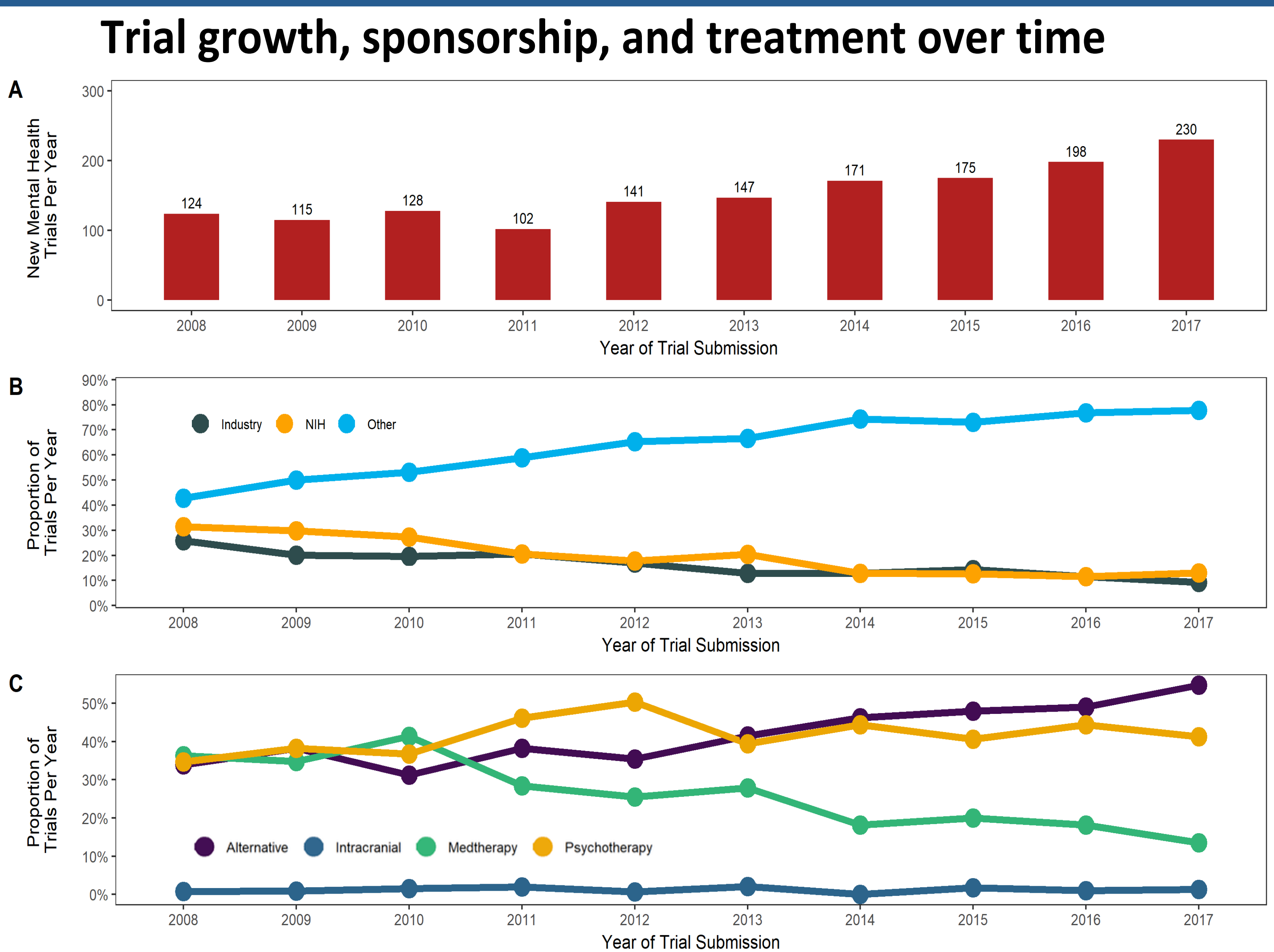




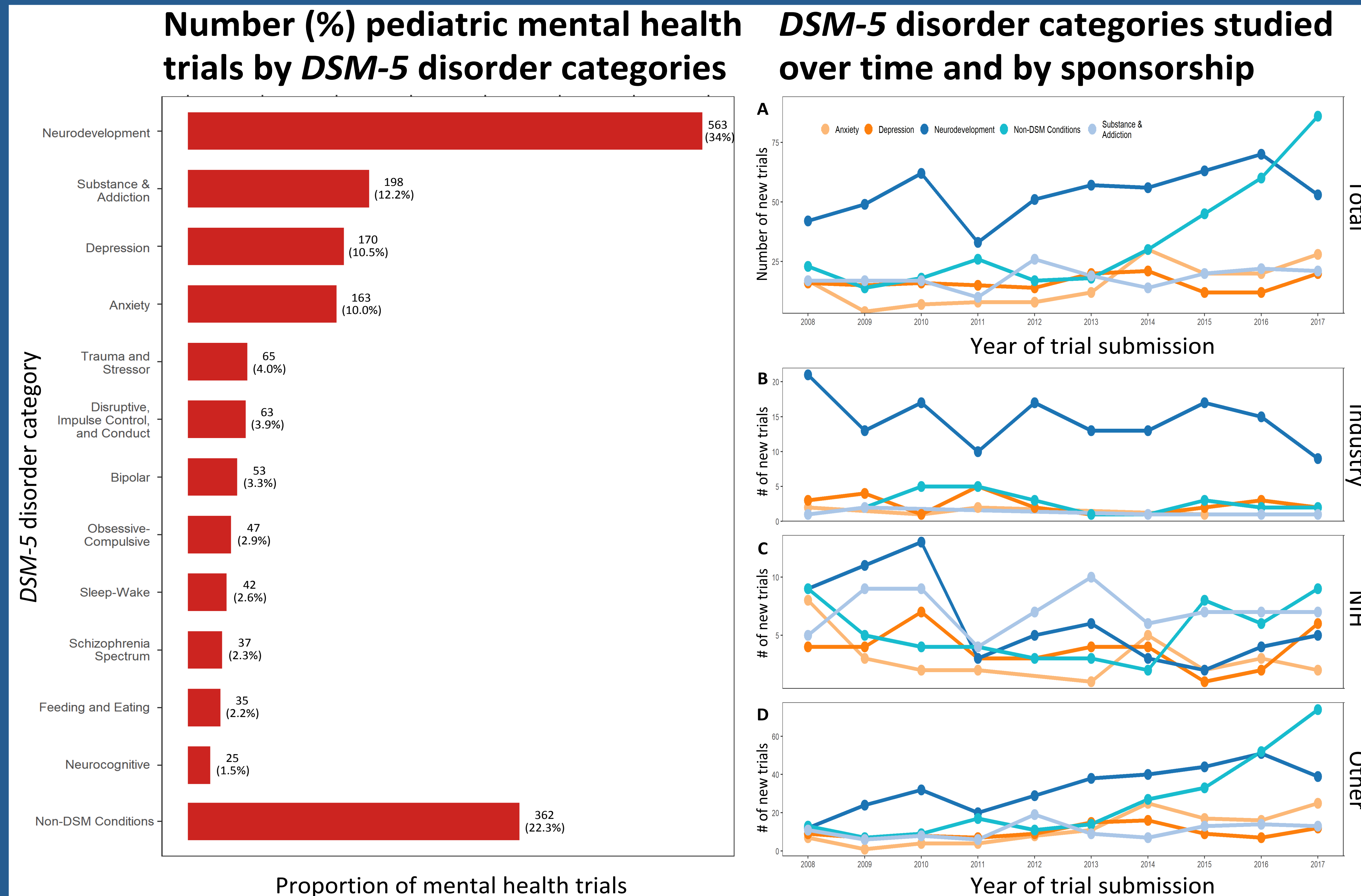
Trends in pediatric mental health clinical trials over the past decade: An analysis of the 1622 trials reported in ClinicalTrials.gov from 2007 – 2018

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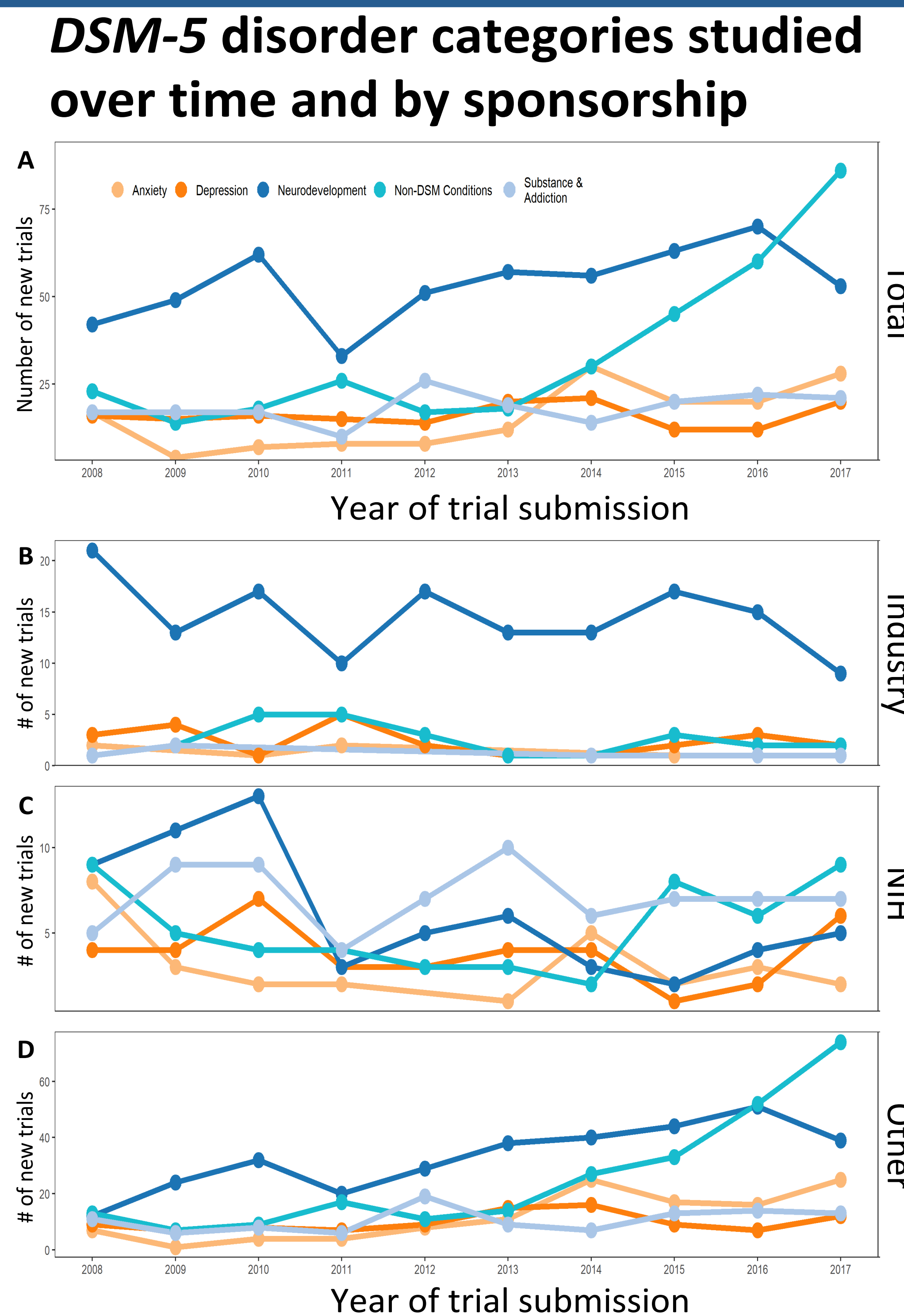
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(A) The total number of pediatric mental health trials grew over the past decade (average annual growth rate [AAGR] 8.2%; $p=0.0012$). Pediatric mental health trials cumulatively comprised 14.5% of all mental health trials over this time period and grew nearly twice as fast as all mental health clinical research (AAGR 4.5%; $p=0.0013$) (data not shown). (B) This figure shows changes in the proportion of sponsors over time; trends are evident. These trends were assessed by analyzing total number of trials by sponsor: Other sponsorship (i.e. academic medical centers and hospitals) grew (AAGR 15.70%; $p=0.0002$), while sponsorship from Industry (AAGR -3.2%, $p=0.24$) and NIH (AAGR -0.3%, $p=0.21$) did not. (C) This figure shows changes in the proportion of treatment types studied over time; trends are evident. These trends were assessed by analyzing total number of trials by treatment: Trials studying psychotherapy (AAGR 10.91%; $p=0.0006$) and alternative treatments (AAGR 13.84%; $p=0.002$) grew, while trials studying pharmacotherapy (AAGR -0.9%, $p=0.15$) did not. Too few trials studied interventional treatments (i.e. ECT, deep brain stim, and transcranial magnetic stim) to assess for monotonic growth trends.



The figure on the left shows the total number of pediatric mental health trials over the past decade stratified by disorders studied. The top five disorder categories (neurodevelopment, substance & addiction, depression, anxiety, and non-*DSM-5* conditions) comprised 89% of trials. The percentages add to >100%, as trials studying multiple disorder categories were counted in each category. The remaining *DSM-5* disorder categories comprised <0.5% of trials and were omitted. (A-D) The top five most studied disorder categories were evaluated over time and by sponsor. (A) Investigation of non-*DSM-5* conditions (e.g. suicidality and wellness) grew (AAGR 22.05%; $p=0.009$), while study of *DSM-5* disorders remained stable. Clinical focus differed by sponsor. (B) The majority of industry trials studied neurodevelopmental disorders (e.g. autism and ADHD) (62% cumulatively). (C) NIH studied a similar proportion of all 5 conditions (10-25% cumulatively). (D) The majority of Other-sponsored trials studied non-*DSM-5* (26% cumulatively) and neurodevelopmental (32% cumulatively) disorders, and both of these disorder categories grew over time.



Background:

- By analyzing the ClinicalTrials.gov database, investigators have identified important changes in their fields (Califf et al., *JAMA* 2012; Arnow et al. *Psychiatry Res* 2019).
- These studies identified important trends in trial sponsorship, design, treatment, and disorders studied.
- This analysis has not been conducted in pediatric mental health trials.

Study Objective:

- To perform an exploratory analysis of the entire portfolio of pediatric mental health clinical trials reported to ClinicalTrials.gov over the past decade and to identify trends in trial growth, treatment type, disorders studied, and trial sponsorship.

Data:

- We obtained records from all 274,416 trials registered in ClinicalTrials.gov from October 1, 2007 to April 30, 2018.
- We identified the subset of trials relevant to pediatric mental health ($n=1622$) using the Medical Subject Heading (MeSH) terms and disease condition terms indexed for each trial by the registry.
- We manually reviewed the official title and study description of each trial to exclude trials not relevant to pediatric mental health and to label the trials by the *DSM-5* disorder categories and treatment types studied.

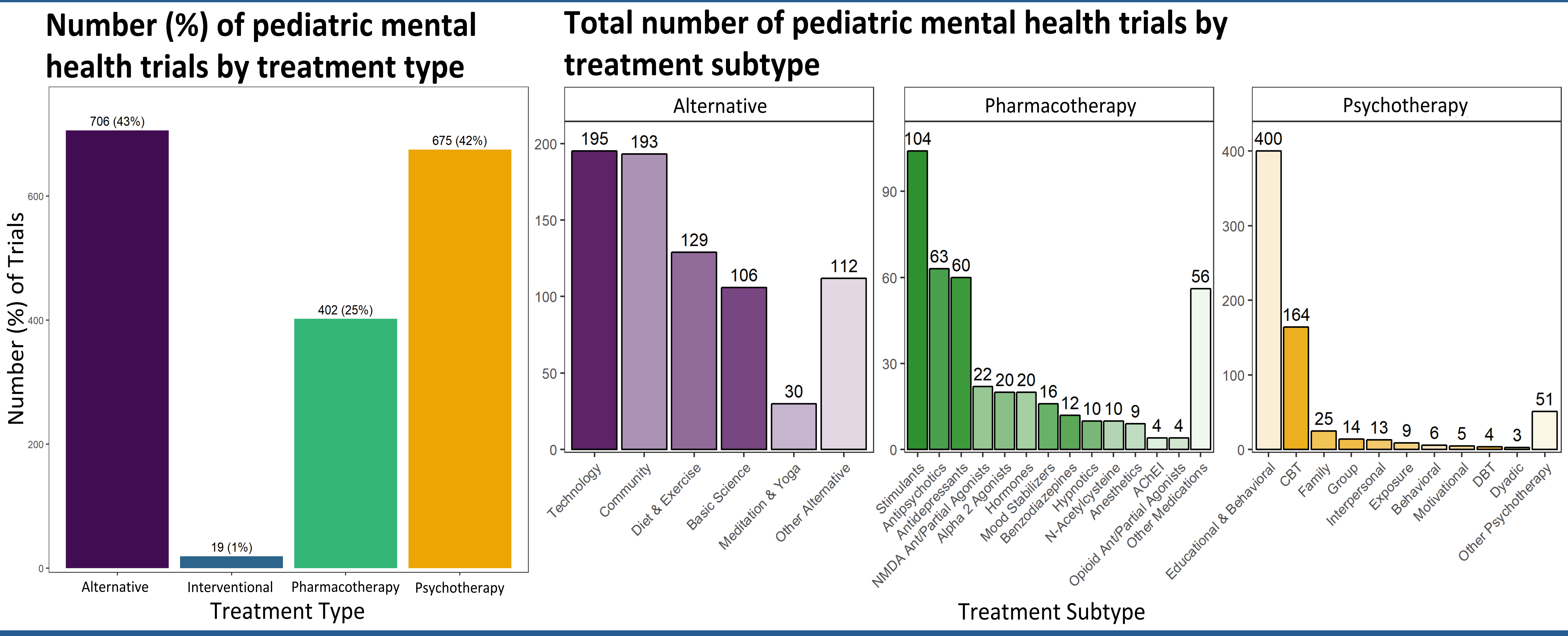
Methodology:

- We analyzed trial growth, treatment type, disorders studied, and trial sponsorship over time.
- Trends over time were assessed using Mann-Kendall tests, and differences between categorical variables were assessed using Pearson χ^2 tests.

Results: (Please see panels to the left)

Discussion:

- There appears to be a growing emphasis on studying pediatric populations in mental health research.
- Ongoing shifts in sponsorship may influence the disorders and treatments studied in mental health.
- Increased study of non-*DSM-5* conditions may reflect a number of variables, such as the growing adoption of the NIMH's RDoC (Research Domain Criteria) initiative.
- The growth of Other sponsors may reflect the growth of non-*DSM-5*-focused philanthropies that have compensated for waning funding from government and industry sources.



Psychotherapy and alternative studies cumulatively comprised 84.8% of all trials. Alternative interventions fell into broad categories, the most prominent being technology (e.g. interactive apps), community (e.g. clinic program evaluations), diet & exercise (e.g. nutritional supplements), and basic science (e.g. fMRI) (81.4% of total). The majority of the pharmacotherapies tested were stimulants, antipsychotics, and antidepressants (55.4% of total). The majority of psychotherapy treatments were educational & behavioral interventions (57.6% of total).

Takeaways:

- ❖ Pediatric mental health trials grew in number and percentage compared to all mental health trials.
- ❖ The number of Other sponsors grew.
- ❖ The number of psychotherapy and alternative treatment trials grew.
- ❖ Five disorder categories comprised the majority of trials, with significant growth of trials studying non-*DSM-5* conditions.
- ❖ Non-*DSM-5* trials grew primarily due to Other sponsorship. Overall disorders studied differed by sponsor.
- ❖ Psychotherapy (mostly behavioral & educational) and alternative (mostly technology & community) treatments comprised the majority of all trials.

Limitations:

- While ClinicalTrials.gov is one of the largest and most comprehensive registries, some trials, such as phase 1 trials and trials studying non-pharmacological treatments, are not required by the FDA to report and may be missing.
- There may be trials excluded from our analysis due to missing or mislabeled keywords in the registry.

Next Steps:

- We plan to further analyze how trial sponsorship may correlate with trial rigor, publication bias, results reporting to the registry, and trial discontinuation.

Disclosures:

- All authors declare no conflicts of interest and did not receive funding for this research.