

Do cross-over trials give accurate results?

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Conclusions

- Cross-over studies are likely to be incorrectly analysed and thereby produce inaccurate results. This could lead to a misinterpretation of how effective the intervention was.
- In one study detailed here, the researcher reported no significant difference in the pumps tested whereas our recalculation of the data found a difference that is statistically as well as clinically relevant.
- A study design needs to follow through in the analysis if the data is to be correctly interpreted, disseminated and put into practice.

Background and Objective

A cross-over design examines within-subject differences. This design can reduce confounding variables as each participant acts as their own control. However this design is only effective if analysed using paired analysis rather than treated as parallel groups.

We examined the analysis methods and conclusions of the 13 RCTs using a cross-over design in our Cochrane systematic review¹ to determine if appropriate methods were used and the effect on interpretation of the results.

Methods

For cross-over RCTs that did not use paired analysis we calculated the mean difference (MD) and standard error (SE) of the mean difference.

Results

- 4 of the 13 cross-over studies used some form of paired analysis
- 9 of the 13 cross-over studies used statistical methods designed for parallel studies

One cross-over study examined for differences between four breast pumps with each pump used by each of the 28 mothers of infants in a neonatal unit. The published article² reported mean volume obtained with each pump and that no statistical difference was found when comparing the four breast pumps. Table 1 and Fig. 1

The researcher made her data available and we calculated the MD(SE) to examine mean within-subject differences (paired analysis). Our results indicated a significant difference that could be as large as 35% greater milk volume obtained between the highest and the lowest pump. Table 2 and Fig. 2

Table 1: Published data analysis

| Milk volume (mls) per 24 hrs Mean ± standard deviation | Pump A | Pump B | Pump C | Pump D |
|---|-----------|-------------|------------|------------|
| | 106 ± 2.6 | 110.6 ± 2.5 | 97.6 ± 2.6 | 86.0 ± 2.5 |

Fig. 1: Mean volume (mls)/24hrs

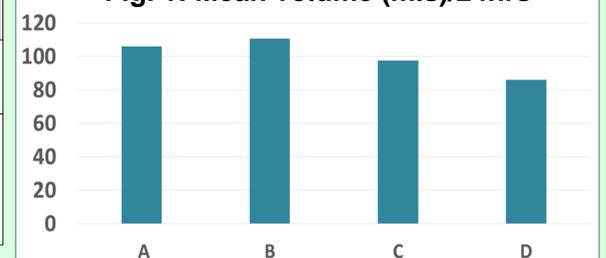
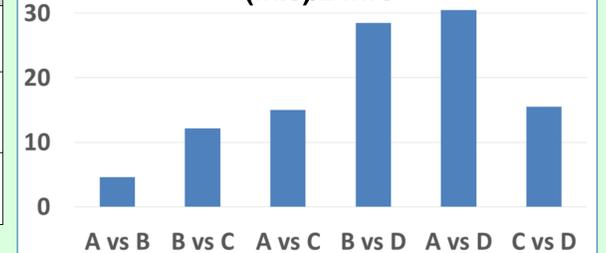


Table 2: Recalculated as paired data

| Milk vol (mls)/24 hrs Mean Difference | A vs B | B vs C | A vs C | B vs D | A vs D | C vs D |
|--|--------|--------|--------|--------|--------|--------|
| | 4.6 | 12.1 | 15.0 | 28.5 | 30.5 | 15.5 |
| Standard Error | 9.2 | 11.1 | 14.5 | 8.4 | 13.8 | 8.8 |

Fig. 2: Mean Difference in volume (mls)/24hrs



Literature cited

1. Becker GE, Smith HA, Cooney F. Methods of milk expression for lactating women. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD006170. DOI: 10.1002/14651858.CD006170.pub4
2. Bernabe-Garcia M, Lopez-Alarcon M, Villegas-Silva R, Rodriguez-Cruz M, Jimenez-Galicia C. Effectiveness of four manual breast pumps for mothers after preterm delivery in a developing country. Journal of the American College of Nutrition 2012;31(1):63–9.