Pediatric Autoimmune Clinical Trial Discontinuation and Non-publication: an Analysis of the National Library of Medicine

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BACKGROUND

- The prevalence of pediatric autoimmune diseases has continued to rise in the previous decade.[1]
- Autoimmune diseases often require complex treatment options that pose challenges to healthcare professionals.
- These obstacles are often met via initiation of clinical trials. The NIH annually invest approximately $1.0 billion to autoimmune research alone.[2]
- The pediatric population poses a multitude of barriers regarding trial enrollment and initiation.[3-5]
- These barriers often result in nonpublication, delayed medical advancements, unnecessary risk, and the squandering of research funds.[6-9]

OBJECTIVES

- Our objectives assessed the characteristics and rates of discontinuation of pediatric autoimmune clinical trials registered with the National Library of Medicine between 2008 and 2021.

METHODS

- Using ClinicalTrials.gov, we performed a cross-sectional study on all pediatric autoimmune clinical trials conducted from 2008 to 2021.
- Trials included in our study were pediatric autoimmune clinical trials with an interventional treatment.
- The following data was extracted: the trial's phase, intervention, autoimmune disease type, trial status, and intervention type.
- We then assessed rates of discontinuation by trial characteristics.
- Lastly, we determined the rates of publication versus nonpublication of completed and discontinued trials.

Results

- From our search, 2009 trials were initially returned, of those 1098 met inclusion criteria.
- The most commonly studied autoimmune disease types were type 1 diabetes (664/1098, 60.5%) and arthritis (164/1098, 15.0%). The most common intervention was pharmacologic (542/1098, 49.4%) (Table 1).
- We found that 17.1% (188/1098) of studies were discontinued and 18.9% (207/1098) were completed.
- 395 trials had a status of completed or discontinued – 91.3% (189/207) of completed trials and 81.9% (154/188) of discontinued trials did not have preliminary results published (Table 2).

	Complete No. (%)	Active No. (%)	Enrolling No. (%)	Discontinued No. (%)	Total No. (%)	Test
Disease Type						
Anemia	3 (33.33)	1 (11.11)	5 (55.56)	0 (0)	9 (0.82)	
DM I	101 (15.21)	36 (5.42)	420 (63.25)	107 (16.11)	664 (60.47)	
HIV	2 (40)	0 (0)	3 (60)	0 (0)	5 (0.46)	
Lupus	12 (33.33)	1 (2.78)	17 (47.22)	6 (16.67)	36 (3.28)	
PANDAS	2 (28.57)	0 (0)	3 (42.86)	2 (28.57)	7 (0.64)	
Thrombocytopenia	9 (20.93)	1 (2.33)	25 (58.14)	8 (18.6)	43 (3.92)	
arthritis	30 (18.18)	10 (6.06)	98 (59.39)	27 (16.36)	165 (15.03)	
celiac	7 (25)	0 (0)	13 (46.43)	8 (28.57)	28 (2.55)	
dermatmyositis or (..	1 (12.5)	0 (0)	6 (75)	1 (12.5)	8 (0.73)	
other	25 (30.12)	5 (6.02)	33 (39.76)	20 (24.1)	83 (7.56)	*X^2(30) = 44.68, P = .041*
sclerosis	15 (30)	3 (6)	23 (46)	9 (18)	50 (4.55)	
Intervention Type						
Behavioral (Device)	15 (17.65)	6 (7.06)	58 (68.24)	6 (7.06)	85 (7.74)	
Behavioral (Mental)	33 (21.15)	9 (5.77)	87 (55.77)	27 (17.31)	156 (14.21)	
Behavioral (Physical Activity)	7 (20.59)	2 (5.88)	20 (58.82)	5 (14.71)	34 (3.1)	
Device (Medical)	34 (17)	11 (5.5)	125 (62.5)	30 (15.00)	200 (18.21)	
Drug	101 (18.63)	25 (4.61)	313 (57.75)	103 (19.00)	542 (49.36)	
Other	15 (23.81)	3 (4.76)	31 (49.21)	14 (22.22)	63 (5.74)	*X^2(18) = 14.47, P = .70*
Surgical Technique	2 (11.11)	1 (5.56)	12 (66.67)	3 (16.67)	18 (1.64)	
Funding Source						
Industry	58	25	202	47	332	
US Federal Grant	19	7	104	18	148	
Other	130	25	340	123	618	*X^2(2) = 2.2, 0.32*

Table 1: Clinical trials for pediatric autoimmune diseases and intervention types by trial status.

	Total No. (%)	Not Published No. (%)	Published No. (%)	Test
Disease Type				
Anemia	3 (0.76)	3 (100.00)	0 (0.00)	
DM I	208 (52.66)	180 (86.54)	28 (13.46)	
HIV	2 (0.51)	1 (50.00)	1 (50.00)	
Lupus	18 (4.56)	16 (88.89)	2 (11.11)	
PANDAS	4 (1.01)	3 (75.00)	1 (25.00)	
Thrombocytopenia	17 (4.3)	16 (94.12)	1 (5.88)	
arthritis	57 (14.43)	49 (85.96)	8 (14.04)	
celiac	15 (3.8)	13 (86.67)	2 (13.33)	
dermatmyositis or (..	2 (0.51)	2 (100.00)	0 (0.00)	
other	45 (11.39)	38 (84.44)	7 (15.56)	
sclerosis	24 (6.08)	22 (91.67)	2 (8.33)	*Fisher's exact = .85*
Intervention Type				
Behavioral (Device)	21 (5.32)	17 (80.95)	4 (19.05)	
Behavioral (Mental)	60 (15.19)	47 (78.33)	13 (21.67)	
Behavioral (Physica..	12 (3.04)	12 (100.00)	0 (0.00)	
Device (Medical)	64 (16.2)	59 (92.19)	5 (7.81)	
Drug	204 (51.65)	178 (87.25)	26 (12.75)	
Other	29 (7.34)	25 (86.21)	4 (13.79)	
Surgical Technique	5 (1.27)	5 (100.00)	0 (0.00)	*Fisher's exact = .24*
Funding Source				
Industry	105 (26.58)	93 (88.57)	12 (11.43)	
US Federal Grant	37 (9.37)	31 (83.78)	6 (16.22)	
Other	253 (64.05)	219 (86.56)	34 (13.44)	*Fisher's exact = .72*
Completion Status				
Complete	207 (52.41)	189 (91.30)	18 (8.70)	
Discontinued	188 (47.59)	154 (81.91)	34 (18.09)	Fisher's exact = .007

Table 2: Publication status of clinical trials for pediatric autoimmune among those whose status was completed or discontinued (n=395)

CONCLUSION

- Our results suggest an alarming rate of discontinuation and non-publication among pediatric autoimmune clinical trials.
- Trial discontinuation is warranted under certain conditions, however the most common reasons are often preventable.[8,10]
- The rates of discontinuation and non-publication may exacerbate barriers to pediatric trials and reveal how subjects' rights are not validated as outlined in The Declaration of Helsinki.[11]
- We urge the AAP, NICHQ, and other institutions to formalize accountability for researchers through process and policy.

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