

QUANTIFICATION OF EARLY TREATMENT DISCONTINUATION

A Retrospective Analysis on 4,810 Participants to CNS Clinical Trials

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1 Methodological issue being addressed

Precisely quantifying the magnitude and temporality of early treatment discontinuation in CNS trials

- Across countries;
- Across dosing regimens.

2 Introduction

- Early treatment discontinuation
 - Is frequent in clinical trials;
 - 40% of participants discontinue within 1 year;
 - Must be considered when running a trial;
 - Only partially detected through self-reported dropout.
- Electronic recording of medication intakes can be performed using smart medication packages:
 - Bottle caps,
 - Blisters,
 - Injectors,
 - Inhalers,
 - Pill dispensers...
- Smart medication packages record a timestamp each time a participant takes their medication (Figure 1).
- The resulting data allows to:
 - Quantify how well a participant follows the regimen;
 - Determine the exact day on which the last dose is taken, which is more precise than other approaches to estimate time to treatment discontinuation.

3 Methods

Data source: electronic medication intake data

- From 7 recent clinical trials;
- Collected;
- Anonymized (participant, drug, smart package, study, sponsor, site);
- Pooled;
- Convenience sample.

Data analysis

Using electronic medication intake data:

1. Actual duration of follow-up for each participant was derived;
2. Event of interest: early treatment discontinuation, for any reason;
3. Sponsor-provided information about who dropped out from the study was used (when available);
4. When not available, early discontinuation status was determined using:

Actual duration < planned duration – 7 days

5. A Kaplan-Meier survival curve was built from the pooled dataset.
6. Implementation adherence (how well a participant took the medication) was computed as the proportion of prescribed doses taken while on treatment.
7. A Cox regression was performed with implementation adherence as a predictor of early treatment discontinuation.

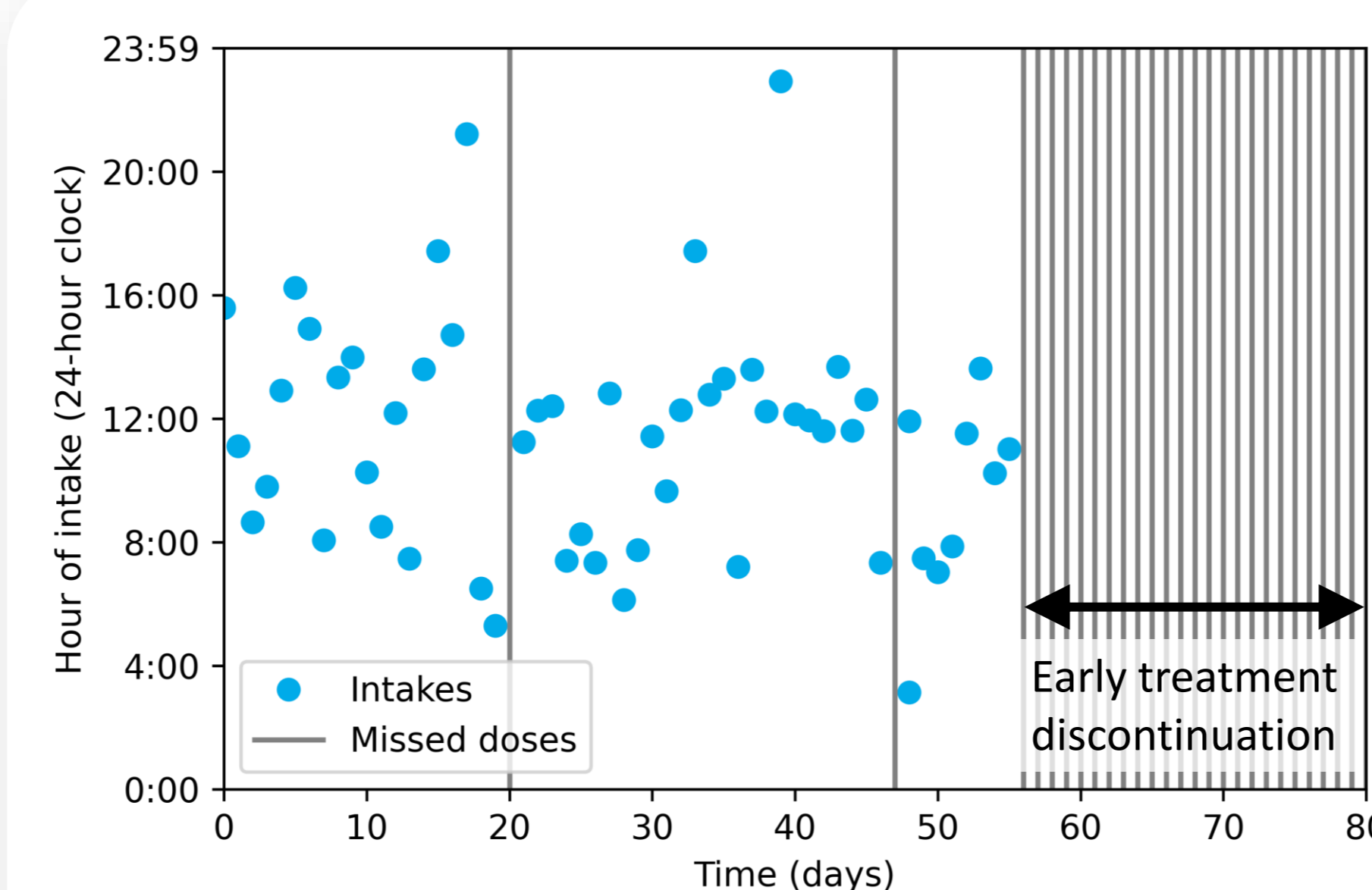


Figure 1. Example of data collected using a smart package for electronic monitoring of adherence. Each dot corresponds to one opening of the smart package.

4 Results and discussion

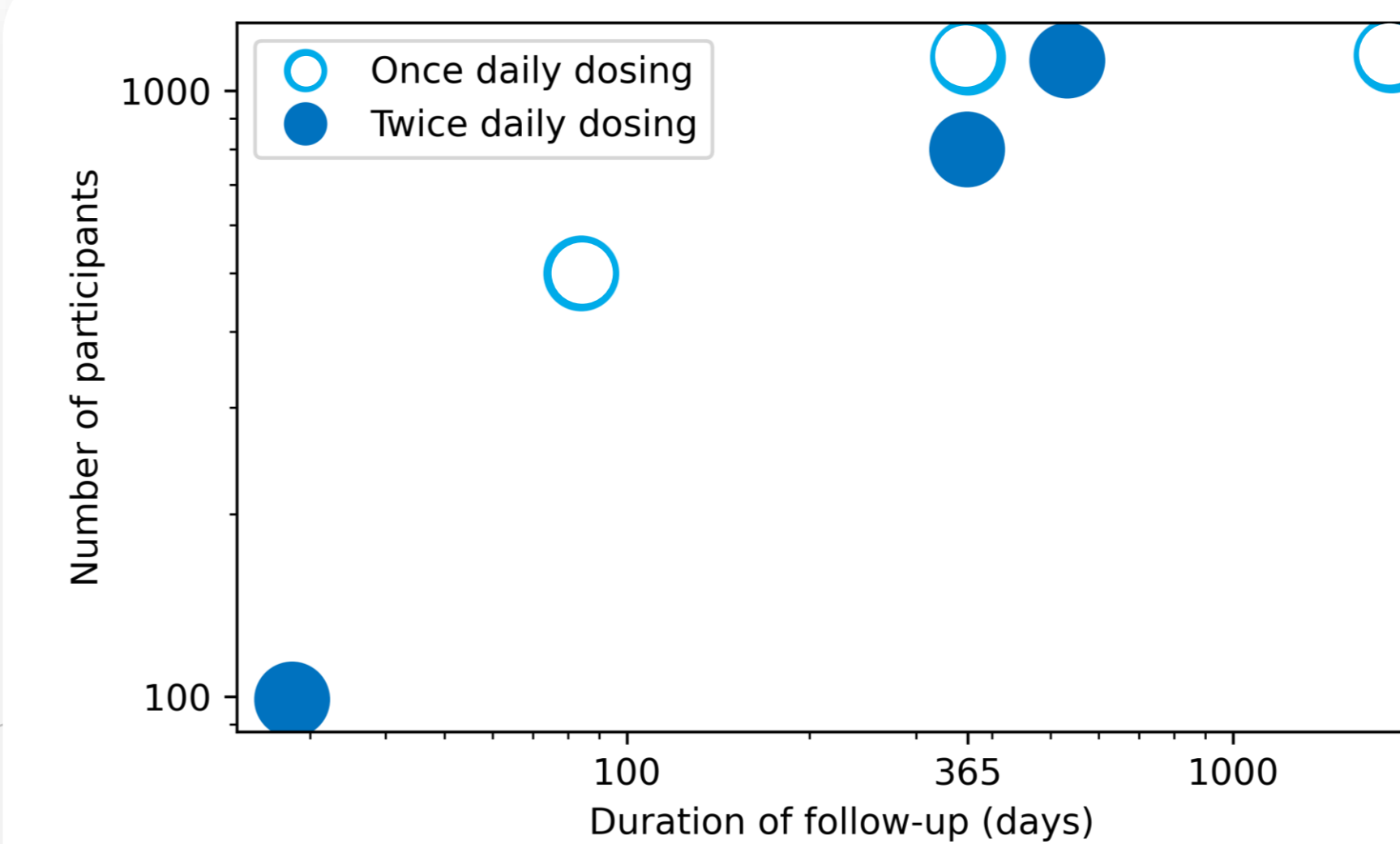


Figure 2. Characteristics of the 7 trials.

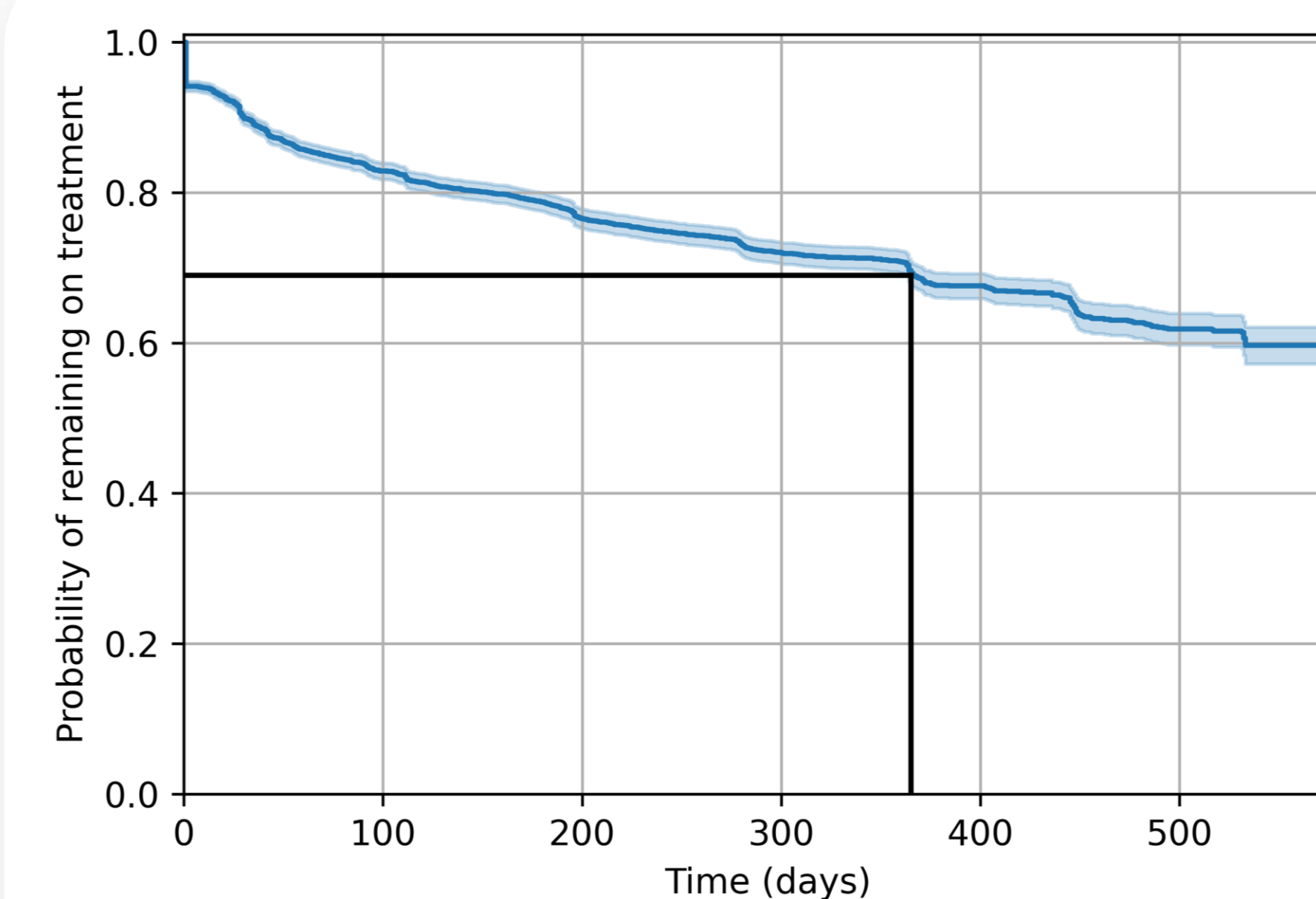


Figure 3. Kaplan-Meier curve of the probability of remaining on treatment over time.

5 Conclusions

- Early treatment discontinuation is common, even in the controlled environment of CNS clinical trials.
- Implementation and early discontinuation are inter-related.
- Hence, monitoring and improving medication adherence is important.

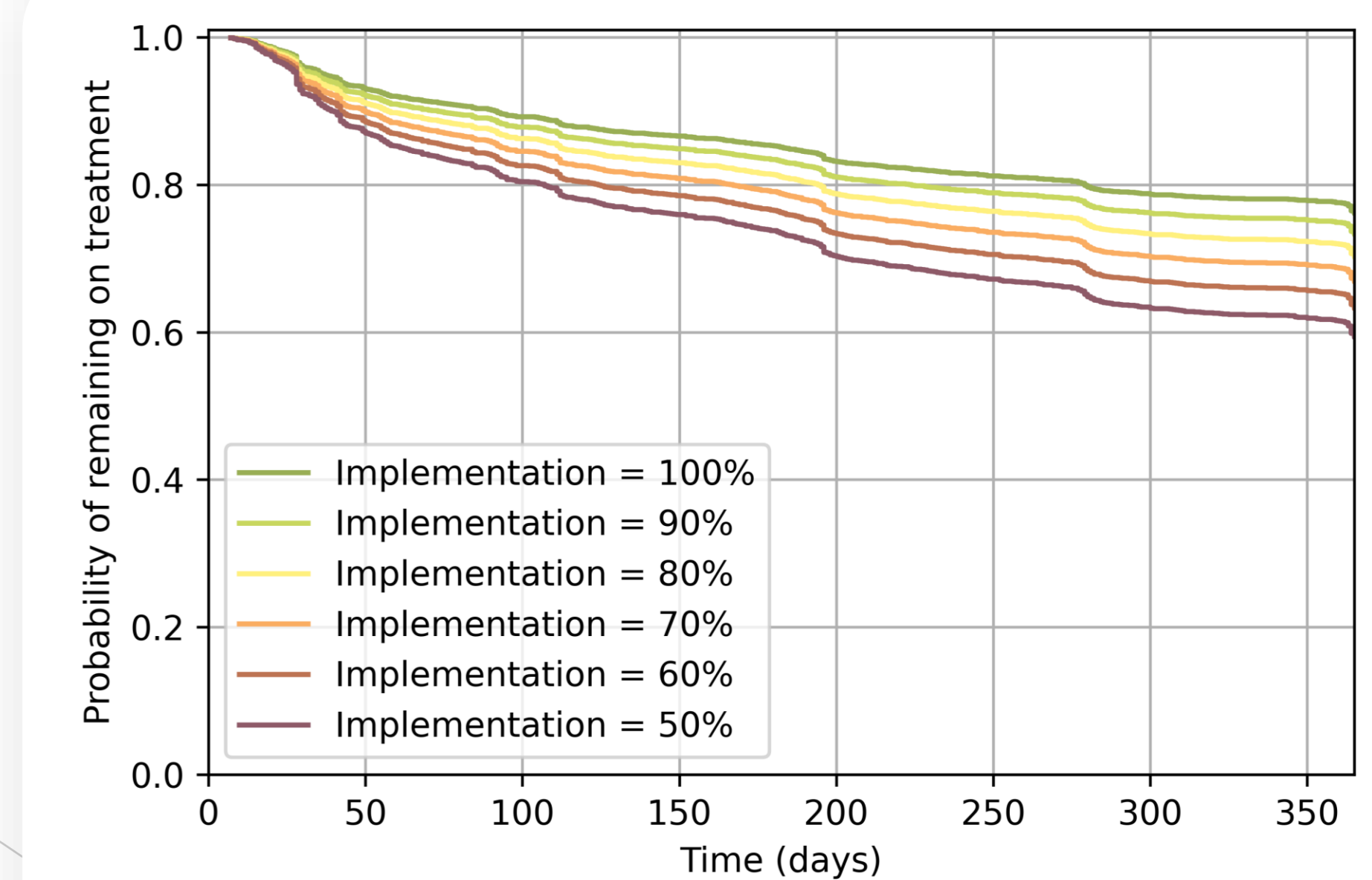


Figure 4. Relation between implementation adherence and the probability of remaining on treatment.

- The median one-year persistence is 69% (Figure 3).
- A worse implementation adherence is significantly associated to a higher risk of treatment discontinuation ($\beta = -1.3, p < 0.005$; Figure 4).
- This is the first study to report a meta-analysis of early treatment discontinuation derived from electronic medication adherence data in CNS trials.
- Previous studies reported early treatment discontinuation pooled across several therapeutic areas. Their results are consistent with the present study.
- The rate of early treatment discontinuation is similar for CNS trials and for other therapeutic areas.

Disclosures

One or more authors report potential conflicts which are described in the program.