For the mild to moderate Alzheimer's patient population, the ADAS-cog is the gold standard for how Alzheimer's patients are assessed. The ADAS-cog is what the FDA has accepted as the main outcome assessment for mild to moderate patients and is the primary efficacy outcome for Alzheimer's disease (AD) drug studies. While the ADAS-cog not the only assessment for Alzheimer's, it is the one most commonly used.

The ADAS-cog does an excellent job of assessing mild to moderate patients with Alzheimer's disease. But for people who suffer from severe Alzheimer's disease, there has been far less research conducted. Because so little research has being done on populations with severe Alzheimer's, few sites and raters have any expertise in assessing these patients.

In fact, there hasn't been a successful phase III Alzheimer's study for the past 15 years, and there hasn't been a new treatment for those suffering from severe Alzheimer's in that same time period, despite the huge interest in research. Surprisingly, more than 100 studies have failed in Alzheimer's in the last 15 years, most of those in the mild to moderate populations.

An Effective Assessment for Severity

There is an assessment that has proven very effective in accurately rating people with severe Alzheimer's disease. The Severe Impairment Battery (SIB) is the most widely utilized psychometrically validated instrument for assessing severe cognitive and behavioral changes in Alzheimer's patients. It targets cognitive issues specifically, since cognition is the number one issue associated with dementia.

The SIB is not commonly used because of the critical scarcity of site raters with experience administering the scale and because researchers are discovering that by the time the mild to moderate progression of Alzheimer's is seen in patients, they are usually too far along in the disease to be helped by many drugs. These factors make the severe patient population harder to treat.

Since it's ultimately the decision of the pharmaceutical company to determine what study they want to conduct and what patient population they want to look at, the vast majority of failed studies over the past 15 years have been in the mild to moderate populations of patients, which have used the ADAS-cog for assessments. When pharmaceutical companies have looked at these failures, they have seen that drug treatment is more beneficial in the mild patient population. So more pharmaceutical companies are targeting to mild cognitive impairment studies, which is essentially a less severe version than mild to moderate.

Because of the lack of training for raters and the fact that the SIB is more sensitive in assessing more severely impaired patients, which most studies don't focus on, the SIB assessment is used far less frequently than other AD scales used in more mild to moderate trials.

A Survey of the Severe Impairment Battery

Last year, we conducted a survey based on the Severe Impairment Battery to give us more information on where training was lacking. We found that 47 percent of experienced AD raters had no experience rating the SIB. This finding becomes understandable given that between 2003 to 2015, per a review of clinicaltrials.gov

studies, only 10 moderate to severe and severe AD trials were found using the SIB as an outcome measure, versus over 130 mild to moderate AD trials, which did not use the SIB.

These results indicate that research studies using the SIB, as their primary efficacy variable, may be ill equipped to detect changes, especially considering that the SIB is a complex scale with intricate administration requirements.

Since scale experience and training are essential in accurately administering scales, a comprehensive training program, which provides raters with enhanced SIB administration experience, is required. This is similar to other trials in which complex neuropsychological assessments are mandated.

A Methodology for Training

The illustration outlines a rater-training program implemented in an industry sponsored interventional clinical trial using SIB the as the primary outcome measure. The training was provided to more than 70 SIB study raters and involved SIB administration and scoring conventions, preparatory pre-investigators' meeting trainings, multiple optional practice sessions, video illustrations of standard administrations, and applied skills evaluations to assess the efficacy of the training.

The SIB assessment has a range of zero to 100. A rating of 100 doesn't mean the patient is perfect. It's just the maximum core a patient can receive. The scoring for the SIB is fairly simple. For instance, if a rater reaches out his or her hand, will the Alzheimer's patient reach out their hand to shake? Can the patient provide a cogent answer to the question, how are you today? Those things receive one or two points on the SIB. So it's a simple scale.

Because the SIB is not widely used, and because the assessment is the primary way the FDA will determine if a drug is effective, if this one assessment fails, the whole study fails. That was another reason why rigor was needed to ensure the approach used in training raters at various sites was robust. We had to make sure they had the understanding of how to administer the assessment because a lack of training leads to lack of experience and use of the SIB.

Of the 70 SIB study raters trained using this comprehensive training program, only two SIB raters, a mere three percent, required remediation following their Applied Skills Evaluation. In addition, of the 86 SIB scale source reviews completed to date, zero raters have required retraining or remediation on the SIB administration and scoring conventions.

Comprehensive Steps to the Training

We normally conduct a five stage training process for the SIB. The first stage is to qualify raters to meet experience requirements. We didn't want someone with two years of Alzheimer's experience that had only done a few assessments. We wanted to ensure they had in-depth experience, dependent on their education. If they had a doctorate degree, we might have allowed less number of years of experience, but we wanted to train people who had a thorough understanding of Alzheimer's assessments in general.

Then we provided the necessary didactic slides, which gave a quick overview of the SIB assessment. The slides illustrated the basic facts outlining what the assessment was about and how to administer it.

Next, we provided administration video overviews where we videotaped the administration of the SIB scale with a mock patient. We demonstrated how the assessment was done. Raters watched the video in its entirety and were then asked to follow along and score the video using SIB materials.

These overviews were challenging for the trainers. If a patient gives an answer that is not relevant, sometimes a rater is allowed to take only that response, and sometimes a rater is allowed to give the patient a prompt. The SIB rating is complex and based on how to score one or two points.

Next is the "Gold Standard Score Review," where we videotaped another assessment and then had raters score along with the assessments. They scored zero, one or two points for each different assessment, and then we measured their score against what we believe to be the gold standard in rating. The gold standard scores are derived from expert clinicians' scores.

The final step is the Applied Skills Assessment. All raters were required to complete an SIB assessment with a mock patient. We saw that they could correctly come up with a score close to 80 percent of the gold standard. But we wanted to make sure that they could actually administer the scale appropriately.

We sat down with each rater individually and videotaped their demonstration of the administration of the scale. We trained to make sure the rater actually conducted the assessment correctly with the Applied Skills Assessment. Immediate feedback was given to the rater by the trained clinician. Raters were graded on a pass/fail basis. If they failed the assessment on their first attempt, they were allowed to try a second time.

In addition to these steps, we also provided an additional optional practice session to introduce additional rigor. We have evidence that the more time someone has to practice training on the SIB scale, the less errors they will make.

Based on the data, the survey clearly demonstrated that a comprehensive training program significantly reduces the number of raters requiring additional follow-up and/or remediation of the SIB.