Subject Registries Reduce Duplicate Subjects Entering CNS Studies

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Abstract

***Background*: Duplicate and professional clinical trial subjects are an increasingly recognized problem and likely contribute to failed CNS studies. The internet, a culture of cheating, and a dramatic increase in the complexity of studies may also contribute to rising numbers of duplicate subjects.**

***Methods*: Utilizing CTSdatabase, one of 3 commercially available subject registries, 16 participating Southern California sites entered 2,584 potential CNS clinical trial subjects who presented for prescreening between October 31st 2011 and March 31st 2013. Prescreening subjects signed an IRB-approved Subject Database Authorization prior to being entered into the registry by site staff. Sites were immediately notified whether or not potential subjects matched with those seen at other sites.**

***Results*: Of 2,584 subjects entered, 190 were same site matches (i.e. brought back to the same site at a later date) and were eliminated from the analysis. "Virtually certain" duplicates (those with a <1/10 million likelihood of matching by chance) made up 7.8% of all prescreens. This is a sharp increase compared with the 3.45% noted when only 9 sites had entered only 1,132 (non-same site) subjects into the registry. Duplicates currently (or too recently) participating in other studies or having participated in studies for exclusionary indications were prevented from entering studies.**

***Conclusion*: Use of a subject registry at prescreen reduced duplicate subjects entering CNS studies. A disturbing number of duplicate subjects were found and this number more than doubled as the number of participating sites increased. To optimize the detection and elimination of duplicate subjects from clinical trials, all sites in a given geographic area should utilize a subject database early in the screening process.**

***Keywords*: Duplicate subjects, professional subjects, subject registry, subject database**

Background

- **Duplicate and professional subjects are an increasingly recognized problem in clinical trials, particularly in CNS. The internet, a culture of cheating, and a dramatic increase in the complexity of studies may also contribute to rising numbers of duplicate subjects.[1-2]**
- **Privately available registries address this problem by comparing identifiers of potential subjects to look for matches and dual enrollment.[3]**
- **Previous reports have found intra-pharma matches (within one pharmaceutical company or one development program) to be in the range of 1.5-5%.[4-5]**
- **Site collaboration between a small number of sites has yielded duplicate subject numbers in the range of 3.5-5%.[6]**

Methods

- **Investigators in Los Angeles, Orange and San Diego counties were contacted by the authors to participate in the subject registry at prescreen.**
- **The sites were provided with a template of the Subject Database Authorization Form ("Authorization") to submit to an Institutional Review Board (IRB) for approval.**
- **Site staff were provided with login information and were trained by CTSdatabase staff.**
- **Potential subjects ("Subjects") were required to sign an IRB-approved Authorization allowing collection of partial identifiers and to provide photo identification.**
- **Site staff accessed the web-based database during the prescreening process and received a match report detailing subject previous study participation.**
- **In case of a match, sites followed HIPAA guidelines in communicating about subject enrollment status.**
- **The authors reviewed all matches which occurred between October 31, 2011 and March 31, 2013 and eliminated same site matches from the dataset.**
- **Matches were considered Virtually Certain ("certain") if there was <1 in 10M likelihood that the match would occur by chance alone, Probable (<1/1M by chance) or Possible (<1/100,000 by chance). Since there were false positives included in the possible matches, only certain and probable matches are reported here.**

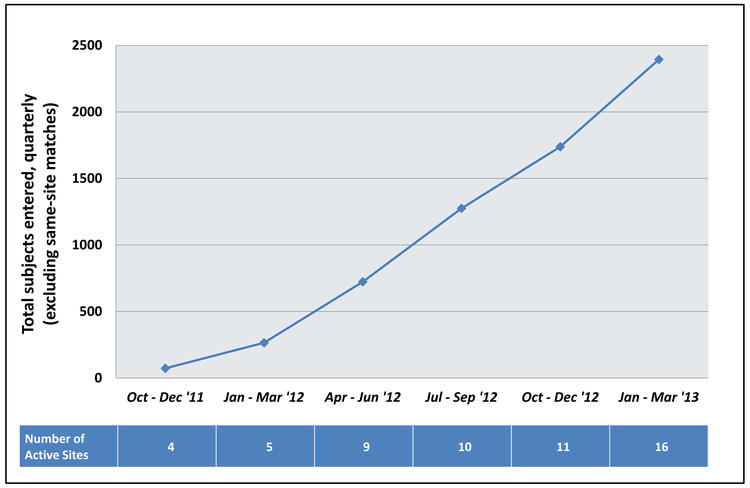

Figure 1: Cumulative subjects entered and number of active sites, by quarter

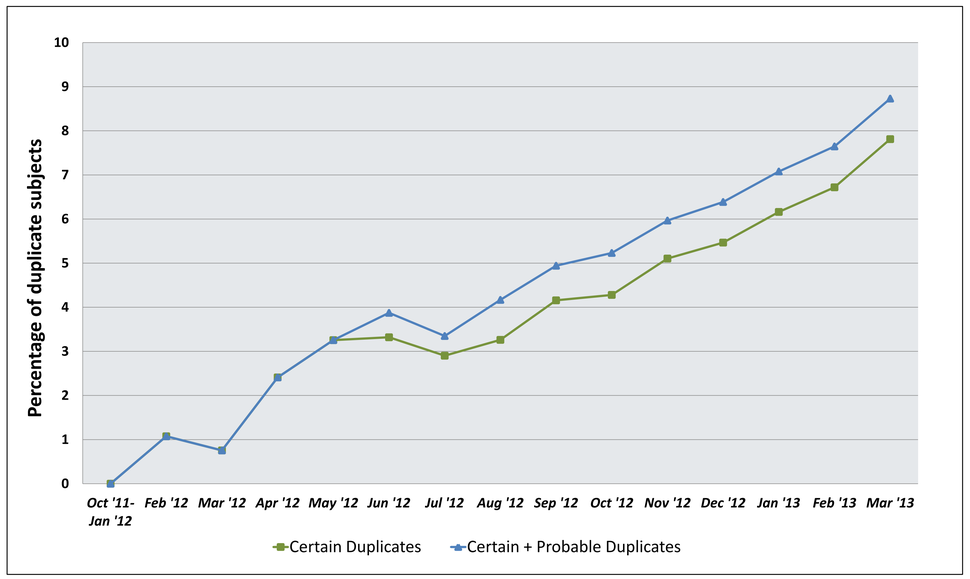

Figure 2: Cumulative percentage of certain and certain+probable duplicates, by month

Results

- **16 participating sites entered 2,584 total potential subjects. 190 of these prescreens were the same subject re-entered at the same site and are, therefore, excluded from the data presented on duplicate subjects. *(Figure 1)***
- **187 certain duplicates were found, accounting for 7.8% of the sample *(Figure 2)*. When probable duplicates were included, this number increased to 209 duplicates, or 8.7% of the sample.**
- **Potential subjects found to be duplicates were prevented at prescreen from entering studies; some sites excluded dozens of potential duplicates.**

Discussion

- **Over time, a prescreen database may capture appropriate subjects as duplicates (e.g. those that have completed a study and waited for an appropriate length of time), as well as inappropriate subjects (e.g. those that are currently in a study or have prescreened for multiple indications).**
- **Even when appropriate duplicates are taken into account, as more sites in this densely populated area were included, the duplicate rate increased sharply.**
- **There were only 3.5-4.2% duplicate prescreens in Aug. 2012 and 4.3-5.3% duplicates in Oct. 2012 (when 1520 prescreens had been entered at only 10 sites).[6]**
- **Concerns over patient privacy and a lack of data sharing between pharmaceutical companies and among investigative sites may assist professional subjects in avoiding detection.**
- **Duplicate and professional subjects, who likely contribute to the problem of failed studies, are a significant problem and must be addressed.**

Conclusions

- **At least 7.8% of the subjects presenting for entry into CNS studies were previously entered at local sites.**
- **As the number of sites rose from 9 to 16, the duplicate rate increased sharply.**
- **Increasing the number of participating sites using a registry makes it more difficult for duplicate subjects to avoid detection by shifting to non-participating sites.**
- **At least 100 potential duplicate subjects were prevented from entering studies due to the simple use of a subject registry.**

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