Methods: Outcome Data Collection

Objective

Early intervention in autism has been shown to yield more positive outcomes compared to late or no intervention (Dawson et al., 2010, 2013; Eikeseth, Klintwall, Jahr, & Karlsson, 2012; Eldevik, Hastings, Jahr, & Hughes, 2012; Reichow, Barton Erin, Boyd Brian, & Hume, 2012). The objective of this project is to synthesize the existing lifetime cost and outcome data and to visually and meaningfully represent the effect that age of intervention has on these variables. This section focuses on our collection of outcome data and our synthesis of studies to show how outcomes vary with age of intervention. It describes our methods of article selection and review, our variable selection, and the calculation of weighted effect sizes at all ages.

Systematic Review

We employed a systematic review of the treatment intervention literature based on methods outlined for Cochrane reviews. This review began first by identifying appropriate key search terms; once these terms were identified and selected, we searched several databases using these terms, which are detailed in Table 1 of the Appendix, and limited our search to articles published between 2003 and 2014, inclusive. Additional articles before 2003 included were found through examining references in articles found in our search. After we exhausted all search methods and the literature that described outcomes of early intervention in ASD was collected, all articles were reviewed for relevance; this includes eliminating some articles that did not have average age of intervention and articles without pre-intervention data. Relevance was assessed by reading the abstract of the article and a more thorough reading of the methods and results section, if needed.

After articles were identified as relevant, they were read over and evaluated for quality using Cochrane assessments. Each article was identified as being weak, moderate, or high quality. The assessment questions employed in this determination are detailed in Table 3 of the Appendix. We retained only medium and high quality studies in our synthesis.

Outcome Variables

Throughout the systematic literature search, we also took note of the variables researchers used to measure the effectiveness of an intervention. After reviewing the literature and in consultation with established experts in the field, we selected the following variables to measure outcomes in autism intervention: adaptive functioning, autism symptoms, intellectual functioning, developmental skills, and socioaffective skills. Descriptions of these variables can be found in Table 1 below.

Table 1: Variable Definitions

Variable	Definition
Adaptive functioning	The severity of autism symptoms a child displays depending on age, including communication skills, social interaction skills, play skills, and stereotypical behavior
Autism symptoms	The ability for an individual to change a destructive behavior into a constructive, socially appropriate behavior
Intellectual functioning	A child's cognitive abilities
Developmental skills	The extent to which a child has developed relative to his her established age milestones
Socioaffective skills	This variable measures the degree to which a child can regulate his/her emotions and behavior to create and maintain relationships (Rivard, Terroux, & Mercier, 2014)

Data collection
After the articles' quality assessment was conducted, articles receiving a moderate to high quality were retained, reviewed again, and the data from those articles were recorded. The data we recorded includes:

1. the averages and standard deviations for selected variables from pre- and post-intervention, or from experimental and control groups;
2. the average age of intervention in the study;
3. the type of intervention (e.g. ABA-based, Floortime);
4. the duration of the intervention;
5. the intensity of the intervention (the number of hours a child received treatment);
6. the delivery method (parent, school, or clinic-based); and
7. the sample size of the groups.

Not all studies included the duration and intensity of the intervention; in these cases we still recorded the data, but assumed the lowest intensity and duration. Since the literature suggests that interventions of greater intensity (over 10 hours) and greater duration (1-2 years) for younger children are more likely to yield robust outcomes, we only included studies with reported intensities of 10 hours per week or more (Granpeesheh, Dixon, Tarbox, Kaplan, & Wilke, 2009; Vivanti, Dissanayake, Zierhut, Rogers, & Team, 2013).

Measuring Effect
Once the data from the literature was collected, we sought to calculate and aggregate the effect the interventions had on all five variables. To do this, we chose to calculate effect sizes, or standard mean differences, for all data points and then aggregate effect

sizes for each variable in each age group. We found the effect size to be an appropriate means of measurement given that is a standardized and scale-free measure and many of the studies we reviewed used a variety of different measures for the variables we studied (Turner & Bernard, 2006).

To calculate effect size, we used Hedge's g, which corrects for small sample sizes; this was important since many of the studies included had relatively small sample sizes. Furthermore, while combining the effect sizes we chose to also weigh effect sizes relative to sample sizes pre- and post-intervention; we did this to ensure the effect sizes were not over or underestimated because of sample size. Below describes the process we employed to aggregate the effect sizes for all variables at all available ages.

To calculate Hedge's g, we first calculated Cohen's *d*, using the following formula:

$$Cohen's\ d = \frac{\bar{X}_E - \bar{X}_C}{s} \tag{1}$$

In Equation 1, the numerator is the mean difference between the experimental and control groups; the denominator is the pooled standard deviation, which was calculated using this formula:

$$s = \sqrt{\frac{SD_E^2 - SD_C^2}{2}} \tag{2}$$

After Cohen's d was calculated, we converted all the effect sizes into Hedge's g using this formula:

$$Hedges's\ g = Cohen's\ d \times \left(1 - \frac{3}{4N - 9}\right) \tag{3}$$

The "N" in Equation 2 was the sum of the sample sizes from each group.

In order to aggregate the effect sizes, the sum of the product of each Hedges's *g* and each corresponding weight (IVW) was divided by the sum of the weight, shown in the equation below:

$$Hedges's\ g^* = \frac{\sum_{i=1}^{n} Hedges'sg\ (i) \times IVW\ Hedges'sg(i)}{\sum_{i=1}^{n} IVW\ Hedges'sg(i)} \tag{4}$$

The weights for each of the effect sizes were calculated using this formula:

$$IVW_{Hedges'\ g} = \frac{1}{(SE_{Hedges'sg})^2} \tag{4}$$

The standard error for each of the data points were calculated using this equation:

$$SE = \sqrt{\frac{1}{n_E} + \frac{1}{n_C} + \frac{d_{cohen}^2}{2(n_E + n_C)}} 1 \times \left(1 - \frac{3}{4(n_E + n_C) - 9}\right) \tag{5}$$

The full data set used to calculate the effect sizes is too large to be included in this document, but is available upon request.

The full list of references of studies included in our effect size calculations can be found in the Appendix.

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Appendix
Table A.2: Search Process for Outcome Data

Web of Science	(autism OR autistic disorder) AND early intervention AND (outcome assessment OR assessment* OR outcome* OR outcome* measure* OR treatment outcome*)
	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (outcome assessment OR outcome* OR outcome* measure* OR patient outcome* OR health outcome* OR treatment outcome*)
	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (health outcome* OR clinical outcome* OR patient reported outcome* OR long-term outcome*)
	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (assessment OR functional outcome* OR social outcome* OR individual outcome*)
	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR age of diagnosis OR age of intervention) AND (outcome assessment OR outcome* OR outcome* measure* OR patient outcome* OR health outcome* OR treatment outcome*)
Medline	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (outcome assessment OR outcome* OR outcome* measure* OR patient outcome* OR health outcome* OR treatment outcome*)
	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (health outcome* OR clinical outcome* OR patient reported outcome* OR long-term outcome*)

	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (assessment OR functional outcome* OR social outcome* OR individual outcome*)
PsycINFO	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (outcome assessment OR outcome* OR outcome* measure* OR patient outcome* OR health outcome* OR treatment outcome*)
	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (health outcome* OR clinical outcome* OR patient reported outcome* OR long-term outcome*)
	(autism OR autis* OR autism spectrum OR autism spectrum disorder*) AND (early intervention OR head start program OR preventative health services OR community health services OR child health services) AND (assessment OR functional outcome* OR social outcome* OR individual outcome*)
ScienceDirect	TITLE-ABSTR-KEY(autism spectrum disorder early intervention) and TITLE-ABSTR-KEY(outcome).
	ALL(autism spectrum disorder early intervention) and TITLE-ABSTR-KEY(health outcome OR long term outcome).
	TITLE-ABSTR-KEY(autism spectrum disorder early intervention) and TITLE-ABSTR-KEY(assessment OR functional outcome OR social outcome OR individual outcome).

Table A.2: Qualitative Assessment Questions

Selection Bias	
Are the individuals selected to participate in the study likely to be representative of the target population?	Very likely
	Somewhat likely
	Not likely
	Can't tell
What percentage of selected individuals agreed to participate?	80-100% agreement
	60-79% agreement
	Less than 60% agreement
	Not applicable
	Can't tell
Rate this section	Strong
	Moderate
	Weak
Study Design	
Indicate the study design	Randomized control trial
	Controlled clinical trial
	Cohort analytic (two groups pre and post)
	Case-control
	Cohort (one group pre + pose
	Interrupted time series
	Other
	Can't tell
Was the study described as randomized?	Yes or No
If Yes, was the method of randomization described?	Yes or No
If Yes, was the method appropriate?	Yes or No
Rate this section	Strong

	Moderate
	Weak
Confounders	
Were there important differences between groups prior to the intervention	Yes
	No
	Can't tell
	Not applicable
If yes, indicate the percentage of relevant confounders that were controlled (either in design (e.g. stratification, matching) or analysis)?	80-100% agreement
	60-79% agreement
	Less than 60% agreement
	Not applicable
	Can't tell
Rate this section	Strong
	Moderate
	Weak
Blinding	
Was (were) the outcome assessor(s) aware of the intervention or exposure status of the participants?	Yes
	No
	Can't tell
	Not applicable
Were the participants aware of the research question?	Yes
	No
	Can't tell
	Not applicable
Rate this section	Strong

	Moderate
	Weak
Data Collection	
Were the data collection tools shown to be valid?	Yes
	No
	Can't tell
	Not applicable
Were the data collection tools shown to be reliable?	Yes
	No
	Can't tell
	Not applicable
Rate this section	Strong
	Moderate
	Weak
Drop Outs	
Were withdrawals and drop-outs reported in terms of numbers and/or reasons per group?	Yes
	No
	Can't tell
	Not applicable
Indicate the percentage of participants completing the study. (If the percentage differs by groups, record the lowest.)	80-100% agreement
	60-79% agreement
	Less than 60% agreement
	Not applicable
	Can't tell
Rate this section	Strong

	Moderate
	Weak
Integrity	
What percentage of participants received the allocated intervention or exposure of interest?	80-100% agreement
	60-79% agreement
	Less than 60% agreement
	Not applicable
	Can't tell
Was the consistency of the intervention measured?	Yes
	No
	Can't tell
	Not applicable
Is it likely that subjects received an unintended intervention (contamination or co-intervention) that may influence the results?	Yes
	No
	Can't tell
	Not applicable
Analyses	
Indicate the unit of allocation	Community
	Organization/Institution
	Practice/Office
	Individual
Indicate the unit of analysis	Community
	Organization/Institution
	Practice/Office
	Individual
Are the statistical methods appropriate for the study design?	Yes

	No
	Can't tell
	Not applicable

Outcome Data Bibliography

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