ENROLLMENT PATTERNS:
Implications for CNS Clinical Trials

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INC Research

The Methodological Question Being Addressed

A. Do clinical trials in CNS follow typical or unique enrollment patterns across the year?

B. How can the enrollment patterns be characterized whether by region or by therapeutic area?

C. What are the likely reasons for observed enrollment patterns?

Introduction (Aims)

Enrollment patterns are often an important consideration in lengthy CNS trials when projecting enrollment timelines and enrollment rates. The ability to predict and achieve the desired enrollment rate can determine the success of the clinical trial because of the impact on data analysis plans, overall study timeline, project budget, and marketing goals of the sponsor. Many factors can influence enrollment rates. Enrollment projections for clinical trials typically account for an expected seasonal pattern of decreased enrollment in Northern Hemisphere Summer (July/August) and Winter (December/January) months. Here, using an archive of four years of enrollment data, we more closely examine enrollment patterns in CNS clinical trials by evaluating site enrollment productivity for observable enrollment patterns across regions and therapeutic areas.

Methods

Data were reviewed on 107 trials enrolling 31,830 subjects at 3,331 investigative sites in CNS trials conducted by INC Research during the years 2011 – 2014, inclusive. Trials were categorized by three CNS therapeutic areas, as defined by business operations (% subjects): psychiatry (55%), analgesia (34%), and neurology (11%). Data were examined in North America and Europe. Enrollment is defined here as subjects consented into the trial. To standardize the evaluation across each of these trials with differing timelines, we developed a productivity ratio formula that summed the number of subjects consented on any given day as an indicator of the number of sites that could produce enrollment on that day, and calculated a site productivity indicator as the dividend of these two variables (# subjects/# site days = site productivity). By consolidating these productivity data into a single 12 month observation period, we were then able to observe trends in enrollment.

Results

In Table 1, the total site days and screened subjects by therapeutic area are presented for four consecutive years inclusive of 2011 through 2014. Across all 3 therapeutic areas, October represented the month in which the most subjects were screened (3,554 or 11% of enrollment). However, when using the productivity ratio, which accounts for the number of sites that were active, this high performance in global enrollment was greatest for analgesia studies only (see Table 2). Analgesia demonstrated the greatest variability and adherence to the expected seasonal patterns, and demonstrated a a bimodal peak in both April and October. Site activity in analgesia was also at a peak in the Fall; the productivity ratio was consequently higher in April as there were less sites enrolling more subjects. When observing the analgesia site productivity by region, Europe's peak was in September just after the Summer respite and North America's peak was in April but not in October. Psychiatry's site productivity followed a flatter distribution. While, psychiatry's enrollment appears to spike in October (Table 1), the number of sites on board also peaked which indicates that the productivity of these sites was not significantly different (see Table 2). Psychiatry's productivity by region, observed separately, re-introduces more variability and a seasonal pattern in Europe. Neurology studies were rather flat in their site productivity pattern as well (see Table 2).

Table 1. Total Site Days and Screened Subjects by Therapeutic Area January 2011 – December 2014

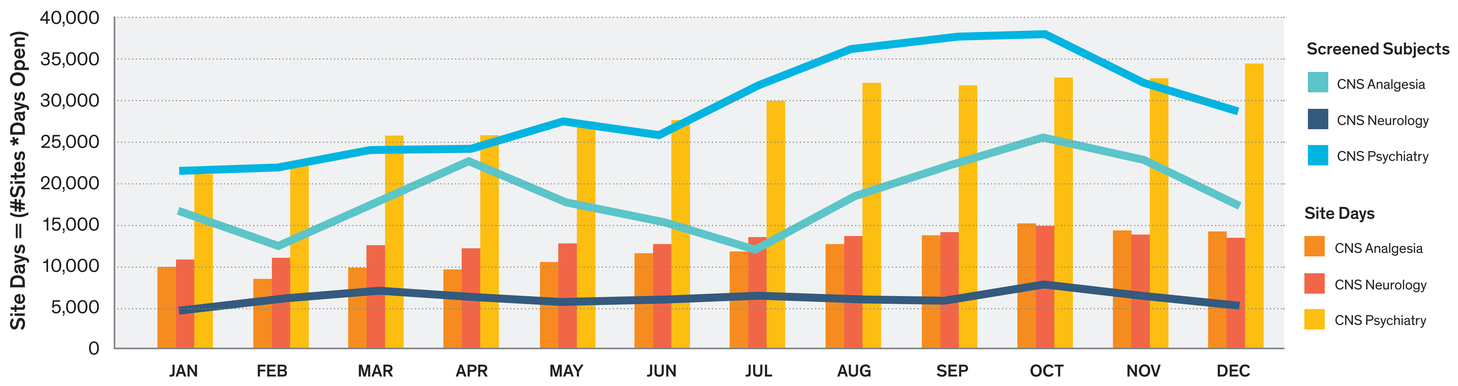
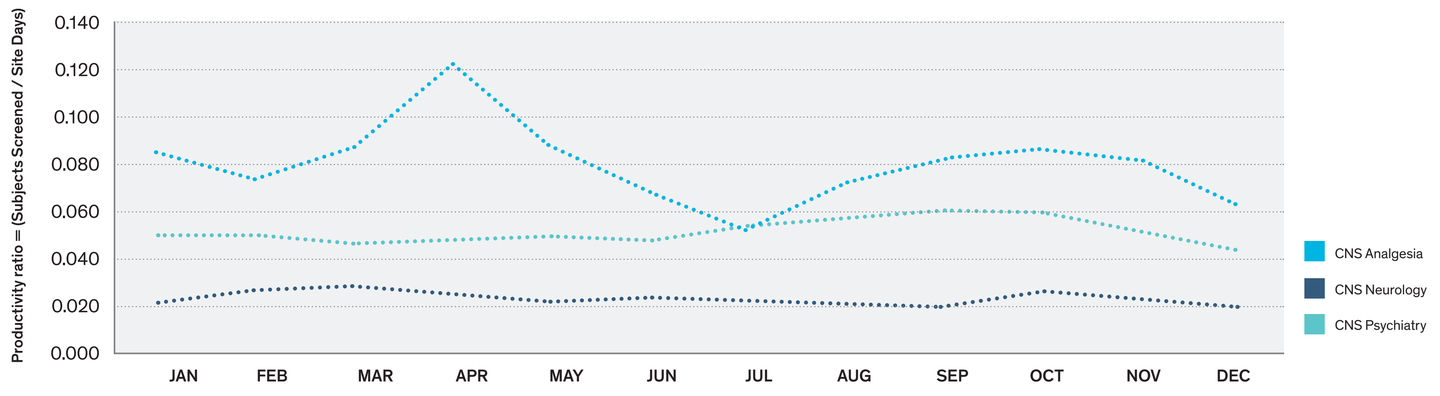


Table 2. Productivity Ratio by Therapeutic Area January 2011 – December 2014



Conclusions

Expected seasonal enrollment variations that are often accounted for in clinical trials were observed in part in this large global dataset of enrollment in CNS clinical trials, with the most consistent site productivity peak being in October. An important consideration is the population under study and the measures taken to bolster enrollment, which may lessen the seasonal variation. Further exploration of these patterns is warranted.

Disclosures

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