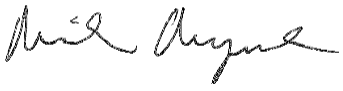
ECHO AUTISM
Statistical Analysis Plan: Amendment 1

Kristin Sohl, MD
Thompson Center for Autism and other Neurodevelopmental Disorders,
University of Missouri
Study Chair



Micah Mazurek, PhD
University of Virginia
Study Co-Chair

Robert A. Parker, ScD
MGH Biostatistics Center

During preparation of the manuscript two errors were identified by the study team.

1. Correction to the Definition of Screening Practice

The original version (from Version 1.1) was:

6.3.1.1 Screening Practice (co-primary endpoint)

Clinical Practice/Behavior was assessed at T1, T2, T3, and T4 by review of a subset of charts from each PCP's practice. Four subsets of charts will be reviewed, with a limit of 25 charts in any group. The groups are:

1. Charts for all children seen for 9-month well-child visits in the 30 days prior to the date of chart review.
2. Charts for all children seen for 18-month well-child visits in the 30 days prior to the date of chart review.
3. Charts for all children seen for 24-month well-child visits in the 30 days prior to the date of chart review.
4. Charts for all children seen for 30-month well-child visits in the 30 days prior to the date of chart review.

If more than 25 well-child visits at a specific age are available for chart review, the most recent 25 well-child visits at a specific age will be reviewed.

Because of the timing and feasibility of doing all chart-reviews in the 2-week interval between the 6th and 7th ECHO clinics, the 30-days was either (a) the 30-days prior to the date of the 7th ECHO clinic; or (b) the 30-days prior to the date of the visit scheduled for chart reviews, if the visit occurred prior to the 7th clinic.

These chart reviews assess the adequacy of screening for each child at each visit. The screening practice is summarized over the four sets of charts as total number screened appropriately / total number of charts reviewed and then converted to a percentage.

For the 9 US sites, adequate screening, as defined by US guidelines consider the use of any general developmental screening tool as appropriate screening for the 9- and 30-month visits. For the 18- and 24-month visits, an ASD specific screen must have been used for the child to be considered correctly screened for Autism.

A different guideline is used in Canada, so that adequate screening was defined differently for the Canadian site. The recommended screening practice in Canada uses a general developmental screening tool at 12- and 18-month well-child visits. Only visits at those times were reviewed at the Canadian site, and children were considered appropriately screened if a general developmental screening tool was administered.

For analysis purposes, the results of each individual chart reviewed (screened or not screened appropriately) is used in the analysis rather than the summary over all charts for a PCP.

PCPs having no well-child visits at baseline would have baseline results imputed if appropriate (Section 8.4.1).

This section has been replaced with the text below (with changes indicated):

6.3.1.1 Screening Practice (co-primary endpoint)

Clinical Practice/Behavior was assessed at T1, T2, T3, and T4 by review of a subset of charts from each PCP's practice. Four subsets of charts will be reviewed, with a limit of 25 charts in any group. The groups are:

1. Charts for all children seen for 9-month well-child visits in the 30 days prior to the date of chart review.
2. Charts for all children seen for 18-month well-child visits in the 30 days prior to the date of chart review.
3. Charts for all children seen for 24-month well-child visits in the 30 days prior to the date of chart review.
4. Charts for all children seen for 30-month well-child visits in the 30 days prior to the date of chart review.

If more than 25 well-child visits at a specific age are available for chart review, the most recent 25 well-child visits at a specific age will be reviewed.

Because of the timing and feasibility of doing all chart-reviews in the 2-week interval between the 6th and 7th ECHO clinics, the 30-days was either (a) the 30-days prior to the date of the 7th ECHO clinic; or (b) the 30-days prior to the date of the visit scheduled for chart reviews, if the visit occurred prior to the 7th clinic.

These chart reviews assess the adequacy of screening for each child at each visit. The screening practice is summarized over the four sets of charts as total number screened appropriately / total number of charts reviewed and then converted to a percentage.

For the 9 US sites, adequate ASD screening, as defined by US guidelines ~~consider the use of any general developmental screening tool as appropriate screening for the 9- and 30-month visits. For~~ requires an ASD specific screen at the 18- and 24-month visits~~, an ASD specific screen must have been used~~ for the child to be considered correctly screened for Autism. The use of a general developmental screen at 9 and 18 months will be a secondary endpoint. The US guidelines specify a general development screening at either 24 or 30 months but the study does not have longitudinal data on children. Therefore, the team decided that the 24- and 3-month general developmental screening data would not be used.

A different guideline is used in Canada, so that adequate screening was defined differently for the Canadian site. The recommended screening practice in Canada uses a general developmental screening tool at 12- and 18-month well-child visits. Only visits at those times were reviewed at the Canadian site, and children were considered appropriately screened if a general developmental screening tool was administered. The Canadian data is included only in the analysis of the secondary endpoint of general developmental screening at 9 (or 12) and 18 months.

For analysis purposes, the results of each individual chart reviewed (screened or not screened appropriately) is used in the analysis rather than the summary over all charts for a PCP.

PCPs having no well-child visits at baseline would have baseline results imputed if appropriate (Section 8.4.1).

2. Need for Missing Data Imputation of Baseline Values

The basic model in Section 10.3.1 did not use baseline value as a predictor, and therefore imputation of baseline values was not needed for the analysis. As such, the following section is removed from the SAP:

8.4.1 Imputing Missing Data for Baseline Measures

Since baseline values are included in the basic modeling analysis of the study (Section 10.3), baseline data for a primary outcome measure (listed in Section 6.3.1) for a PCP will be imputed using multiple imputation if there is data at three- and six-months for the outcome measure for that PCP.

Such missing data would occur if there are no well-child visits or no ASD child visits at baseline for a PCP. Imputation for a primary outcome will only be done if it allows us to include at least 5% more individuals in the analysis for a primary outcome measure. Several PCPs had very low volume offices, so that before embarking on multiple imputation we are requiring that there be sufficient information to be gained to make the additional complexity worthwhile.

Data will be imputed from the distribution of site specific values of the baseline data. Imputation will not be done for other measures.

3. Additional Changes

Because of the change in the definition of screening practice Section 10.3.2 is removed from the SAP. This text is included for completeness:

10.3.2 Sensitivity Efficacy Analyses

Because of differences in screening practices at one site, the primary efficacy analysis of screening will be repeated with the data from this site removed to ensure robustness of conclusions.