

Clinical Trials in Down Syndrome

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Introduction

- Estimates suggest that somewhere between 50-80% of individuals with DS have at least one co-occurring medical conditions¹.
- Recognizing this, in 1997 the NIH committed \$3 million dollars in funding to DS-specific clinical trials (CTs)². Funding remained somewhat steady from 1997-2017.
- In 2018, the NIH launched the INCLUDE project, contributing to progressive increases in funding for research in DS through 2024³.
- These projects could improve the quality of life and overall health of individuals with DS. They could also provide insight into these co-occurring conditions for individuals without DS. The INCLUDE project has increased funding supporting CTs for individuals with DS from an average of \$23.2 million per year to \$85.7 million per year post-INCLUDE³.

To identify research opportunities, it is beneficial to examine the impact of the INCLUDE project on the number of and types of clinical trials receiving funding in the field of DS.

Methods

Searched ClinicalTrials.gov with the terms “Down”, and “Trisomy 21” for trials registered 1999-2024. Studies were reviewed for meeting criteria as a CT (used an intervention to target a biomedical health or behavioral condition in humans) and inclusion of individuals with DS.

PROCEDURE:

CTs were grouped and summarized by target condition. Across target condition we described:

- Sample characteristics:** number of clinical trials, age range, sample size, % including those with mosaic DS
- Study design:** duration of study, trial design, type of intervention, trial phase
- Productivity:** % of trials complete, % of trials with published results

Results

389 trials > 138 trials > 11 target conditions

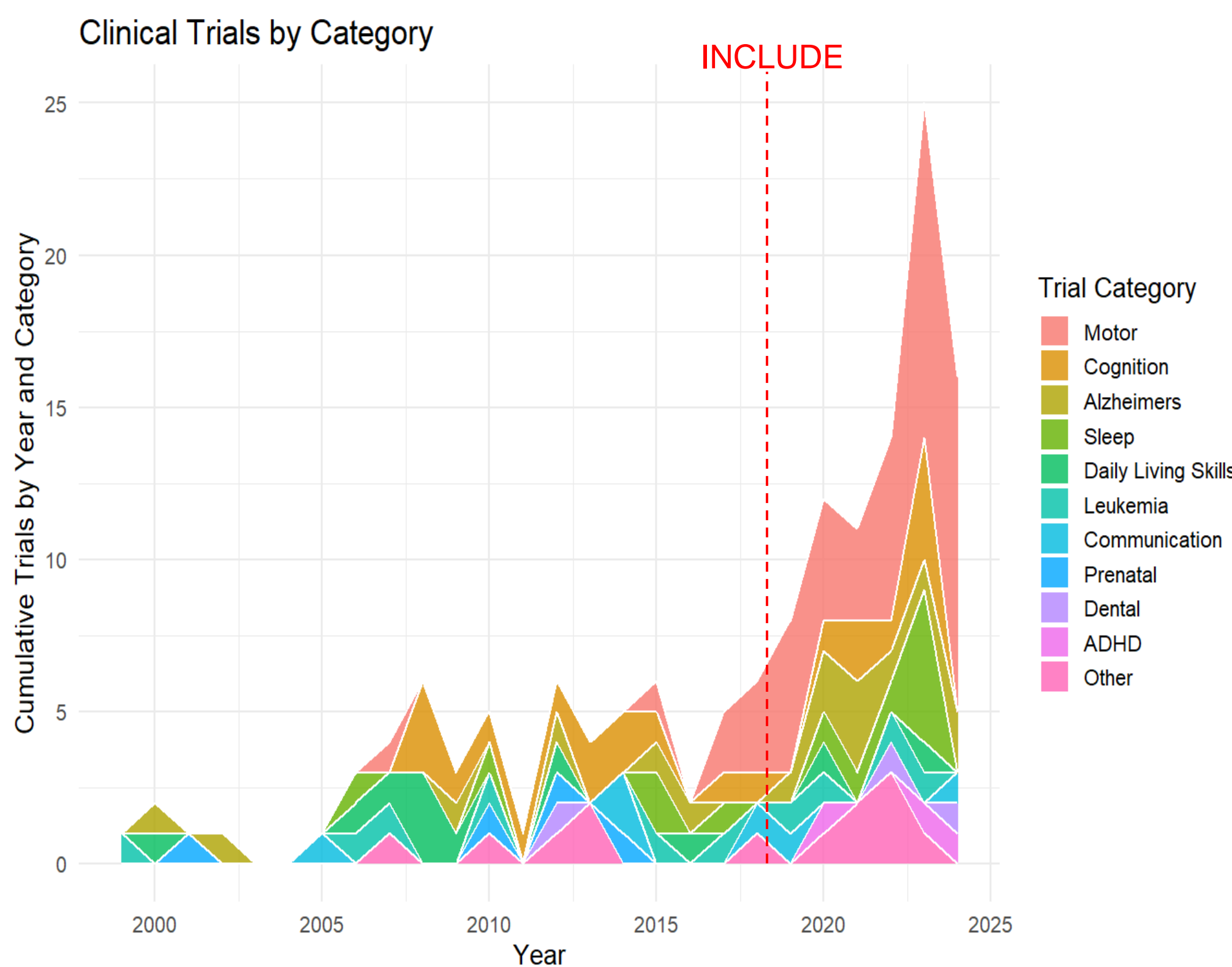
Search yielded 389 studies. Only 138 registered studies were true CTs and related to DS. Across these, 11 target conditions emerged.

Trials Per Year by Target Condition Pre and Post INCLUDE				
	n	Pre- INCLUDE		Post- INCLUDE
TOTAL	138	3.11(2.18)	↑	12.13(7.59)
Motor Functioning	46	0.21(0.54)	↑	5.38(3.89)
Cognition	24	0.68(0.89)	↑	1.13(1.36)
Alzheimer's	17	0.32(0.92)	↑	1.38(0.92)
Sleep	13	0.26(0.56)	↑	1.0(1.69)
Daily Living Skills	11	0.47(0.77)	↓	0.25(0.46)
Leukemia	10	0.26(0.45)	↑	0.63(0.52)
Communication	7	0.21(0.54)	↑	0.25(0.46)
Prenatal	4	0.21(0.42)	↓	0(0.00)
Dental	3	0.05(0.23)	↑	0.25(0.46)
ADHD	3	0(0.00)	↑	0.38(0.52)
Other	13	0.26(0.56)	↑	1.0(1.07)

- Other (any target condition with <3 CTs) included: DS Regression Disorder (n=2), hypothyroidism (n=2), quality of life (all remaining n=1), bone metabolism, oxygenation, pharmacokinetics, infection, dermatology, hematology, mental health, and vision.

Discussion

- CTs spanned both well documented (motor functioning) and emerging (regression disorder) areas of DS research. The total # of CTs, average # of CTs per year, and diversity of CTs all increased post-INCLUDE, suggesting a positive impact of INCLUDE funding on CTs in DS.
- There was growth in the number of CTs across many target condition post-INCLUDE. The most dramatic increase in CTs occurred across motor skills.



Future Directions

- <10% of CTs specifically included individuals with mosaicism. Several co-occurring conditions are more common for individuals with mosaicism compared to other causes of DS⁴. Inclusion of these individuals in CTs warrants attention.
- Several common co-occurring conditions were not addressed (e.g. Autism⁵) as well as those with low-incidence rates (e.g. chronic pain, gout⁶). More work is needed here.
- Treatment across target conditions generally utilized therapeutic or pharmacological intervention. Opportunities exist for the use of AI/machine learning in treatment.

Limitations

- Some funding bodies and institutions do not require CTs to be registered. CTs have likely been conducted that are not reported on ClinicalTrials.gov.
- Information on ClinicalTrials.gov is provided by CT sponsors and investigators. It may not be perfectly accurate or up-to-date.

Trial Characteristics by Target Condition									
	Sample Characteristics			Study Design				Productivity	
	Age Range (years)	Sample Size M(SD)	% Including Mosaic	Duration (months) M(SD)	Randomized, Blinded/Open Label/Other	Therapeutic/ Medical/Other	Phase1/Phase2/ Phase3/Phase4/ NA*	% Completed Trials	% Published
Motor Functioning	0-69	40.0(29.1)	0%	3.6(3.9)	35/10/1	45/1/0	0/0/0/46	72%	33%
Cognition	0-80	76.3(7.1)	8%	5.2(3.9)	21/3/0	6/18/0	5/14/4/1/4	63%	62%
Alzheimer's	14-≥ 50	109.5(103.6)	6%	21.7 (14.6)	3/14/0	5/12/0	5/6/3/1/4	35%	82%
Sleep	0->18	68.1(78.5)	0%	9.5(10.0)	11/2/0	9/4/0	0/2/0/0/11	38%	46%
Daily Living Skills	0-17	141.5(107.2)	27%	9.4(10.8)	9/2/0	3/8/0	1/4/4/0/4	64%	55%
Leukemia	0->22	1499.6(2522.9)	50%	27.6(21.7)	1/9/0	0/9/1	2/3/6/0/0	20%	50%
Communication	0-21	49.1(42.8)	0%	6.8(3.5)	4/3/0	6/1/0	0/2/1/0/4	57%	57%
Prenatal	16-60	7023.5(12027.1)	NA	NA	0/0/4	0/4/0	1/0/0/0/3	100%	100%
Dental	4-70	26.7(11.6)	0%	8.7(9.3)	3/0/0	1/2/0	1/2/0/0/1	66%	100%
ADHD	6-24	76.0(21.2)	0%	4.1 (2.9)	3/0/0	0/3/0	1/1/0/1/0	0%	0%
Other	0->18	91.7(132.5)	8%	8.2(7.9)	4/9/0	4/7/2	1/4/2/2/4	69%	69%

Sources and Funding

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