# Decisions: Academic site perspective

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Disclaimers: I am often an N of 1.

We don't do many trials as an academic site anymore because they are too cumbersome and difficult.

If you know that in 9 of the last 10 CNS trials you have had to modify the protocol in X, Y and Z way-- just start there.

# Disclosures

- Professor, Dept of Psychiatry; Henry B. Dielmann Chair, University of Texas Health Science Center, San Antonio
- Consultant:  Indivior, Acadia, Click Therapeutics, Boehringer Ingelheim, Karuna, Bristol Myers Squibb, Alkermes
- Speaker: Otsuka, Janssen

# Multiple protocol amendments

- Number of amendments going up, amendments are highly disruptive, representing the largest single cause of unplanned delays and unbudgeted expense.
- The total average time to implement an amendment has nearly tripled during the past decade
- The time from identifying the need to implement now taking an average of 260 days.
- If you know that you have made similar amendments in similar trials or maybe competitors have—just start that way

# Problems with amendments

- Tufts Center for the Study of Drug Development (Tufts CSDD)examined data from 836 phase I-IIB/IV protocols ; 136 randomly selected amendments. 52 protocols
- 57% of protocols had at least one substantial amendment, and nearly half (45%) of these amendments were deemed "avoidable."
- Protocols with at least one substantial amendment had fewer actual screened and enrolled patients relative to the original baseline plan than did those protocols without an amendment.
- The median direct cost to implement a substantial amendment was US$141,000 for a phase II protocol and $535,000 for a phase III protocol.
- Sites ask for them and hate them!

Getz K, Smith Z, Botto E, Murphy E, Dauchy A. New Benchmarks on Protocol Amendment Practices, Trends and their Impact on Clinical Trial Performance. Ther Innov Regul Sci. 2024 May;58(3):539-548. doi: 10.1007/s43441-024-00622-9. Epub 2024 Mar 4. PMID: 38438658.


# Trials are too complex; sequencing problems

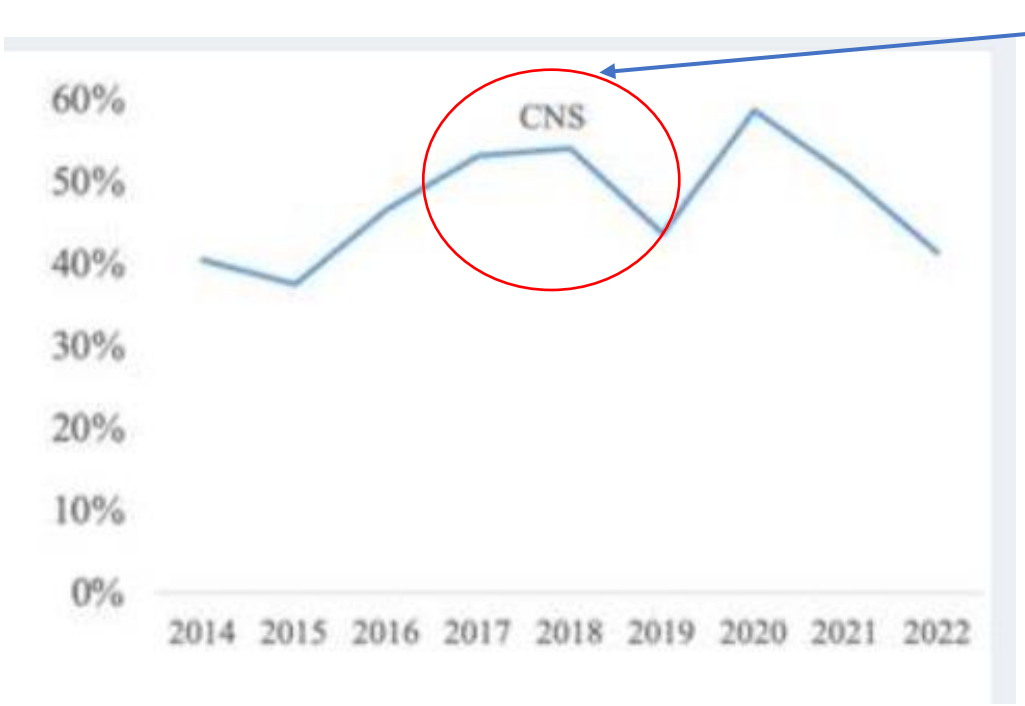
- Requirements for rating have gotten absurd; years of experience are not as important as doing it right
- Too many websites
- Too many devices
- Too much training too early requiring retraining
- Stop sending drug ---WAIT!!!
- Stop training raters before the IRB—WAIT!!
- By the time gets through IRB already amendments

# Trials are too complex to begin with

- Choose your primary and secondary endpoints and leave it alone
- Stop stuffing the taco; it makes the tortilla break
- Too many assessments and time spent at clinic
- KISS  Keep it Simple St____d
- Ask site and people with lived experience to pre-review for feasibility

Markey N, Howitt B, El-Mansouri I, Schwartzenberg C, Kotova O, Meier C. Clinical trials are becoming more complex: a machine learning analysis of data from over 16,000 trials. Sci Rep. 2024 Feb 12;14(1):3514. doi: 10.1038/s41598-024-53211-z. PMID: 38346965; PMCID: PMC10861486.

# Complexity in CNS Trials




When we stopped doing clinical trails

Markey N, Howitt B, El-Mansouri I, Schwartzenberg C, Kotova O, Meier C. Clinical trials are becoming more complex: a machine learning analysis of data from over 16,000 trials. Sci Rep. 2024 Feb 12;14(1):3514. doi: 10.1038/s41598-024-53211-z. PMID: 38346965; PMCID: PMC10861486.