UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND

RTRU
Rehabilitation Teaching & Research Unit

Death of the RCT?

Can single-case experimental research designs effectively evaluate complex health interventions?

Rachelle Martin
PhD candidate and Professional Practice Fellow,
RTRU, Department of Medicine, University of Otago, Wellington

Thanks to supervisors & consultant

Assoc Prof Will Taylor

Assoc Prof Lois Surgenor

Assoc Prof Neville Blampied (UC)

Dr Fi Graham

Rumen Manolov, Department of Behavioural Sciences Methods, University of Barcelona

UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND

RTRU
Rehabilitation Teaching & Research Unit

The RCT – strength & limitations?

Strengths

- Determine treatment effectiveness
- Reduce risk of bias
  - Control the intervention
  - Strict inclusion criteria

Limitations

- End up knowing a lot about the ‘average’ response
- Inclusion criteria can limit ability to apply findings to ‘real’ populations
- Intervention may have been too controlled – no longer representing what happens in real-world practice

Complex [rehabilitation] interventions

Characteristics

- Aim is to vary the intervention in response to changes in the recipient
  - Not applying a set of tasks/activities/techniques to a de-contextualised individual
- Involvement of humans – their choices, agency etc
- Therapeutic alliance & engagement within the process
- Often delivered over a longer period of time
  - when lots of other things are happening in their lives…
- Broader concepts of health – therefore health outcomes not able to measured so 'directly'
  - Eg BSBF outcomes may be easier to quantify than participation outcomes


Throw
the
baby
out
with
the
bath
water?

Single-case experimental designs (SCEDs)

- Prospective and intensive study of the individual who serves as his or her own control
- Repeated measurement of outcomes (dependent variables) before (baseline phase) and during the implementation (intervention phase) of the intervention (independent variable)
- Systematic comparison of the level, trend and variability of the data from each case between baseline and intervention phases permits determination of the presence or absence of any treatment effect for that case
- Evaluate who responded (and who did not respond) to the intervention under which conditions, based on individual characteristics of participants

What SCED graphs look like…

- Can reflect progress or change across time
- More nuanced understanding of empirical data
- Who did, and who didn't, respond
- Intervention continues to be delivered in a tailored fashion … rather than being limited by experimental design

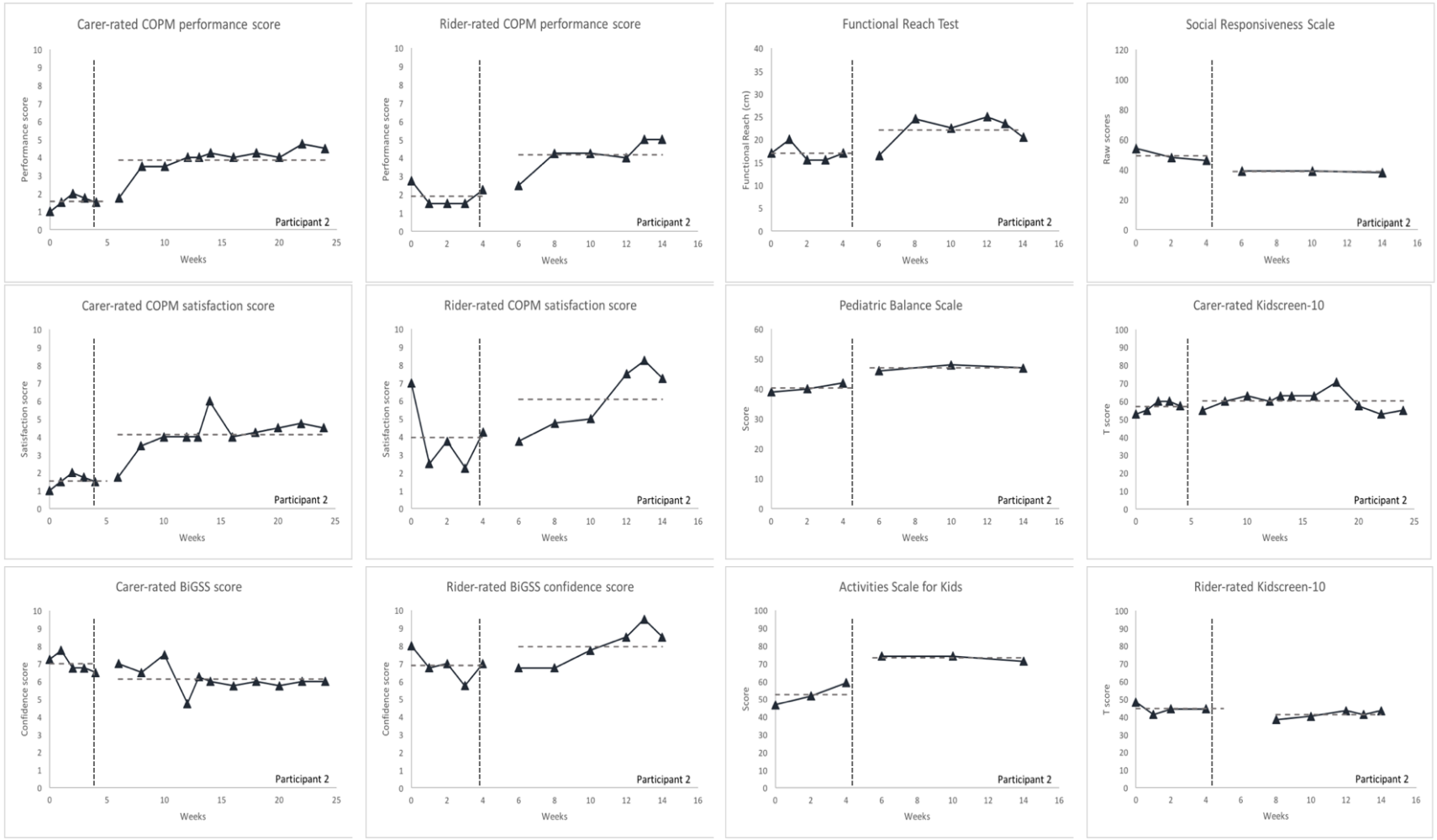


Figure 6: Participant 2 graphs per dependent variable

Internal validity?

- Oxford Centre for Evidence-Based Medicine (2011) now rank the randomised n-of-1 trials as Level 1 evidence for treatment decision purposes in individual patients, alongside systematic reviews of RCTs

- Development of quality assessment tools and reporting guidelines, aimed at improving the methodological quality, and consistency in reporting, of SCEDs.

- Development of analysis tools (R packages) and tutorials
- Publication of key papers re design and analysis

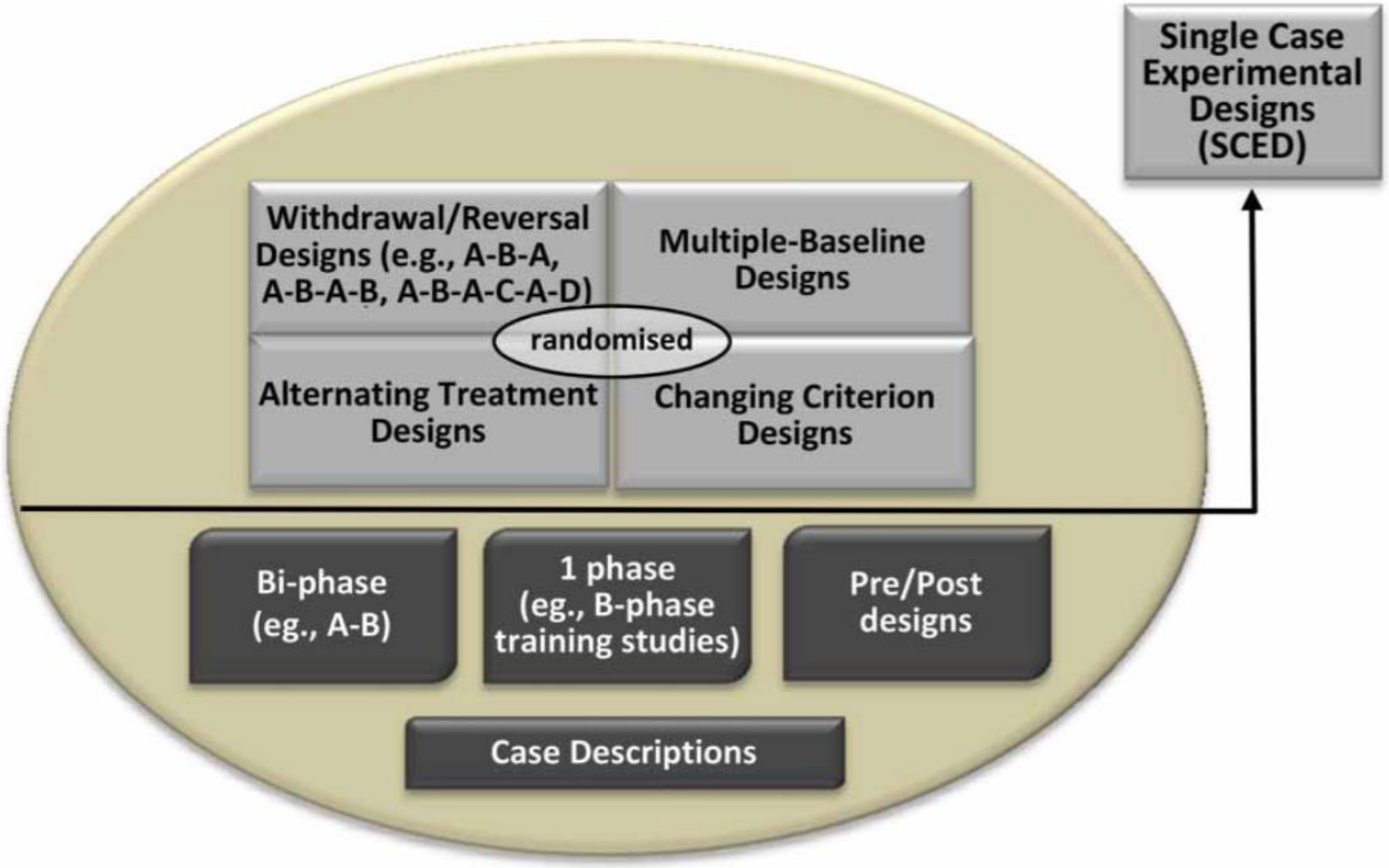


Figure 1. A taxonomy of common designs using a single participant

Robyn Tate et al. 2013

A SCED case example…

Participant 2

7 year old, male, with CP

Independent walking with frame in community settings

PBS 39/56
ASK 47/100
SRS 58

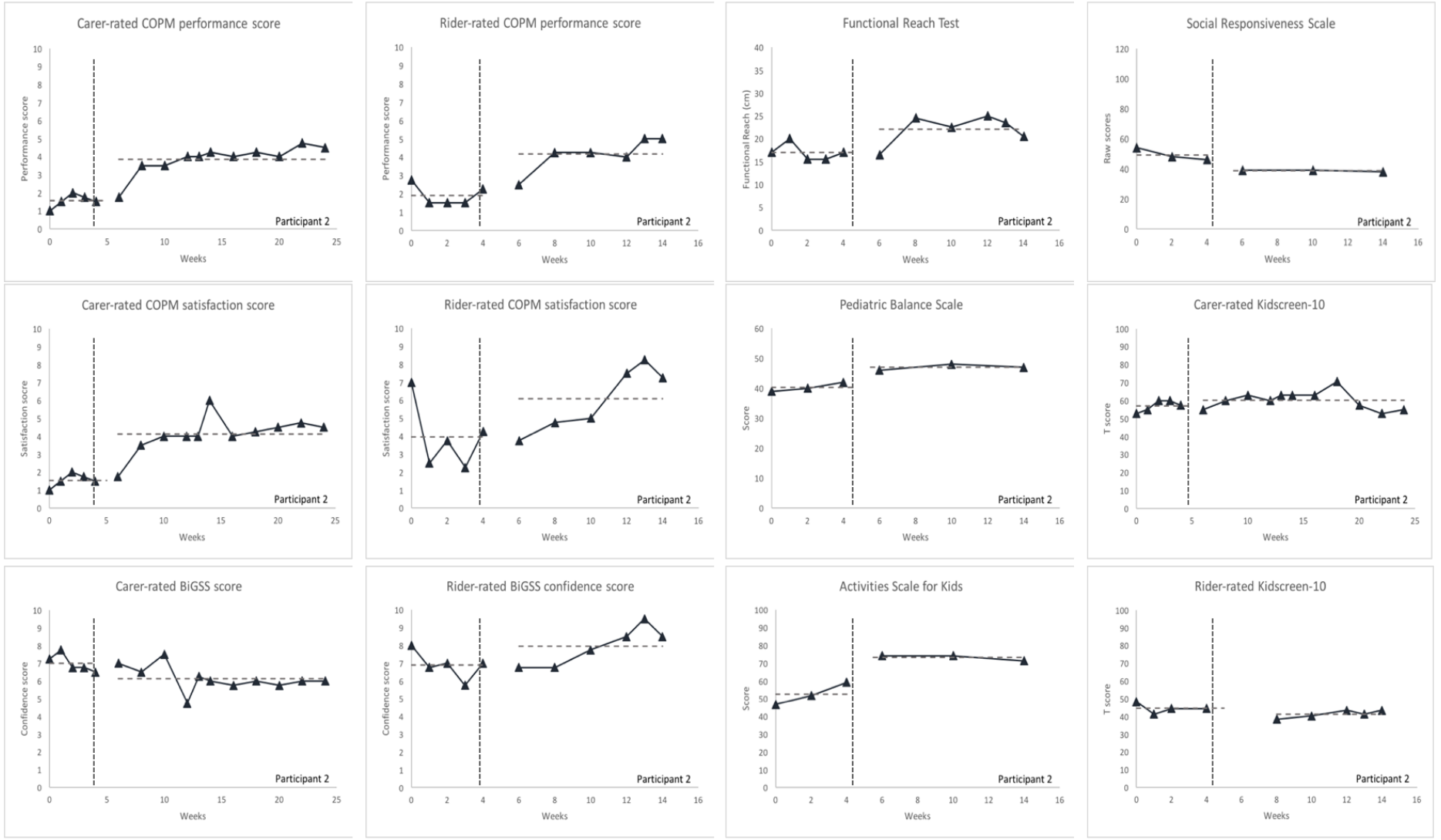
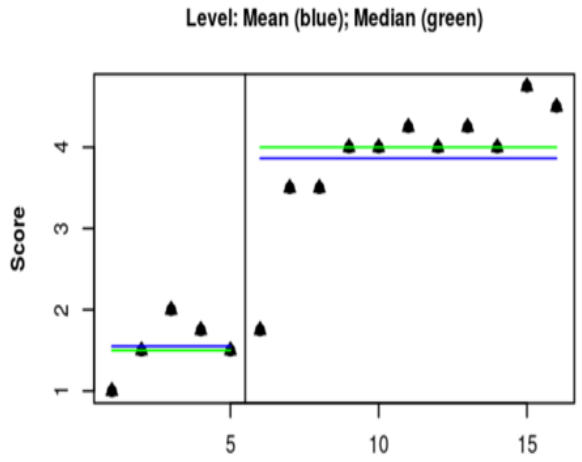
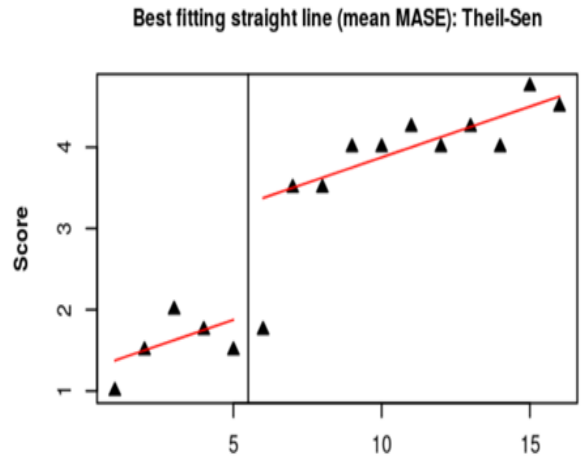
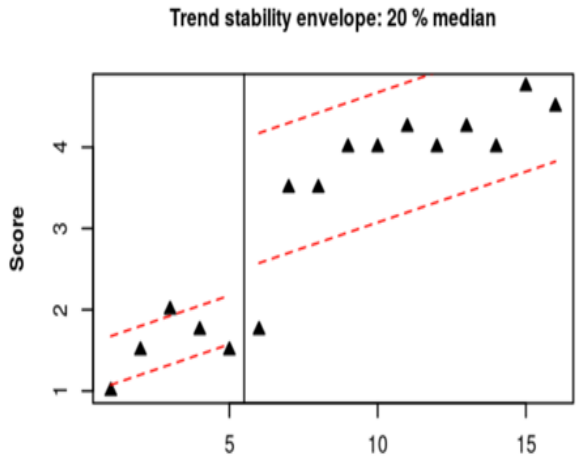


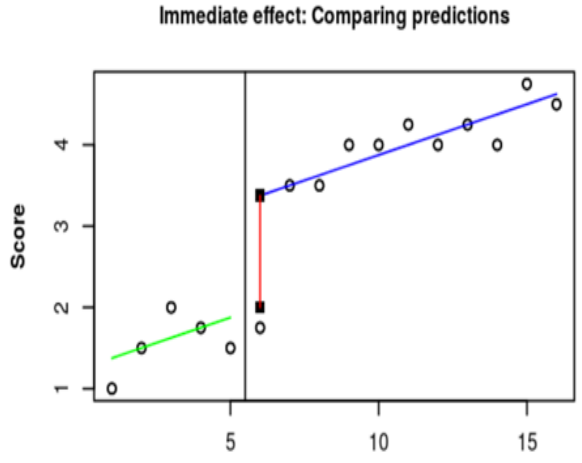
Figure 6: Participant 2 graphs per dependent variable

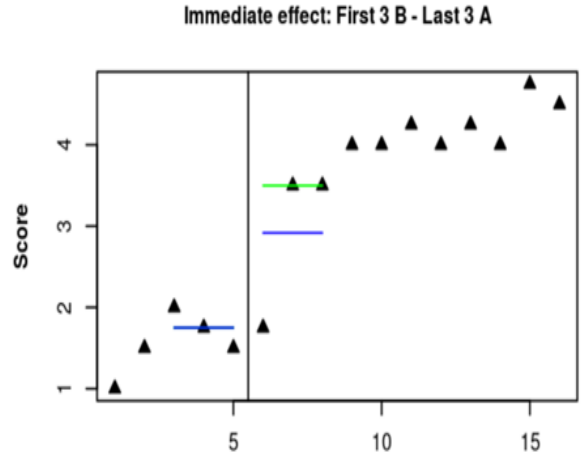
Quantification procedures for visual analysis

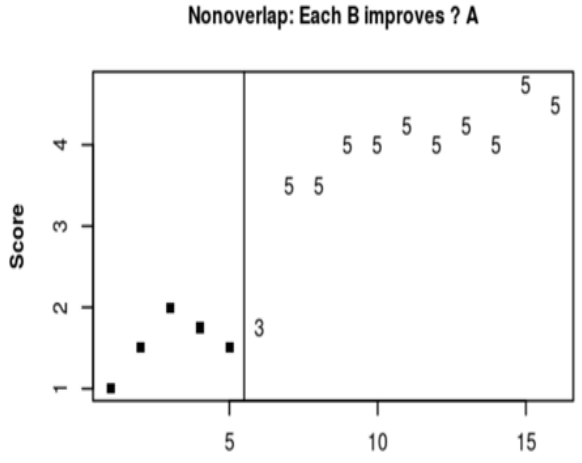




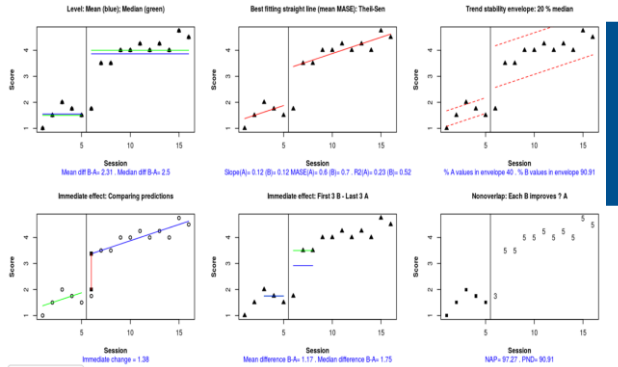








P2 visual analysis findings



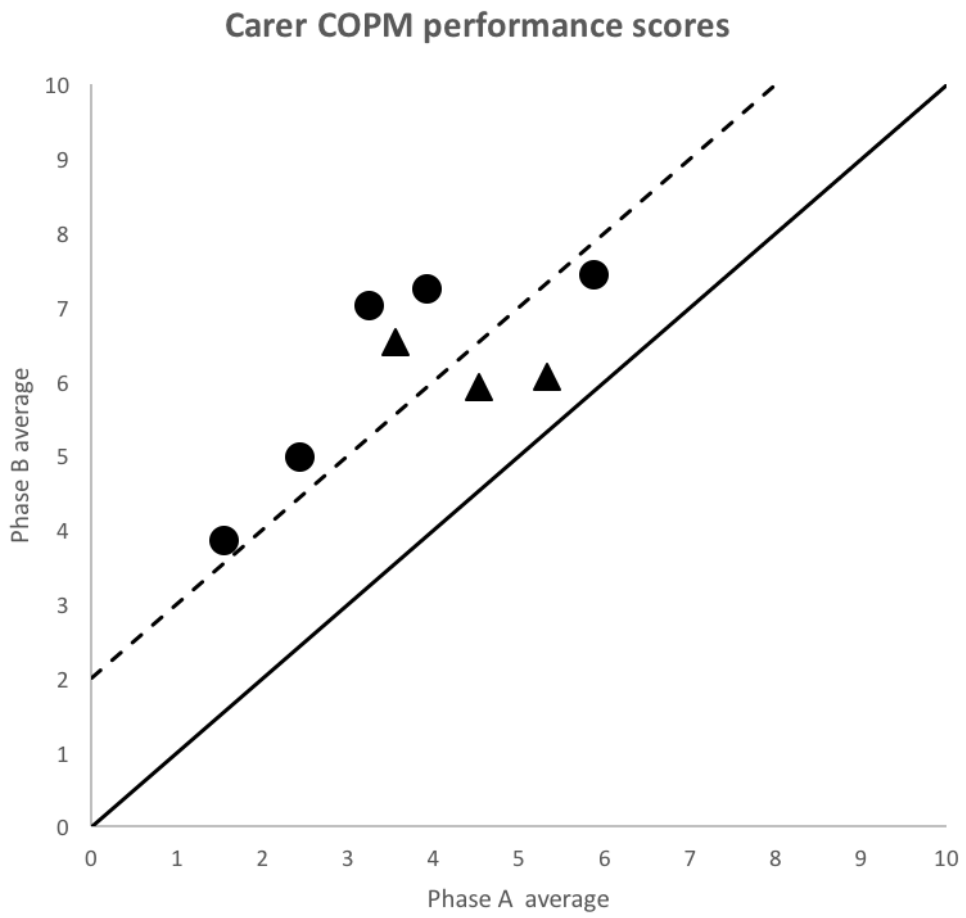
Dependent variable	Level change (Mean Difference/ Median Difference)	Slope (phase A/ phase B)	Trend stability envelope – % of data within 20% median (phase A/ phase B)	Immediate change (comparing predictions)	Immediate effect (Mean Difference / Median Difference)	Non-overlap of all pairs (NAP)	Percent of non-overlapping data (PND)	Comments	Intervention effect (yes /no)
Carer COPMp	2.31 / 2.25	0.12 / 0.12	40 /100	1.38	1.17 / 1.75	97.27	90.91	Minimal slope BL BL data variability Immediate effect Minimal data overlap	Yes
Carer COPMs	2.56 / 2.5	0.12 / 0.12	40 / 82	1.5	1.33 / 1.75	97.27	90.91	Minimal slope BL BL data variability Immediate effect Minimal data overlap	Yes
Carer BiGSS	-0.86 / -0.75	-0.22 / -0.08	100 / 91	0.3	0.33 / 0.25	13.64	0	Negative level change Significant data overlap	No
Rider COPMp	2.27 / 2.75	0 / 0.38	60 / 100	1.81	1.92 / 2.75	96.67	83.33	No slope BL but some instability of data Some overlapping data	Yes
Rider COPMs	2.13 / 2.38	-0.5 / 0.88	20 / 100	1.48	1.08 / 1	85	50	BL negative slope; unstable data Moderate data overlap	With reservations
Rider BiGSS	1.06 / 1.12	-0.38 / 0.58	100 / 100	0.79	0.5 / -0.25	73.33	50	BL negative slope Stable data	With reservations

Visual analysis comments

General comments

- Rider able to reliably score: completed with attention and consideration to score given, although data point 1 appears to be an aberration
- 'Stable' clinical presentation – no other obvious factors that could impact on study findings / evidence of intervention effect
- Clinically, most change expected in COPM, FRT, PBS and ASK dependent variables
- Carer-rated COPMp and COPMs scores improved, while the BiGSS confidence score reduced; rider-rated KS-10 demonstrates change in a negative direction; carer-rated KS-10 is dropping off at the end of the intervention as well
- ASK, PBS and SRS seem to demonstrate a tendency towards improvement in the measure in the baseline - *regression towards the mean*?

Modified Brinley Plot & effect sizes



8/8 demonstrated improvements in means between phases

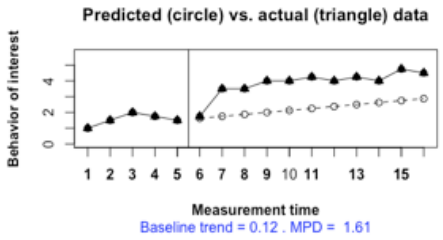
5/8 were beyond MCID

HPS *d*-statistic = effect size comparable with Cohen's *d*
Carer-rated COPM performance: ES=1.4 (variance = 0.084)

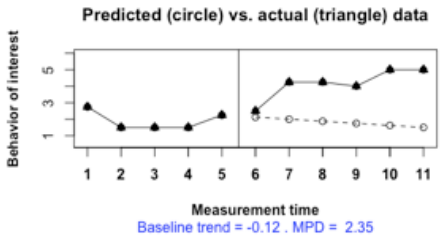
Also analysing differences between groups

UNIVERSITY of OTĀGO
Te Whare Wānanga o Otāgo NEW ZEALAND
RTRU
Rehabilitation Teaching & Research Unit

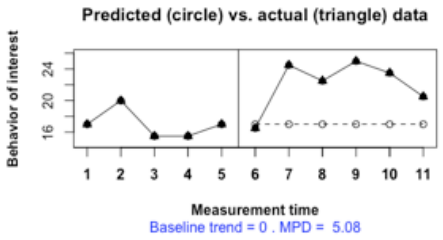
Mean Phase Difference Procedure



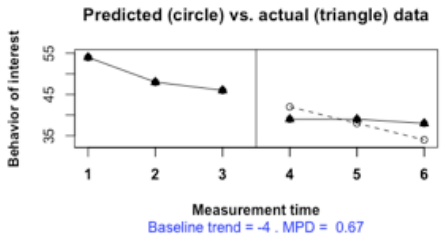
Carer COPMp



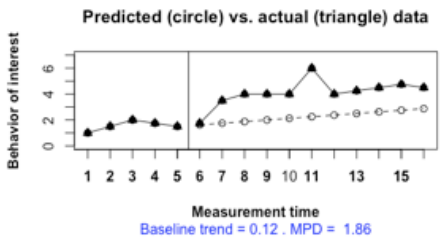
Rider COPMp



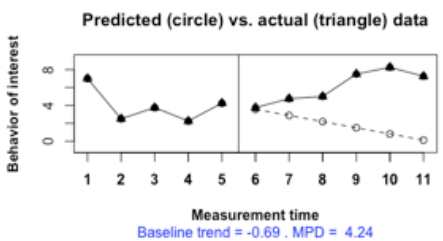
FRT



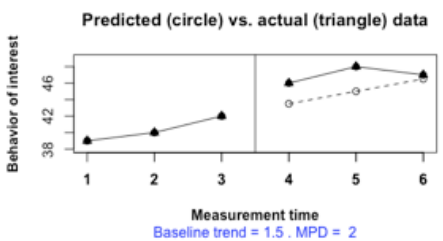
SRS



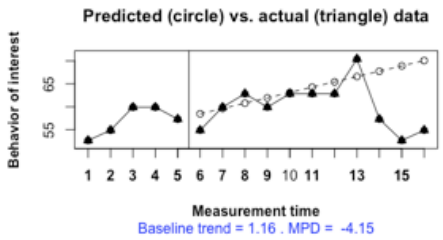
Carer- COPMs



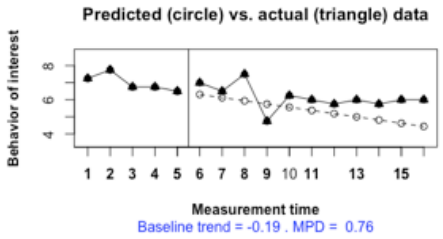
Rider COPMs



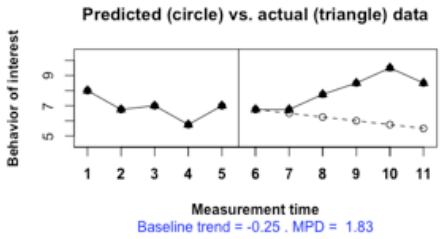
PBS



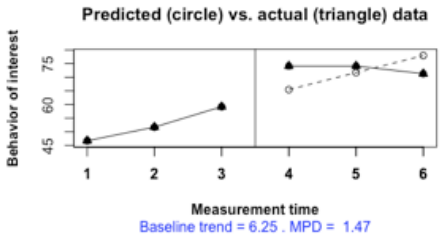
Carer KS-10



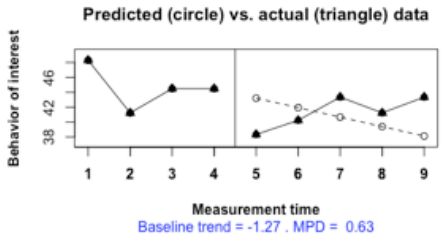
Carer BiGSS



Rider BiGSS

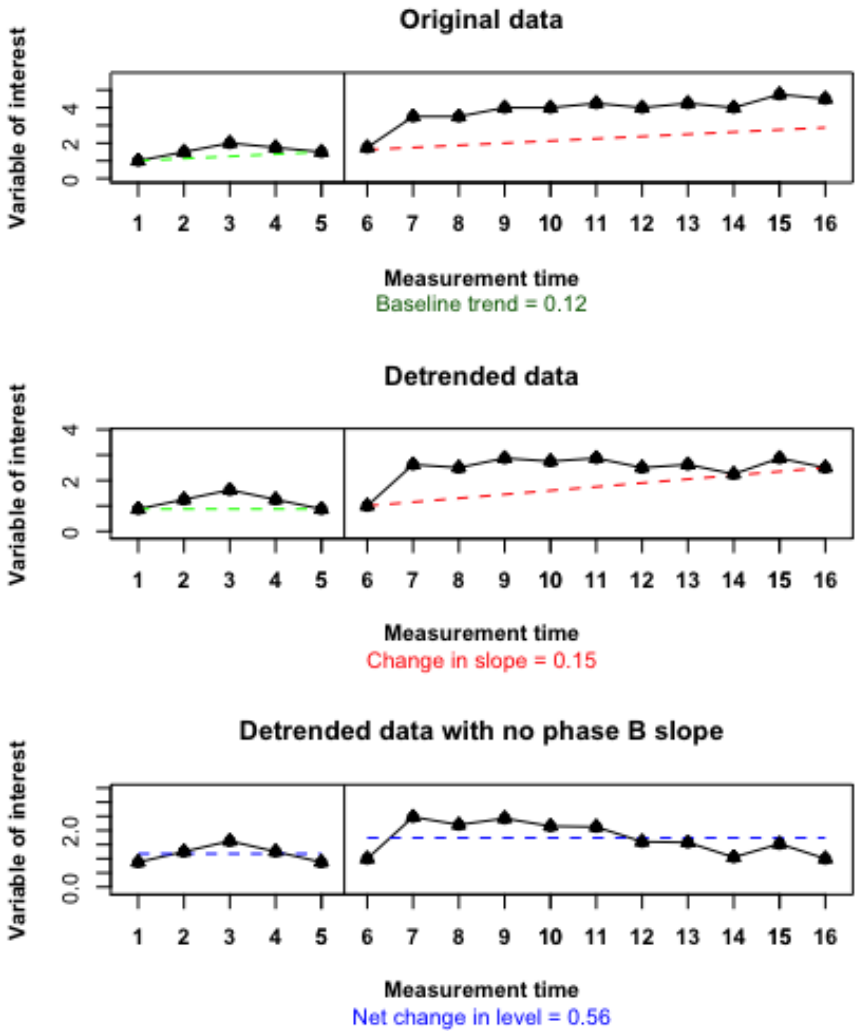


ASKp



Rider KS-10

Slope and level change procedure



MPD and SLC procedure data for P2

Non-standardised means for P2:

COPMp = 2.31

COPMs = 2.56

PBS = 6.67

	Mean Phase Difference outputs		Slope and Level Change outputs		
	Baseline Trend (BLT)	Mean Phase Difference (MPD)	Baseline trend estimate (BTE)	Slope change estimate (SCE)	Net level change estimate (NLCE)
Carer COPMp	0.12	1.61	0.12	0.15	0.56
Carer COPMs	0.12	1.86	0.12	0.15	0.81
Carer BiGSS	-0.19	0.76	-0.19	0.09	0.2
Rider COPMp	-0.12	2.35	-0.12	0.62	1.39
Rider COPMs	-0.69	4.24	-0.69	1.39	2.45
Rider BiGSS	-0.25	1.83	-0.25	0.6	0.93
Carer KS-10	1.16	-4.15	1.16	-1.16	-0.3
Rider KS-10	-1.27	0.63	-1.27	2.52	-2.65
FRT	0	5.08	0	0.8	3.08
PBS	1.5	2	1.5	-1	3.17
ASK-p	6.25	1.47	6.25	-7.65	9.53
SRS	-4	0.67	-4	3.5	-2.17

Analysis matrix for P2

Positive intervention effect (raw mean difference change)	Clinically meaningful change?	Positive change when considering baseline stability?	Clinically meaningful change when considering baseline stability?	Intervention effect considering all aspects of data using VA information?
Carer-rated COPMp	+	+	-	
Carer-rated COPMs	+	+	-	
Rider-rated COPMp	+	+	+	+
Rider-rated COPMs	+	+	-	
FRT	+	+	+	-
PBS	+	-		
ASKp	+	-		
SRS	-			
Carer-rated KS-10	-			

Data analysis & statistical inference in SCED's

- **Rejects sampling theory**
- **Does not average over participants**
- **Does not use NHST-based inference**

- An experimental effect is demonstrated when dependent measures show change when and only when the treatment is introduced
- A SCED provides demonstration of a causal relation if the data across all phases of the study indicate at least three replicated demonstrations of an effect

What can I report?

- Participants who demonstrated a positive response
  - How many outcomes?
  - Which participants demonstrated most change?
  - Was this change greater than MCID?

- Dependent variables that most consistently demonstrated change
  - Which ones showed change greater than MCID?

- Size of the intervention effect across participants

What can I report?

- Dependent variables showing the most consistent evidence of an effect when considering baseline stability
- Describe how the intervention effect seen varied depending on key participant characteristics
  - predominant physical or psychosocial impairments of the participants

External validity?

- Generalisability is a key critique of SCED's
- Development of methods of analysis allowing for meta-analysis
  - possibility of combining studies thereby adding to external validity and generalisation
  - Use HPS *d*-statistics and variance data
- Results are very useful for clinicians
  - As the study is progressing
  - Ability to apply clinical reasoning skills to the range of responses seen

Limitations & challenges

- Balancing internal validity requirements with pragmatic study design factors a significant issue within the design and conduct of this study
- THR intervention was not controlled in any way
  - No attempt was made to determine procedural fidelity of the intervention
  - But careful reporting of the dosage and type of activities that were delivered to the participants
- Study design not able to establish which part of the THR intervention lead to changes in specific outcomes

Limitations & challenges

- Selecting outcome measures that suited a wide range of riders and impairments was challenging

- OM pragmatic considerations needed to be carefully considered
  - resources and assessment demands placed on participants when multiple data points are required

- Analysis – range of options and can be difficult to determine best
  - greatly improved in the last few months!

Strengths

- Random allocation of participants into one of the three baseline phase lengths
- High recruitment and retention rates for this study - including a range of diagnoses reflective of the diverse people who access the CRDA service
- Rigorous analysis process considering
  - internal validity
  - how clinically meaningful the changes were
  - findings from study are easily interpreted and can be readily applied in clinically meaningful ways
  - individuals' responses to the THR intervention

Death of the RCT?

- Fit for purpose

- More use of SCED's
  - Especially evaluating effectiveness of interventions with individuals
  - Are the RCT findings replicated in clinical settings?
  - Exploring varied responses to treatments
  - Where limited populations
  - Where diverse populations
  - Where intervention complexity is a good thing!

The attention that SCED studies give to individual responses supports the development of evidence-based practice by contributing knowledge not only about whether an intervention works in controlled and ideal circumstances, but also on how it may work, for the range of people who access it, in different clinical settings.

Do we need to let more than one type of study design get into the
‘bath’ that is researching intervention effectiveness?

Key SCED references

- Evans, J. J., Gast, D. L., Perdices, M., & Manolov, R. (2014). Single case experimental designs: Introduction to a special issue of Neuropsychological Rehabilitation. *Neuropsychological Rehabilitation*, *24*(3-4), 305–314. http://doi.org/10.1080/09602011.2014.903198
- Kratochwill, T. R., Hitchcock, J. H., Horner, R. H., Levin, J. R., Odom, S. L., Rindskopf, D. M., & Shadish, W. R. (2013). Single-case intervention research design standards. *Remedial and Special Education*, *34*(1), 26–38. http://doi.org/10.1177/0741932512452794
- Kratochwill, T. R., Hitchcock, J., Horner, R. H., Levin, J. R., Odom, S. L., Rindskopf, D. M., & Shadish, W. R. (2010). What Works Clearinghouse: Single-Case Design Technical Documentation. Retrieved February 24, 2016, from http://eric.ed.gov/?id=ED510743
- Manolov, R., & Moeyaert, M. (2016). How Can Single-Case Data Be Analyzed? Software Resources, Tutorial, and Reflections on Analysis. *Behavior Modification*, 0145445516664307. http://doi.org/10.1177/0145445516664307
- Manolov, R., & Moeyaert, M. (2017). Recommendations for Choosing Single-Case Data Analytical Techniques. *Behavior Therapy*, *48*(1), 97–114. http://doi.org/10.1016/j.beth.2016.04.008
- Tate, R. L., Perdices, M., & Rosenkoetter, U. (2016). The Single-Case Reporting Guideline In BEhavioural Interventions (SCRIBE) 2016: Explanation and elaboration. *Archives of Scientific …*. http://doi.org/10.1037/arc0000027
- Tate, R. L., Perdices, M., McDonald, S., Togher, L., & Rosenkoetter, U. (2014). The design, conduct and report of single-case research: resources to improve the quality of the neurorehabilitation literature. *Neuropsychological Rehabilitation*, *24*(3-4), 315–331. http://doi.org/10.1080/09602011.2013.875043
- Tate, R. L., Perdices, M., Rosenkoetter, U., Wakim, D., Godbee, K., Togher, L., & McDonald, S. (2013). Revision of a method quality rating scale for single-case experimental designs and n-of-1 trials: the 15-item Risk of Bias in N-of-1 Trials (RoBiNT) Scale. *Neuropsychological Rehabilitation*, *23*(5), 619–638. http://doi.org/10.1080/09602011.2013.824383