Modelling Tumour Growth

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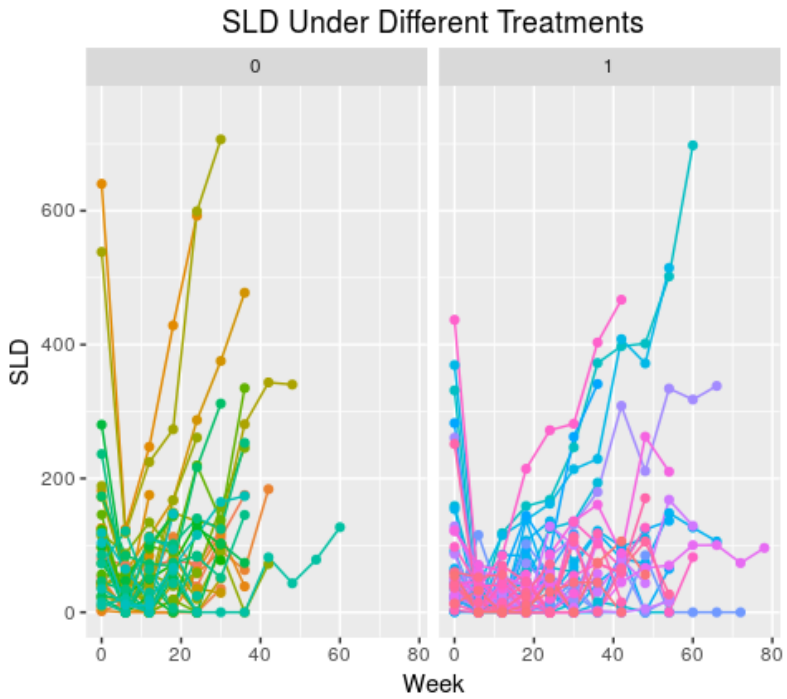
Problem Re-cap

Aim:
To compare different cancer treatments.
Data:
SLD = sum of longest diameters of the tumours in one patient.



Our Model

GAMM (Generalised Additive Mixed Model).

$$y_{ij} = \beta_0 + f(t_i \star b_j) + \varepsilon_{ij}, \quad \varepsilon_{ij} \sim N(0, \sigma^2), \quad b_j \sim N(0, \sigma_b^2)$$

Where $y = SLD$, $t = time$, $i = measurement$, $j = patient$.

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Decisions:

- How to include random effects, b_j.
- How to include treatment effects.
- How to incorporate dependence in successive measurements.

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$$y_{ij} = \beta_0 + f(t_i) + b_{0j} + b_{1j} t_i + b_{2j} t_i^2 + \varepsilon_{ij}, \quad \varepsilon_{ij} \sim N(0, \sigma^2), \quad b_{kj} \sim N(0, \sigma^2_{b_k})$$

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Where $y = SLD$, $t = time$, $i = measurement$,
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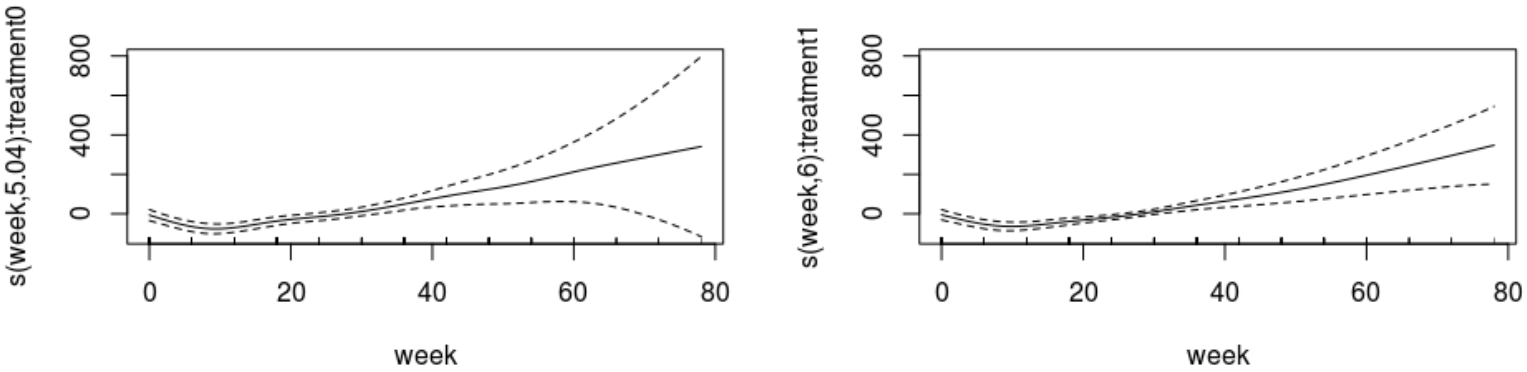
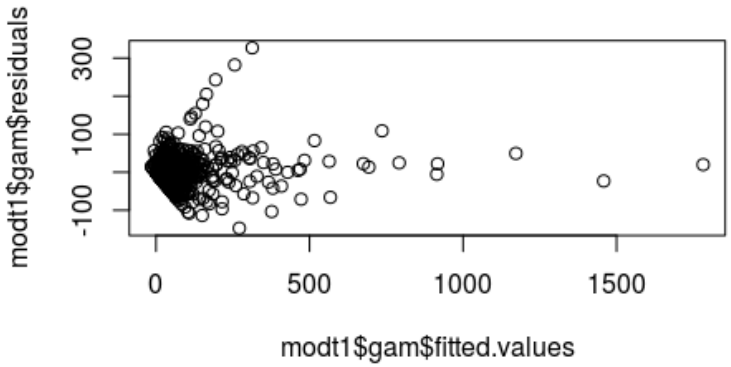
Model 1

Fitted smooths of the SLD as a function of time for each treatment.



Residual plot for the model.



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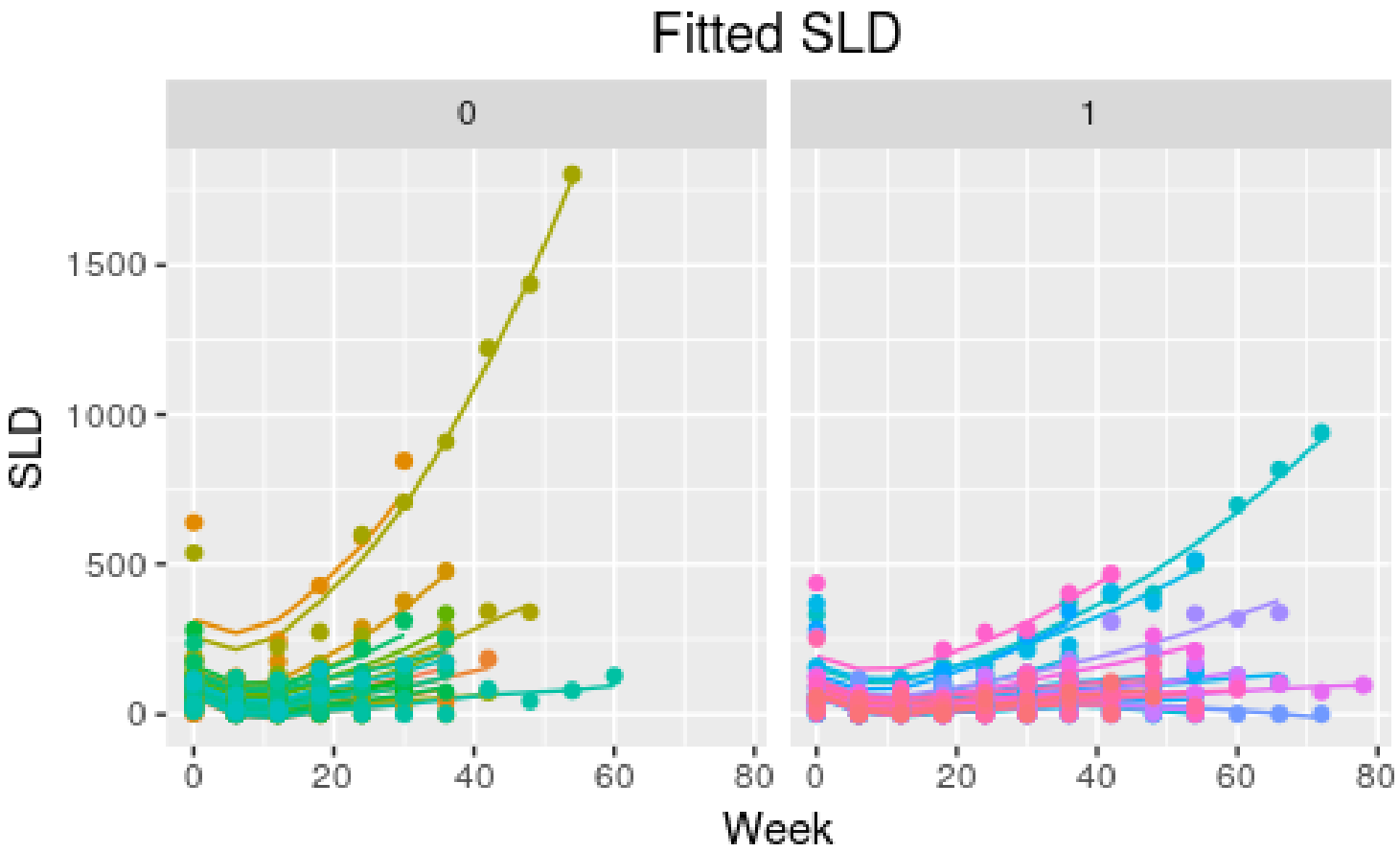
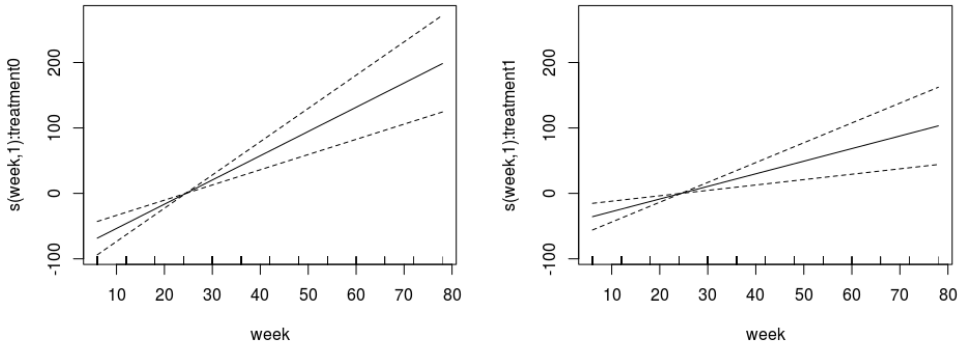
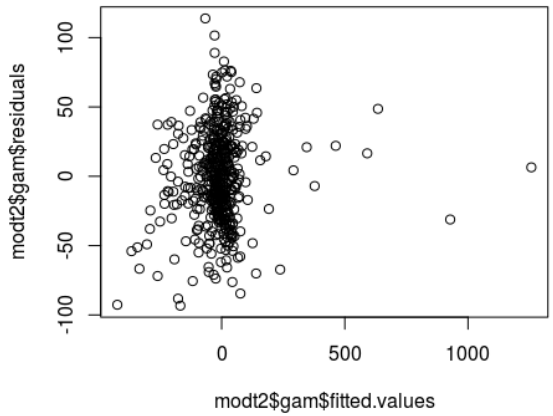


Model 2: Response = SLD - SLD(0)

Fitted smooths of the change in SLD from baseline SLD as a function of time.



Residual plot for the model.



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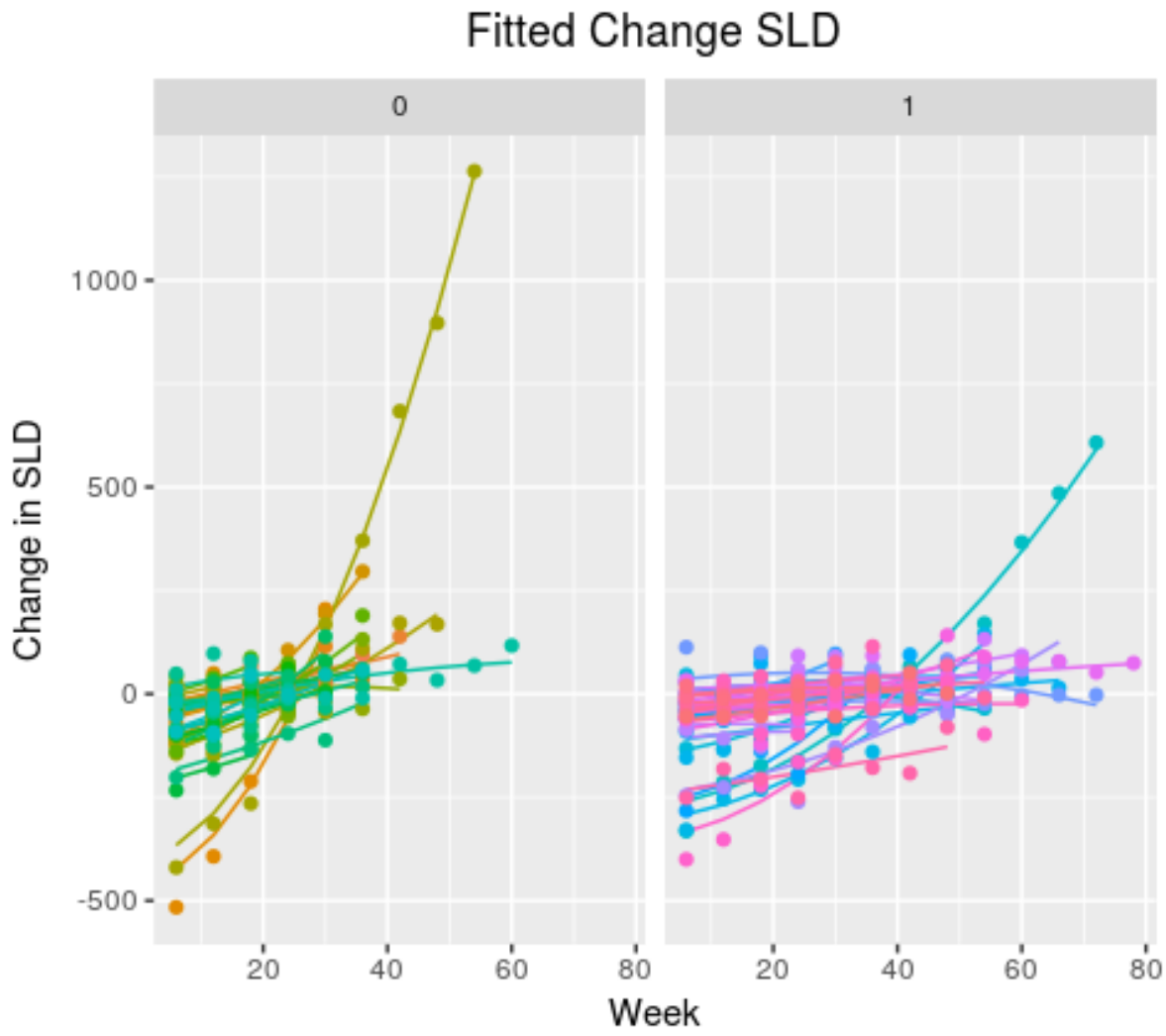
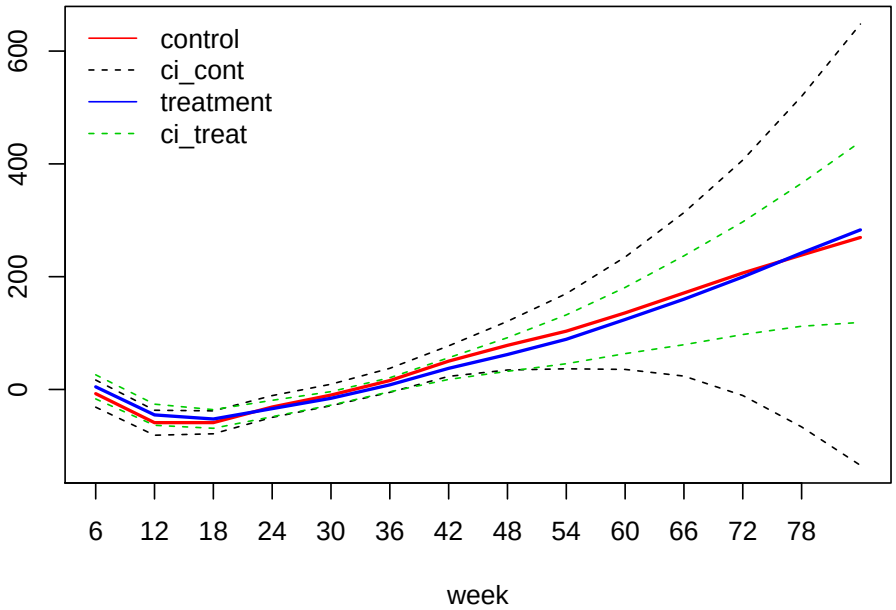
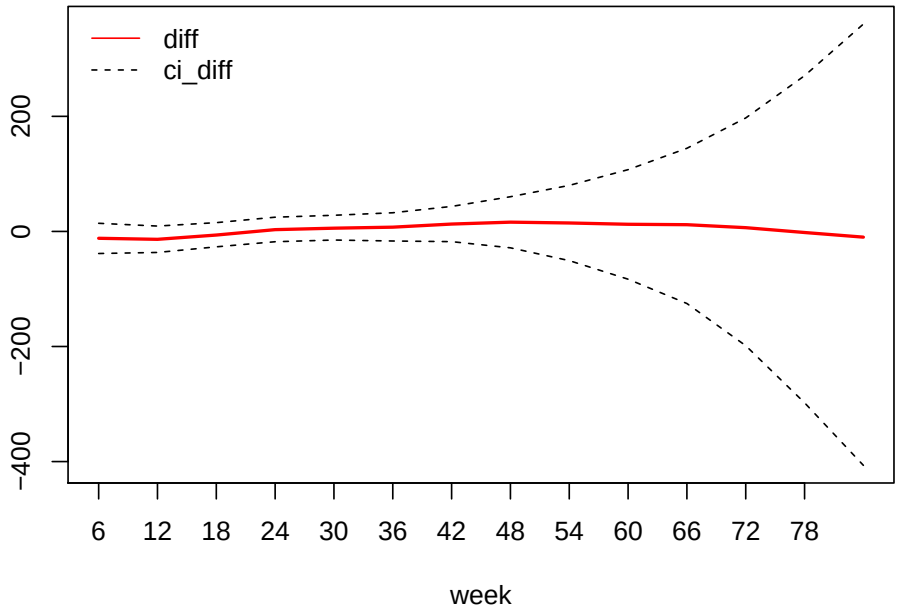


Difference in Control and Treatment for Model 1





Benefits of New Approach

- Current models for tumour growth cannot be statistically distinguished but there is high variability in the predictive results for an individual patient.
- In the absence of a physically motivated model, it is natural to let the data choose the model.
- The new approach is a natural extension to the PK model framework.
- A mixed model allows for information from other patients to inform predictions for an individual patient.

Future Work

- Explore how to include more flexible random effects.
- Include more explanatory variables:
  - To identify outliers;
  - To improve model fit.
  - To identify factors that have significant effect on tumour growth.
- How to use the model to set up a statistical framework to identify a treatment effect.
- Joint modelling with survival end-point.

Thank you for listening.
Any questions?