Dynamic Predictions of Visual Acuity in Uveitis

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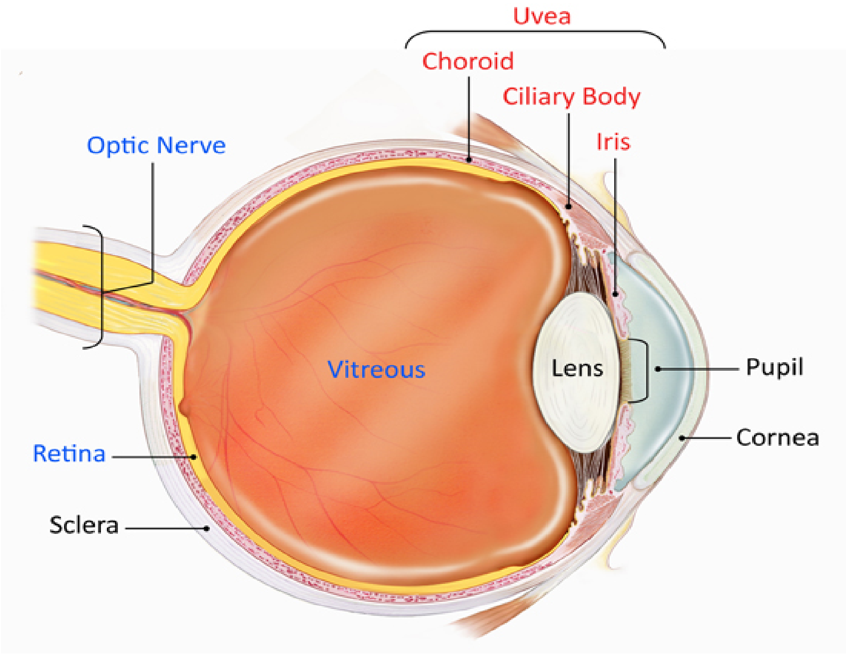
Motivation

- Uveitis - inflammation (INF) $\rightarrow$ blindness

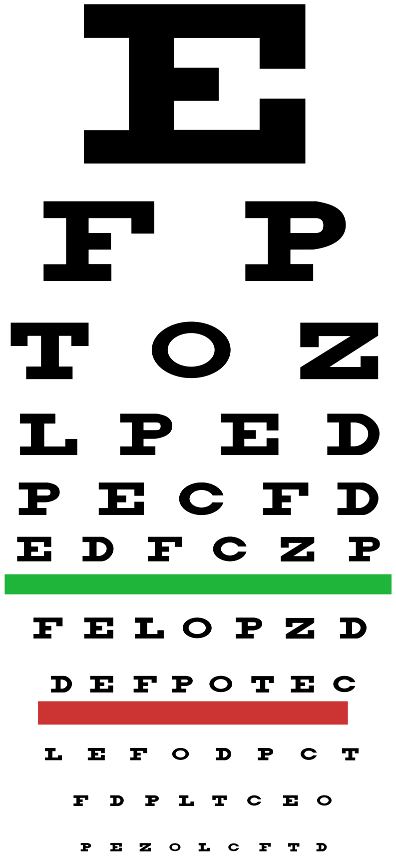


Influences visual acuity (VA)

Motivation (cont'd)

- 365 patients visiting the Rotterdam Eye Hospital
  - ▷ Data recorded since 2000
  - ▷ Mean follow-up visit is equal to 2.5 years
  - ▷ Time-varying covariates: **Visual Acuity (VA), Inflammation (INF), Complications (COM)**

Motivation (cont'd)



1	20/200
2	20/100
3	20/70
4	20/50
5	20/40
6	20/30
7	20/25
8	20/20
9	
10	
11	

Motivation (cont'd)

Feet	Decimal	LogMAR
20/200	0.10	1.00
20/160	0.13	0.90
20/125	0.16	0.80
20/100	0.20	0.70
20/80	0.25	0.60
20/63	0.32	0.50
20/50	0.40	0.40
20/40	0.50	0.30
20/32	0.63	0.20
20/25	0.80	0.10
20/20	1.00	0.00

Motivation (cont'd)

Feet	Decimal	LogMAR
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20/100	0.20	0.70
20/80	0.25	0.60
20/63	0.32	0.50
20/50	0.40	0.40
20/40	0.50	0.30
20/32	0.63	0.20
20/25	0.80	0.10
20/20	**1.00**	**0.00**

Motivation (cont'd)

Feet	Decimal	LogMAR
20/200	**0.10**	**1.00**
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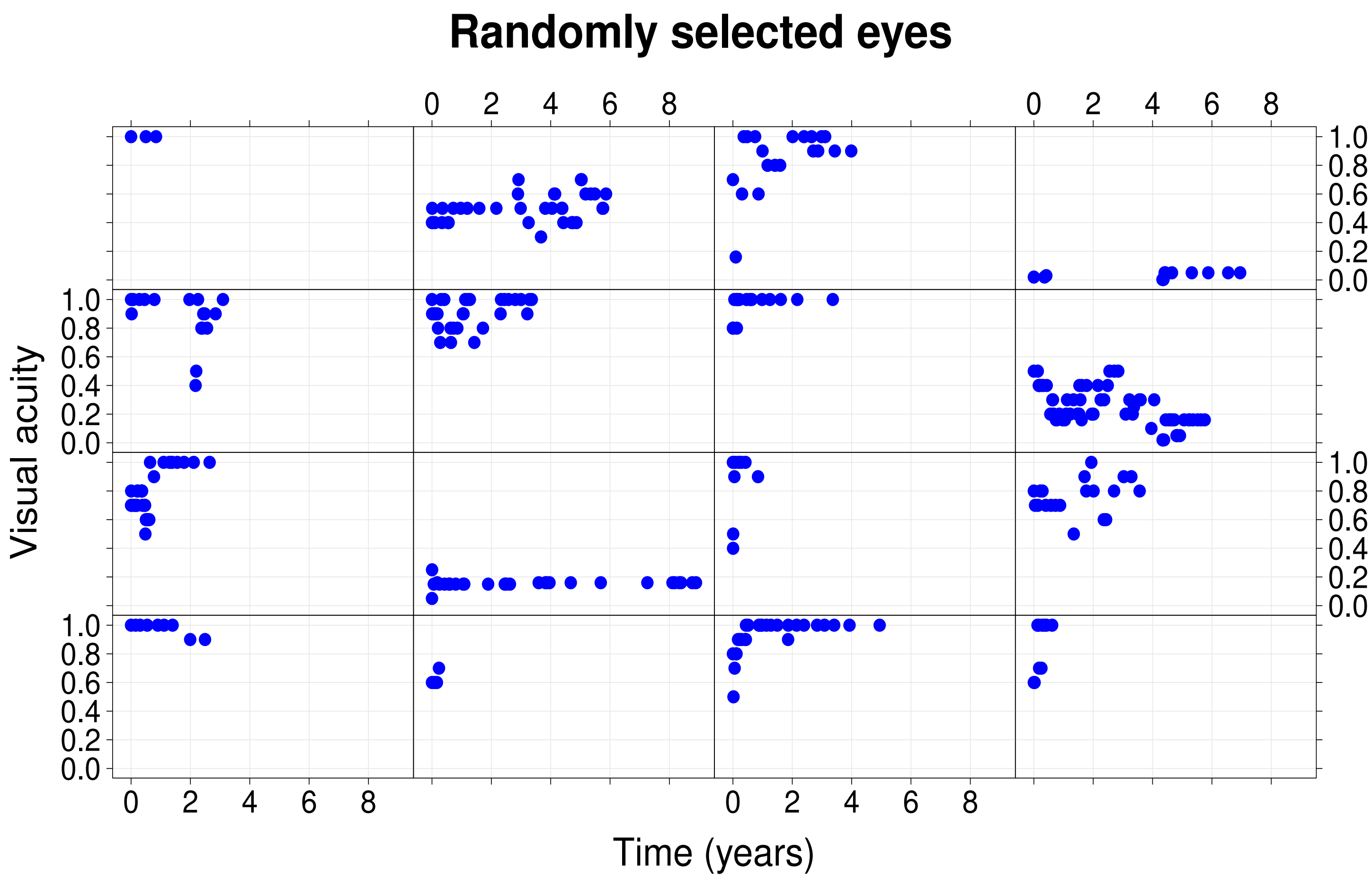
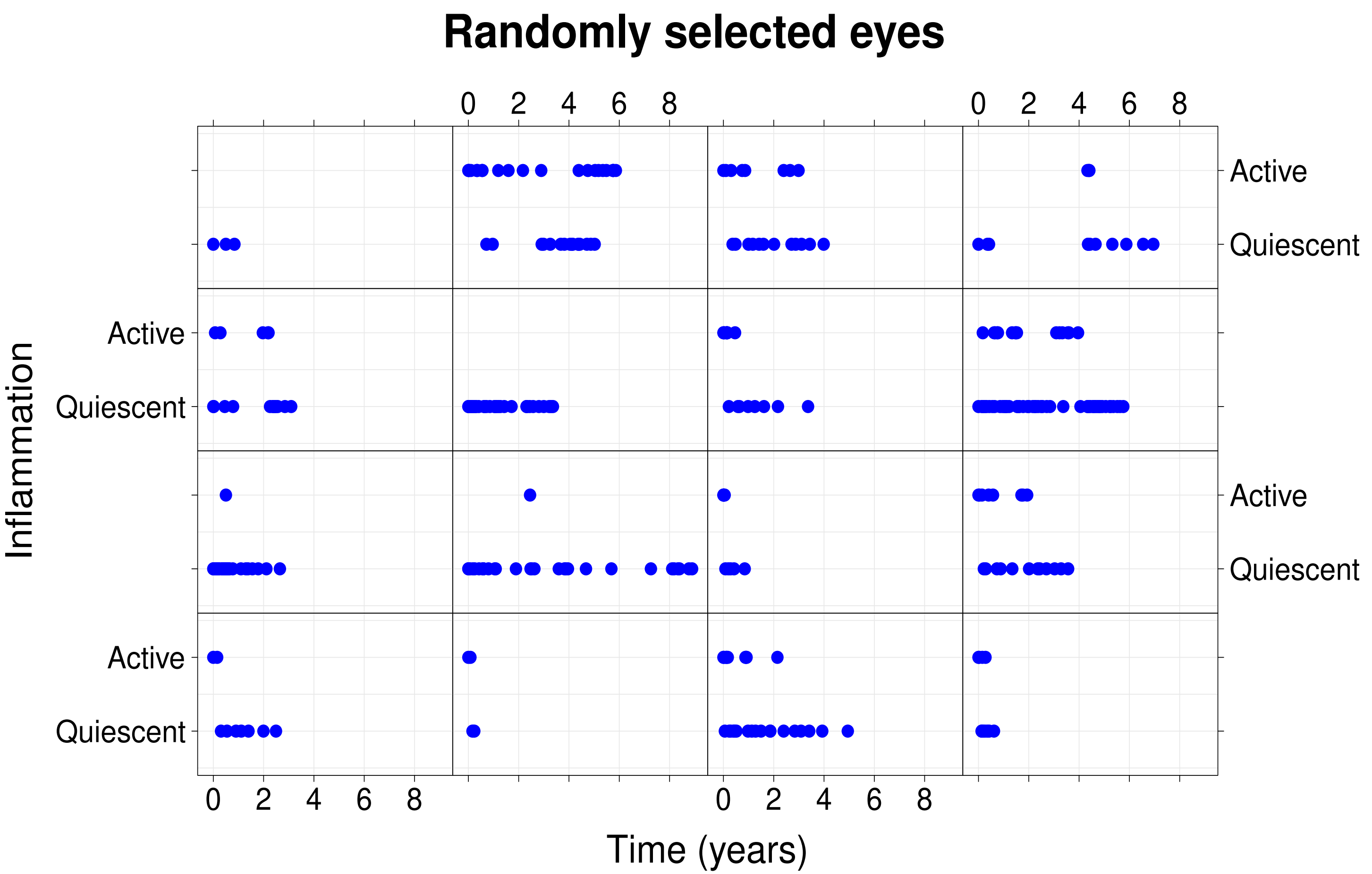
20/63	0.32	0.50
20/50	0.40	0.40
20/40	0.50	0.30
20/32	0.63	0.20
20/25	0.80	0.10
20/20	1.00	0.00

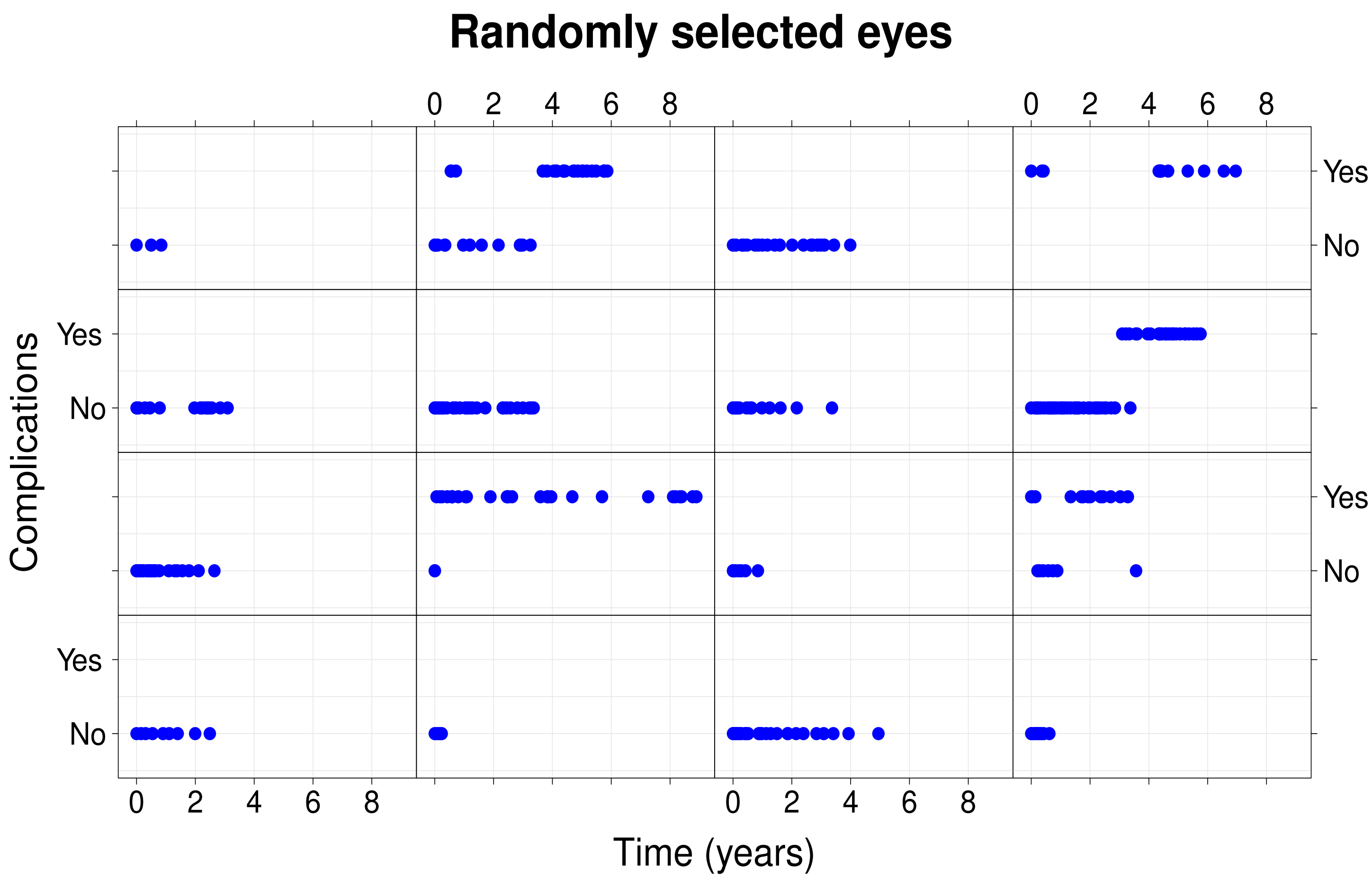
Motivation (cont'd)



Motivation (cont'd)



Motivation (cont'd)



Motivation (cont'd)

Predict future VA measurements in patients with uveitis

Analysis

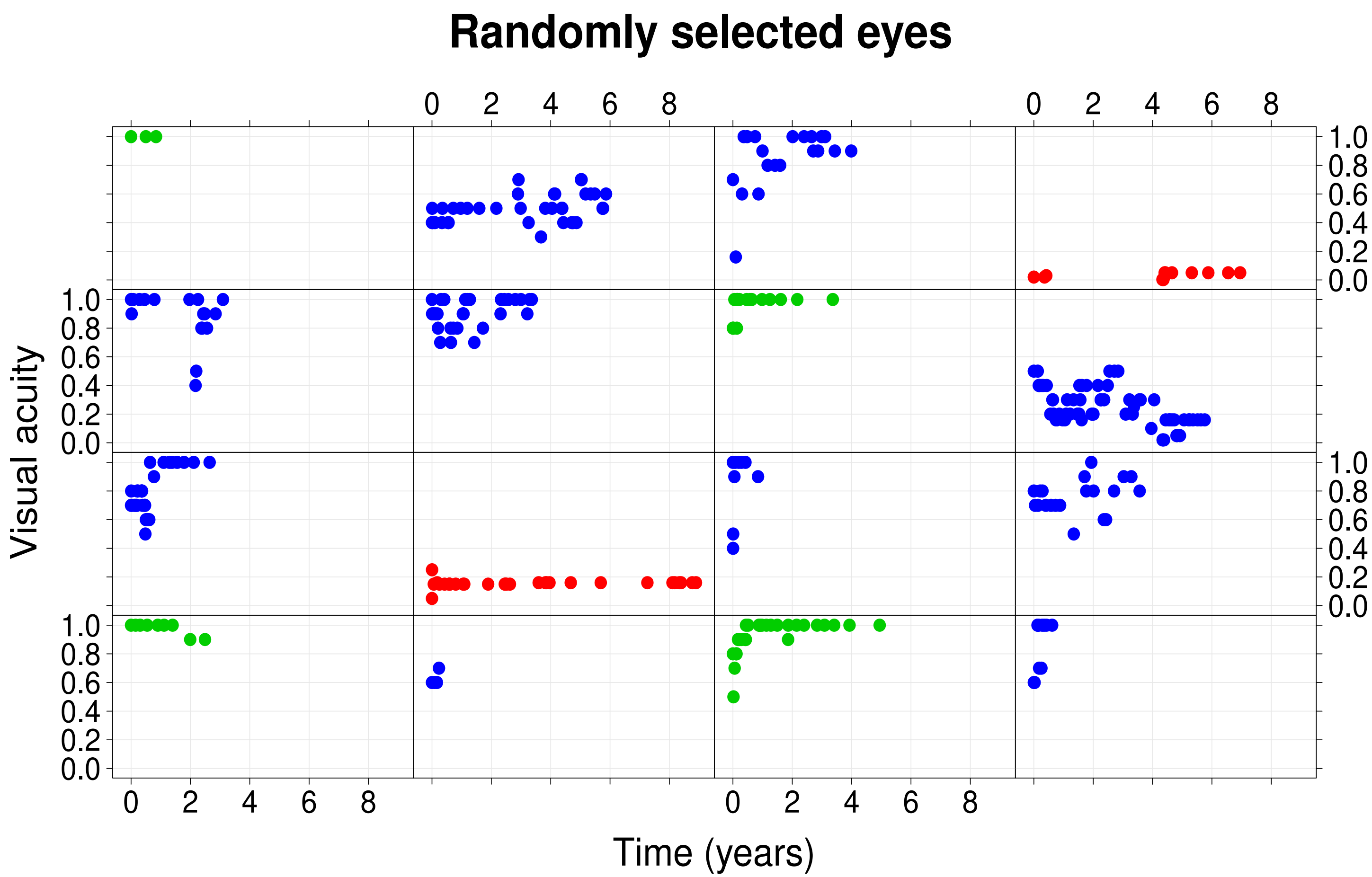
Better predict VA?

- Special features

  1. Clusters (Stable/Unstable patients)

    ▷ Latent classes

Analysis (cont'd)



Analysis (cont'd)

- Mixed models

$$y_{\mathsf{VA}_i} = x_{\mathsf{VA}i}^\top \beta_{\mathsf{VA}} + z_{\mathsf{VA}i}^\top b_{\mathsf{VA}i} + \epsilon_i, \qquad \epsilon_i \sim N(0, \Sigma_i)$$

where

▷ β_{VA} denotes the fixed effects

▷ $b_{\mathsf{VA}i} \sim N(0, D)$ denotes the random effects

Analysis (cont'd)

- Mixed models

$$y_{\mathsf{VA}_i} = \boxed{x_{\mathsf{VA}i}^\top \beta_{\mathsf{VA}}} + z_{\mathsf{VA}i}^\top b_{\mathsf{VA}i} + \epsilon_i, \qquad \epsilon_i \sim N(0, \Sigma_i)$$

where

▷ β_{VA} denotes the fixed effects

▷ $b_{\mathsf{VA}i} \sim N(0, D)$ denotes the random effects

Analysis (cont'd)

- Mixed models

$$y_{\mathsf{VA}_i} = x_{\mathsf{VA}i}^\top \beta_{\mathsf{VA}} + \boxed{z_{\mathsf{VA}i}^\top b_{\mathsf{VA}i}} + \epsilon_i, \qquad \epsilon_i \sim N(0, \Sigma_i)$$

where

- ▷ β_{VA} denotes the fixed effects
- ▷ $b_{\mathsf{VA}i} \sim N(0, D)$ denotes the random effects

Analysis (cont'd)

- Mixed models

$$y_{\mathsf{VA}i\mathbf{c}} = x_{\mathsf{VA}i}^\top \beta_{\mathsf{VA}\mathbf{c}} + z_{\mathsf{VA}i}^\top b_{\mathsf{VA}i\mathbf{c}} + \epsilon_i, \qquad \epsilon_i \sim N(0, \Sigma_i),$$

where

- ▷ $\beta_{\mathsf{VA}\mathbf{c}}$ denotes the fixed effects
- ▷ $b_{\mathsf{VA}i\mathbf{c}} \sim N(0, D_{\mathbf{c}})$ denotes the random effects
- ▷ $\mathbf{c}$ denotes the class

Analysis (cont'd)

Better predict VA?

- Special features

  2. Multiple outcomes (VA, INF, COM, . . .) $\rightarrow$ high dimensional model

     ▷ Penalties

     ▷ Model averaging

Analysis (cont'd)

- Multivariate Mixed Models **(Scenario Ia)**

$$y_{\text{VA}i\mathbf{c}} = x_{\text{VA}i}^{\top}\beta_{\text{VA}\mathbf{c}} + z_{\text{VA}i}^{\top}b_{\text{VA}i\mathbf{c}} + \boxed{\boldsymbol{\alpha}_{\mathbf{c}} y_{\text{INF}i\mathbf{c}}} + \epsilon_i, \qquad \epsilon_i \sim N(0, \Sigma_i)$$

$$\texttt{logit}(y_{\text{INF}i\mathbf{c}}) = x_{\text{INF}i}^{\top}\beta_{\text{INF}\mathbf{c}} + z_{\text{INF}i}^{\top}b_{\text{INF}i\mathbf{c}}$$

where

- ▷ $\beta_{\text{VA}\mathbf{c}}$ and $\beta_{\text{INF}\mathbf{c}}$ denote the fixed effects
- ▷ $b_{i\mathbf{c}} = (b_{\text{VA}i\mathbf{c}}, b_{\text{INF}i\mathbf{c}}) \sim N(0, D_{\mathbf{c}})$ denotes the random effects
- ▷ $\mathbf{c}$ denots the class
- ▷ $\boxed{\boldsymbol{\alpha}_{\mathbf{c}}}$ association between outcomes

Analysis (cont'd)

- Multivariate Mixed Models **(Scenario Ib)**

$$y_{\text{VA}i\mathbf{c}} = x_{\text{VA}i}^\top \beta_{\text{VA}\mathbf{c}} + z_{\text{VA}i}^\top b_{\text{VA}i\mathbf{c}} + \boxed{\boldsymbol{\alpha}_{\mathbf{c}} y_{\text{COM}i\mathbf{c}}} + \epsilon_i, \qquad \epsilon_i \sim N(0, \Sigma_i)$$

$$\texttt{logit}(y_{\text{COM}i\mathbf{c}}) = x_{\text{COM}i}^\top \beta_{\text{COM}\mathbf{c}} + z_{\text{COM}i}^\top b_{\text{COM}i\mathbf{c}}$$

where

- $\beta_{\text{VA}\mathbf{c}}$ and $\beta_{\text{COM}\mathbf{c}}$ denote the fixed effects
- $b_{i\mathbf{c}} = (b_{\text{VA}i\mathbf{c}}, b_{\text{COM}i\mathbf{c}}) \sim N(0, D_{\mathbf{c}})$ denotes the random effects
- $\mathbf{c}$ denots the class
- $\boxed{\boldsymbol{\alpha}_{\mathbf{c}}}$ association between outcomes

Analysis (cont'd)

- Multivariate Mixed Models **(Scenario II)**

$$y_{\mathsf{VA}i\mathbf{c}} = x_{\mathsf{VA}i}^\top \beta_{\mathsf{VA}\mathbf{c}} + z_{\mathsf{VA}i}^\top b_{VAi\mathbf{c}} + \boxed{\boldsymbol{\alpha}_{1\mathbf{c}} y_{INFi\mathbf{c}}} + \boxed{\boldsymbol{\alpha}_{2\mathbf{c}} y_{\mathsf{COM}i\mathbf{c}}} + \epsilon_i, \qquad \epsilon_i \sim N(0, \Sigma_i)$$

$$\texttt{logit}(y_{\mathsf{INF}i\mathbf{c}}) = x_{\mathsf{INF}i}^\top \beta_{\mathsf{INF}\mathbf{c}} + z_{\mathsf{INF}i}^\top b_{\mathsf{INF}i\mathbf{c}}$$

$$\texttt{logit}(y_{\mathsf{COM}i\mathbf{c}}) = x_{\mathsf{COM}i}^\top \beta_{\mathsf{COM}\mathbf{c}} + z_{\mathsf{COM}i}^\top b_{\mathsf{COM}i\mathbf{c}}$$

where

- ▷ $\beta_{\mathsf{VA}\mathbf{c}}$, $\beta_{\mathsf{INF}\mathbf{c}}$ and $\beta_{\mathsf{COM}\mathbf{c}}$ denote the fixed effects
- ▷ $b_{i\mathbf{c}} = (b_{\mathsf{VA}i\mathbf{c}}, b_{\mathsf{INF}i\mathbf{c}}, b_{\mathsf{COM}i\mathbf{c}}) \sim N(0, D_{\mathbf{c}})$ denotes the random effects
- ▷ $\mathbf{c}$ denots the class
- ▷ $\boxed{\boldsymbol{\alpha}_{1\mathbf{c}}}$ and $\boxed{\boldsymbol{\alpha}_{2\mathbf{c}}}$ association between outcomes

Estimation

- **Bayesian** framework

  ▷ Latent classes

  * $\pi_{ic} \sim Dirichlet(A_c)$

    $A_c = A_1, \ldots, A_C$

  ▷ Multiple outcomes

  * Penalties
  * Model averaging

Estimation

- **Bayesian** framework

  ▷ Latent classes

  * $\pi_{ic} \sim Dirichlet(A_c)$

    $A_c = A_1, \ldots, A_C$

  ▷ Multiple outcomes

  * **Penalties $\rightarrow$ Shrinkage priors (Scenario II)**
  * Model averaging

Estimation

- **Bayesian** framework
  - ▷ Latent classes
    - * $\pi_{ic} \sim Dirichlet(A_c)$
      $A_c = A_1, \ldots, A_C$
  - ▷ Multiple outcomes
    - * Penalties
    - * **Model averaging $\rightarrow$ Posterior probabilities (Scenario Ia and Ib)**

Estimation (cont'd)

Bayesian model averaging: Posterior probability for each model (m)

$$P(M_m \mid D) = \frac{P(D \mid M_m) \boldsymbol{P(M_m)}}{\sum_{m=1}^{M} P(D \mid M_m) \boldsymbol{P(M_m)}},$$

where

- D: data
- $\boldsymbol{P(M_m)}$ prior for the models

Estimation (cont'd)

Bayesian model averaging: Posterior probability for each model (m)

$$P(M_m \mid D) = \frac{\boldsymbol{P(D \mid M_m)}\, P(M_m)}{\sum_{m=1}^{M} \boldsymbol{P(D \mid M_m)}\, P(M_m)},$$

where

- D: data
- $\boldsymbol{P(D \mid M_m)} = \int P(D \mid \theta_m, M_m) P(\theta_m \mid M_m) d\theta_m$

Likelihood **Priors**

Estimation (cont'd)

Bayesian model averaging: Posterior probability for each model (m)

$$P(M_m \mid D) = \frac{\boldsymbol{P(D \mid M_m)}\, P(M_m)}{\sum_{m=1}^{M} \boldsymbol{P(D \mid M_m)}\, P(M_m)},$$

where

- D: data
- $\boldsymbol{P(D \mid M_m)} = \int P(D \mid \theta_m, M_m) P(\theta_m \mid M_m) d\theta_m$

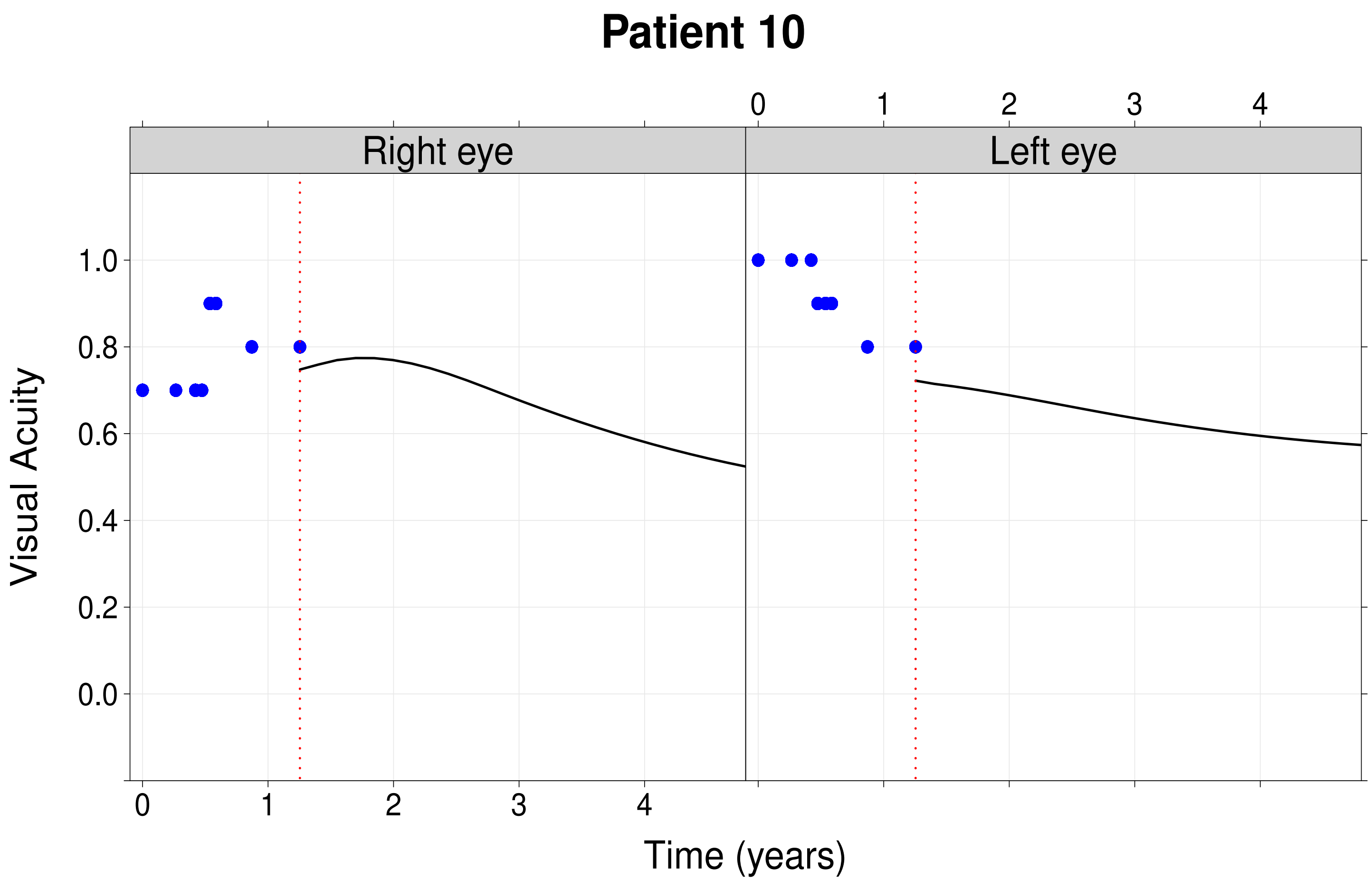
Likelihood **Priors**

Results: **Scenario Ia** $\rightarrow P(M_{\text{INF}} \mid D) = 1$ and **Scenario Ib** $\rightarrow P(M_{\text{COM}} \mid D) = 0$

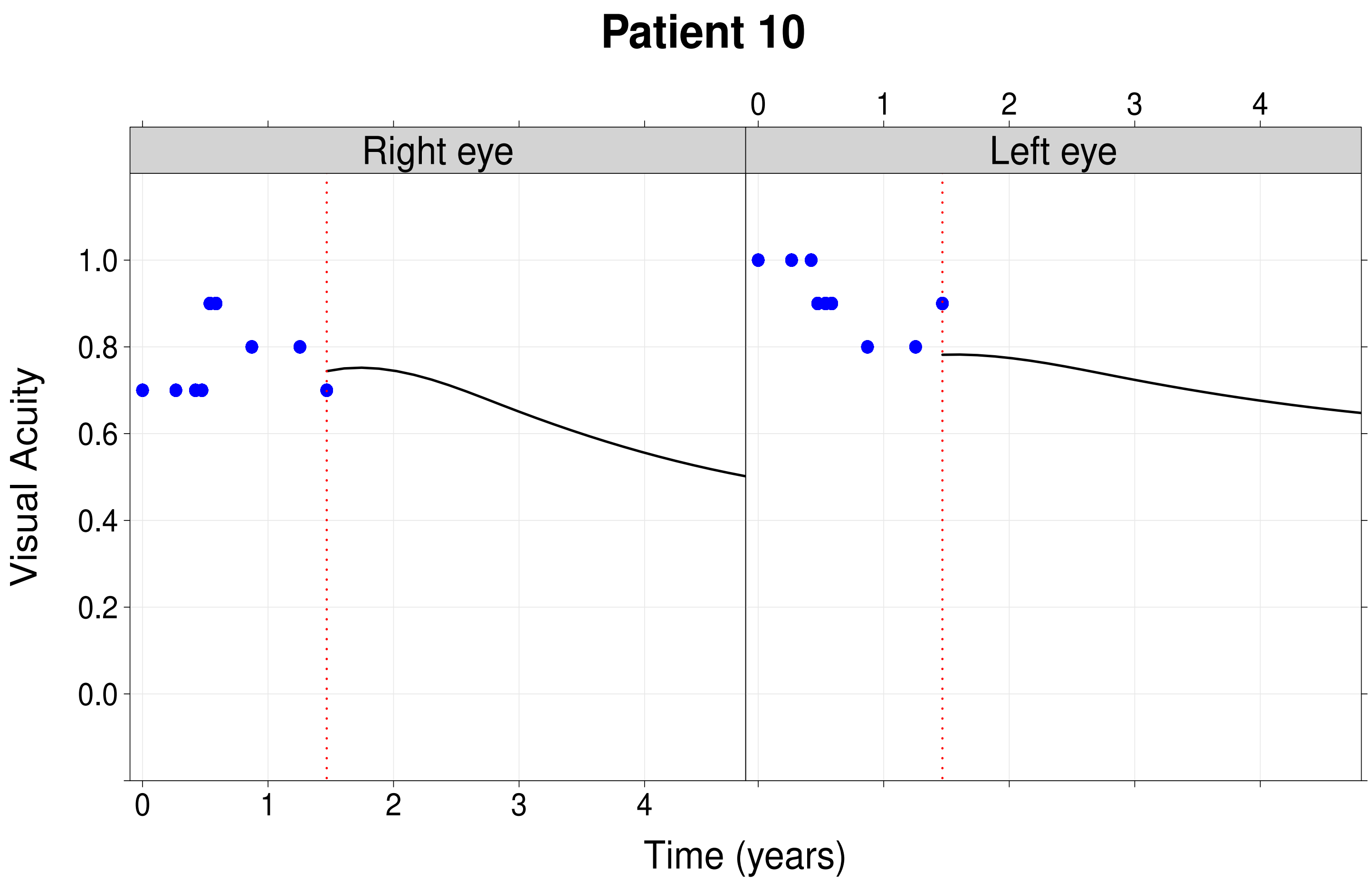
Predictions

Predictions for VA

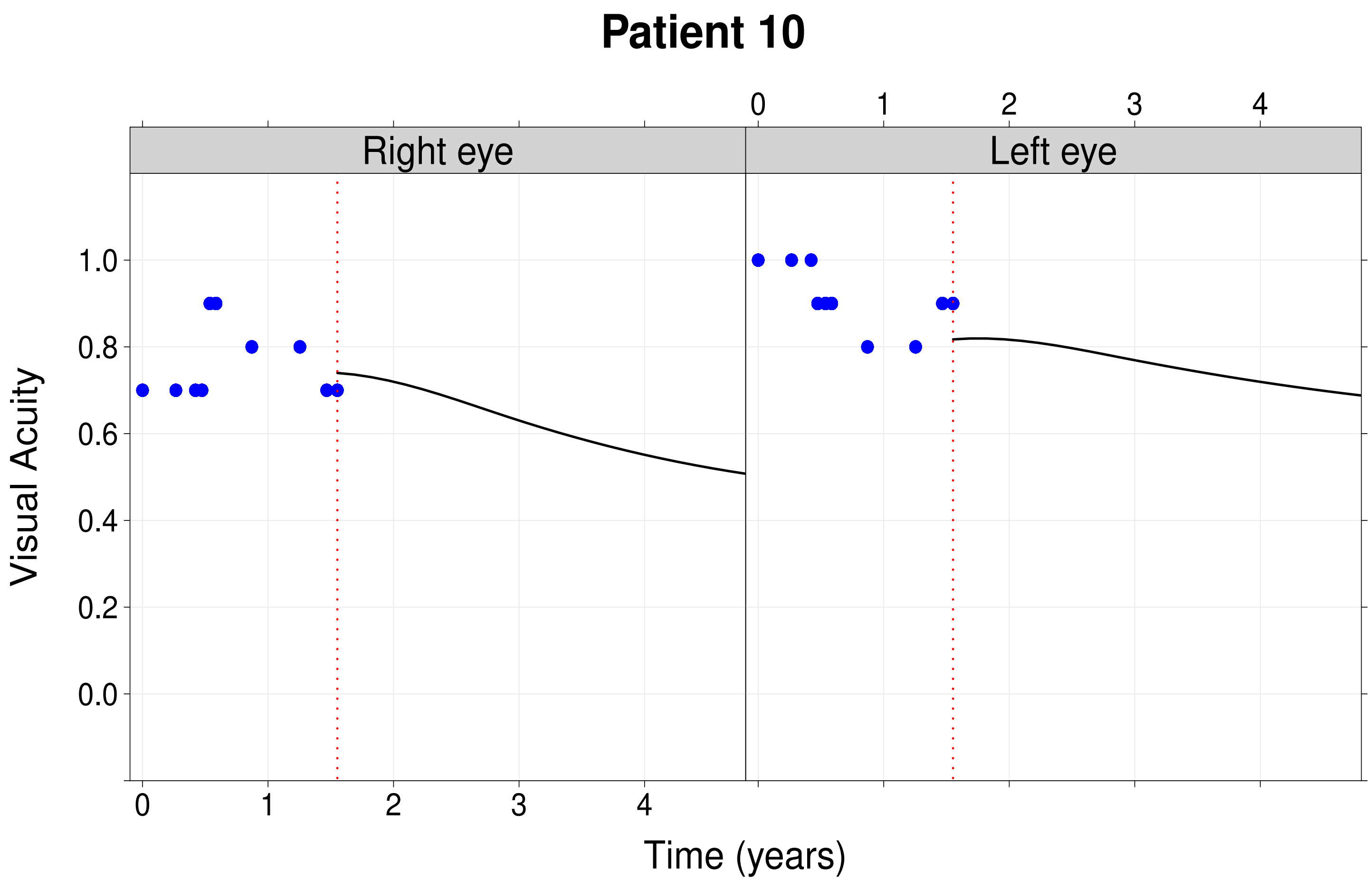
Predictions



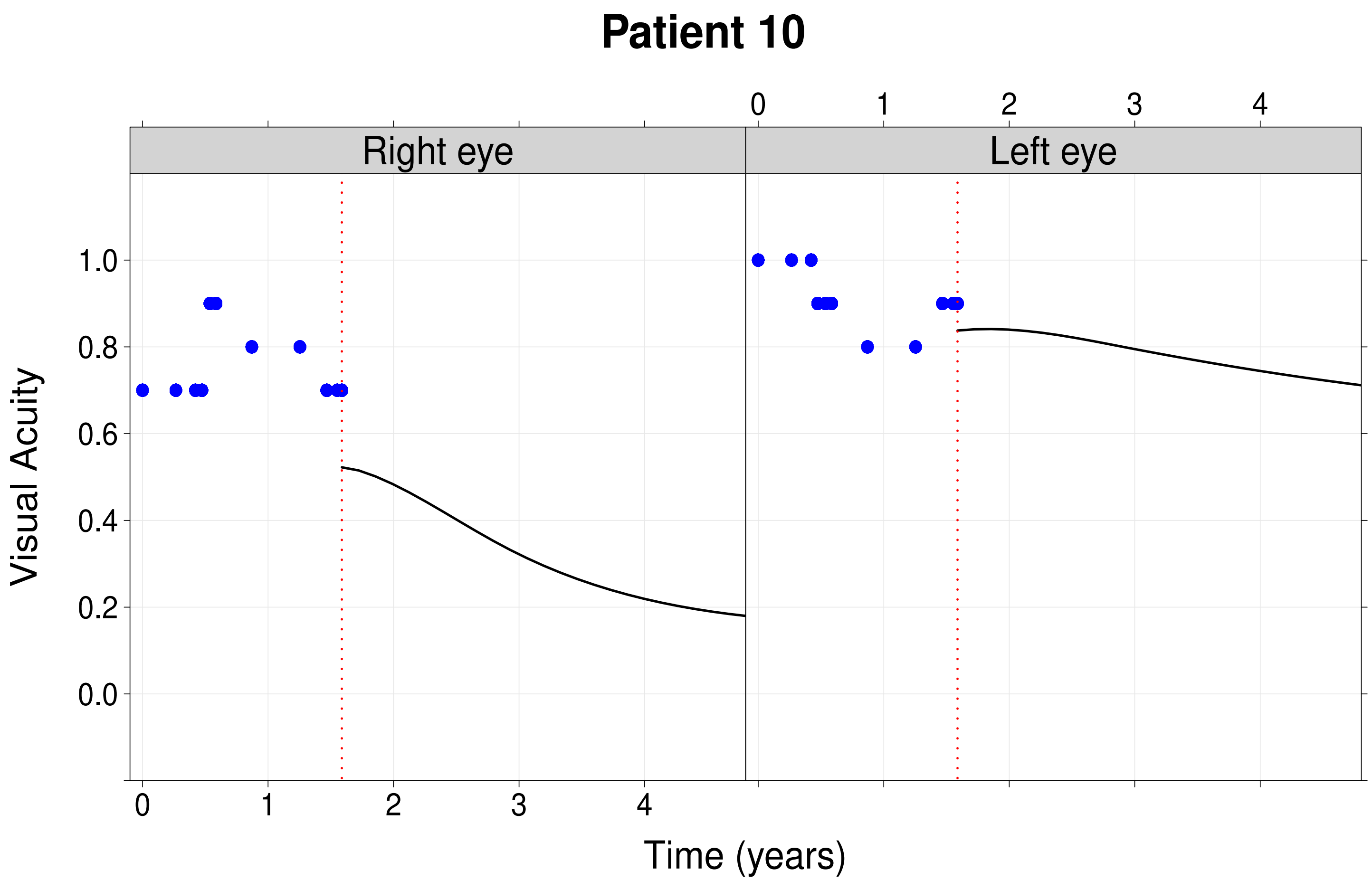
Predictions (cont'd)



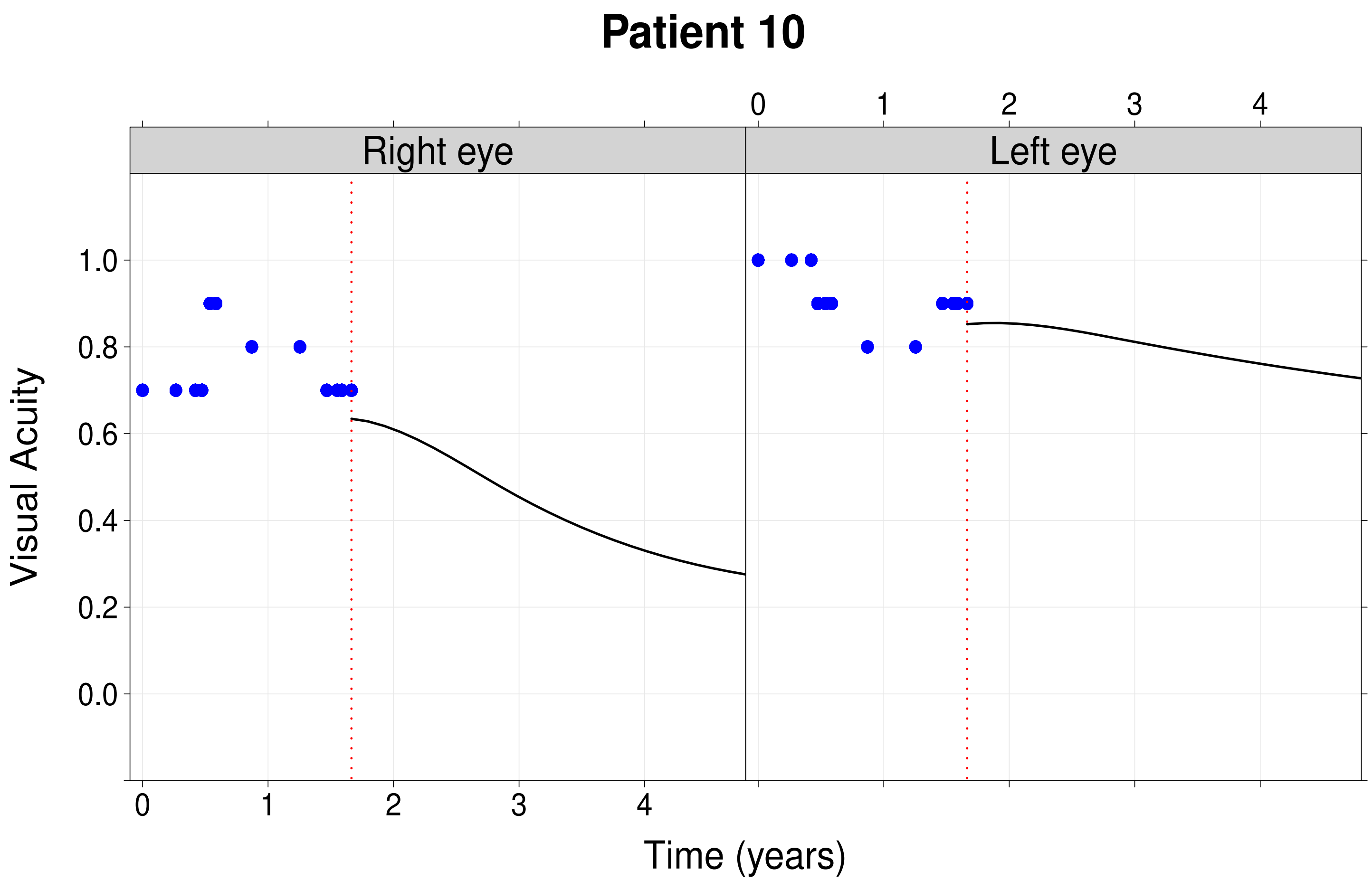
Predictions (cont'd)



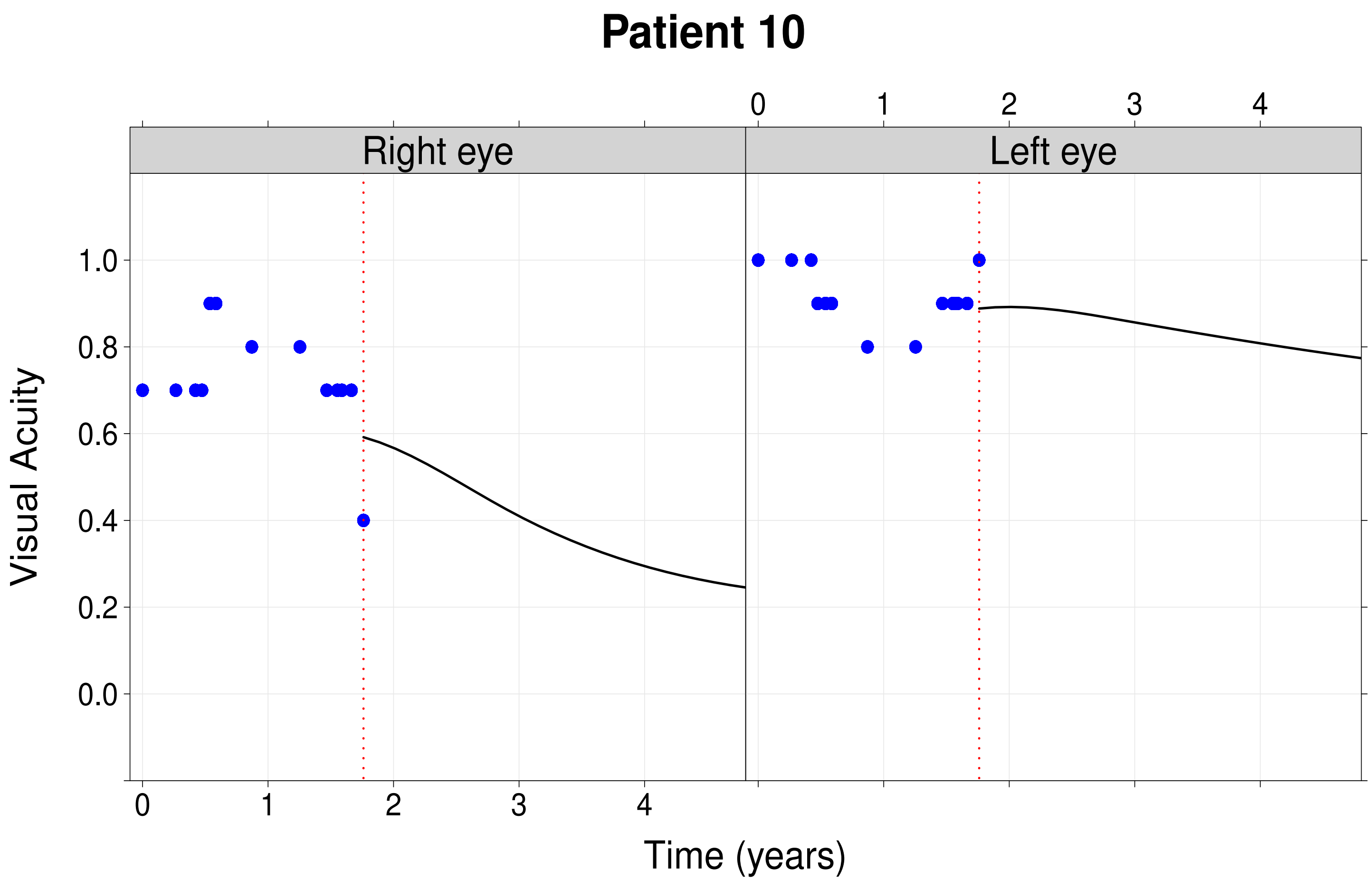
Predictions (cont'd)



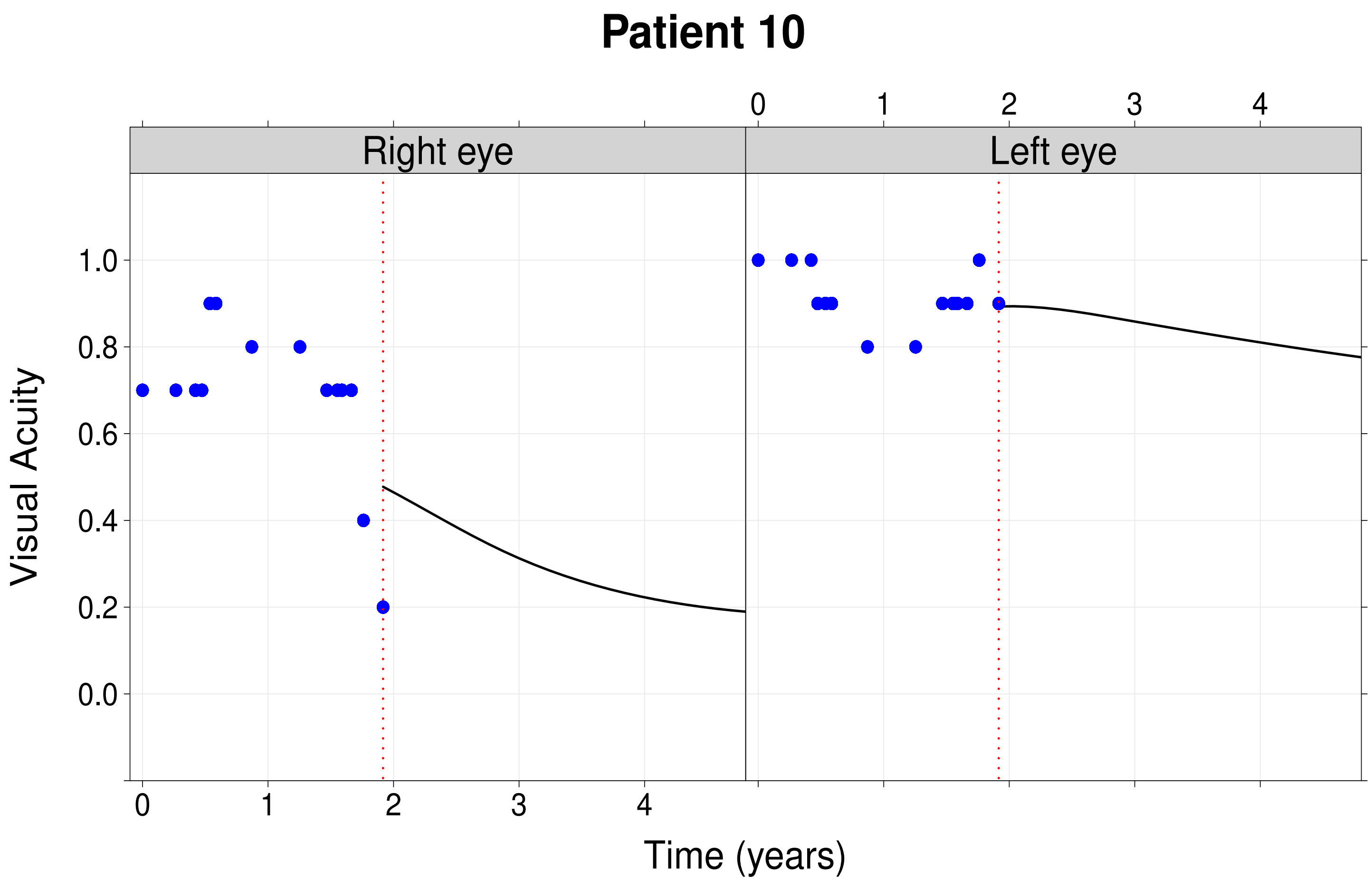
Predictions (cont'd)



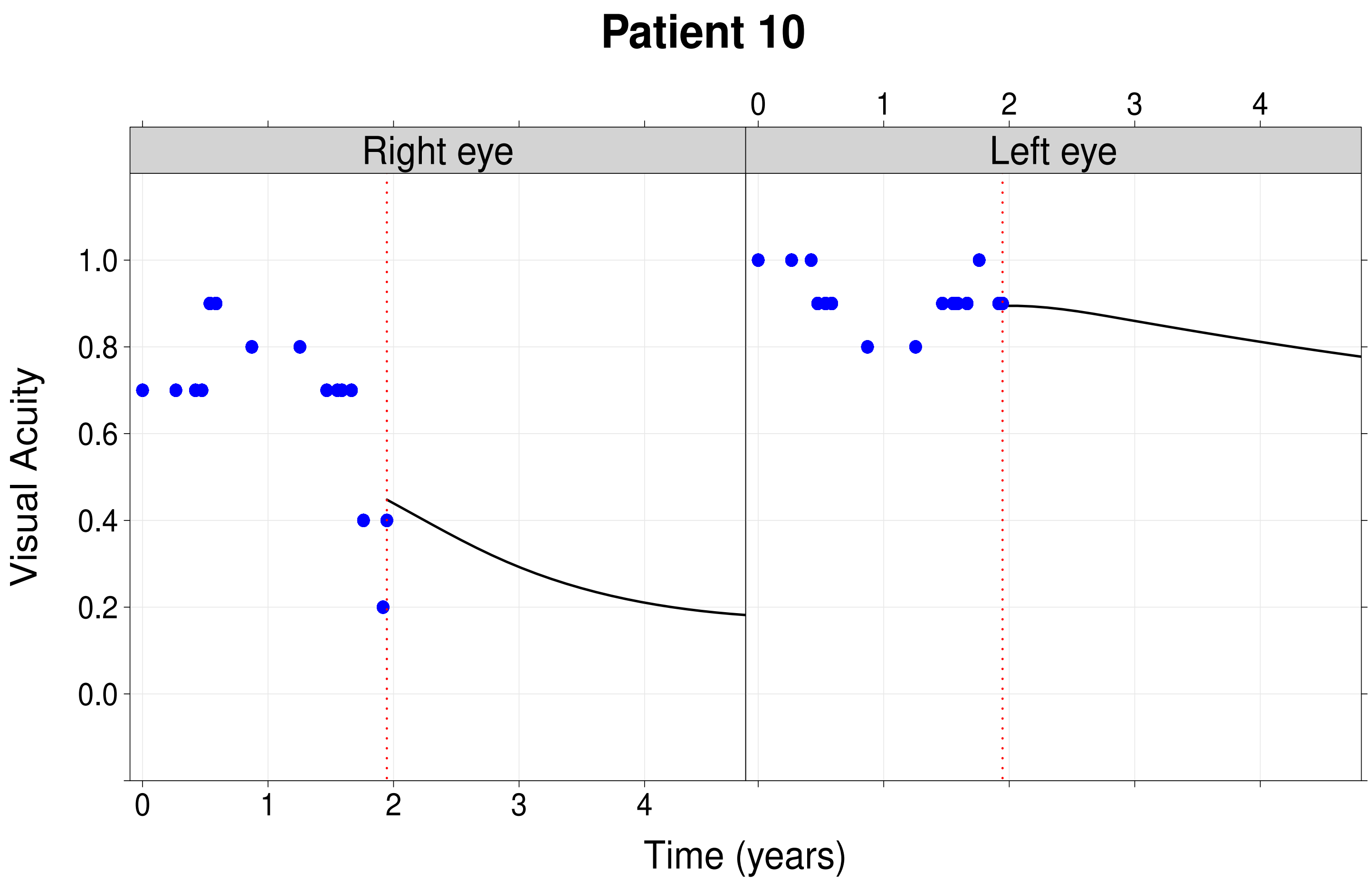
Predictions (cont'd)



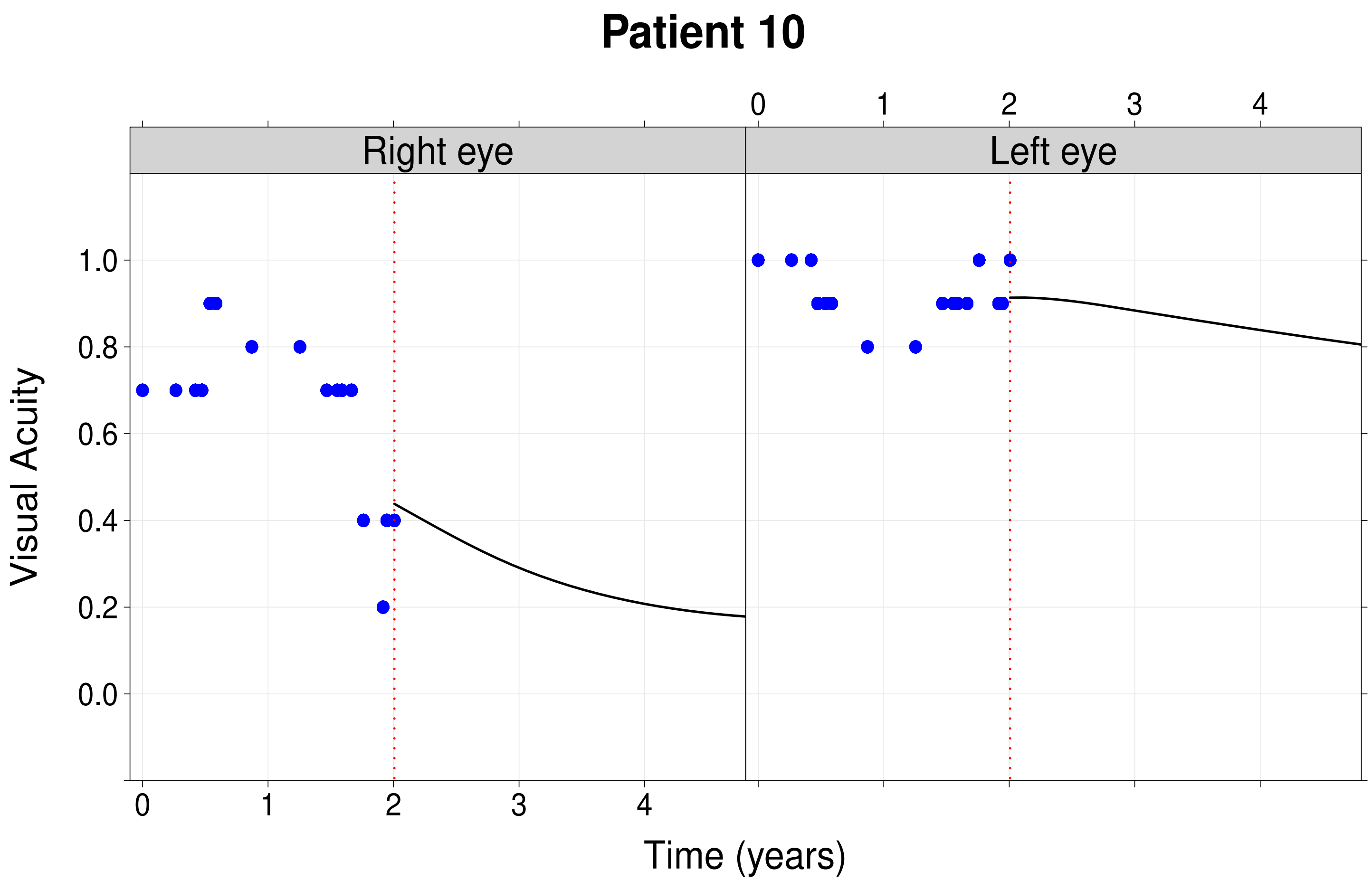
Predictions (cont'd)



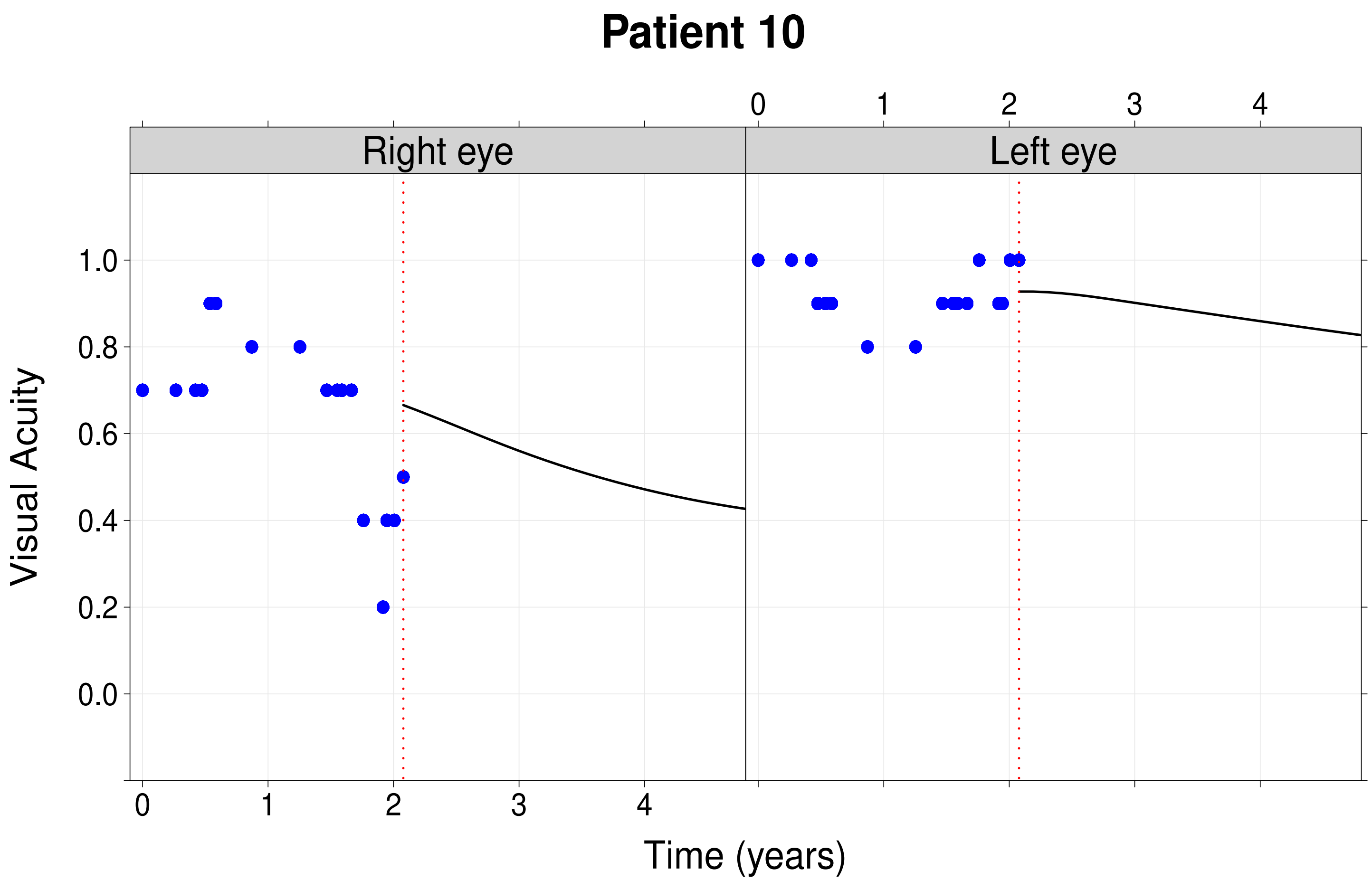
Predictions (cont'd)



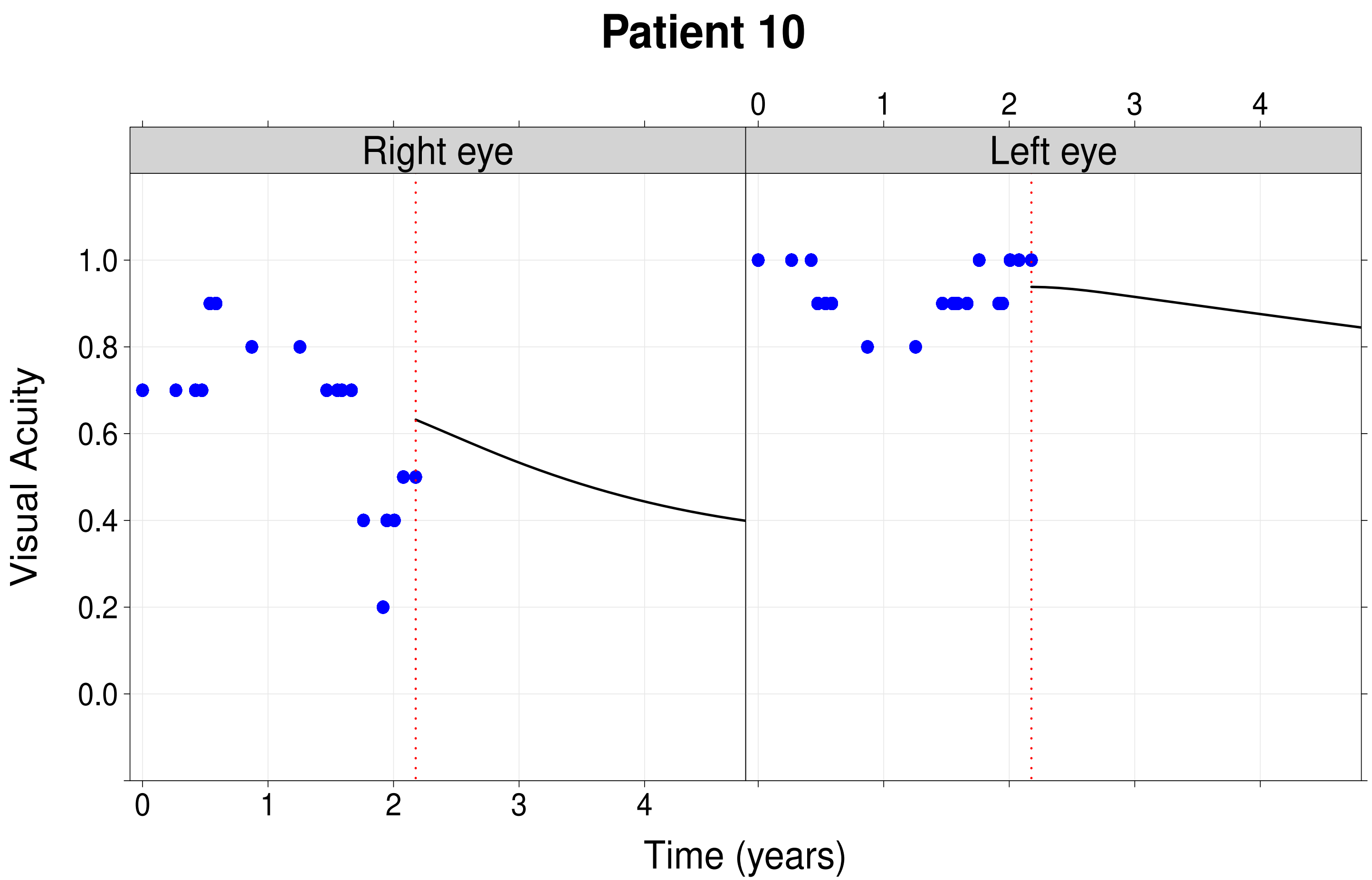
Predictions (cont'd)



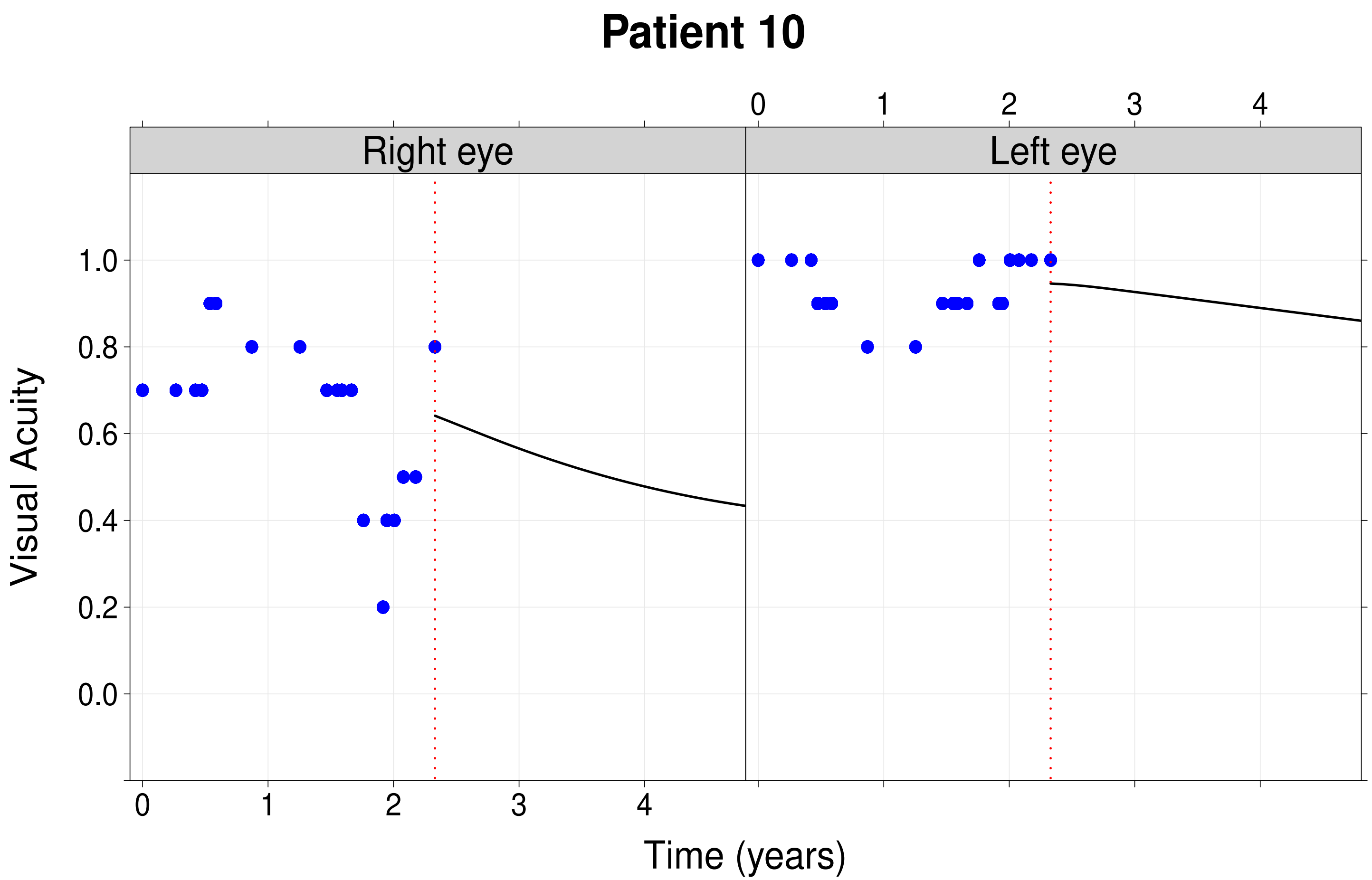
Predictions (cont'd)



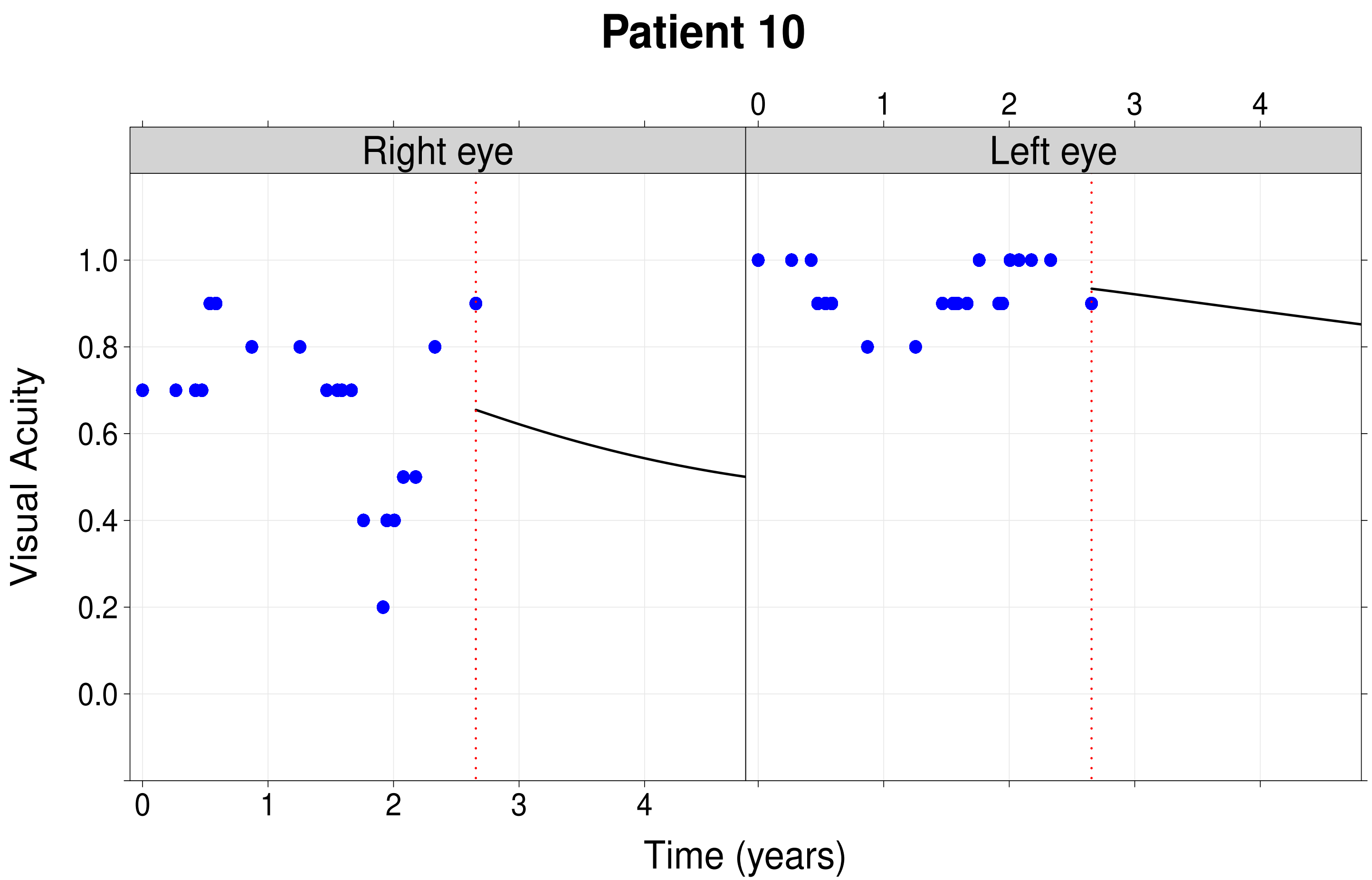
Predictions (cont'd)



Predictions (cont'd)



Predictions (cont'd)



Predictions (cont'd)

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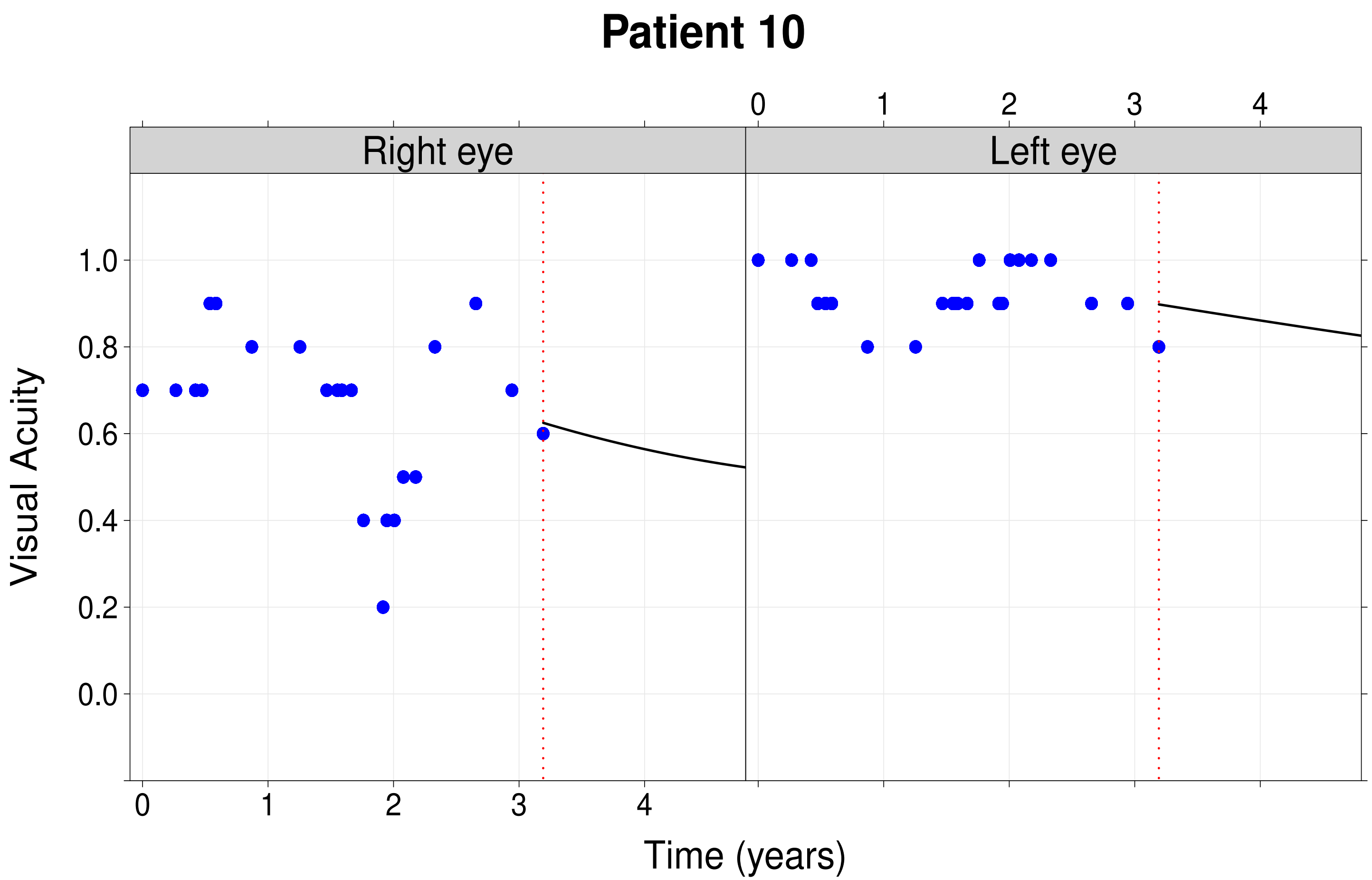

Predictions (cont'd)

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Predictions (cont'd)

Predictions (cont'd)

Evaluation

- **Clinical point of view**
  - ▷ **GOOD** $= |$ logMAR(observedVA) - logMAR(predictedVA) $| <=$ 0.3

Evaluation (cont'd)

- Cross validation

  ▷ 5-fold cross-validation

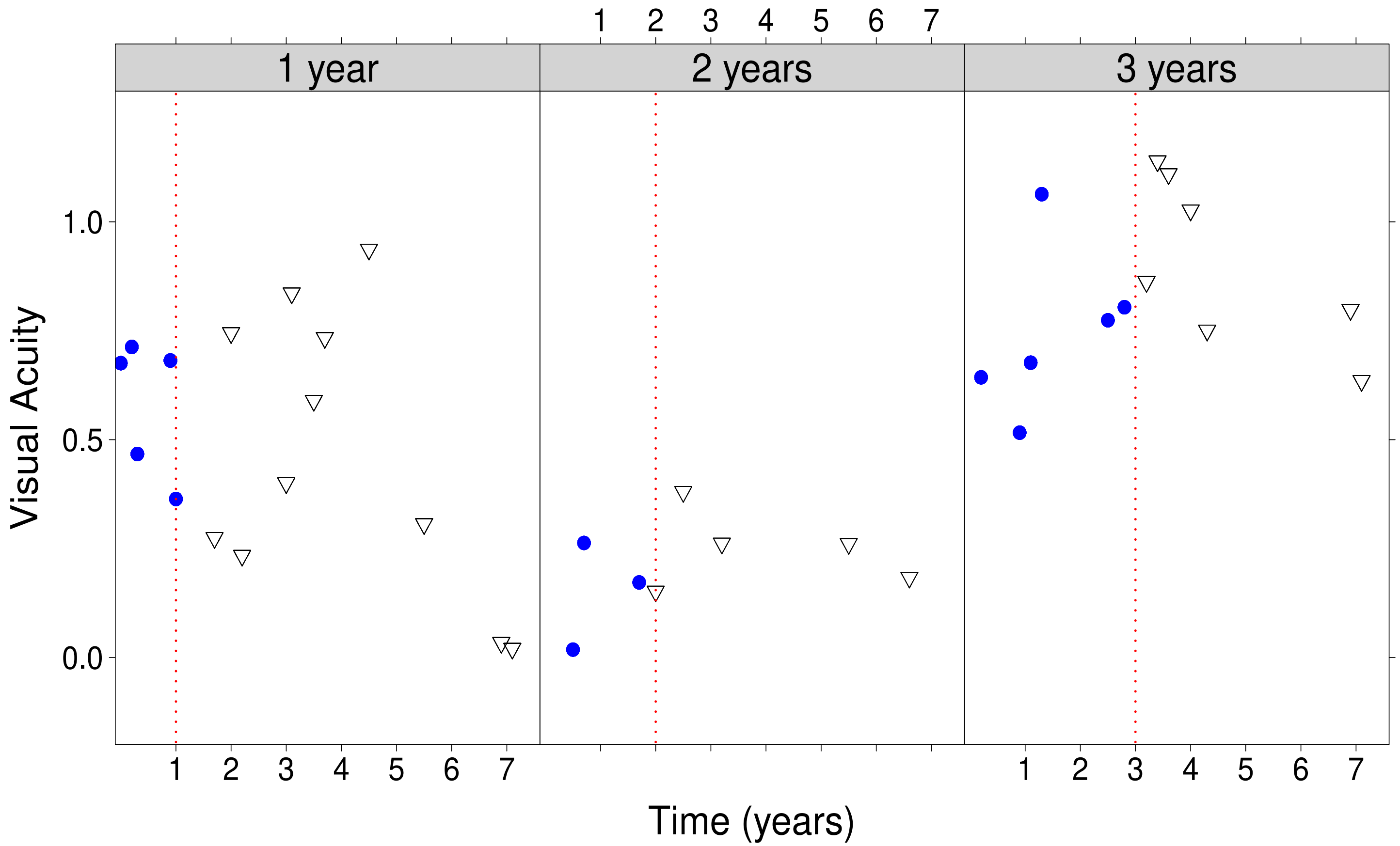
  ▷ Split data 5 subsets

  ▷ fit $\rightarrow$ 4 subsets

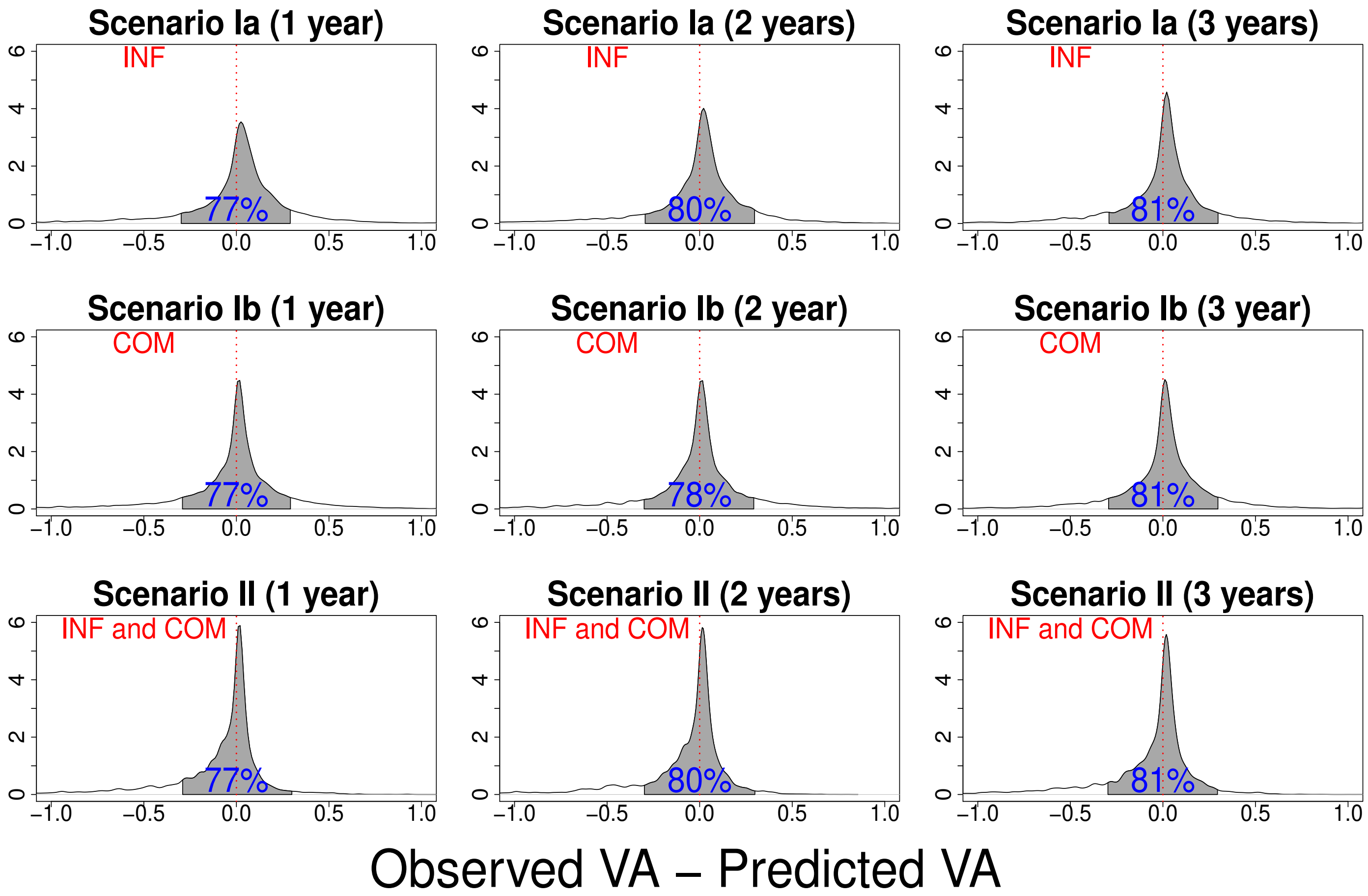
  ▷ calculate **GOOD** $\rightarrow$ 1 subset

  Repeated 10 times

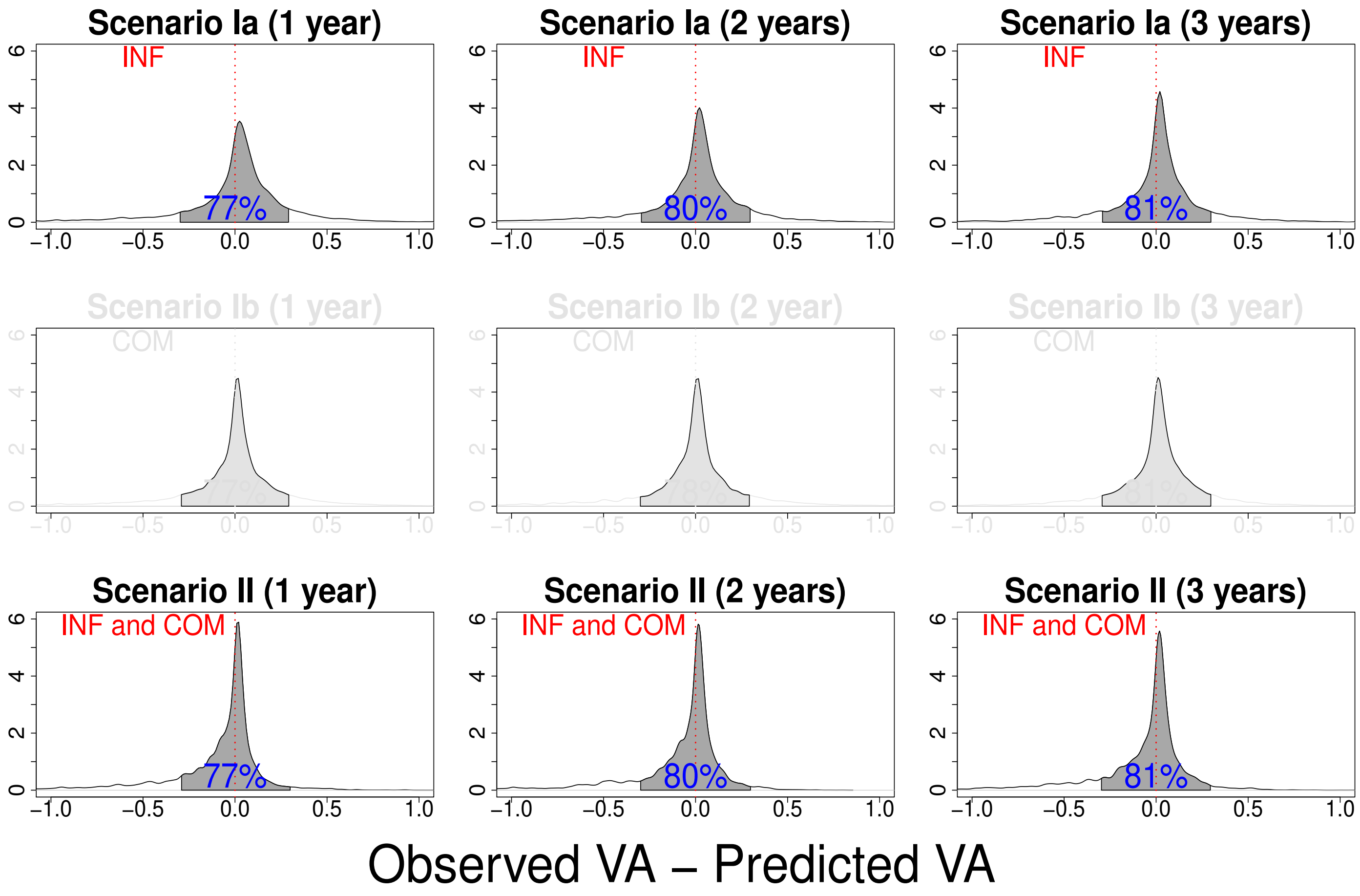
Evaluation (cont'd)



Evaluation (cont'd)



Evaluation (cont'd)



Conclusion

- predictions of VA

Limitations

- ▷ No correlation between the eyes
- ▷ different features of the time-varying covariates
- ▷ more features and time-varying covariates for shrinkage
- ▷ external validation

Thank you!