

Repeated Measures Design

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Common design: Repeated measures designs

- Take measurements on same subject over time or under different conditions.
- Same basic idea as a randomized block design:
 - treatment effects measured on ``units" that are similar as possible.

Repeated measures designs

Advantages

- Precision determined by variation within same subject;
- May be the only design that answers the questions of interest.
 - For example, how do measurements on an individual change over time?

Repeated measures designs

Disadvantages

- May not be feasible
- May not give realistic assessments of treatment effects
- Analyses more difficult
 - usually need to take into account associations between observations taken from same individual

Repeated measures designs

Cross-over Designs

- Subjects receive every treatment
- Most common is ``two-period, two-treatment''
 - Subjects are randomly assigned to receive either
 - A in period 1, B in period 2 or
 - B in period 1, A in period 2

Repeated measures designs

Cross-over Designs

- Important assumption: No carry-over effects
 - effect of treatment received in each period is not affected by treatment received in previous periods.
- To minimize possibility of carry-over effects
 - “wash-out” time between the periods in which treatments are received.

Cross-over designs: Example

- Treatments: Impermeable (IP) / Semi-Permeable (SP)
- Outcomes: Skin temperature, heat storage, oxygen consumption
- Protocol:
 - 6 men studied under both types of clothing.
 - 3 men randomized to order (IP, SP), 3 men to (SP, IP)

Rissanen and Rintamaki (1997) Ergonomics p. 141-150.

Cross-over designs: Example

- Why a crossover design and not a completely randomized design ?
- Would expect large amounts of variability in heat storage, oxygen consumption, etc. from different men.
- Would expect small variability in these measures from the same man at two different times

Cross-over designs: Example 2

- Effects of fluids on exercise capacity.
- Treatments: (N) no drink, (W) water, (I) isotonic glucose electrolyte and (H) hypotonic glucose electrolyte.
- Outcome is ``time to exhaustion."''
- 12 subjects available.

Cross-over designs: Example 2

Possible designs

- Completely randomized?
- Randomized block?
- Cross-over:
 - Each subject observed under each condition
 - Randomize order.
 - One week period between observations.

Cross-over designs: Example 2

- Precision determined by variation in ``time to exhaustion'' by a subject over multiple occasions.
 - Avoids basing precision on variation in time to exhaustion between different subjects

Cross-over designs: Examples

- Both examples illustrate importance of
 - “wash-out period” and
 - randomizing/balancing the order that treatments are applied.

Completely randomized design or
randomized block design or
a cross-over design?

- Is the natural variability within a subject likely to be small relative to the natural variability across subjects?
- Are there likely to be carry-over effects?
- Are there likely to be "drop-outs"?
- Is a cross-over design feasible?

Completely randomized design or
randomized block design or
a cross-over design?

- No definitive statistical answer to the question.
- Answer depends on knowledge of
 - experimental material and
 - the treatments to be studied

Measurements over time (longitudinal studies)

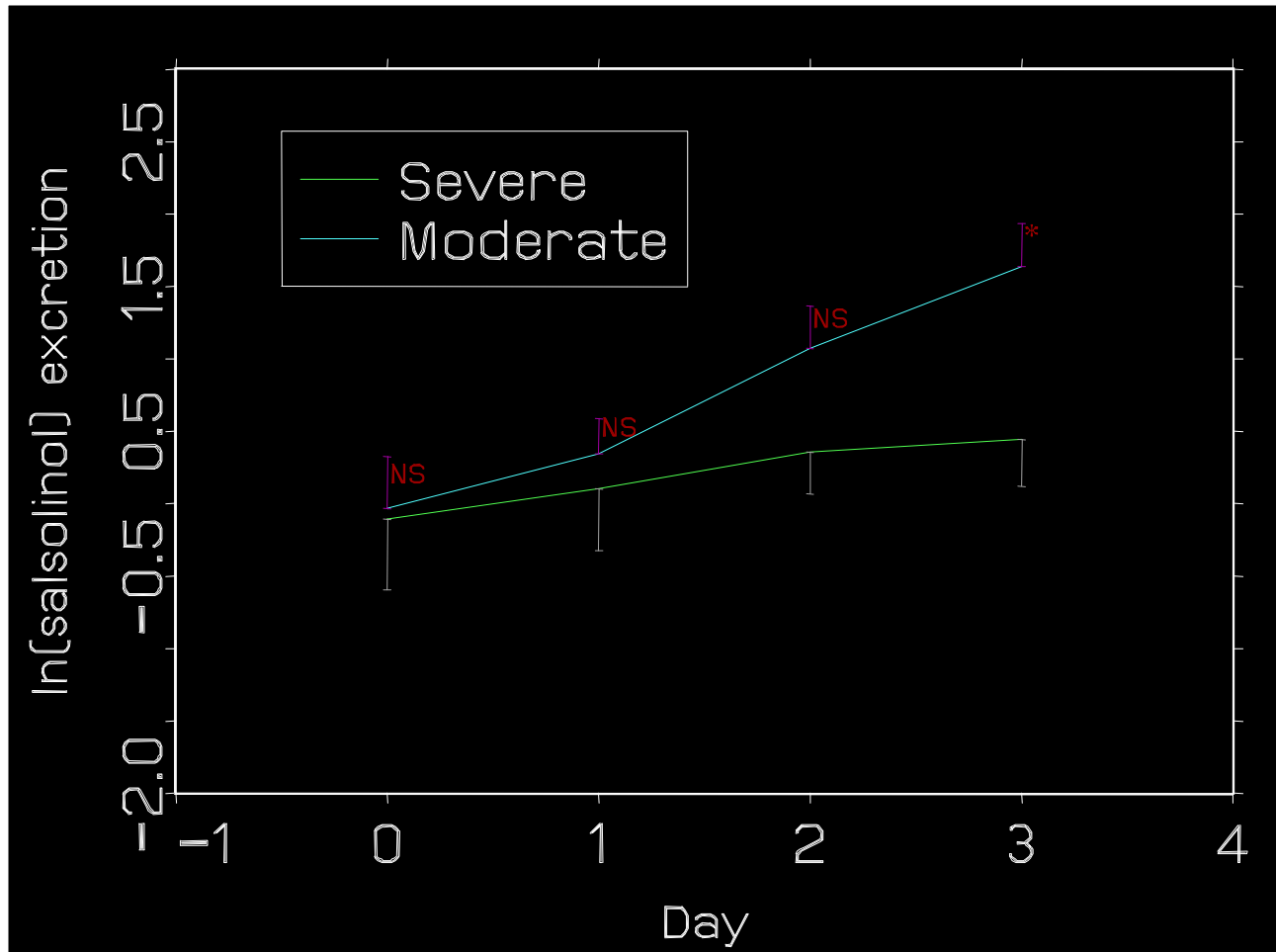
- Advantage:
 - May be the only design that answers questions of interest
- Disadvantages:
 - Analyses can be difficult
 - Can be biased due to dropouts, especially if dropout related to treatment being studied

Measurements over time

- Important to consider individual subject profiles over time.
- Ignoring individual subjects can give misleading impression of
 - variation
 - direction of effects

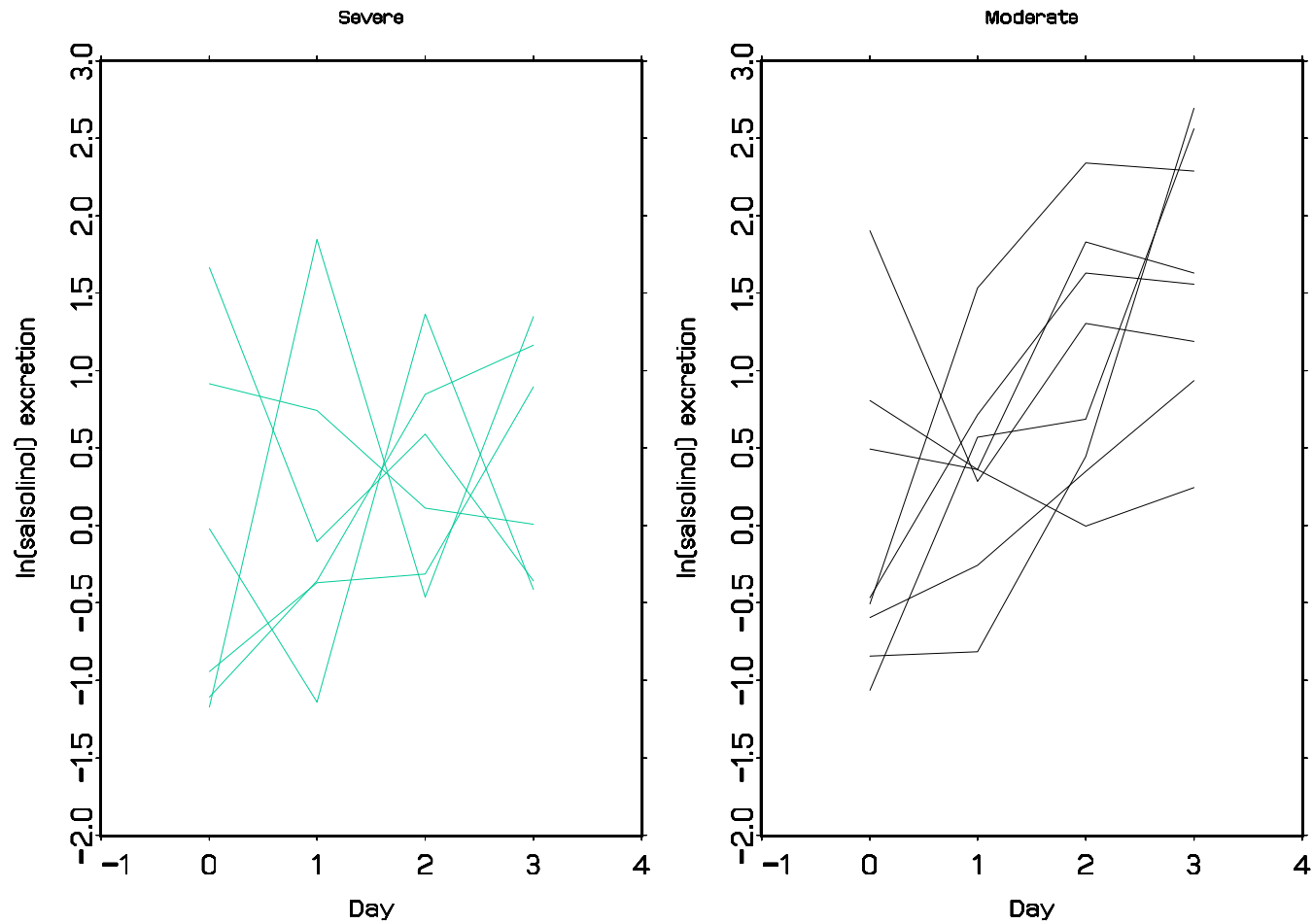
Ignoring individual patients can misrepresent variation

Modified data from Crowder and Hand. Analysis of Repeated Measures

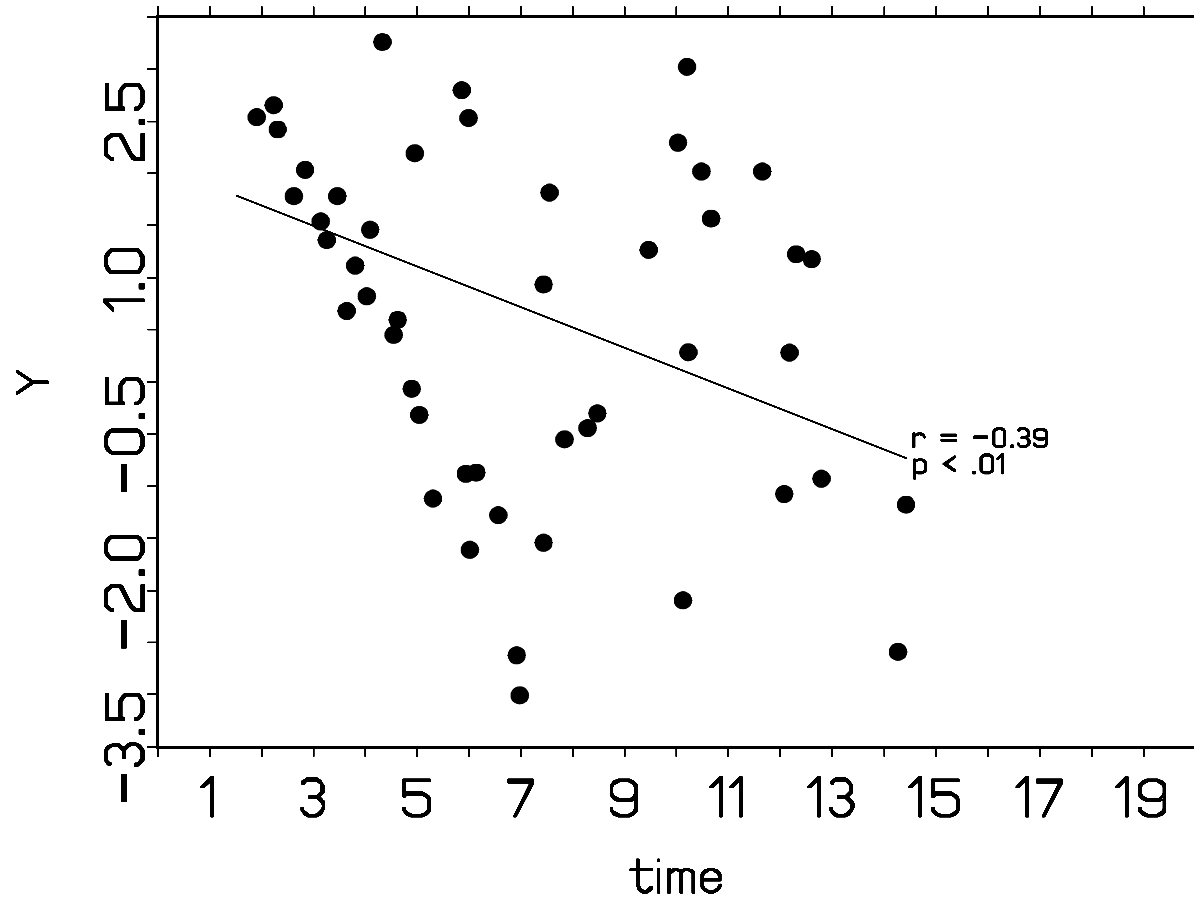


Ignoring individual patients can misrepresent variation

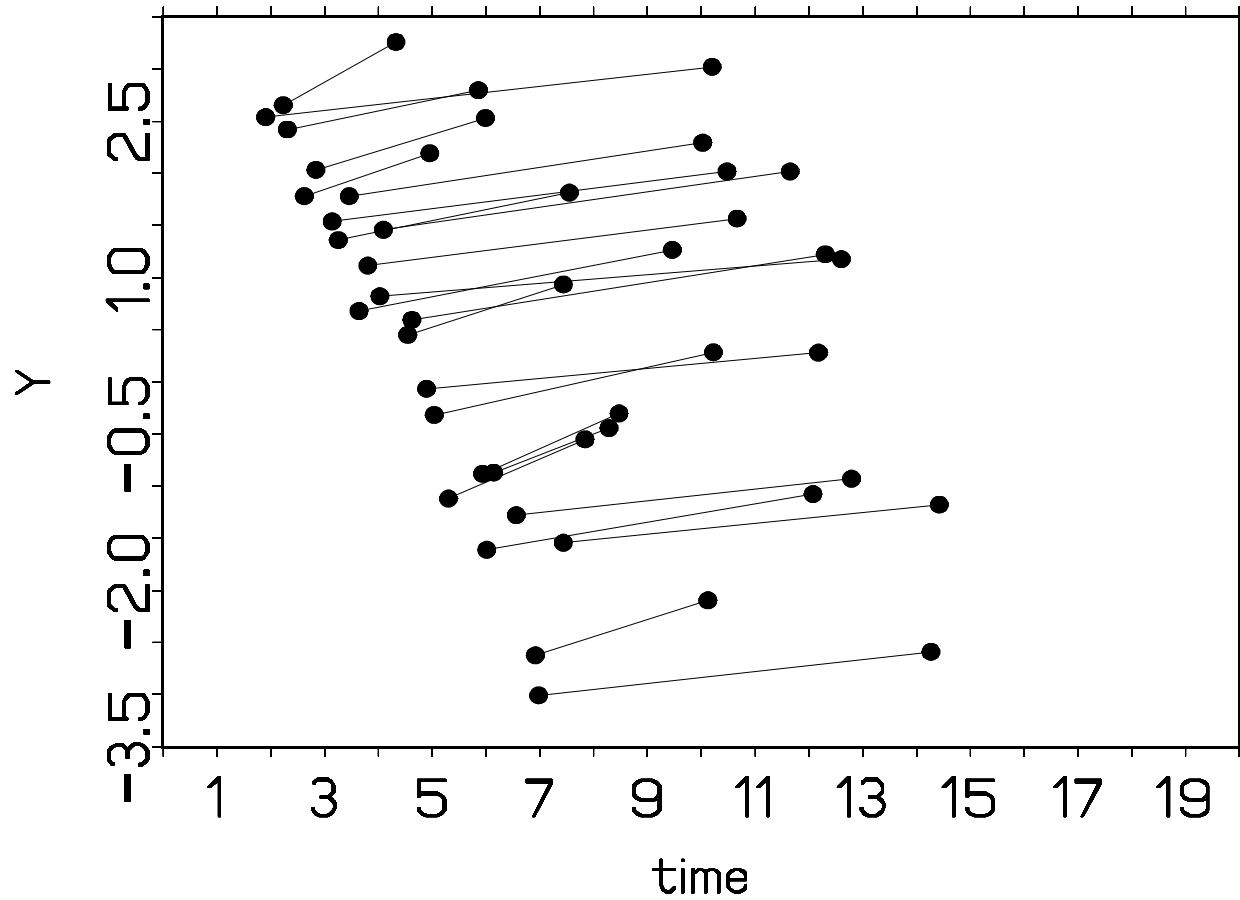
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Ignoring individual patients can misrepresent direction of effects



Ignoring individual patients
can misrepresent direction of effects

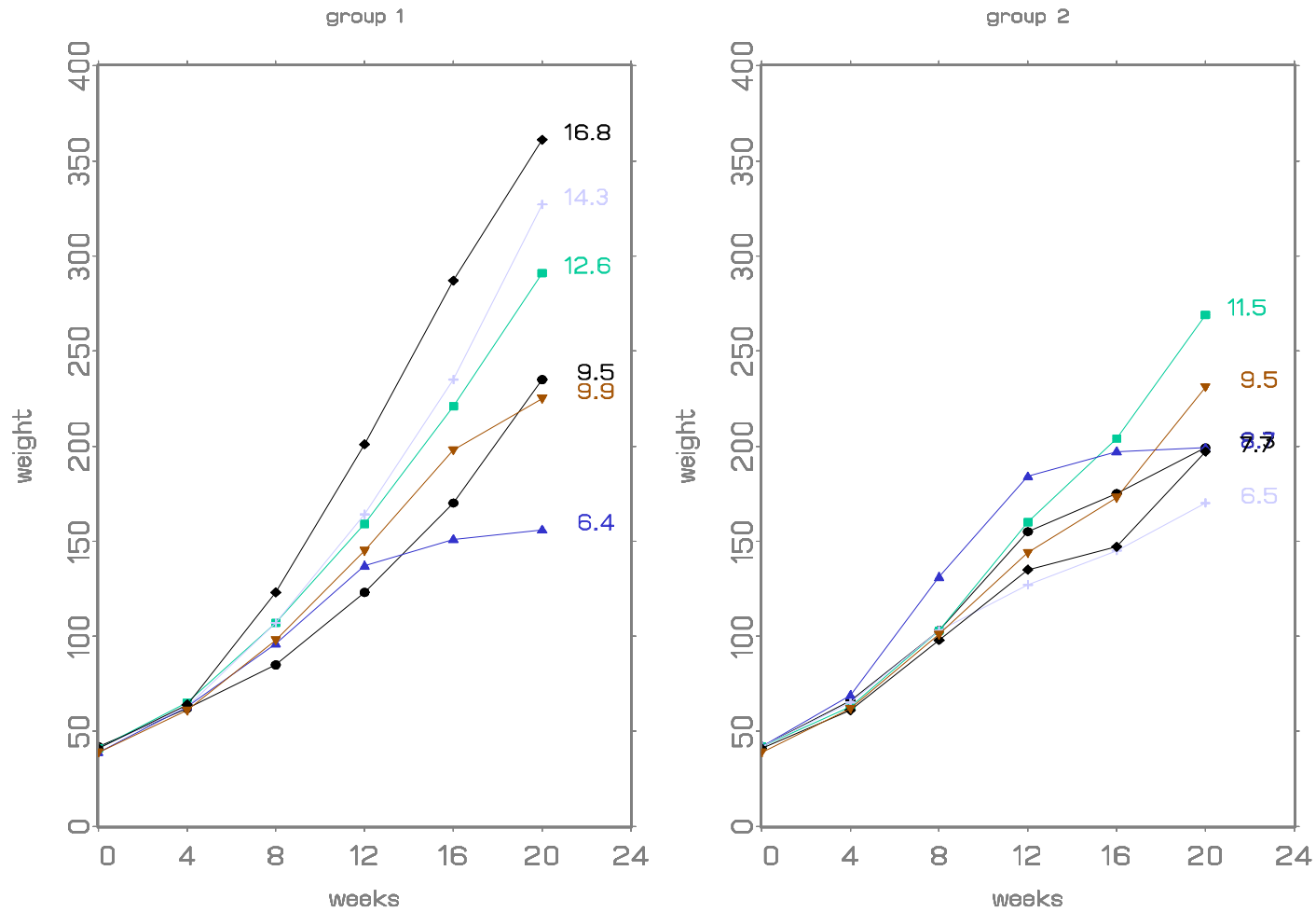


Analysis by summary measures

- Matthews et al recommend analysis by *summary measure*
- Common summary measures are
 - individual slopes
 - area under curve

Example of Analysis by individual slopes.

Data from Crowder and Hand



Example of Analysis by individual slopes.

Data from Crowder and Hand

Group 1	Group 2
9.5	8.3
12.6	11.5
6.4	8.7
14.3	6.5
16.8	7.7
9.9	9.5

Analyze this as a standard 2 group problem.

Analysis by summary measures.

Senn, BMJ, 1990

- **Advantages**
 - Easy
 - Summary measures may have an interpretation
- **Disadvantages**
 - Makes sense with different lengths of follow-up?
 - Effect of predictors measured at time points within subject?
 - Can a single summary measure can capture entire curve?

Handling dropouts in longitudinal studies

- Possible approaches.
- Analyze only those who complete therapy.
 - May bias results, especially if reason for dropout is related to outcome

Handling dropouts in longitudinal studies

- Use "Last Observation Carried Forward (LOCF)" method.
 - After patient has withdrawn, use the last observation.
 - Could bias results; last observation may not reflect true state of subject
 - Does not provide reasonable assessment of uncertainty
 - Generally dismissed as a method for handling dropouts

Handling dropouts in longitudinal studies

- Modeling the dropout process
 - Requires assumptions and sophisticated modeling methods.
- No generally accepted method for handling dropouts.