Donna Brogan problem

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1 Introduction

The question arises as to whether in the case of two treatment groups and two timepoints does MMRM reduce exactly to ANCOVA.

- Does if matter if the analysis is adjusting for baseline (i.e. not including baseline in MMRM response.).

- Does it matter if response is observed value or is a change score? Consider the article by Brogan and Kutner [@Brogan1980] Here are all the responses bundled into a single markdown code block:

```
I'll explain the key differences between using a linear model and a random
effects model for your clinical trial scenario.

Linear Model (e.g., ANCOVA):

In a linear model, you would typically analyze the post-treatment measurements
as your dependent variable, with treatment group as a predictor and
pre-treatment measurements as a covariate. This approach:

- Treats all observations as independent
- Handles missing post-treatment data through complete case analysis (dropping those cases)
- Assumes the relationship between pre and post measurements is the same for all subjects
- Same error variance for all observations
```

```
Random Effects Model (Mixed Model):

This approach would model both time points together and account for the fact
that measurements from the same person are correlated. Key features:

- Includes subject-specific random effects to account for individual differences
- Can handle missing data more efficiently (uses all available data)
- Allows for different variances at different time points
- Models the correlation between repeated measurements within subjects

For your specific case, the random effects model has several advantages:

1. It can use all available data, including subjects who only have pre-treatment measurements
2. It accounts for the correlation between pre and post measurements from the same person
3. It provides more accurate standard errors by modeling the dependency structure

The basic random effects model for your case might look like this in R:

```r
lmer(outcome ~ time * treatment + (1|subject))
```

Yes, the linear model can be seen as a special case of the random effects model where the random effects variance components are set to zero. This means:

1. In mathematical terms, if we write a random effects model as: $y = X + Zu +$ where:

   - X represents the fixed effects
   - Zu represents the random effects
   - is the error term

   When we set $Var(u) = 0$, the random effects term Zu disappears, and we're left with: $y = X +$ which is the standard linear model

2. This relationship is why random effects models are sometimes called "mixed models" - they mix both fixed effects (like your linear model) and random effects together. The fixed effects portion is essentially the same as what you'd have in a linear model.

3. You can actually test this relationship formally using a likelihood ratio test comparing the models, though there are some technical considerations since you're testing on the boundary of the parameter space (variance can't be negative).

This hierarchical relationship between the models is one reason why random effects models are so flexible - they can "collapse" down to simpler models when the data suggest that's appropriate. Would you like me to explain more about how this relationship plays out in practice with your clinical trial data? "'

2   Methods

Set up the model, no covariates, in both settings with 3 observations per group. Work out analytic formula

- Repeat for unequal variances
- Repeat w covariates

3 Methods

4 Results

5 Code

6 References

6.1 Prerequisites

In development

6.2 Step-by-Step Implementation

In development

6.3 Key Takeaways

In development

6.4 Further Reading

In development