ARE SITE DIFFERENCES DRIVING OUTCOMES? THE CENTRAL ROLE OF EXPECTATIONS IN OA RCTS.

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PURPOSE:

- **RCTs** often show **differences in results across clinical sites**
- Adjusting for site effects is common, but may reduce statistical precision
 → Especially in OA trials with small site sizes
- This Post-Hoc analysis investigates the role of site disparities and expectations in the prognostic response of patients in OA trials

METHOD:

- Post-hoc analysis from a knee OA trial with 173 patients across 18 sites (site size: 2–18 patients).
- This analysis was performed on:
 - All Sites
 - Sites with at least 10 subjects (9 sites)
- Subject response was measured using WOMAC Pain response.
- Baseline expectations were measured with the MPsQ questionnaire.
- The analysis evaluated:
 - The relationship between sites and baseline expectations
 - The effects of site variability and patient expectations on outcome variance and treatment effect estimation

RESULTS

 Site-level differences accounted for only a marginal proportion of patient expectations

(17.4% for all sites and only 12.5% for larger sites)

 Site-level differences accounted for the WOMAC Pain Response to the same extent

(16.2% for all sites and only 12.7% for larger sites)

- When adjusting for patient expectations, the explanatory role of site disparities ceased to be significant
- Site-average expectations and WOMAC response strongly correlated (r = 0.54 for all sites and r = 0.73 for larger sites)
- Adjusting for sites, the precision of the treatment effect decreased (-6.3%)
- Adjusting for individual expectations, this precision increased (+15%)

CONCLUSION

- Site-related differences in patient expectations are small and possibly due to random variation.
- Patient expectations better than sites explain the variability in treatment responses.
- Adjusting for expectations is more effective than adjusting for sites in improving trial precision.
- Site adjustment may not be necessary when expectations are accounted for.
- Highlights the importance of incorporating patient-centered measures (like expectations) into RCT analyses to improve power and reduce variability.



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You should account for Individual Expectations Rather than Site Disparity



Accounting for Site Disparity Accounting for Expectations



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SUPPLEMENTARY MATERIAL

	Sites	Expectations
Explanation of WOMAC-Pain Response for all Sites (as a R ²)	16.2% (p = 0.43)	14% (p < 0.001)
Explanation of WOMAC-Pain Response for Larger Sites (as a R ²)	12.7% (p = 0.55)	13.1% (p < 0.001)
Change in precision of treatment effect estimation	-6.3%	+15%

Comparison of the performance of Sites and Expectations to improve analysis precision

This significant but small relationship between Sites and Expectations is consistent with our OARSI 2024 Abstract

Features Groups	R ²
Psychological Subject Profile	24.65%***
Psychological Subject State	7.27%**
Contextual Subject Profile	8.67%***
Average Site Effect	<mark>18.27%***</mark>
Average Country Effect	1.17%
Interaction with Site	16.55%***
Disease Intensity	3.12%*

Variance of the Expectations explained by each group of features. (*: p<0.05, **:p<0.01, ***:p<0.001) DOI: 10.1016/j.joca.2024.02.744

Full abstract and video presentation on:

Why Covariate Adjustment Is Important?



Sample Size

Link between Study Analysis Precision and Sample Size and the role of Adjustment for Prognostic Factors