Delfini "Within-Patient Design" Critical Appraisal Considerations in the Context of Hyperhidrosis

A sizable number of hyperhidrosis studies utilize "within-patient designs" (see other **synonyms** below) in which a subject serves as his or her own control. The evaluation of these studies does not lend itself to checklist considerations in the same way as in a primary superiority trial—although all checklists should be used as guidance only as all studies are contextual.

Key consideration is always: **what can explain the results other than truth**. Below is a list of considerations that may be useful in assessing the likely reliability of these studies and their clinical usefulness. Considerations include those obtained through review of sources on the topic (incomplete list below), considerations from our expertise and our usual critical appraisal tools: primary studies, cross-over design and safety, including the work of Austin Bradford Hill.

Considerations

#	Area	Item of Interest
1.	Considerations	Distinguish between internal and external validity considerations
2.	Initial	Outcomes should include QOL. With these studies, QOL should probably also accompany objective outcomes.
3.	Initial	Subject serving as own control makes a good match with respect to confounders. Consideration should be given as to whether baseline equity between sites is important to assess. It may not be when evaluating outcomes compared to baseline and not "differences between site and site."
4.	Design	Were useful experimental features employed in the study, such as randomization of affected patient sites? If not, was that likely to matter?
5.	Design	Is the comparator reasonable?
6.	Design	Is there a cross-over element? If yes, see Delfini critical appraisal considerations for cross-over designs.
7.	Selection	Many or most baseline characteristics are likely to be balanced in within-patient trials. For example, age, smoking, medications and dosages of medications, etc. are balanced.
8.	Performance	Evaluate the potential for co-interventions, including cross contamination or inappropriate exposure.
9.	Performance	Evaluate blinding, or lack of, and potential to affect the outcomes. And what was the likely success of blinding, if done?
10.	Performance	What is the duration of follow-up and is it appropriate? What was the duration for the outcome measure? If meant to be permanent, was it? If temporary, is there a dose/response relationship at least with respect to application of the intervention and its cessation which improves with reapplication?
11.	Performance	Were any quality control measures reported? (Examples: interobserver reliability; elimination of potential confounders; instructions to subjects, etc.)
12.	Performance	Was adherence evaluated?
13.	Assessment	Evaluate potential for attrition bias to affect results, keeping in mind subject is own control. How was loss of subjects handled and was it appropriate?
14.	Assessment	Is raw data reported?
15.	Measurement	Could seasonal effects affect the outcomes?
16.	Measurement	How often did measurement occur? Do the number of time points measured seem reasonable?
17.	Measurement	What discussion is provided about baseline variables to establish improvement? Can a baseline to measure against actually be established? If a wholly subjective outcome is being evaluated, is there confirmatory support

		in a hard outcome?
18.	Measurement	What is the validity of the measurement methods?
19.	Results	Were the results consistent, by subject, in the trajectory for the outcomes?
20.	Results	What is the length of time between application of the intervention and improvement?
21.	Results	Are there compelling patterns intra- and/or inter-study?
22.	Results	Are outcomes reported selectively?
23.	Results	If carry-over is employed, could that affect results?
24.	Considerations	Do factors for replicability matter in this specific context?
25.	Considerations	Is this a small n study? If yes, there are implications for both internal and external validity.
26.	Considerations	Safety

Synonyms

Synonyms for Within-Patient Design include—

1. Contralateral Controlled Study
2. Half-Side Comparison Study
3. Open Left-Versus-Right Side Trial
4. Right-left Comparison Study
5. Self-Controlled Case Series
6. Sham Control Study
7. Side-Controlled Study
8. Single Case Design
9. Single Subject Experimental Design
10. Single-Blinded Right-Left Comparison Study
11. Split Face
12. Within-Group Design