

Understanding the drivers of placebo response in Atopic Dermatitis: A meta-analysis of randomized controlled clinical trials

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Learning Objectives:

- To quantify and understand factors driving the the placebo effect
- To provide an understanding of role protocol design, such as the use of topical anti-inflammatories

Take Aways:

- In trials of systemic medication for atopic dermatitis, placebo rates are higher in trials that allow use of topical anti-inflammatory agents
- The placebo rates have increased over time, when considering trial start dates

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Methodology

Study Design:

- 68 studies from a meta-analysis of systemic immunomodulatory treatments for AD
- Only studies with a placebo arm where EASI 75 was measured were included

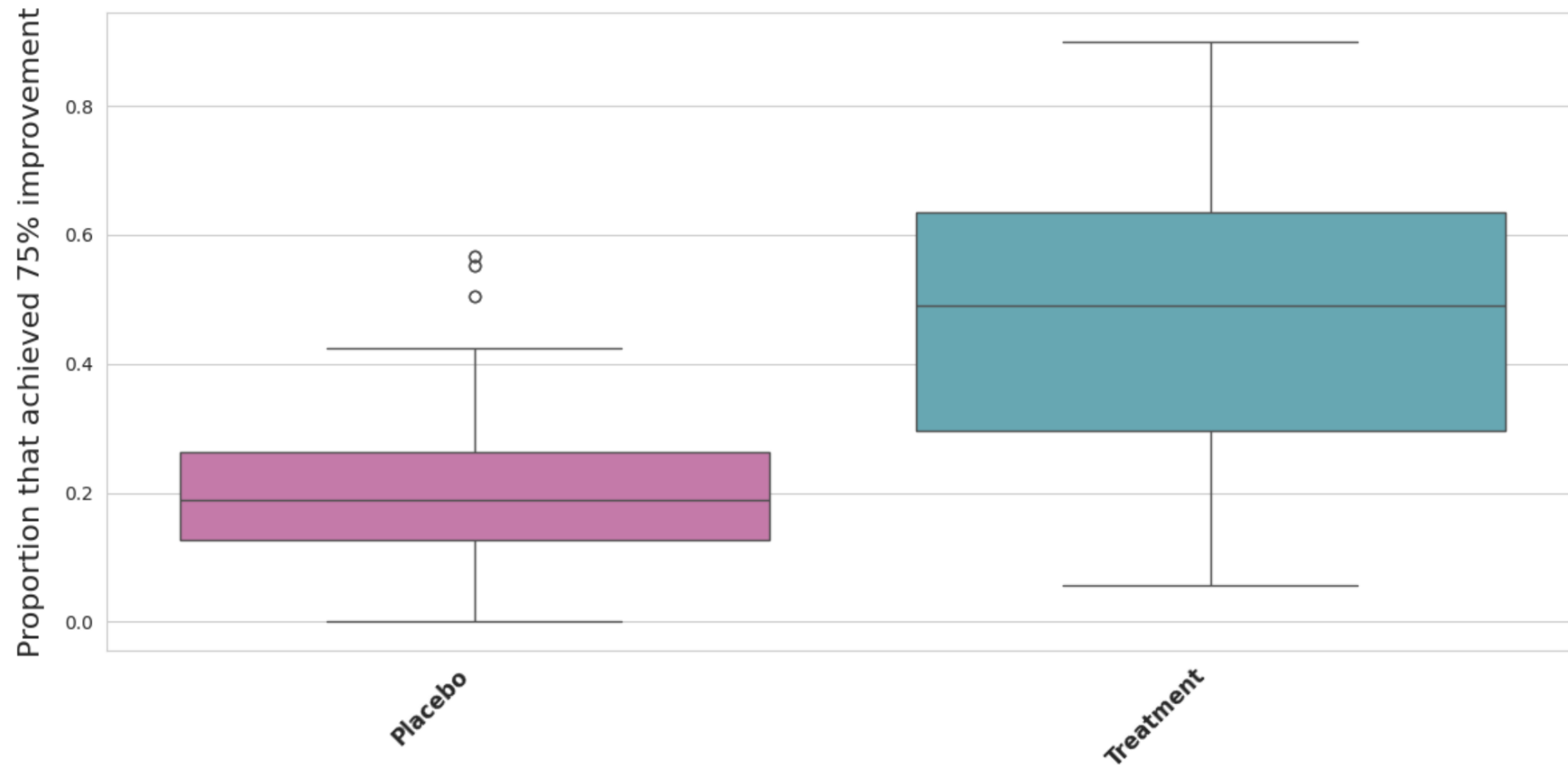
Outcome:

- Proportion of patients in placebo arm achieving 75% improvement in EASI score

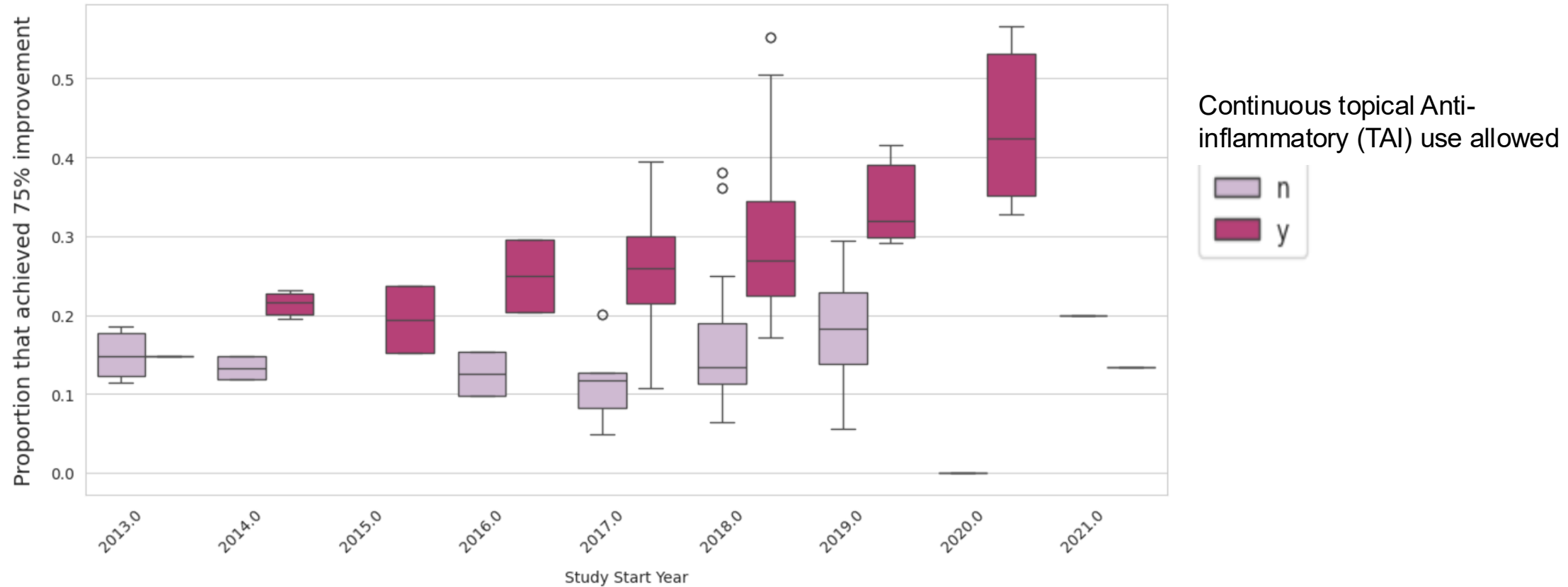
Analysis:

- Multivariate linear regression model, with a 5% level of significance.
- Predictors: Topical anti-inflammatory use, systemic drug class (biologic, JAK inhibitor, traditional, or other), study start date, trial duration, blinding, baseline disease severity and patient age (pediatric, adults or both).

Distribution of Outcome by Treatment Arm



Distribution of Placebo Rates over time, stratified by use of TAI



*Topical Anti-inflammatory (TAI) use based on whether study allowed continued use during study vs use as-needed/rescue

Regression Results : Placebo Rates (PR)

	PR Est. (95% CI)
Intercept	12% (5.7, 19.2)
Topical anti-inflammatory use: No (Ref) Yes	- 16% (13.0, 19.0)
Study Start Year: (Ref. 2013)	
2014	-12.9% (-23.8, -0.2)
2015	-3.3% (-15.9, 9.3)
2016	-0.6% (-9.3, 8.2)
2017	2.1% (-4.6, 8.8)
2018	4.3% (-0.2, 10.9)
2019	4.0% (-4.2, 12.3)
2020	23% (13.3, 33.2)
2021	9.2% (-3.4, 21.7)

16% higher placebo rates for studies allowing topical anti-inflammatory use

Studies started after 2016 trended towards higher placebo rates. Placebo rates were 22% higher in 2020 than in 2013

Regression Results : Placebo Rates (PR)

	PR Est. (95% CI)
Duration (in weeks)	-0.02% (-0.2, 0.2)
Age group: (Ref. Adults only)	
Both (pediatric and adults)	2.5% (-7.8, 2.8)
Pediatric only	0.6% (-6.1, 4.9)
Disease severity: (Ref. High)	-
Low	1.2% (-3.8, 6.3)
Medium	2.7% (-1.7, 7.1)
Drug Class: (Ref. Biologics)	
JAK inhibitor	-3.3% (-7.4, 0.7)
Other	13.3% (3.0, 26.2)
Traditional	-8.6% (-23.2, 6.1)

Few statistically significant difference in placebo rates when assessing duration, age groups, disease severity, or drug class

Discussion / conclusions

- In trials of systemic treatments for atopic dermatitis, placebo rates are higher in trials allowing topical anti-inflammatory treatments and have increased over time; these two variables accounted for 50% of the variance in the data
- Future research will explore drivers of increasing placebo rates in trials with later start dates
- Although clinical trials have important differences from real-world practice, data from placebo arms can help to fill gaps in our understanding of the natural history of disease activity over time

Acknowledgments



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