Using GAMs to asess effect of biomarkers on treatment effect

Elizabeth, Nicole & Karim

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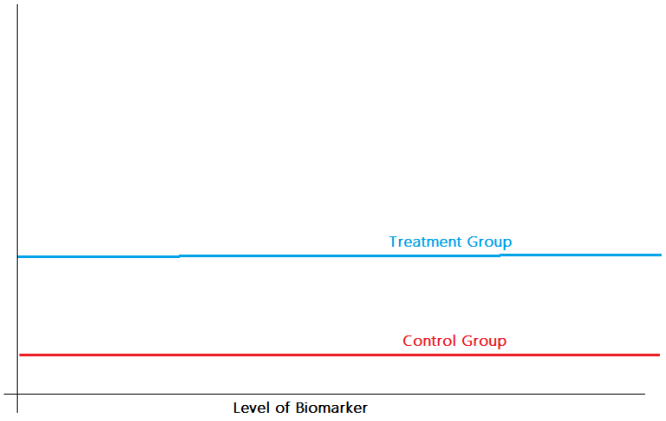
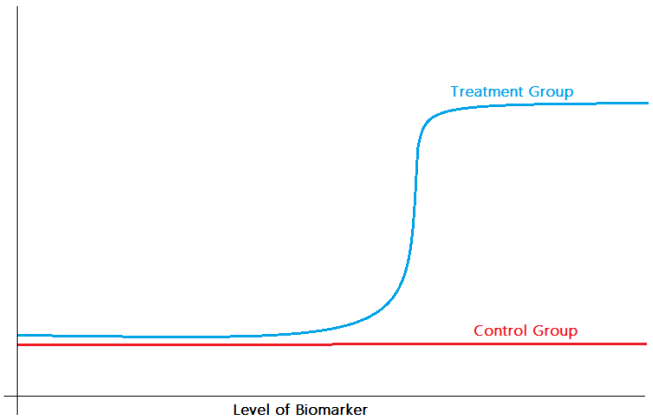
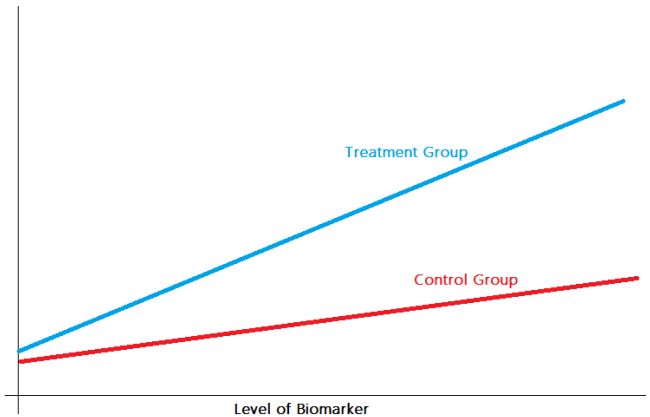
Survival as a function of the Biomarker



Need to...

- estimate from the data these functions of the biomarker.
- use the functions to find a suitable cutoff point.

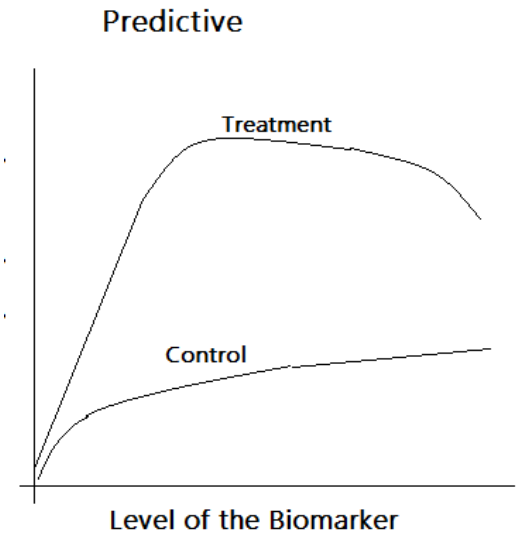


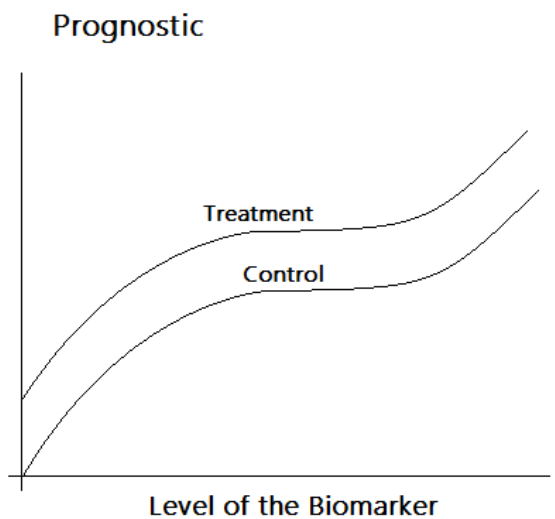


Proportional Hazards and GAMs

Proportional Hazards Model:

- Hazard function $h_i(t) = \exp(\beta_1 x_{1i} + ... + \beta_p x_{pi}) h_0(t)$ is the hazard of individual i dying at time t, where $h_0(t)$ is the hazard baseline.
- Proportional hazards model (with GAM):
  $\log(\frac{h_i(t)}{h_0(t)}) = \beta\,\text{treat}_i + f_{treat_i}(\text{biomarker}_i)$ where β is the treatment main effect and treat_i is 1 if i is in the treatment group and 0 otherwise.





- The GAM fits a model as a linear function of basis functions.
- We can see how $f_0(\text{biomarker})$ differs from $f_1(\text{biomarker})$

Example:

Mayo clinic primary biliary cirrhosis (PBC) data:

- Survival with patents with PBC.
- Treatment: D-penicillamine, and placebo.
- Biomarker: billirubin (mg/dl).
- $\log(\frac{h_i(t)}{h_0(t)}) = \beta\,\text{treat}_i + f_{treat_i}(\text{billirubin}_i)$