

An Exploratory Analysis of the Effect of the Severity Difference Between Positive and Negative Symptoms at Baseline on Last Visit Total PANSS Change From Baseline

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INTRODUCTION

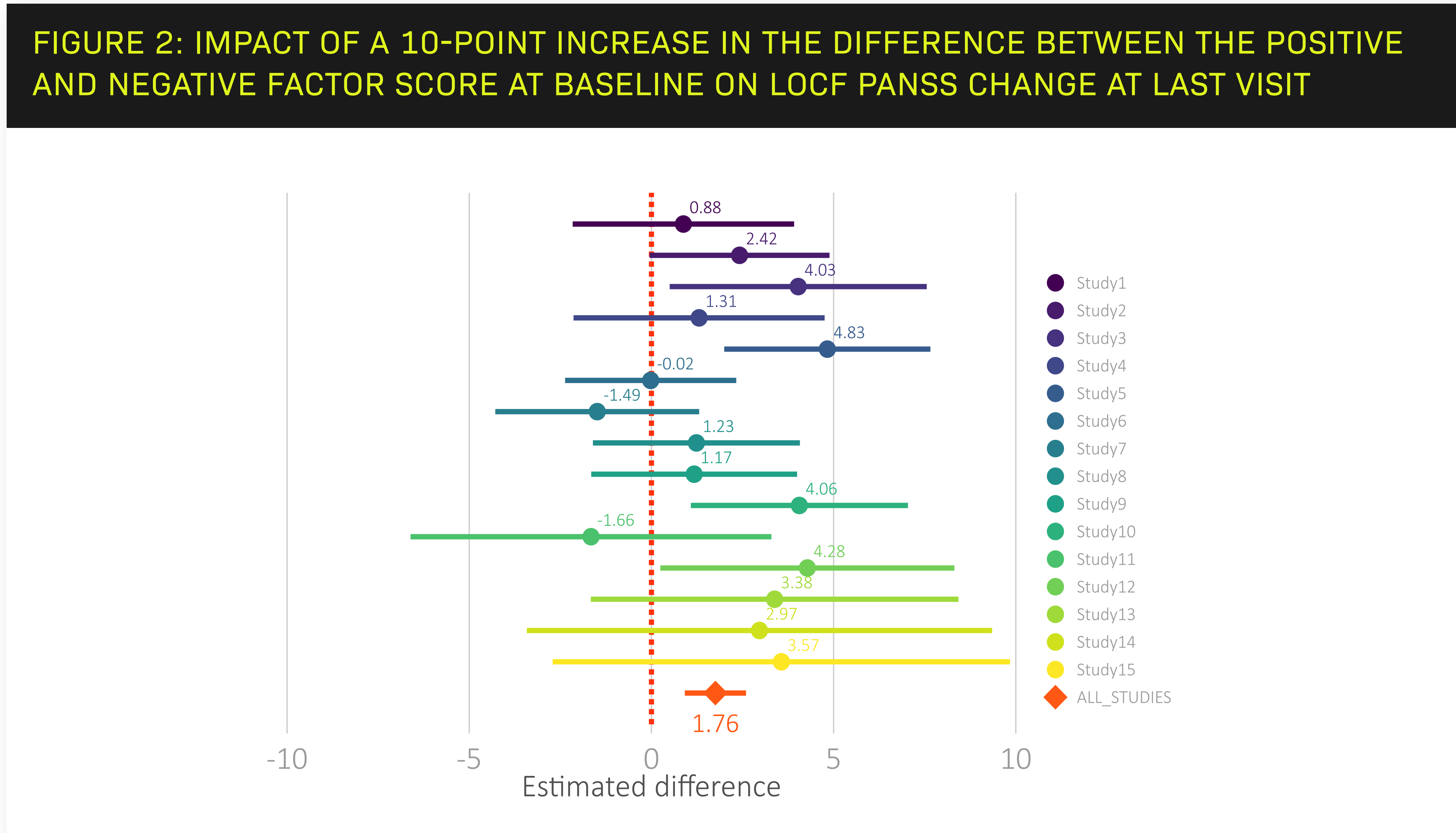
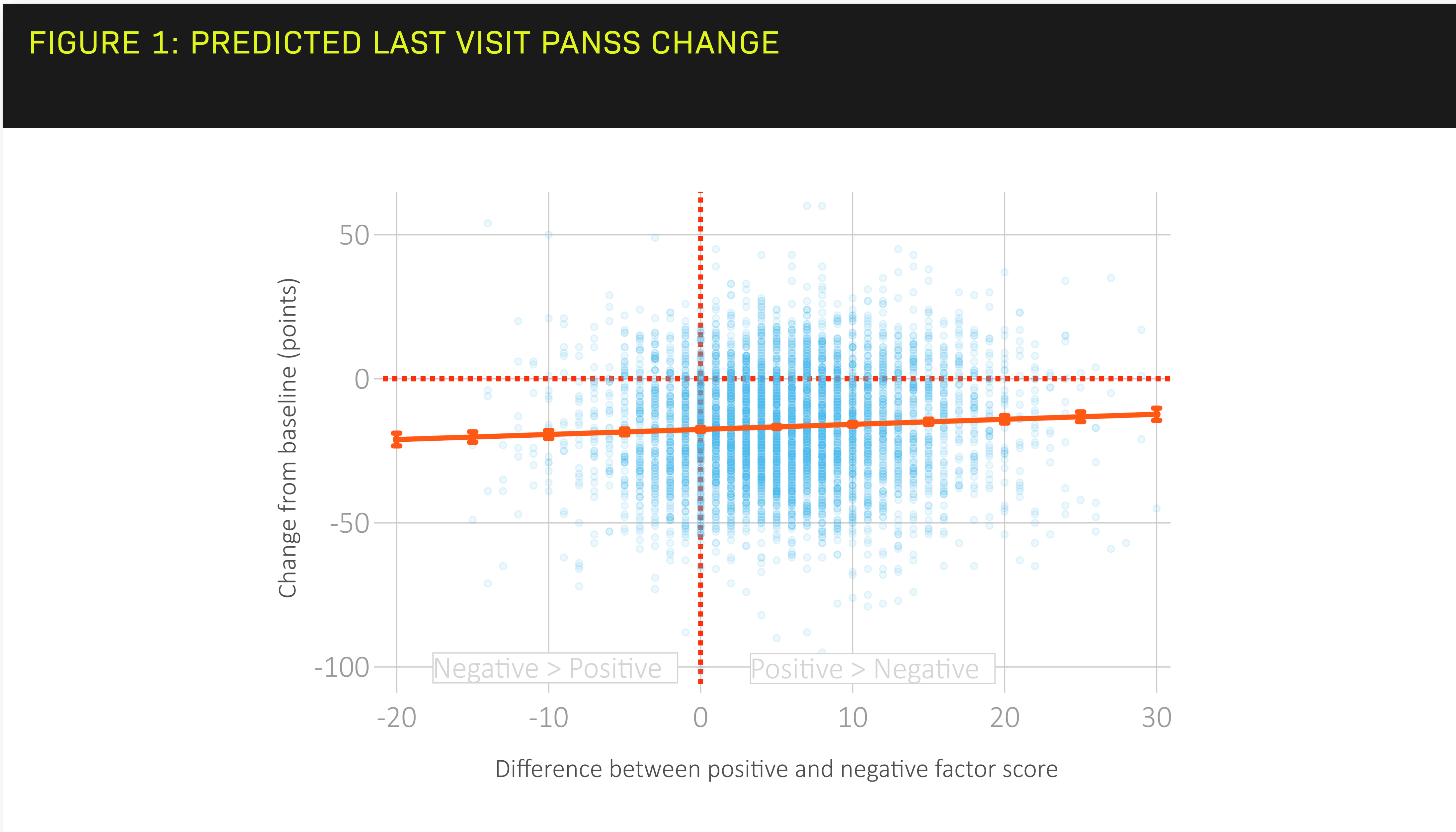
- There is evidence that subjects entering trials with greater symptom severity show larger drug response and larger drug placebo difference in acute and negative symptom trials (Furukawa, 2015; Leucht, 2019).
- We have previously reported the impact of baseline severity of negative symptoms on the end of treatment change in PANSS in acute schizophrenia studies (Kott, 2021).
- In the current analysis we expand on our prior analyses and assess the impact of baseline difference between positive and negative factor scores on end of treatment total PANSS change.

METHODS

- Baseline PANSS and last visit LOCF change from baseline in PANSS was obtained from 15 acute schizophrenia clinical trials.
- Baseline difference between the positive and negative factor scores at baseline was calculated.
- We fitted a single regression model with study included as a fixed effect.
- Additionally, we fitted individual models for each study.
- Given the exploratory nature of the analysis, no correction for multiple testing was applied.

RESULTS

- Data from 5,025 randomized subjects were included in the analysis.
- The mean baseline difference between positive and negative factor score was 5.6(+/- 6.3) points and ranged from -15 to 38 points (Figure 1).
- An increasing baseline predominance of positive factor over the negative factor decreased the last visit LOCF PANSS improvement.



DISCUSSION

- We have previously reported a positive relationship between the baseline severity of negative factor score and end of treatment improvement in the total PANSS.
- Our current findings expand on this observation by indicating that larger predominance of positive symptoms over negative symptoms decreases the end of treatment improvement in the total PANSS in the blinded data.
- While the impact is overall small and some heterogeneity was observed between individual studies, roughly a point of the overall PANSS change is lost for a 6 point difference between the positive and negative factor scores at baseline.
- This finding is to a large degree unexpected and would require confirmation in independent samples and unblinded data.
- If confirmed, it would underline the importance of the presence of negative symptoms on the likelihood of improvement in the total PANSS in acute schizophrenia trials.

REFERENCES

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- Leucht, Stefan; Chaimani, Anna; Mavridis, Dimitris; Leucht, Claudia; Huhn, Maximilian; Helfer, Bartosz et al. (2019): Disconnection of drug-response and placebo-response in acute-phase antipsychotic drug trials on schizophrenia? Meta-regression analysis. In Neuropsychopharmacology 44 (11), pp. 1955–1966. DOI: 10.1038/s41386-019-0440-6.
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