Effects of the Pandemic on Subjects Enrolled in Alzheimer's Disease Trials

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ABSTRACT

Background: Duplicate and professional subjects are a significant issue in clinical trials, particularly those in CNS and pain, where subjective endpoints allow potential subjects to magnify their symptoms in order to meet inclusion criteria. Even in Alzheimer's Disease trials, subjects may participate in concurrent trials to take advantage of different MOAs or to increase the chances of getting an effective treatment. Alternatively, they may be professional subjects, who, for instance, may participate in a Cognition in Schizophrenia study at one site and an Early AD study at another. The failure to address the problem of duplicate and professional subjects can lead to problems with both subject safety and data integrity.
Objectives: To determine if there were pandemic-associated effects on the percentage of duplicate subjects found in clinical trials of Alzheimer's Disease by comparing those added to the CTSdatabase subject registry in the 2 years before the onset of the pandemic compared to the two years during the pandemic.
Methods: We looked at pooled study data for all subjects that screened for an Alzheimer's Disease study in protocols that used CTSdatabase between February 2018 and March 2022. Actionable matches are defined as those that violated protocol I/E (including concurrent enrollment, participation in another study less than the number of days required or previously enrolled in a study for a prohibited indication). The number of actionable matches was divided by the number of subjects screened to determine the percentage of inappropriate subjects (duplicates or otherwise) for that study. The number of screened subjects was also divided into two equal parts for each study based on enrollment date, with March, 2020, as the dividing point for when the pandemic began in earnest. Actionable matches were tallied for each half of enrollment.
Results: Of 1279 subjects entered into Phase 3 Alzheimer's Disease studies using CTSdatabase over the last 4 years, 4.7% (60) were excluded due to participating in another study concurrently, within an exclusionary timeframe or for an exclusionary diagnosis. While there was a trend toward more subjects being excluded during the pandemic, there was no significant difference in the percentage of those excluded before the onset of the pandemic and after the pandemic (3.9 vs 5.5%, p= 0.18).
Conclusion: While there was a trend toward a higher percentage of potential Alzheimer's Disease subjects excluded during the pandemic, this was not significant. The percentage excluded (4.7%) overall was striking, given the indication. We hypothesize that while some of these subjects (and their caregivers were professional subjects, many may have been seeking an effective treatment, i.e. they were duplicate, but not professional, subjects. A subject registry such as CTSdatabase is an important tool in identifying these subjects and either eliminating them or understanding how they may affect study results.

BACKGROUND

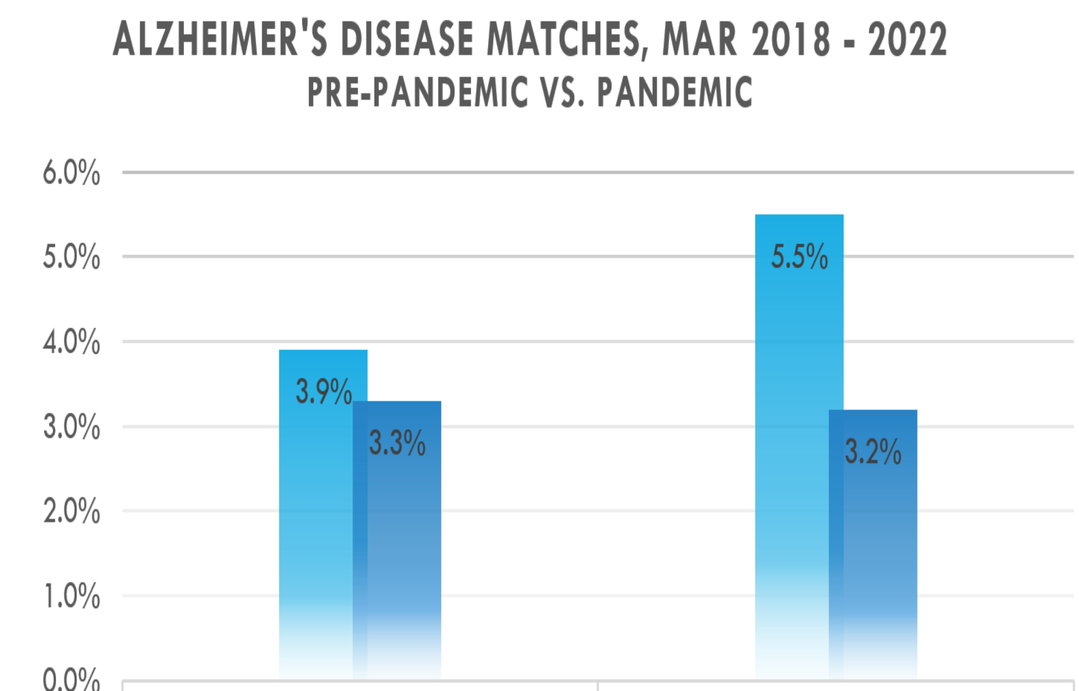
- Duplicate and professional subjects are a significant problem in clinical trials, particularly in studies with subjective endpoints, such as in CNS or pain.[1]
- The problem of duplicate subjects in clinical trials of Alzheimer's Disease has been previously described, and included both professional subjects – those who are participating in multiple studies in order to collect stipends – and those that are duplicate subjects but not professionals – they want efficacy for themselves or their loved ones, not financial reward.[3]
- Data integrity is compromised when professional subjects purposely deceive with regard to inclusionary symptoms, excluded conditions, adherence to investigational product or previous study participation.[2] CTSdatabase is a subject registry which uses partial identifiers to track duplicate and professional subjects across sites and sponsors.

METHODS

We looked at pooled study data for all subjects that screened for an Alzheimer's Disease study in protocols that used CTSdatabase between February 2018 and March 2022. Actionable matches are defined as those that violated protocol I/E (including concurrent enrollment, participation in another study less than the number of days required or previously enrolled in a study for a prohibited indication). The number of actionable matches was divided by the number of subjects screened to determine the percentage of inappropriate subjects (duplicates or otherwise) for that study. The number of screened subjects was also divided into two equal parts for each study based on enrollment date, with March, 2020, as the dividing point for when the pandemic began in earnest. Actionable matches were tallied for each half of enrollment.

RESULTS

- Of 1279 subjects entered into Phase 3 Alzheimer's Disease studies using CTSdatabase over the last 4 years, 4.7% (60) were excluded due to participating in another study concurrently, within an exclusionary timeframe or for an exclusionary diagnosis.
- While there was a trend toward more subjects being excluded during the pandemic, there was no significant difference in the percentage of those excluded before the onset of the pandemic and after the pandemic (3.9 vs 5.5%, p= 0.18).



Although there is a trend toward a greater percentage of AD patients excluded during the pandemic (3.9 vs 5.5%, p= 0.18), it was not statistically different from those excluded pre-pandemic.
*All CNS data was previously reported in a poster from ASCP, 2022[4]

DISCUSSION & CONCLUSION

- In clinical trials of AD, subjects might be dual enrollers in order to take advantage of different MOAs/increase the chances of getting an effective treatment *or* they may be professional subjects who wish to collect multiple stipends.
- While there was a trend toward a greater percentage of excluded subjects in AD studies during the pandemic, this number, as in our previously reported pooled CNS data[4], did not reach statistical significance.
- A subject registry such as CTSdatabase is an important tool in eliminating these problematic subjects from AD trials.

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