EVIDENCE OF RATER EXPECTATION BIAS

Cognitive Performance

- All subjects were aged 60 or older and had completed the Mini Mental State Examination (MMSE) and National Adult Reading Test (NART) at baseline.
- All subjects were told that the purpose of the study was to investigate how people of varying ages performed on a cognitive test.
- Half of the subjects were told that participants change from younger to older or from older to younger across visits.
- Half of the subjects were told that participants changed from 60 to 70 years or from 70 to 80 years.
- All subjects read an article suggesting that age was related to cognitive decline.
- Half of the subjects read an article suggesting that age was unrelated to cognitive decline.
- The results suggested that subjects’ expectations may influence not only performance on a cognitive test but also whether subjects meet criteria for dementia.

Rater Expectation Bias

- Among 100 subjects, 50 neurologists and 50 non-neurologist physicians/psychologists who viewed a series of videotaped assessments of patients with dementia (probable Alzheimer’s disease) at baseline, 6 and 12 months.
- Raters were blinded to order.
- The results suggested that having different raters across visits may reduce placebo response.

Interpersonal Psychiatric Assessment

- Participants, clinicians and clinical graduate students listened to an audiocassette of an actor portraying an adducted mentally healthy female.
- Participants were asked to rate the patient on a 10 point Likert scale.
- Ratings of the subject were significantly lower on the additive scale than on the subtractive scale.

EVIDENCE OF SUBJECT EXPECTATION BIAS

Cognitive Performance

- 14 subjects with asthma received each of the following interventions in random order across four visits (1-7 days apart).
- Albuterol inhaler
- Placebo inhaler
- Sham acupunture
- No intervention

- The results suggested that having different raters across visits may reduce placebo response.

Antihistamines

- None of these studies have been replicated in controlled double-blind placebo-controlled studies.
- Follow-up assessments have a significant therapeutic effect in clinical trials and may inﬂuence measurement of subject improvement.

**Number of Study Visits**

- **Single Versus Multiple Raters – Comparative Visits**
  - 14 subjects with Generalized Anxiety Disorder completed a week multi-site study using 30 subjects (10 per site) who received placebo and active treatment phases.
  - No intervention
  - Albuterol resulted in significantly greater improvement in FEV1 than placebo inhaler, sham acupuncture and no intervention control.
  - Higher severity differences at baseline and 4 visits in the single-rater group.

**EVIDENCE OF CAREGIVER EXPECTATION BIAS**

Caregiver Reports

- 14 subjects with Alzheimer’s disease ADIP responsive to the following scales at 2 time points measured 1 year apart.
  - Global change using the Clinical Global Impression Scale (7-point scale), the Hamilton Depression Scale (17-item scale) and the Zarit Burden scale.
  - Caregiver reports of disease severity and Alzheimer’s disease were at 3 levels.

- Caregivers consistently reported signiﬁcantly lower levels of quality of life at higher levels of symptom severity.

- Caregiver reports showed an overall decrease with increasing severity levels.

- Results suggest significant differences in disease severity across the three intervention groups.

- Caregiver reports demonstrated statistically signiﬁcant differences in reported improvement compared to the no intervention control.

- Results suggest greater placebo response in patient-reported outcomes than in objective measurements.

**EVIDENCE OF RATER SUBJECT EXPECTATION BIAS**

Caregiver Reports

- 14 subjects with Alzheimer’s disease ADIP responsive to the following scales at 2 time points measured 1 year apart.
  - Quality of life on a 0-10 scale.
  - Demerit of life on a 0-10 scale.
  - Suffering scale.

- Caregivers consistently reported signiﬁcantly lower levels of quality of life at higher levels of symptom severity.

- Caregiver reports showed an overall decrease with increasing severity levels.

- Results suggest significant differences in disease severity across the three intervention groups.

- Caregiver reports demonstrated statistically signiﬁcant differences in reported improvement compared to the no intervention control.

- Results suggest greater placebo response in patient-reported outcomes than in objective measurements.

**CONCLUSIONS**

The studies reviewed here suggest that subject expectations, caregiver expectations of patient and caregiver relationship impacts, diagnosis, increase placebo response and decrease signal detection.

Taken together, these results suggest that the following methodological approaches contribute to the high placebo response.

- Randomization
- Blinding
- Duplicate administration
- Single versus multiple raters
- Caregiver reports
- Analytical approaches

The studies reviewed here suggest that subject expectations, caregiver expectations, patient and caregiver relationship impacts, diagnosis, increase placebo response and decrease signal detection.

To date, these results suggest that the following methodological approaches contribute to the high placebo response.

- Randomization
- Blinding
- Duplicate administration
- Single versus multiple raters
- Caregiver reports
- Analytical approaches

The studies reviewed here suggest that subject expectations, caregiver expectations, patient and caregiver relationship impacts, diagnosis, increase placebo response and decrease signal detection.