies adequately accounted for concomitant interventions that might confound observed effectiveness and this should be standardized in future research. (Warren, 2011, p. 124-125)

[Evidence Source]

Maglione (2012)

Surveillance of the literature pertaining to the Warren report was conducted by AHRQ in January 2012 and October 2012 (Maglione, 2012). Conclusions pertaining to ABA therapies that address the currency of the 2011 report are presented below:

- Original conclusions regarding low strength of evidence for Early Intensive Behavioral Interventions (EIBI) are possibly out of date due to new RCTs and long-term follow-up of previously included studies.
- Original conclusion regarding insufficient evidence for parent training is possibly out of date due to several new RCTs.
- For Key Question 2 [what are the modifiers of outcome for different treatments or approaches (frequency, duration or intensity of treatment, characteristics of child or family, training of therapy provider)], conclusions are still valid, with the exception of impact of provider type, which may possibly be out of date. (p. ii)

[Evidence Source]

DRAFT

AHRQ Draft Report Update (2014)

Given this evidence of additional research, AHRQ elected to update the Warren report, focusing only on behavioral interventions. They published their draft report in January 2014. A summary of the findings is below:

> We included 51 unique studies comprising 37 randomized trials and 14 nonrandomized, comparative studies (16 good, 31 fair, and 4 poor quality) published since the prior review. The quality of studies improved compared with that reported in the earlier review. Young children receiving high intensity applied behavior analysis-based early intervention over extended time frames commonly displayed substantial improvement in cognitive functioning and language skills relative to community controls. The magnitude of these effects varied across studies, potentially reflecting poorly understood modifying characteristics related to subgroups of children. Early intensive parent training programs modified parenting behaviors during interactions; however, data were more limited about their ability to improve developmental skills beyond language gains for some children. Social skills interventions varied in scope and intensity and showed some positive effects on social behaviors for older children in small studies. Evidence for play/interaction-based approaches suggested that joint attention interventions may be useful for young and preschool children with ASD when targeting joint attention skills; data on the effects of such interventions in other areas were limited. (AHRQ draft, 2014, p. v)

Of the 51 included studies, 25 addressed interventions included in this report (EIBI except when delivered as an educational intervention, symbolic play and joint attention interventions, parent training). Three studies addressed EIBI, 12 studies addressed parent training, nine studies addressed play and/or interaction based approaches and one evaluated the addition of parent training to individuals using risperidone. Some characteristics of the included studies are reported in the table below:

**Table 2 Summary of new studies from AHRQ draft report update**

| Intervention Type | Intensity Range | Duration Range | Age Range |
|---|---|---|---|
| EIBI (excluding educational interventions) | 15 to 26 hours/week[2] | 24 months | 15 to 54 months |
| Parent training | 30 minutes sessions X 10 to 30 | 12 weeks to 2 years | 18 to 66 months |

[2] The study with 15 hours included an additional 16 hours of parent delivered treatment

| Intervention Type | Intensity Range | Duration Range | Age Range |
|---|---|---|---|
| | hours/week home based ABA[3] | | |
| Play/Interaction Based Interventions[4] | 20 minutes 2X/day, 5 days/week to 3 hours/week[5] | 6 to 12 weeks | 21 to 82 months |
| Parent Training in addition to Risperidone | 11 sessions + boosters, 1 home visit | 16 weeks | 4 to 14 years |

With regard to the impact of intensity or duration on treatment effectiveness, the authors report the following:

- In a retrospective cohort study of EIBI, treatment duration was not determined to be a significant predictor of outcome after controlling for other variables.
- In one parent training RCT evaluating ESDM (12 one hour sessions plus treatment as usual), total intervention hours (range zero to 16 hours/week, mean 1.5 hours/week for intervention group vs. 3.7 hours/ week for control) were associated with improved developmental and vocabulary scores, as was younger child age.

With regard to strength of the evidence, the authors reach the following conclusions:

> A growing evidence base suggests that children receiving early intensive behavioral and developmental interventions (e.g., many hours of intervention a week over the course of 1-2 years) show substantial improvements in cognitive and language skills over time compared with children receiving low-intensity interventions, community controls, and eclectic non-ABA based intervention approaches. With this growing literature, our confidence (strength of evidence) in the effects of ABA-based early intensive approaches on cognitive and language outcomes is moderate, based on the need for additional research that identifies which groups of children benefit the most from specific high intensity approaches.

[3] The study that included 30 hours/week of home based ABA compared this group to three other interventions: special ed classroom (mean 13 hours/week), low-intensity, home based manualized intervention (mean 8 hours/week) and 1:1 behavioral intervention that included a 5 day parent training component (mean 13 hours/week). This study found no significant differences in cognitive or adaptive scores between groups, but did find differences in educational outcomes favoring the intensive ABA group.
[4] Typically delivered in addition to other treatment as usual
[5] Four of the studies did not report treatment intensity

> Our strength of evidence in these high intensity interventions to affect adaptive behavior skills, social skills, and core ASD symptom severity is low. At present it is challenging to understand which high intensity variants most robustly impact these domains for specific children and in general the impact of these skill domains is less consistent.
>
> A growing evidence base suggests that children receiving early joint attention-related intervention in combination with other interventions show substantial improvements in joint attention and language skills over time. Within this growing literature, our confidence (strength of evidence) in this effect is moderate, based on the need for additional research that identifies which groups of children benefit the most from this approach and how this intervention relates to other ongoing concurrent offered interventions. Results from a variety of play-based interventions also suggest that young children often display short-term improvements in early play, imitation, language, and social interaction skills. However, our confidence in these estimates is low, and substantial evidence that these short-term improvements are linked to broader indices of change over time is lacking (AHRQ draft, p. 75).
>
> The evidence base for parent training interventions is moderate for their impact on early language and communication skills and low for impact on ASD symptom severity and early cognition. There is not yet sufficient data from this literature base to understand impact on adaptive behavior skills. Available studies indicate variable responses, with modest improvement for some children in some approaches, but limited improvement in other parent training paradigms. (AHRQ draft, 2014, p. 67)

*Parent-mediated Early Intervention*

<u>Oono (2013)</u>

A review of parent-mediated early intervention in children less than seven was completed by the Cochrane Collaboration in April 2013 (Oono, 2013). It included 17 RCTs (one of which was identified in the AHRQ surveillance report, and eight of which were included in the original Warren report) and drew the following conclusions:

> Overall, we did not find statistical evidence of gains from parent-mediated approaches in most of the primary outcomes assessed (most aspects of language and communication - whether directly assessed or reported; frequency of child initiations in observed parent-child interaction; child adaptive behaviour; parents' stress), with findings largely inconclusive and inconsistent across studies. However, the evidence for positive change in patterns of parent-child interaction was strong and statistically significant (shared attention: standardized mean difference (SMD) 0.41; 95% confidence interval (CI) 0.14 to 0.68, P value <

> 0.05; parent synchrony: SMD 0.90; 95% CI 0.56 to 1.23, P value < 0.05). Furthermore, there is some evidence suggestive of improvement in child language comprehension, reported by parents (vocabulary comprehension: mean difference (MD 36.26; 95% CI 1.31 to 71.20, P value < 0.05). In addition, there was evidence suggesting a reduction in the severity of children's autism characteristics (SMD -0.30, 95% CI -0.52 to -0.08, P value < 0.05). However, this evidence of change in children's skills and difficulties as a consequence of parent-mediated intervention is uncertain, with small effect sizes and wide CIs, and the conclusions are likely to change with future publication of high-quality RCTs. (Oono, 2013, p. 2)

This conclusion differs from that of the AHRQ draft report, for unclear reasons. It may be because Oono 2013 limited their population to children less than seven, or it may be that the AHRQ draft included more recent studies, since there is nearly a year difference in the literature search end dates (July 2013 for the AHRQ draft and August 2012 for Oono 2013). It also may be variable interpretation of the strength of the evidence by different authors. Indeed, the Oono 2013 review does find a statistically significant benefit in language comprehension and autism severity, outcomes that the AHRQ draft authors assess as having moderate and low strength of evidence respectively. However, Oono 2013 downgrades these findings because they are based on parent self report, and have small effect sizes and wide confidence intervals.

[Evidence Source]

DRAFT

**Adolescents and Young Adults (Ages 13 to 30)**

Lounds (2012)
Only one poor quality case series evaluated ABA-based intensive behavioral therapy, precluding conclusions regarding efficacy in this age group (Lounds, 2012).

[Evidence Source]

**Evidence Summary**

Based on the evidence presented in this document (Warren, 2011; AHRQ draft, 2014; Oono, 2013), there is moderate strength of evidence that EIBI improves cognitive and language skills, and low strength of evidence that EIBI improves adaptive behavior skills, social skills, and core symptoms of autism, although improvements are inconsistent. Parent-mediated early intervention improves early language and communication skills, including shared attention and parent synchrony (moderate strength of evidence), and may have some impact on autism symptom severity and early cognition (low strength of evidence). Play-/interaction-based interventions improve child joint attention and language skills (moderate strength of evidence) and play, imitation and social interaction skills (low strength of evidence). The evidence is insufficient to evaluate the effectiveness of ABA on children and adolescents older than twelve. The evidence is insufficient to determine whether there are any factors that modify the effectiveness of ABA therapy.

DRAFT

GRADE-INFORMED FRAMEWORK

The HERC develops recommendations by using the concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for carrying out the steps involved in developing recommendations. There are four elements that determine the strength of a recommendation, as listed in the table below. The HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations. Balance between desirable and undesirable effects, and quality of evidence, are derived from the evidence presented in this document, while estimated relative costs, values and preferences are assessments of the HERC members.

| Indication/Intervention | Balance between desirable and undesirable effects | Quality of evidence | Resource allocation | Values and preferences | Recommendation |
|---|---|---|---|---|---|
| ***Children aged 1 to 12 years at initiation*** | | | | | |
| Early Intensive Behavioral Interventions | Benefit on cognitive and language skills | Moderate | High | Low variability | Recommendation for coverage (strong recommendation) |
| | Benefit on adaptive behavior, social skills and overall autism severity | Low | High | Low variability | |
| Parent training interventions | Increased joint attention and parent synchrony, and improved early language and communication skills | Moderate | Moderate | Low variability | Recommendation for coverage (strong recommendation) |
| | Lessened overall severity of autism and improved early cognition | Low | Moderate | Low variability | |
| Play/interaction-based interventions (including joint attention interventions) | Improvements in joint attention and language skills | Moderate | Low | Low variability | Recommendation for coverage (strong recommendation) |
| | Short-term improvements in play, imitation, social skills | Low | Low | Low variability | |
| ***Adolescents and young adults*** | | | | | |
| ABA | Unknown | Insufficient | Moderate for focused, high | Low variability | Recommend noncoverage of |

DRAFT

| Indication/Intervention | Balance between desirable and undesirable effects | Quality of evidence | Resource allocation | Values and preferences | Recommendation |
|---|---|---|---|---|---|
| | | | for more comprehensive | | intensive ABA therapies *(weak recommendation)* Recommendation for coverage for specific problem behaviors with focused interventions *(weak recommendation)* |

Note: GRADE framework elements are described in Appendix A

DRAFT

SUMMARY CONCLUSIONS

**Children ages 1 to 12**

Applied behavior analysis (ABA), including early intensive behavioral intervention (EIBI), is recommended for coverage[6] for treatment of autism spectrum disorder[7] (*strong recommendation*).

> Rationale: This strength of recommendation was based on sufficient (moderate quality) evidence and expert input, including testimony on parent/caregiver values and preferences.

Specifically, EIBI (for example, UCLA/Lovaas or ESDM), is recommended for coverage for up to 25 hours per week for a maximum of three years.

> Rationale: The 25-hour limit would be similar to other payers in Oregon that were mandated through SB 365 and earlier Warren report had demonstrated 25 hours per week was effective. There is no evidence that increased intensity beyond this level yields improved outcomes. The duration limit is based on the fact that EIBI studies have a duration of 2-3 years

Initial coverage of EIBI should be provided for up to six months. Ongoing coverage should be based on demonstrated progress towards meaningful predefined objectives (objectives should be achieved as a result of the EIBI, over and beyond gains that would be expected to arise from maturation alone) using standardized, multimodal assessments, no more frequently than every six months *(strong recommendation).* Examples of such assessments include Vineland, IQ tests (Mullen, WPPSI, WISC-R), language measures, behavior checklists (CBCL, ABC), and autistic symptoms measures (SRS).

> Rationale: Ensuring that patients are making meaningful progress is important to ensure quality outcomes and effective use of resources. The six month assessment was chosen based on expert input and subcommittee deliberation to allow for sufficient time for progress while not being burdensome to providers and plans.

Less intensive ABA-based interventions

If EIBI is not indicated, has been completed, or there is not sufficient progress toward multidimensional goals, then less intensive behavioral ABA-based interventions (such as parent training, play/interaction based interventions, and joint attention interventions)

[6] These conclusions apply to the Oregon Health Plan as governed by the Prioritized List of Health Services and to no other health plan.
[7] Autism spectrum disorder should be diagnosed by a qualified health care professional according to DSM-5 criteria.

are recommended for coverage to address core symptoms of autism and/or specific problem areas *(strong recommendation)* for up to 8 hours per month. In extenuating circumstances (e.g severe aggressive behavior that is responding to interventions but requires increased intensity), an additional 8 hours per month is recommended for coverage. Initial coverage should be provided for six months. Ongoing coverage should be based on demonstrated progress towards meaningful predefined objectives or emergence of new problem behaviors.

> Rationale: Not all autistic children require comprehensive therapy and less intensive interventions will be appropriate for many, or appropriate for those who have completed intensive intervention. Evidence supports these less intensive interventions in this age group. Eight hours was chosen based on a wide range of intensity in the literature, expert input, and previous HERC Prioritized List guideline precedent.

Parent/caregiver involvement and training is recommended to be a component of treatment *(strong recommendation).*

> Rationale: Evidence and expert input indicated that parental involvement in ABA is a key part of effective treatment. Parent delivered therapy is effective.

### Individuals ages 13 and older

Intensive ABA is not recommended for coverage for treatment of autism spectrum disorder in persons ages 13 and older (*weak recommendation*).

> Rationale: There is insufficient evidence to support intensive ABA treatment at older ages.

For individuals age 13 and older, targeted behavioral interventions, including focused ABA*, are recommended for coverage for up to 8 hours per month, up to 6 months, only to address specific problem behaviors (*weak recommendation*). Behaviors eligible for coverage include those which place the member at risk for harm or create significant daily issues related to care, education, or other important functions. The interventions should involve predefined behavioral objectives that would result in socially important and sustainable outcomes for the individual. Ongoing coverage should be based on demonstrated progress towards meaningful predefined objectives with ongoing proof of medical appropriateness, or emergence of new problem behaviors.

DRAFT

Rationale: According to the trusted evidence source, there is insufficient evidence to support ABA-based interventions in this age group. Public comment and some expert testimony involved submission of many single subject research design studies to support treatment in this age group, but the quality of this evidence did not meet predetermined criteria for inclusion. The subcommittee agreed that problem behaviors can be challenging to the individual, caregivers, and society and it is reasonable to consider targeted interventions for specific problem behaviors as long as there are clear objectives, progress toward meaningful predefined goals and ongoing proof of medical appropriateness. The net result was to recommend targeted interventions including ABA-based treatments for limited intensity to address problem behaviors. Six months was chosen based on expert testimony and subcommittee discussion that more frequent assessments would potentially be burdensome to providers and plans.

Parent/caregiver involvement and training is encouraged *(weak recommendation)*

Note: The evidence for the treatment of conditions comorbid with autism spectrum disorder is beyond the scope of this evidence summary.

DRAFT

## POLICY LANDSCAPE

No quality measures were identified when searching the National Quality Measures Clearinghouse pertaining to autism and applied behavior analysis.

This report is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide HERC in making informed decisions about the prioritization of health care services for the Oregon Health Plan.

The Center is not engaged in rendering any clinical, legal, business or other professional advice. The statements in this document do not represent official policy positions of the Center. Researchers involved in preparing this document have no affiliations or financial involvement that conflict with material presented in this document.

DRAFT

## Appendix A. GRADE Element Descriptions

| Element | Description |
|---|---|
| Balance between desirable and undesirable effects | The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted |
| Quality of evidence | The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted |
| Resource allocation | The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted |
| Values and preferences | The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted |

**Strong recommendation**

***In Favor:*** The subcommittee is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

***Against:*** The subcommittee is confident that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

**Weak recommendation**

***In Favor:*** the subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

***Against:*** the subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

**Quality of evidence across studies for the treatment/outcome**

***High*** = Further research is very unlikely to change our confidence in the estimate of effect.

***Moderate*** = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

***Low*** = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

***Very low*** = Any estimate of effect is very uncertain.

DRAFT

## Appendix B. Potentially Applicable Codes

| CODES | DESCRIPTION |
|---|---|
| **ICD-9 Diagnosis Codes** | |
| 299.00 | Autistic disorder, current or active state |
| 299.01 | Autistic disorder, residual state |
| 299.10 | Childhood disintegrative disorder, current or active state |
| 299.11 | Childhood disintegrative disorder, residual state |
| 299.80 | Other specified pervasive developmental disorders, current or active state |
| 299.81 | Other specified pervasive developmental disorders, residual state |
| 299.90 | Unspecified pervasive developmental disorder, current or active state |
| 299.91 | Unspecified pervasive developmental disorder, residual state |
| | |
| **ICD-10 Diagnosis Codes** | |
| F84.0 | Autistic disorder |
| F84.2 | Rett's syndrome |
| F84.3 | Other childhood disintegrative disorder |
| F84.5 | Asperger's syndrome |
| F84.8 | Other pervasive developmental disorders |
| **ICD-9 Volume 3 (Procedure Codes)** | |
| None | |
| **Procedure Codes** | |
| *Until July, 2014, no specific procedure codes exist for Applied Behavior Analysis. The list below provides examples of how various state Medicaid agencies covering ABA instruct providers to bill. Temporary codes shown in italics will be available starting July, 2014.* | |
| 90834 | Psychotherapy, 45 min |
| 90837 | Psychotherapy, 60 min |
| *0359T* | *Behavior identification assessment, by the physician or other qualified health care professional, face-to-face with patient and caregiver(s), includes administration of standardized and non-standardized tests, detailed behavioral history, patient observation and caregiver interview, interpretation of test results, discussion of findings and recommendations with the primary guardian(s)/caregiver(s), and preparation of report* |
| *0360T* | *Observational behavioral follow-up assessment, includes physician or other qualified health care professional direction with interpretation and report, administered by one technician; first 30 minutes of technician time, face-to-face with the patient* |
| *0361T* | *…additional 30 minutes* |
| *0362T* | *Exposure behavioral follow-up assessment, includes physician or other qualified health care professional direction with interpretation and report, administered by physician or other qualified health care professional with the assistance of one or more technicians; first 30 minutes of technician(s) time, face-to-face with the patient* |
| *0363T* | *… additional 30 minutes* |
| *0364T* | *Adaptive behavior treatment by protocol, administered by technician, face-to-face with one patient; first 30 minutes of technician time* |
| *0365T* | *…additional 30 minutes* |

DRAFT

| CODES | DESCRIPTION |
|---|---|
| *0366T* | *Group adaptive behavior treatment by protocol, administered by technician, face-to-face with two or more patients; first 30 minutes of technician time* |
| *0367T* | *….additional 30 minutes* |
| *0368T* | *Adaptive behavior treatment with protocol modification administered by physician or other qualified health care professional with one patient; first 30 minutes of patient face-to- face time* |
| *0369T* | *Adaptive behavior treatment with protocol modification, additional 30 minutes* |
| *0370T* | *Family adaptive behavior treatment guidance, administered by physician or other qualified health care professional (without the patient present)* |
| *0371T* | *Multiple-family group adaptive behavior treatment guidance, administered by physician or other qualified health care professional (without the patient present)* |
| *0372T* | *Adaptive behavior treatment social skills group, administered by physician or other qualified health care professional face-to-face with multiple patients* |
| *0373T* | *Exposure adaptive behavior treatment with protocol modification requiring two or more technicians for severe maladaptive behavior(s); first 60 minutes of technicians' time, face-to-face with patient* |
| *0374T* | *each additional 30 minutes of technicians' time face-to-face with patient (List separately in addition to code for primary procedure)* |
| G1076 | Activity therapy, such as music, dance, art or play not for recreation, related to the care and treatment of patient's disabling mental health problems (45 min or more) |
| G1077 | Training and educational services related to the care and treatment of patient's disabling mental health problems (45 min or more) |
| H0002 | Behavioral health screening to determine eligibility for admission to treatment program |
| H0004 | Behavioral health counseling and therapy, per 15 minutes |
| H0031 | Mental health assessment by non-physician |
| H0032 | Mental health service plan development by non-physician |
| H2000 | Comprehensive multidisciplinary evaluation |
| H2010 | Comprehensive medication services, per 15 minutes |
| H2019 | Therapeutic behavioral service, per 15 minutes |
| H2020 | Therapeutic behavioral service, per diem |
| H2027 | Psychoeducational service, per 15 min |
| T1023 | Screening to determine the appropriateness of consideration of an individual for participation in a specified program, project or treatment protocol, per encounter |
| T1024 | Evaluation and treatment by an integrated, specialty team contracted to provide coordinated care to multiple or severely handicapped children, per encounter |
| T1027 | Family training and counseling for child development, per 15 min |
| T2013 | Habilitation, educational, waiver, per hour |
| T2026 | Specialized childcare, waiver, per diem |

Note: Inclusion on this list does not guarantee coverage

DRAFT

## Appendix C. HERC Guidance Development Framework

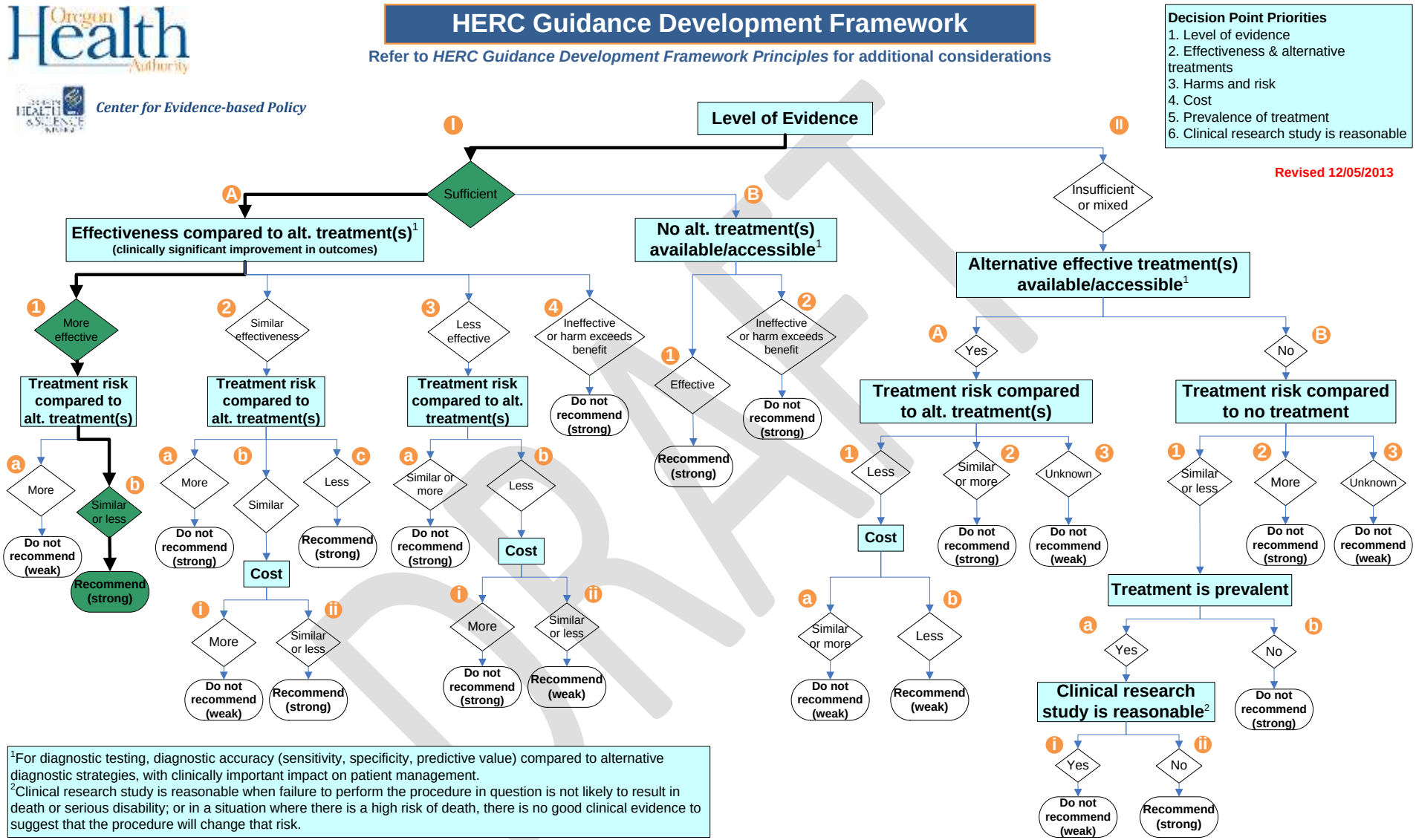
*HERC Guidance Development Framework Principles*

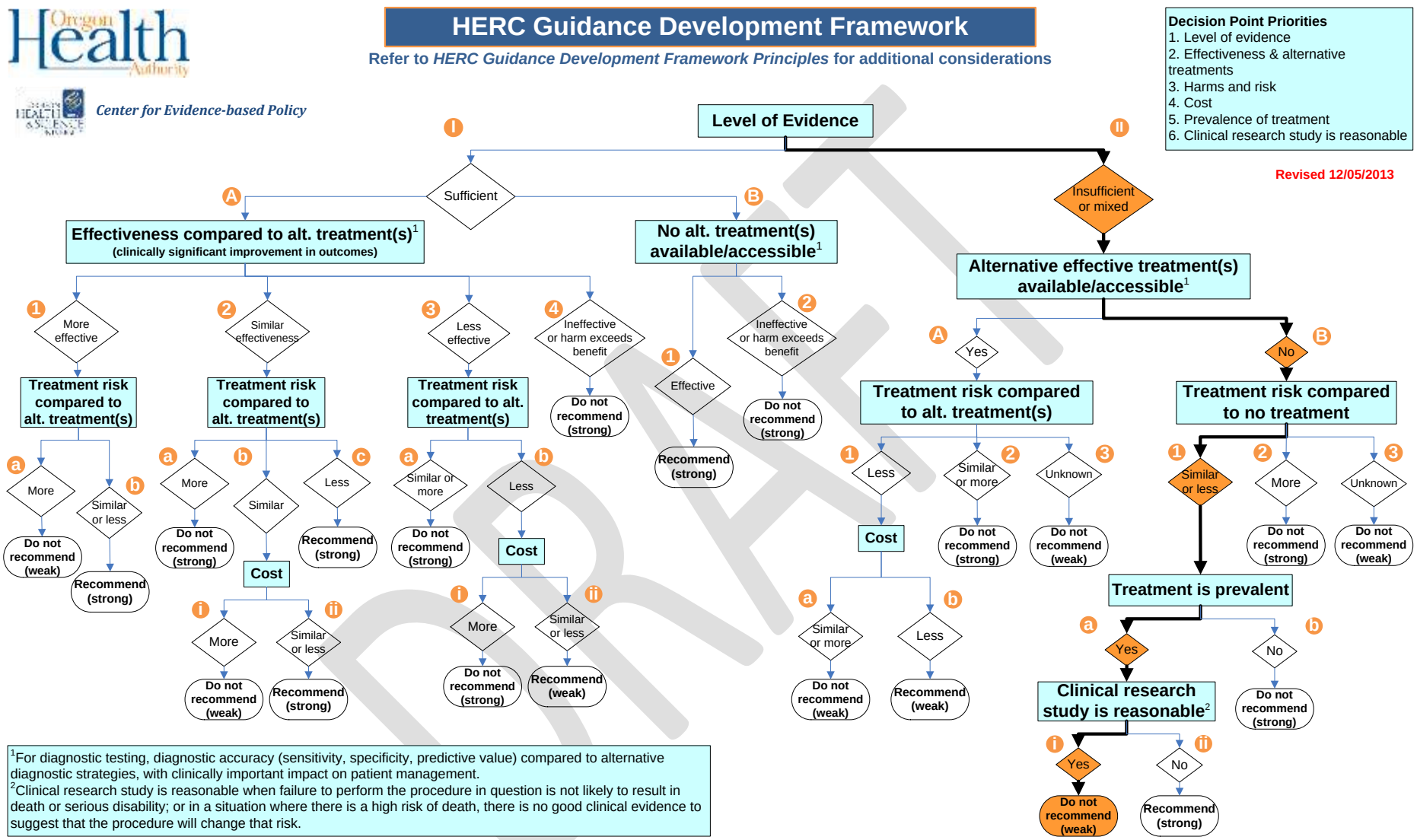
This framework was developed to assist with the decision making process for the Oregon policy-making body, the HERC and its subcommittees. It is a general guide, and must be used in the context of clinical judgment. It is not possible to include all possible scenarios and factors that may influence a policy decision in a graphic format. While this framework provides a general structure, factors that may influence decisions that are not captured on the framework include but are not limited to the following:

- Estimate of the level of risk associated with the treatment, or any alternatives;
- Which alternatives the treatment should most appropriately be compared to;
- Whether there is a discrete and clear diagnosis;
- The definition of clinical significance for a particular treatment, and the expected margin of benefit compared to alternatives;
- The relative balance of benefit compared to harm;
- The degree of benefit compared to cost; e.g., if the benefit is small and the cost is large, the committee may make a decision different than the algorithm suggests;
- Specific indications and contraindications that may determine appropriateness;
- Expected values and preferences of patients

DRAFT

## ABABA-based Treatments for Children Aged 1 to 12, including EIBI and Other Less Intensive Interventions




Oregon Health Authority
Center for Evidence-based Policy
HERC Guidance Development Framework
Refer to HERC Guidance Development Framework Principles for additional considerations
Decision Point Priorities
1. Level of evidence
2. Effectiveness & alternative treatments
3. Harms and risk
4. Cost
5. Prevalence of treatment
6. Clinical research study is reasonable
Revised 12/05/2013
Level of Evidence
Sufficient
Insufficient or mixed
Effectiveness compared to alt. treatment(s)[1] (clinically significant improvement in outcomes)
No alt. treatment(s) available/accessible[1]
More effective
Similar effectiveness
Less effective
Ineffective or harm exceeds benefit
Effective
Ineffective or harm exceeds benefit
Treatment risk compared to alt. treatment(s)
Treatment risk compared to alt. treatment(s)
Treatment risk compared to alt. treatment(s)
Do not recommend (strong)
Recommend (strong)
Do not recommend (strong)
More
Similar or less
Do not recommend (weak)
Recommend (strong)
More
Similar
Less
Do not recommend (strong)
Cost
Recommend (strong)
Similar or more
Less
Do not recommend (strong)
Cost
More
Similar or less
Do not recommend (weak)
Recommend (strong)
More
Similar or less
Do not recommend (strong)
Recommend (weak)
Alternative effective treatment(s) available/accessible[1]
Yes
No
Treatment risk compared to alt. treatment(s)
Treatment risk compared to no treatment
Less
Similar or more
Unknown
Cost
Similar or more
Less
Do not recommend (weak)
Recommend (weak)
Do not recommend (strong)
Do not recommend (weak)
Similar or less
More
Unknown
Do not recommend (strong)
Do not recommend (weak)
Treatment is prevalent
Yes
No
Clinical research study is reasonable[2]
Do not recommend (strong)
Yes
No
Do not recommend (weak)
Recommend (strong)
[1]For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
[2]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.
DRAFT

## Appendix D. Key References from Evidence Sources

### References for Included Studies in Oono 2013


Aldred C, Green J, Adams C. A new social communication intervention for children with autism: pilot randomised controlled study suggesting effectiveness. *Journal of Child Psychology and Psychiatry* 2004;45(8):1420–30. *{published data only}*

Carter AS, Messinger DS, Stone WL, Celimli S, Nahmias AS, Yoder P. A randomised controlled trial of Hanen's "More Than Words" in toddlers with early autism symptoms. *Journal of Child Psychology and Psychiatry* 2011;52(7):741- 52. *{published data only}*

Casenhiser DM, Shanker SG, Stieben J. Learning through interaction in children with autism: preliminary data from a social-communication-based intervention. *Autism* 2013; 17(2):220–41. *{published data only}*

Dawson G, Rogers S, Munson J, Smith M, Winter J, Greenson J, et al. Randomized controlled trial of an intervention for toddlers with autism: the Early Start Denver M model. *American Academy of Pediatrics: Pediatrics* 2010;125(1):e17–23. *{published data only}*

Drew A, Baird G, Baron-Cohen S, Cox A, Slonims V, Wheelwright S, et al. A pilot randomised controlled trial of a parent training intervention for pre-school children with autism. *European Child and Adolescent Psychiatry* 2002;11 (6):266–72. *{published and unpublished data}*

Green J, Charman T, McConachie H, Aldred C, Slonims V, Howlin P, et al. Parent-mediated communication-focused treatment in children with autism (PACT): a randomised controlled trial. *Lancet* 2010;375(9732):2152–60. *{published data only}*

Jocelyn LJ, Casiro OG, Beattie D, Bow J, Kneisz J. Treatment of children with autism: a randomised controlled trial to evaluate a caregiver-based intervention program in community day-care centres. *Journal of Developmental & Behavioral Pediatrics* 1998;19(5):326–34. *{published data only}*

Kasari C, Gulsrud AC, Wong C, Kwon S, Locke J. Randomized controlled caregiver mediated joint engagement intervention for toddlers with autism. *Journal of Autism and Developmental Disorders* 2010;40(8):1045-56. *{published data only}*

Nefdt N, Koegel R, Singer G, Gerber M. The use of a self- directed learning program to provide introductory training in pivotal response treatment to parents of children


DRAFT

with autism. *Journal of Positive Behavior Interventions* 2010;12 (1):23–32. *{published data only}*

Pajareya K, Nopmaneejumruslers K. A pilot randomised controlled trial of DIR/Floortime™ parent training intervention for pre-school children with autistic spectrum disorders. *Autism* 2011;15(5):563-77. *{published data only}*

Rickards AL, Walstab JE, Wright-Rossi RA, Simpson J, Reddihough DS. A randomised controlled trial of a home- based intervention program for children with autism and developmental delay. *Journal of Developmental and Behavioral Pediatrics* 2007;28(4):308–16. *{published data only}*

Roberts J, Williams K, Carter M, Evans D, Parmenter T, Silove N, et al. A randomised controlled trial of two early intervention programs for young children with autism: centre-based with parent program and home-based. *Research in Autism Spectrum Disorders* 2011;5(4):1553-66. *{published data only}*

Siller M. A parent-mediated intervention to increase responsive parental behaviors and child communication in children with ASD: a randomized clinical trial. Journal of Autism and Developmental Disorders 2012. *{published data only}*

Silva LTM, Schalock M, Ayres R, Bunse C, Budden S. Qigong massage treatment for sensory and self-regulation problems in young children with autism: a randomized controlled trial. *American Journal of Occupational Therapy* 2009;63(4):423-32. *{published data only}*

Smith T, Groen AD, Wynn JW. Randomized trial of intensive early intervention for children with pervasive developmental disorder. *American Journal on Mental Retardation* 2000;105(4):269–85. *{published data only}*

Tonge B, Brereton A, Kiomall M, Mackinnon A, King N, Rinehart N. Effects on parental mental health of an education and skills training program for parents of young children with autism: a randomised controlled trial. *American Academy of Child and Adolescent Psychiatry* 2006; 45(5):561–9. *{published data only}*

Wong VCN, Kwan QK. Randomized controlled trial for early intervention for autism: a pilot study of the Autism 1- 2-3 Project. *Journal of Autism and Developmental Disorders* 2010;40(6):677-88. *{published data only}*

DRAFT