Control group design shapes treatment effects in aphasia randomized controlled trials: insights from a systematic review and meta-analysis

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1. Introduction

- ↑ in behavioral randomized controlled trials (RCTs) for aphasia[1]
- Control groups have received limited attention[2]
- Work from related fields suggests that choice of control group influences trial effect sizes[3,4,5]

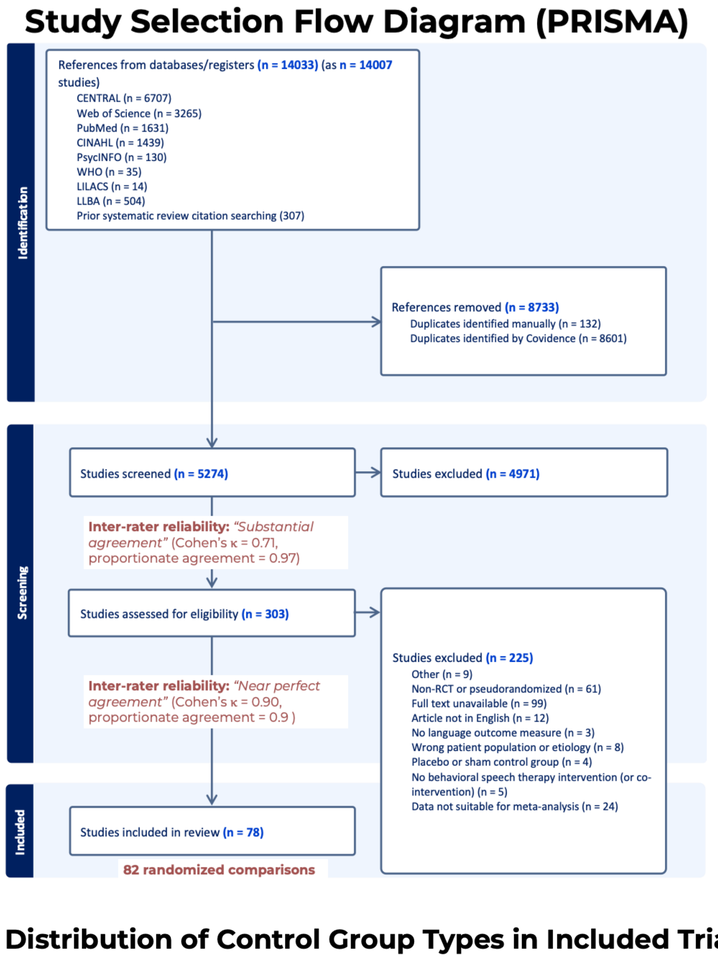
We examined whether control group design similarly shapes outcomes in aphasia RCTs.

2. Methods

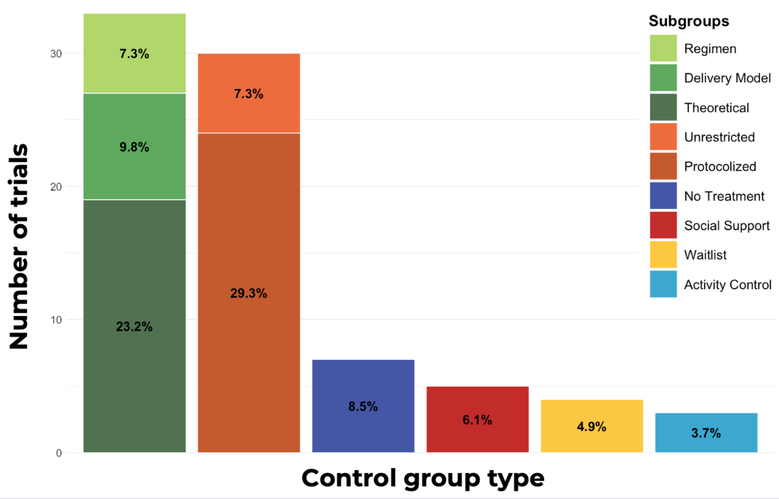
- **Design:** Systematic review and meta-analysis of RCTs evaluating behavioral language interventions for post-stroke aphasia.
- **Comparators:** Trials coded into nine predefined control types
- **Outcomes**: Three domains (severity, expressive, receptive); effect size = Hedges' g (post-treatment).
- **Models:** Pooled estimates (random effects), test for subgroup differences (Qbetween), Benjamini-Hochberg FDR correction
- **Validity checks**: Heterogeneity (Q/I^2), influence analyses, (leave-one-out), publication bias (Doi plots, LFK index), risk of bias (Cochrane Risk of Bias-1).

3. Results

Study Selection Flow Diagram (PRISMA)

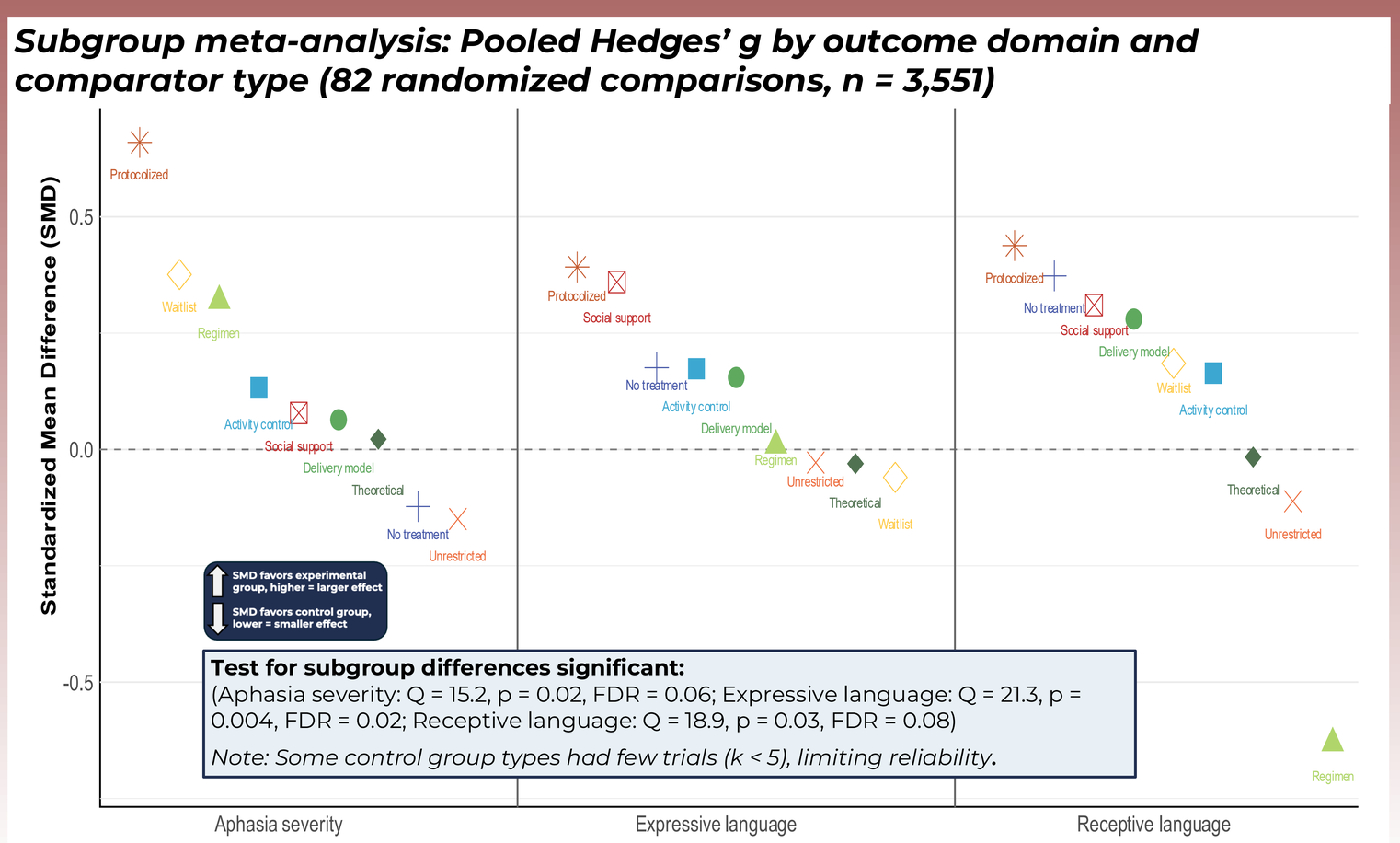


Distribution of Control Group Types in Included Trials



RCT effect sizes vary systematically by control group design: Protocolized usual care > theoretical comparators

Subgroup meta-analysis: Pooled Hedges' g by outcome domain and comparator type (82 randomized comparisons, n = 3,551)



Test for subgroup differences significant:
(Aphasia severity: Q = 15.2, p = 0.02, FDR = 0.06; Expressive language: Q = 21.3, p = 0.004, FDR = 0.02; Receptive language: Q = 18.9, p = 0.03, FDR = 0.08)

Note: Some control group types had few trials (k < 5), limiting reliability.

No treatment: No intervention during study period.
Waitlist: No treatment; intervention offered post-study.
Usual care: (a) Unrestricted routine care/services; (b) Protocolized, structured intervention reflecting typical clinical practice.
Social support: Social activities without structured tasks intended to improve language ability.
Active comparator: Alternative intervention differing in (a) theoretical approach (e.g., phonological vs. semantic), (b) delivery model (e.g., in person vs. virtual), or (c) regimen (e.g., high vs. low intensity).
Activity control: Structured cognitive exercises without targeted language therapy components.

4. Discussion & Conclusion

1. **Similarly labeled controls (i.e., 'usual care') vary widely in content and dosage.** *Leads to **vastly different trial effect sizes**: protocolized usual care g=0.39–0.66 (expressive k=18; receptive k=15; severity k=17; CIs exclude 0), whereas unrestricted usual care g=−0.15 to −0.03 (severity k=2; receptive k=3; expressive k=4; wide CIs).*

2. **Control groups receiving language therapy do not uniformly reduce effect sizes.** ***Protocolized usual care shows relatively larger trial effects*** *(g=0.39–0.66; k=15–18; CIs≠0)* ***vs theoretical active comparators*** *≈0 (g=−0.03 to 0.02; k=7–15); other active comparators are more variable (delivery g≈0.06–0.28, k=5–7; regimen g≈−0.63–0.32, k=1–4) with wide CIs (small k).*

3. **Passive controls are infrequently used and inconsistently implemented.** *Leading to **variable and underpowered estimates** : no-treatment g=−0.12 (severity k=2), 0.18 (expressive k=4), 0.37 (receptive k=3), 0.49 (functional k=3); waitlist g=0.38 (severity k=1), −0.01 (expressive k=4), 0.19 (receptive k=3), −0.02 (functional k=1) — wide CIs*

4. **Social support and activity controls may isolate common factors (e.g., attention, social and cognitive engagement) but are underutilized.** *Underutilized → underpowered (k=2–3), but both control types showed positive effects: social support (g≈0.08–0.36) > activity control (g≈0.08–0.13).* ***Suggests graded change associated with attention/engagement/expectancy contributions.***

5. Limitations & Future Directions

- Small number of studies in some control group categories limits precision.
- Diversity of experimental interventions adds complexity.
- Gaps in methodological reporting complicate interpretation and synthesis.
- Limited functional communication outcomes reported.
- **Comparator selection should reflect trial phase and purpose.**

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Scan for more information about this work and other research at our center!

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