Generalized linear mixed-effects model (GLMM) trees

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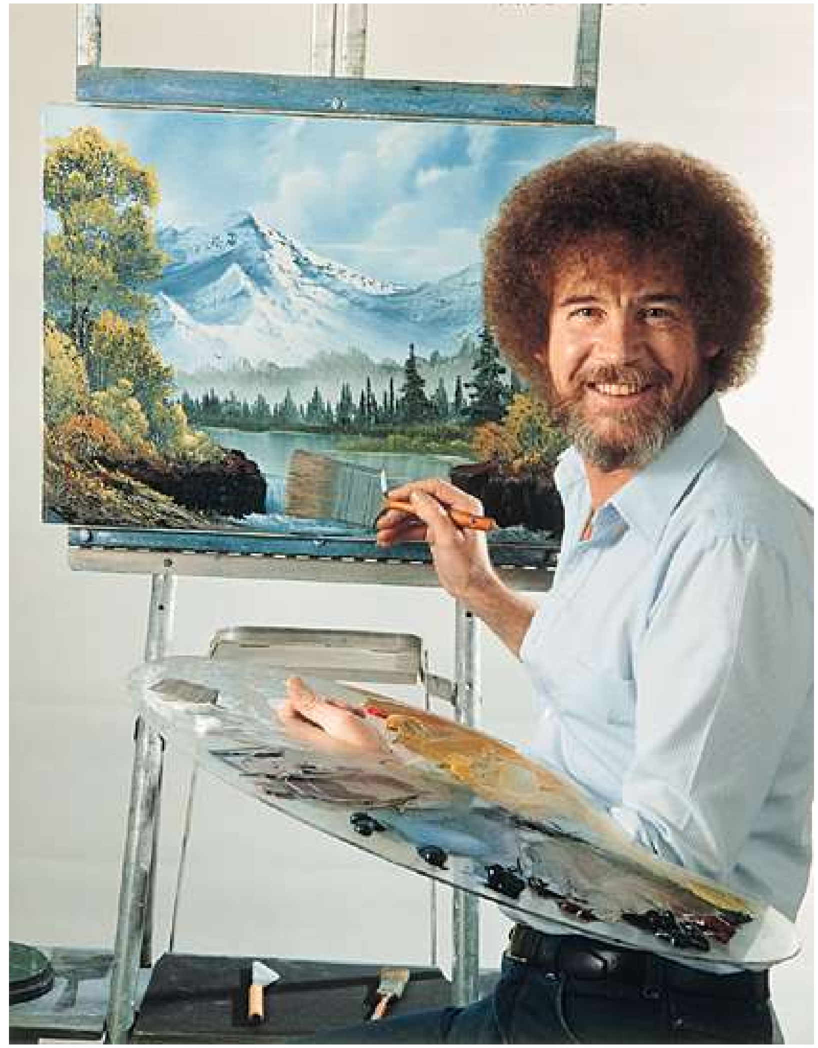


Slides, scripts and data:

https://github.com/marjoleinF/GLMMtree_webinar

Trees: Very short history

Early methods:

- Automated interaction detection (AID Morgan & Sonquist, 1963)
- Classification and regression trees (CART; Breiman et al., 1984)
- ID3 (Quinlan, 1986)
- C4.5 (Quinlan, 1993)

Unbiased recursive partitioning:

- Generalized unbiased interaction detection and estimation (GUIDE; Loh, 2002)
- Conditional inference trees (ctree; Hothorn, Hornik & Zeileis, 2006)
- Model-based recursive partitioning (MOB; Zeileis, Hothorn & Hornik, 2008)

R package: partykit

Model-based recursive partitioning (Zeileis et al., 2008)

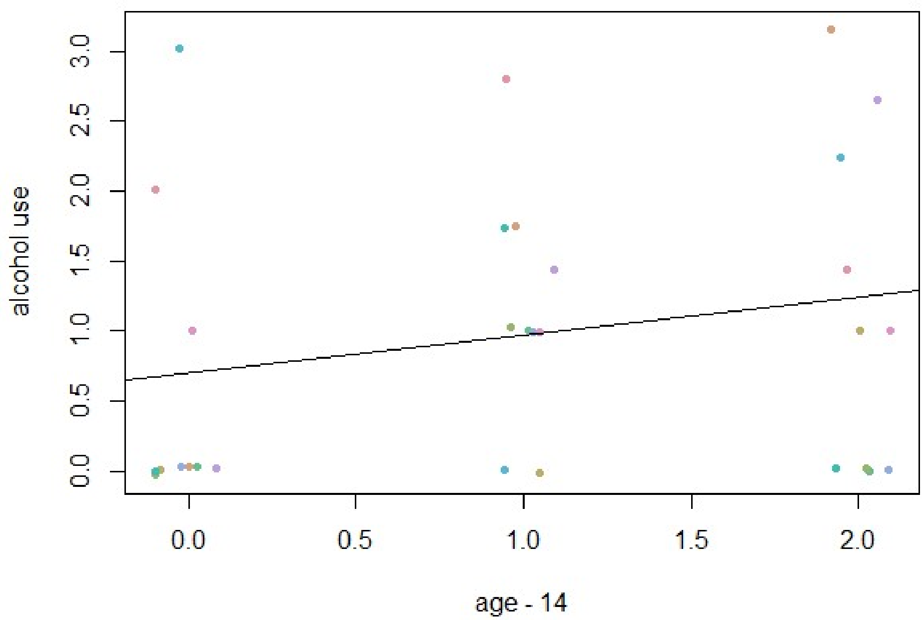
Global parametric model may not fit all observations well:

$$y_i = x_i^\top \beta + \epsilon_i$$

Example: Alcohol use trajectories

82 adolescents, 3 time points:

- Age: 14, 15, or 16 (***X***)
- Alcuse: the primary response (***Y***)



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Model-based recursive partitioning (Zeileis et al., 2008)

Global parametric model may not fit all observations well.

Using covariates, find subgroups with better-fitting local models:

$$y_i = x_i^\top \beta_k + \epsilon_i$$

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MOB algorithm:

1. Fit parametric model to observations in current node.
2. Perform a *parameter stability test* w.r.t. each of the covariates.
3. If at least one of the covariates has *p* value ≤ α , select variable with lowest *p* value for splitting.
4. Repeat steps 1-3 in the two resulting nodes.

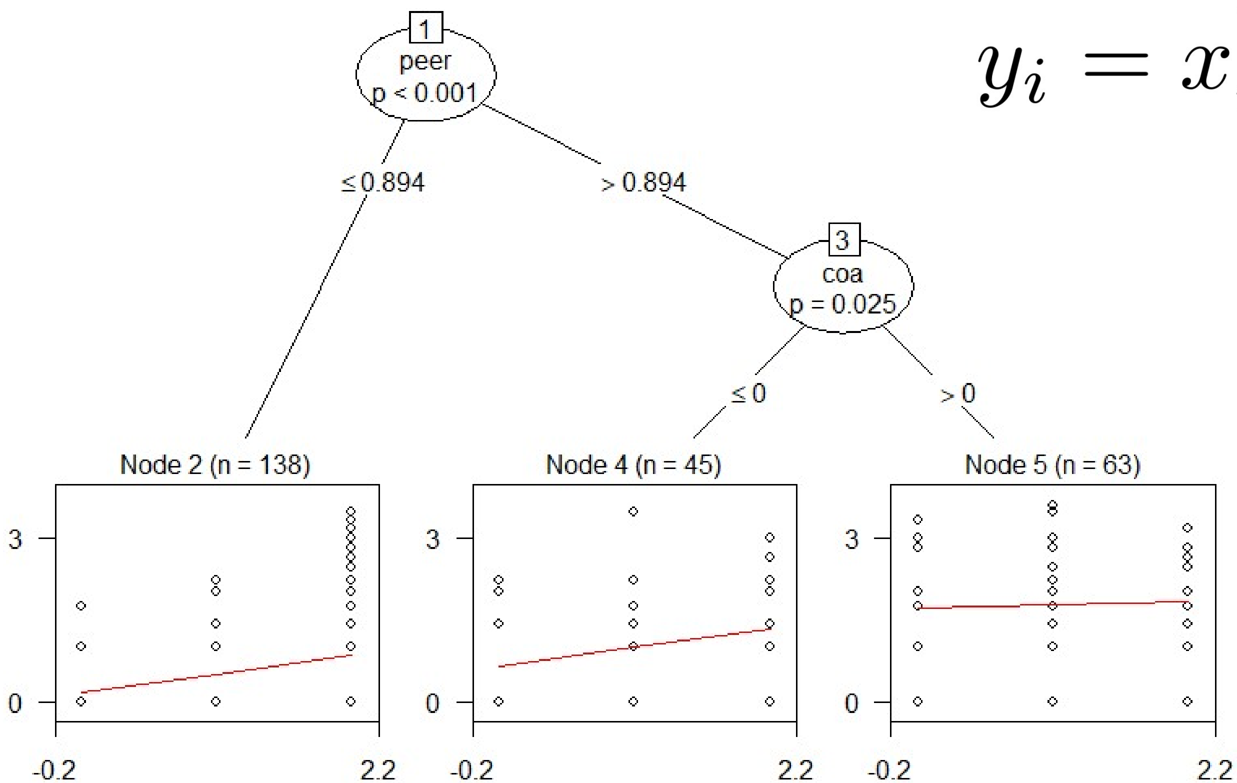
Example: Alcohol use trajectories

82 adolescents, 3 time points:

- Age: 14, 15, or 16 (***X***)
- Alcuse: the primary response (***Y***)
- Additional covariates:
  - Coa: 1 if child of an alcoholic parent; 0 otherwise
  - Male: 1 if male; 0 if female
  - Peer: a measure of peer alcohol use at age 14

Model-based recursive partition

```r
library("partykit")
lt <- lmtree(alcuse ~ age | coa + male + peer, data = alco)
```



$$y_i = x_i^\top \beta_k + \epsilon_i$$

Mixed-effects model

(G)LMM:

$$y_{ij} = x_{ij}^\top \beta + z_{ij}^\top b_i + \epsilon_{ij}$$

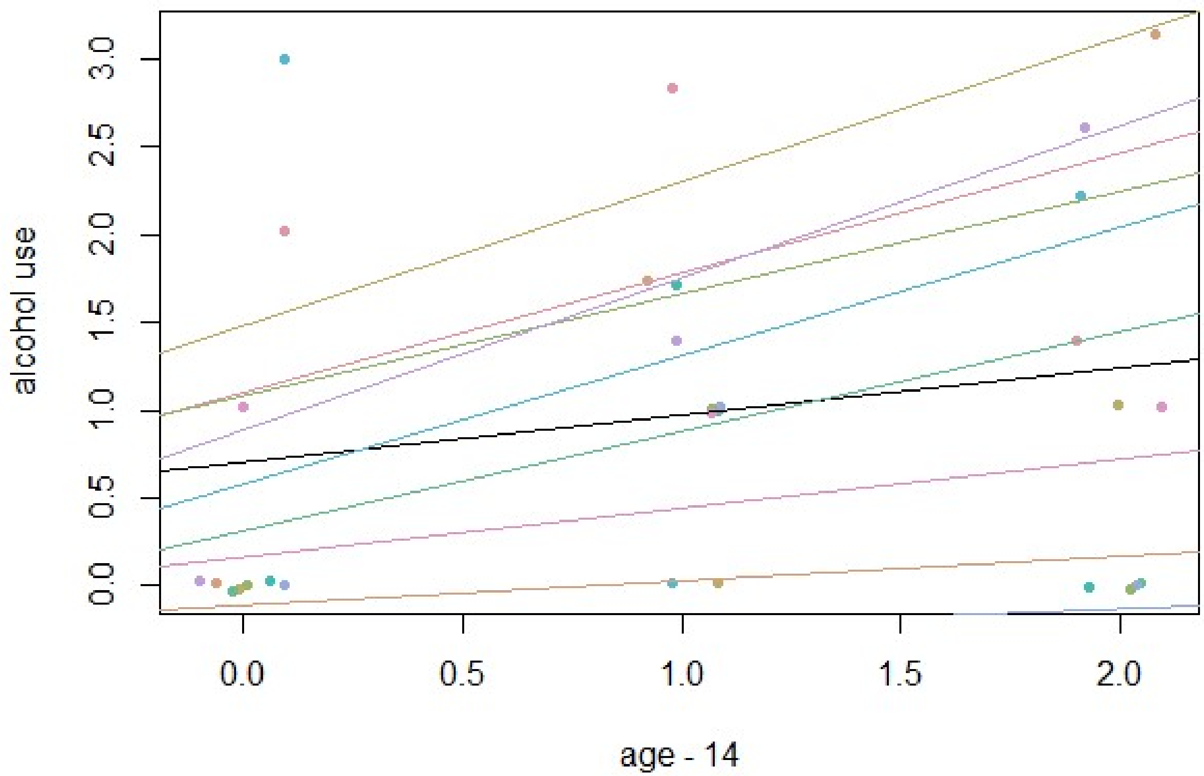
Example: Alcohol use trajectories

82 adolescents, 3 time points:

- Age: 14, 15, or 16 (***X***)
- Alcuse: the primary response (***Y***)

- Id: numerical identifier for subject (***Z***)

Mixed-effects model



$$y_{ij} = x_{ij}^\top \beta + z_{ij}^\top b_i + \epsilon_{ij}$$

Mixed-effects model

(G)LMM:

$$y_{ij} = x_{ij}^\top \beta + z_{ij}^\top b_i + \epsilon_{ij}$$

(G)LMM tree (Fokkema et al., 2018):

$$y_{ij} = x_{ij}^\top \beta_k + z_{ij}^\top b_i + \epsilon_{ij}$$

Example: Alcohol use trajectories

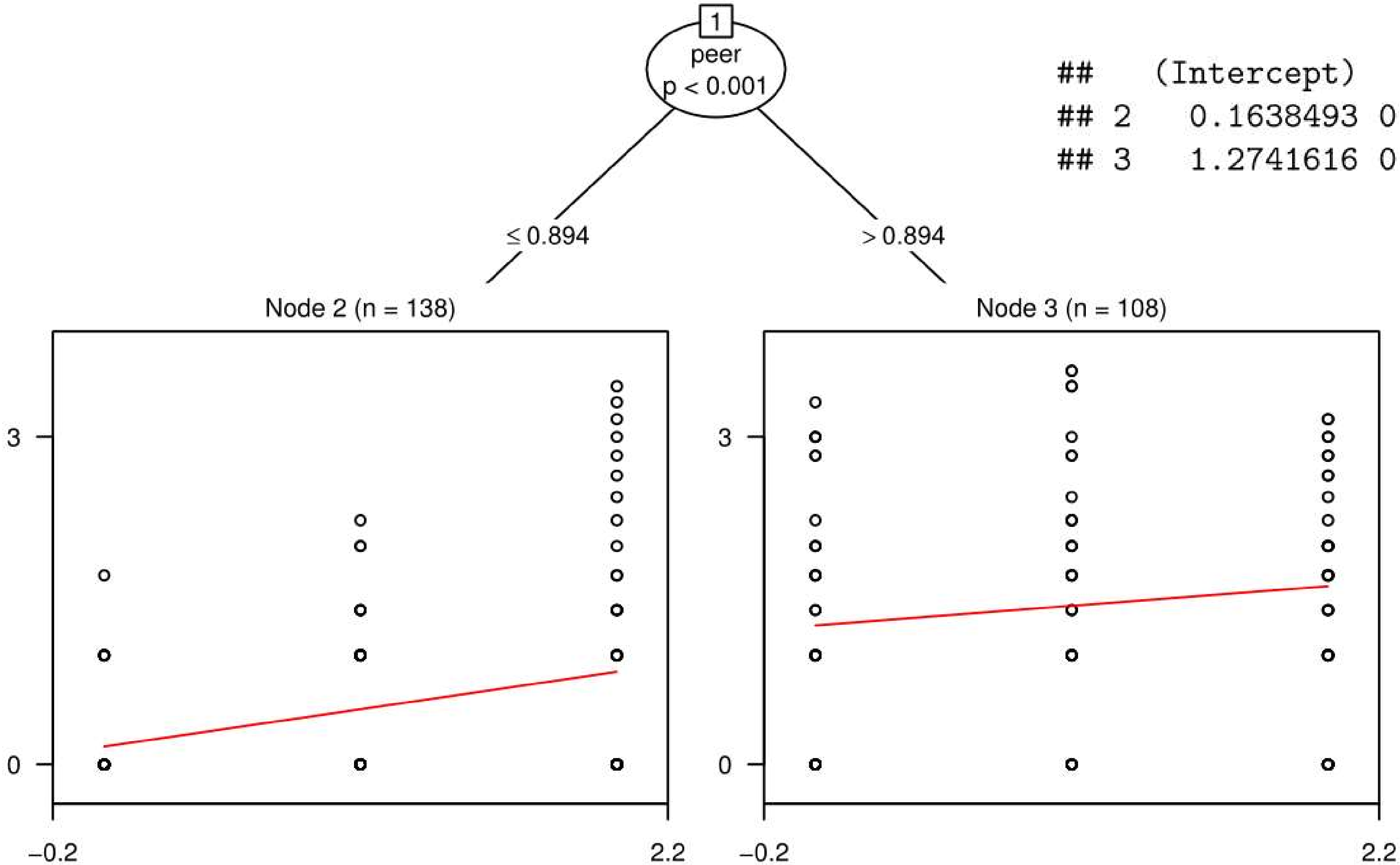
82 adolescents, 3 time points:

- Age: 14, 15, or 16 (***X***)
- Alcuse: the primary response (***Y***)
- Additional covariates:
  - Coa: 1 if child of an alcoholic parent; 0 otherwise
  - Male: 1 if male; 0 if female
  - Peer: a measure of peer alcohol use at age 14
- Id: numerical identifier for subject (***Z***)

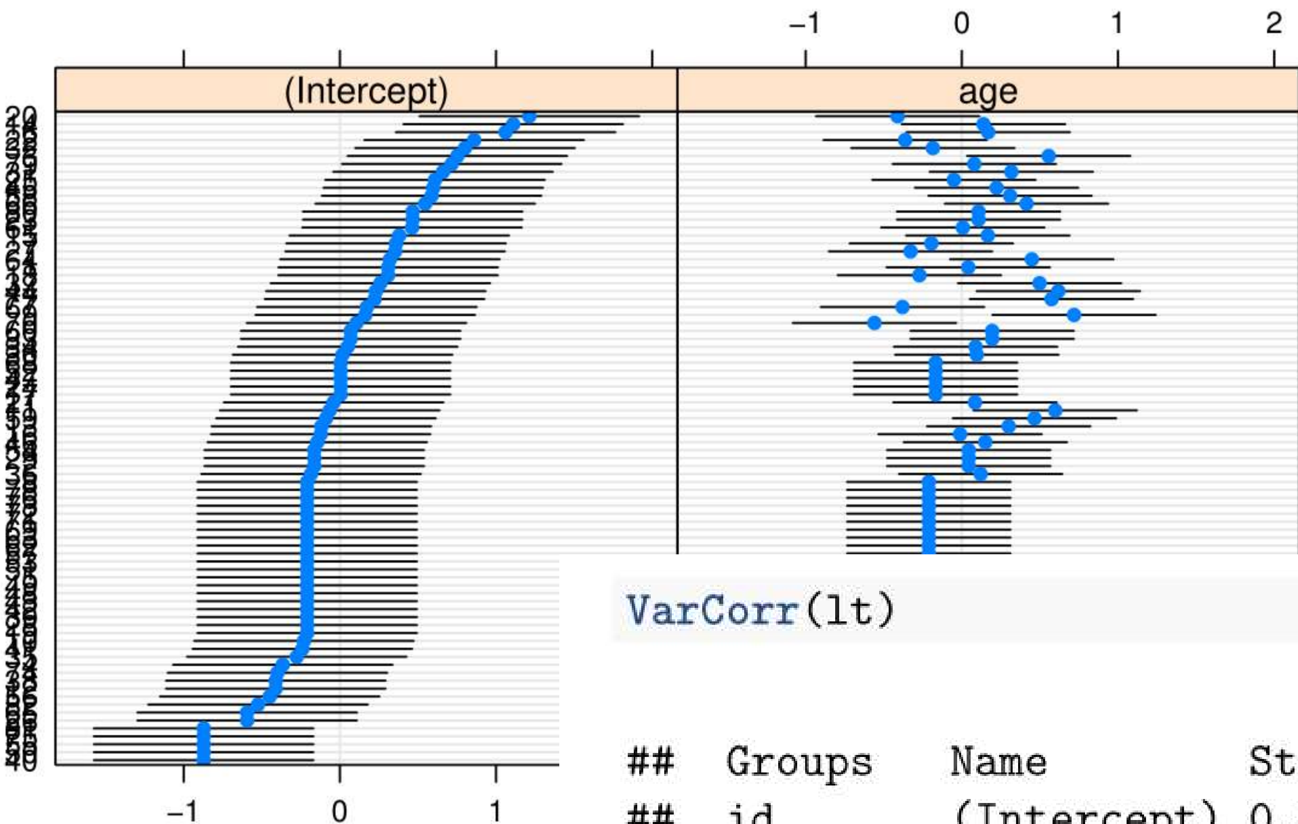
```r
lt <- lmertree(alcuse ~ age | (age|id) | coa + male + peer, data = alco,
               cluster = id)
```

```r
fixef(lt)
```

```
##   (Intercept)       age
## 2   0.1638493 0.3423005
## 3   1.2741616 0.1790998
```



```r
lt <- lmertree(alcuse ~ age | (age|id) | coa + male + peer, data = alco,
               cluster = id)
```




```r
VarCorr(lt)
```

```
## Groups   Name        Std.Dev. Corr
## id       (Intercept) 0.57947
##          age         0.39048  -0.127
## Residual             0.58077
```

Example: Stage fright trajectories

37 music majors filled out diaries prior to performances over the course of an academic year:

- diary: time metric, cumulative total of diaries filled out (***X***)
- na: negative affect score from PANAS ***(Y)***
- id: unique musician identification number (***Z***)

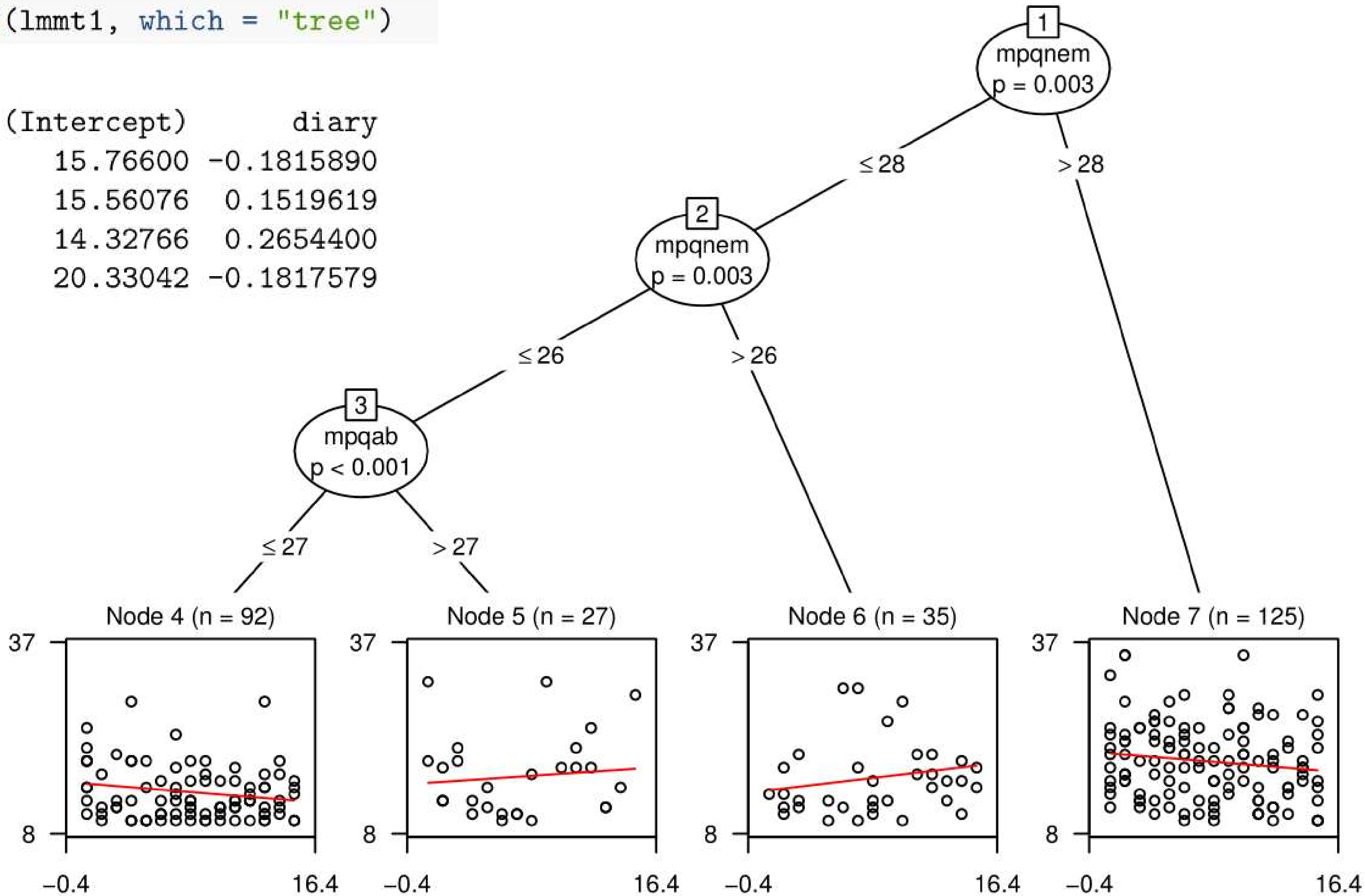
Covariates (level II):

- gender
- instrument: Voice, Orchestral, or Piano
- mpqab: absorption scale from MPQ
- mpqpem: positive emotionality scale from MPQ
- mpqnem: negative emotionality scale from MPQ
- audience: Instructor, Public, Students, or Juried (level I)

```r
lmmt1 <- lmertree(na ~ diary | (diary|id) | gender + instrument +
                  mpqab + mpqpem + mpqnem + mpqcon, data = music, cluster = id)
```

```r
fixef(lmmt1, which = "tree")
```

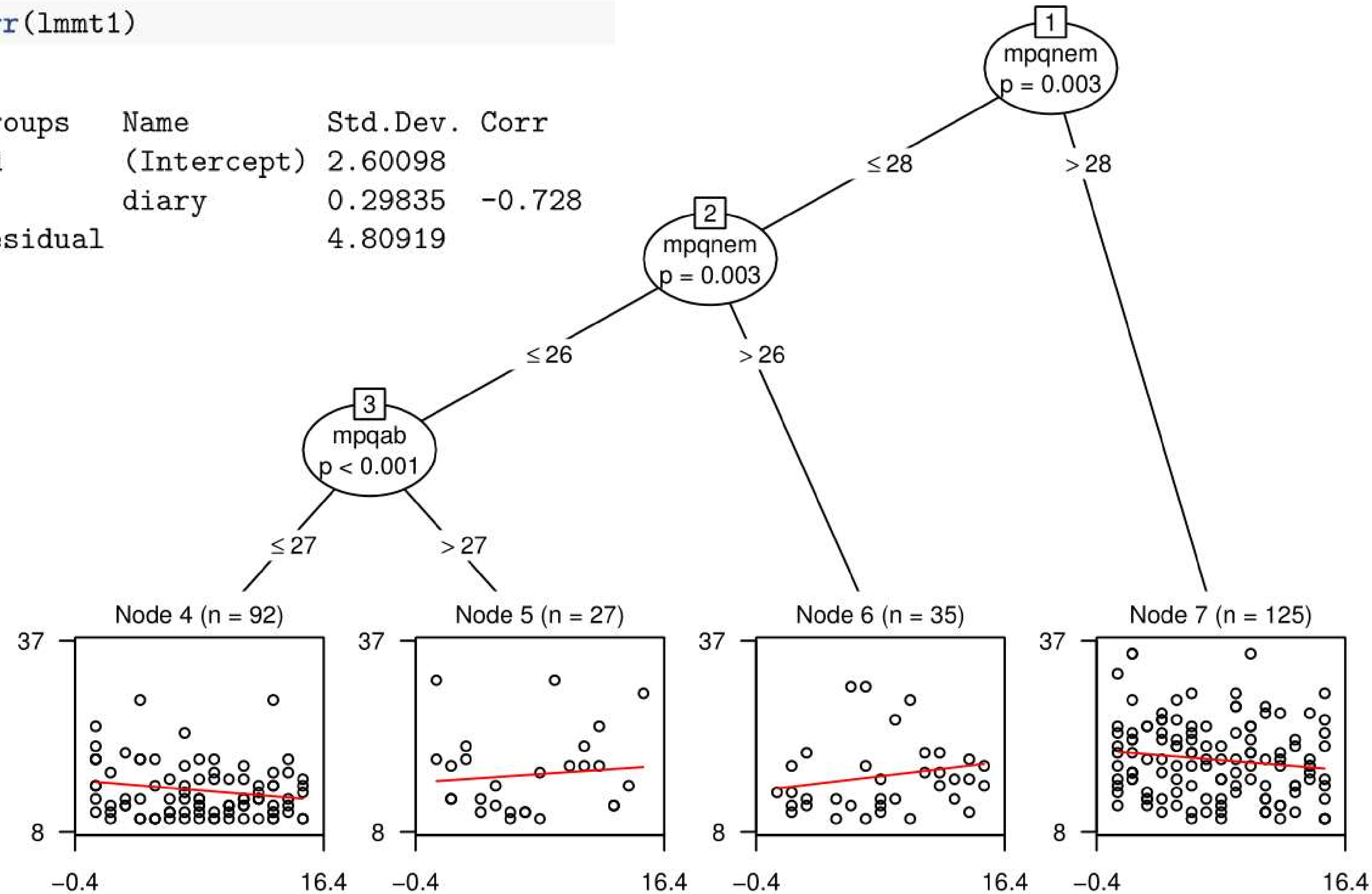
```
##   (Intercept)       diary
## 4    15.76600 -0.1815890
## 5    15.56076  0.1519619
## 6    14.32766  0.2654400
## 7    20.33042 -0.1817579
```



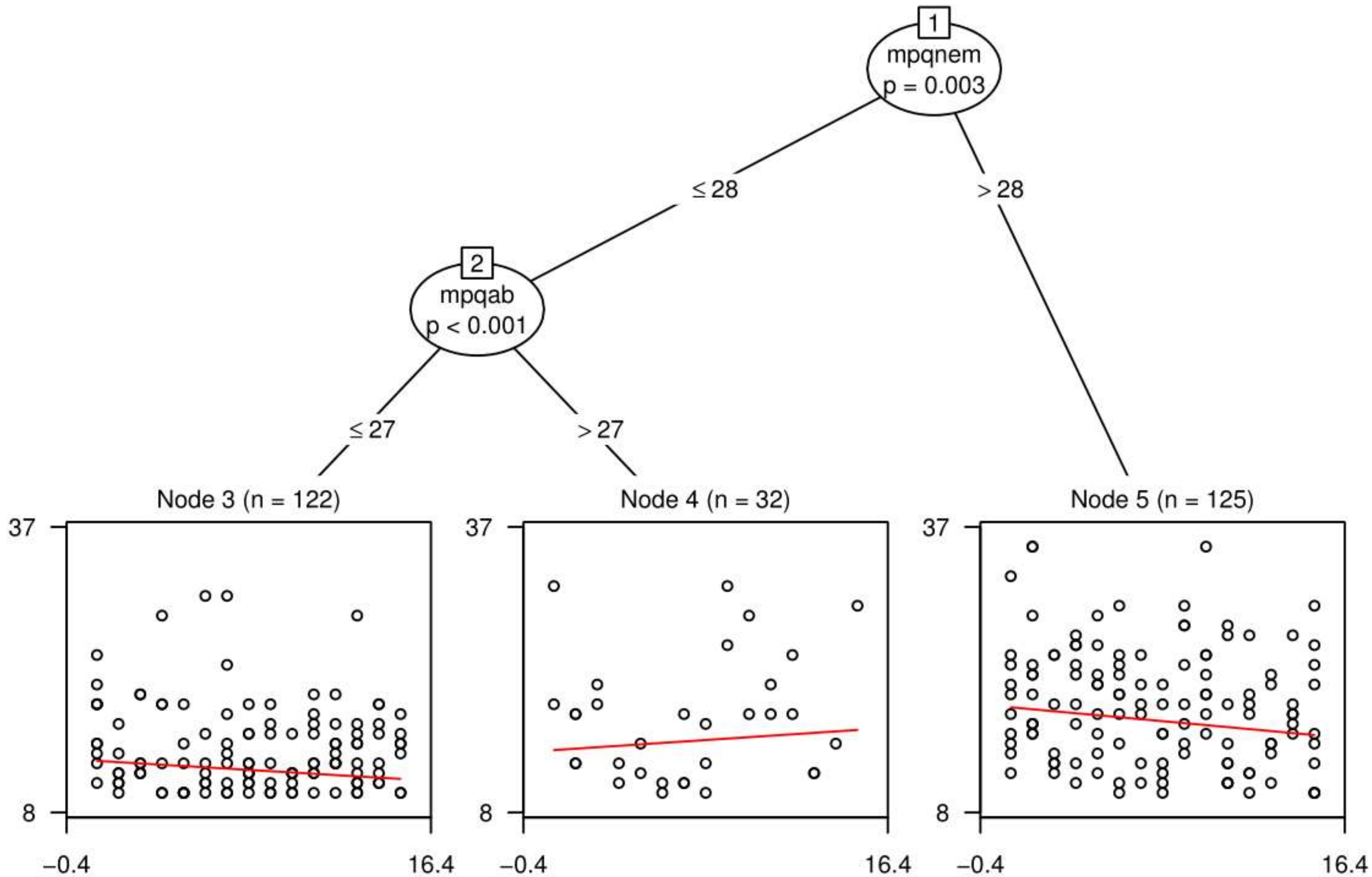
```r
lmmt1 <- lmertree(na ~ diary | (diary|id) | gender + instrument +
                      mpqab + mpqpem + mpqnem + mpqcon, data = music, cluster = id)
```

```r
VarCorr(lmmt1)
```

```
##  Groups   Name        Std.Dev. Corr
##  id       (Intercept) 2.60098
##           diary       0.29835  -0.728
##  Residual             4.80919
```



```r
lmmt2 <- lmertree(na ~ diary | audience + (diary|id) | gender + instrument +
                  mpqab + mpqpem + mpqnem + mpqcon, data = music, cluster = id)
```



```r
lmmt2 <- lmertree(na ~ diary | audience + (diary|id) | gender + instrument +
                  mpqab + mpqpem + mpqnem + mpqcon, data = music, cluster = id)
```

```r
fixef(lmmt2, which = "global")
```

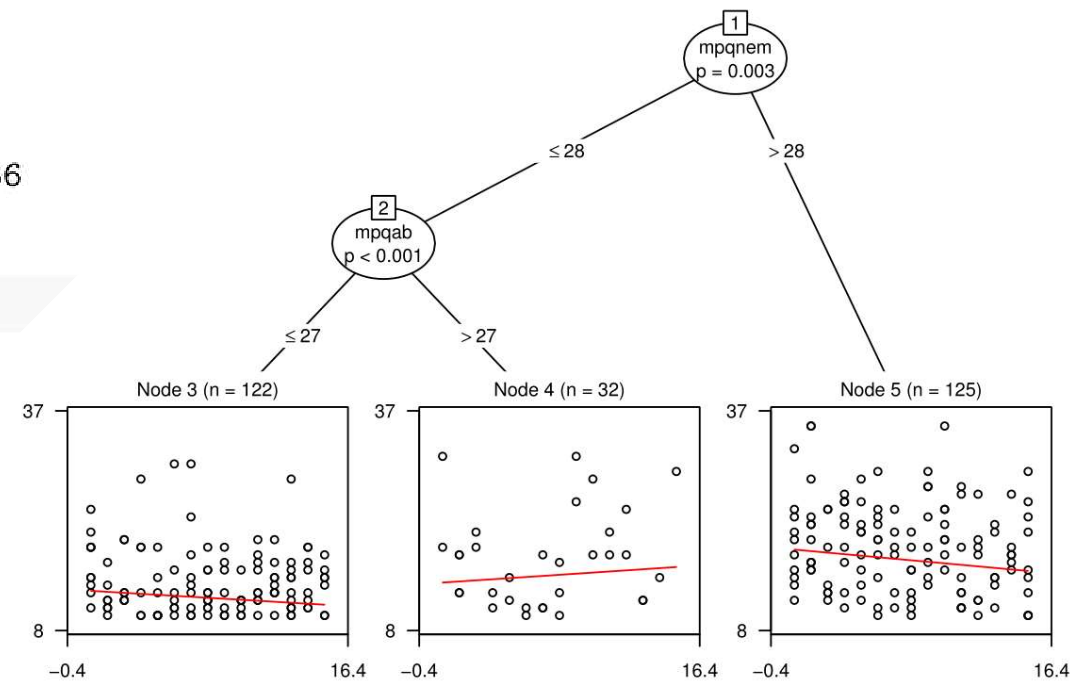
```
##     audienceJuried Recital audiencePublic Performance
##                   3.983440                   3.288610
##         audienceStudent(s)
##                   4.072934
```

```r
VarCorr(lmmt2)
```

```
##  Groups   Name        Std.Dev. Corr
##  id       (Intercept) 2.26847
##           diary       0.25583  -0.736
##  Residual             4.51190
```

```r
fixef(lmmt2, which = "tree")
```

```
##   (Intercept)      diary
## 3    13.37823 -0.1308454
## 4    14.19399  0.1460969
## 5    18.89028 -0.2011977
```



Closing remarks

- GLMM trees can be used to detect subgroups that show differences in any *fixed-effects parameter(s)* of interest, in *any GLMM*
- Ongoing and future work:
  - GAM trees: Detect subgroups in generalized non-linear (mixed-effects) models
  - Detect subgroups and differences in *random-effects* parameters

References

Breiman, L., Friedman, J., Olshen, R., & Stone, C. (1984). *Classification and regression trees.* New York: Wadsworth.

Fokkema, M., Smits, N., Zeileis, A., Hothorn, T. & Kelderman, H. (2018). Detecting treatment-subgroup interactions in clustered data with generalized linear mixed-effects model trees. *Behavior Research Methods, 50*(5), 2016-2034.

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Loh, W. Y. (2002). Regression trees with unbiased variable selection and interaction detection. *Statistica Sinica*, 361-386.

Lucock, M., Barkham, M., Donohoe, G., Kellett, S., McMillan, D., Mullaney, S., ... & Delgadillo, J. (2017). The role of Practice Research Networks (PRN) in the development and implementation of evidence: The Northern improving access to psychological therapies PRN case study. *Administration and Policy in Mental Health and Mental Health Services Research, 44*(6), 919-931.

Morgan, J. N., & Sonquist, J. A. (1963). Problems in the analysis of survey data, and a proposal. *Journal of the American Statistical Association, 58*, 415–434.

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Quinlan, J. R. (1993). *C4.5: Programs for machine learning.* San Francisco: Kaufmann Publishers.

Zeileis, A., Hothorn, T., & Hornik, K. (2008). Model-based recursive partitioning. *Journal of Computational and Graphical Statistics, 17*(2), 492-514

Example: Treatment subgroups

Improving Access to Psychological Therapies project (Lucock et al., 2017).

Patients receiving mental-health services in the UK, either:

- LI: low intensity treatment (guided self-help)
- HI: high intensity treatment (psychotherapy)

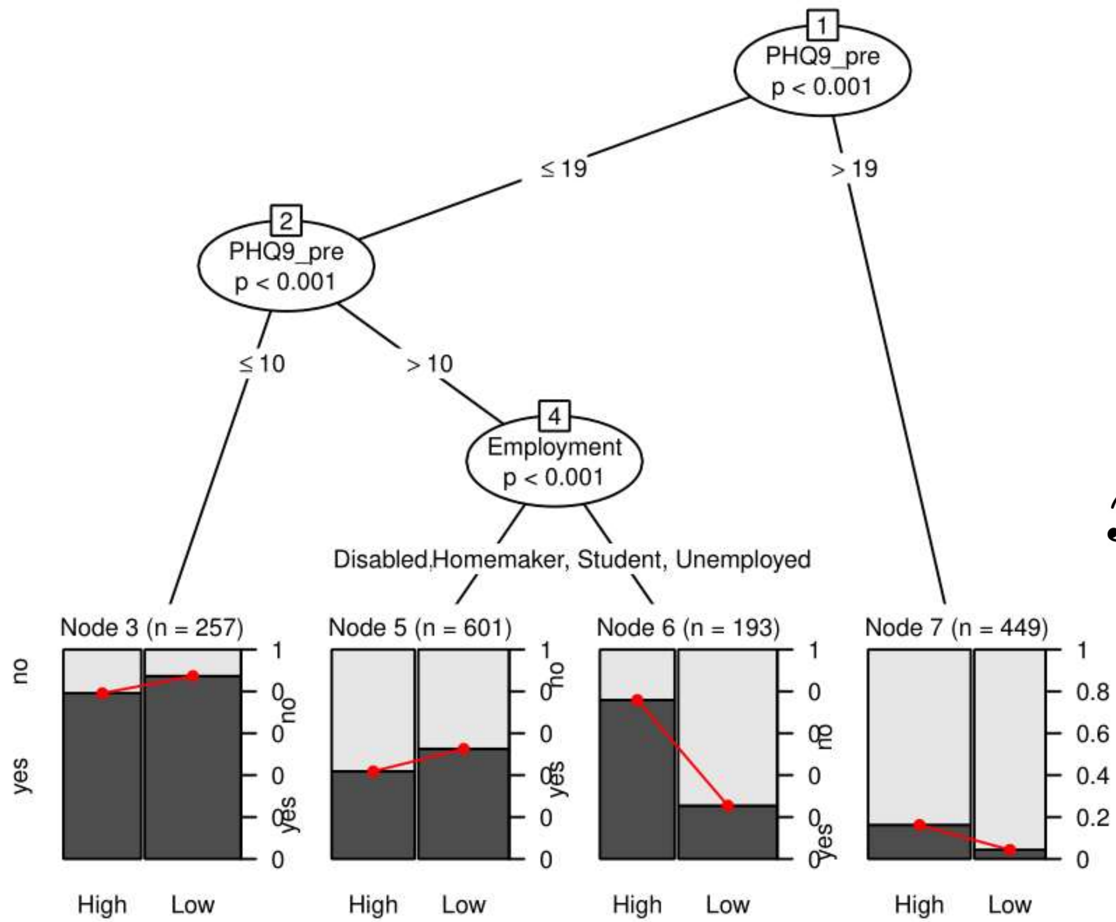
Aim: Identify which patients benefit most from HI vs. LI

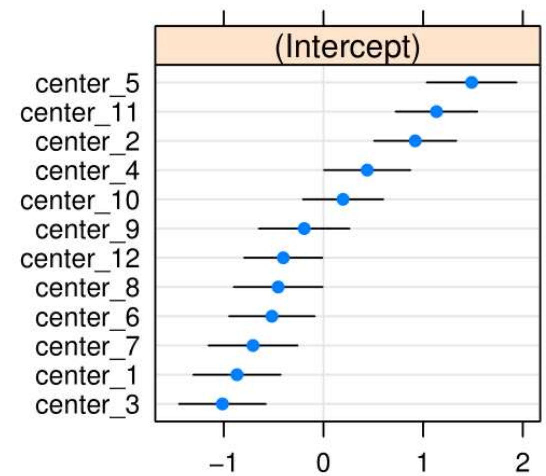
Example: Treatment subgroups

N = 1,500 observations, 13 variables:

- Response (***Y***): recovered (yes, no)
- Predictor (***X***): treatment type (HI vs LI)
- 10 covariates (***U***):
  - PHQ9_pre (baseline depression measure)
  - GAD7_pre (baseline anxiety measure)
  - WSAS_pre (baseline work and social functioning)
  - Age, Gender, Ethnicity
  - …
- Indicator for treatment center (***Z***)

```r
trt_tree <- glmertree(recovered ~ Treatment | center | Age + PHQ9_pre +
                      GAD7_pre + WSAS_pre + Gender + Ethnicity +
                      Diagnosis + Employment + Disability + Medication,
                      data = SMART, family = binomial)
```





$$x_{ij}^{\top}\beta_k + z_{ij}^{\top}b_i \,.$$

```r
trt_tree <- glmertree(recovered ~ Treatment | center | Age + PHQ9_pre +
                        GAD7_pre + WSAS_pre + Gender + Ethnicity +
                        Diagnosis + Employment + Disability + Medication,
                        data = SMART, family = binomial)
```

```r
VarCorr(trt_tree)
```

```
##  Groups Name        Std.Dev.
##  center (Intercept) 0.82557
```

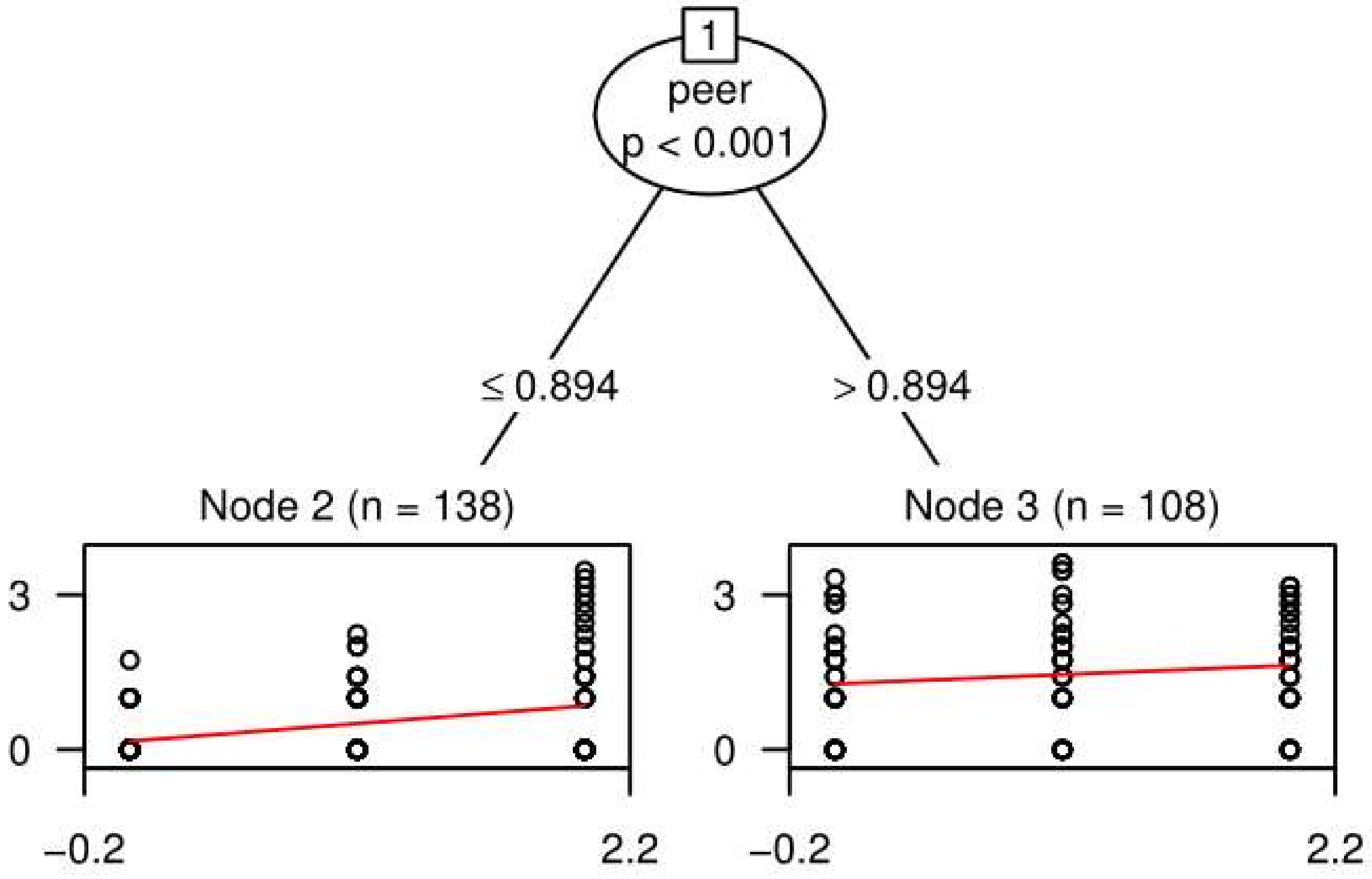
```r
fixef(trt_tree)
```

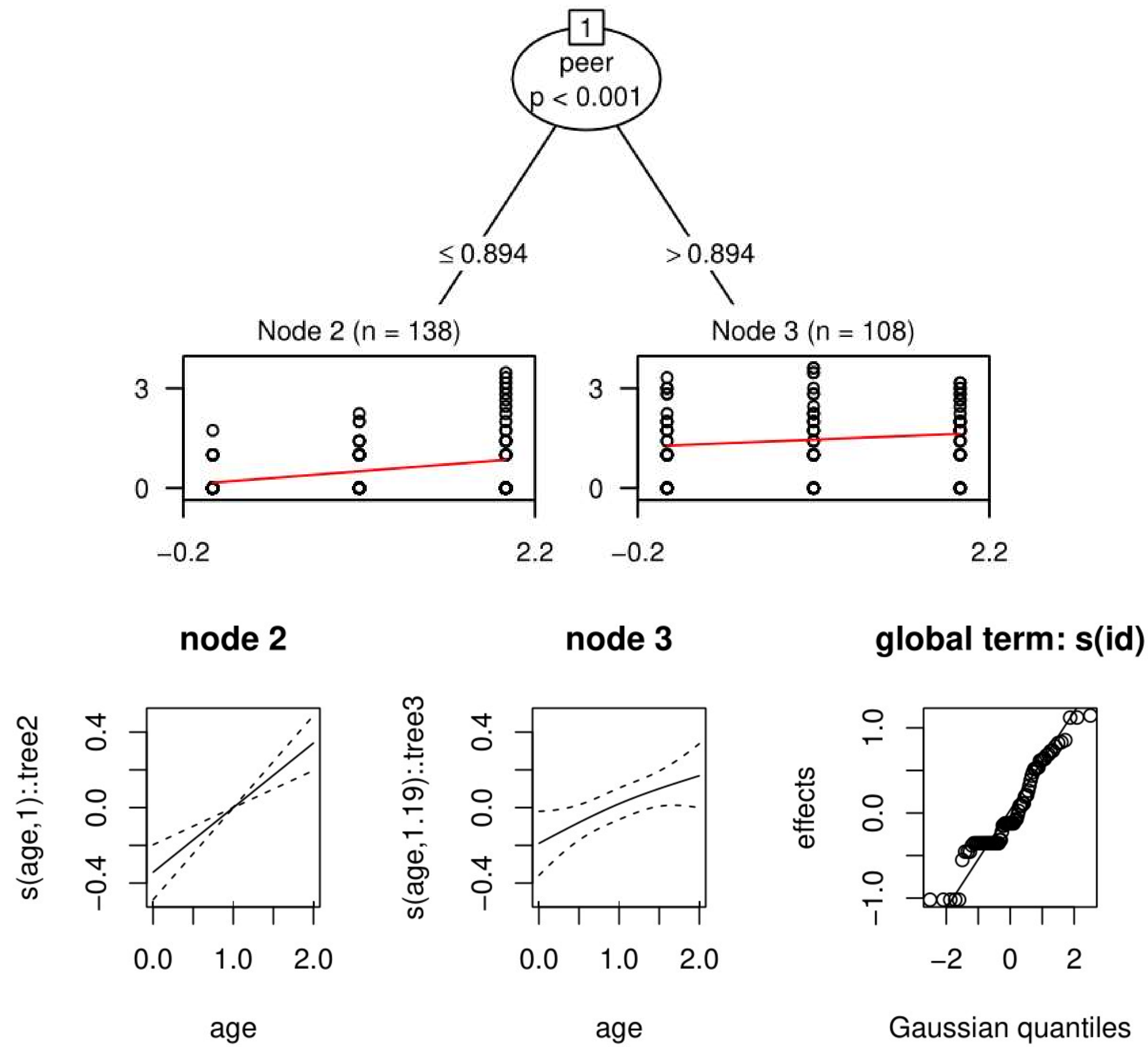
```
##    (Intercept) TreatmentLow
## 3    1.5406327    0.5620038
## 5   -0.2995581    0.4400173
## 6    1.1087452   -2.3810215
## 7   -1.8839567   -1.5372864
```

$$x_{ij}^{\top}\beta_k + z_{ij}^{\top}b_i \cdot$$

GAM trees: Alcohol use

```
gt <- gamtree(alcuse ~ s(age, k = 3) | s(id, bs = "re") | coa + male + peer,
         data = alco, cluster = alco$id, verbose = FALSE)
```

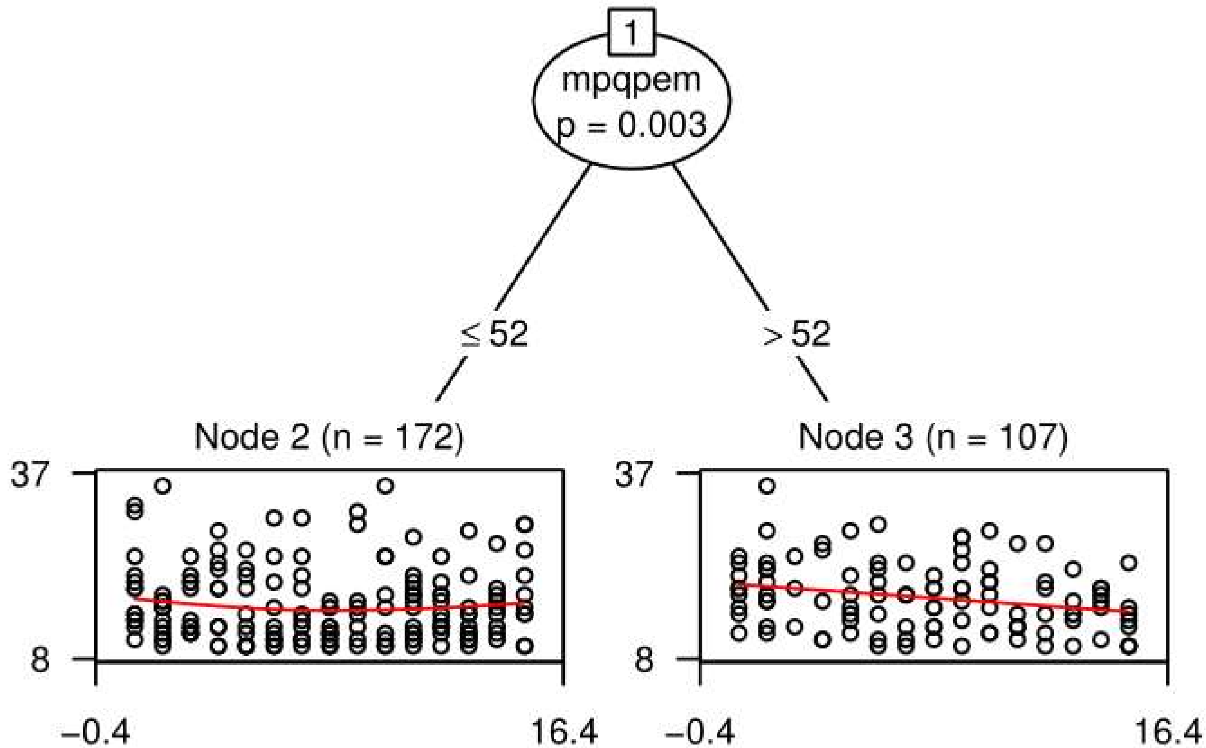


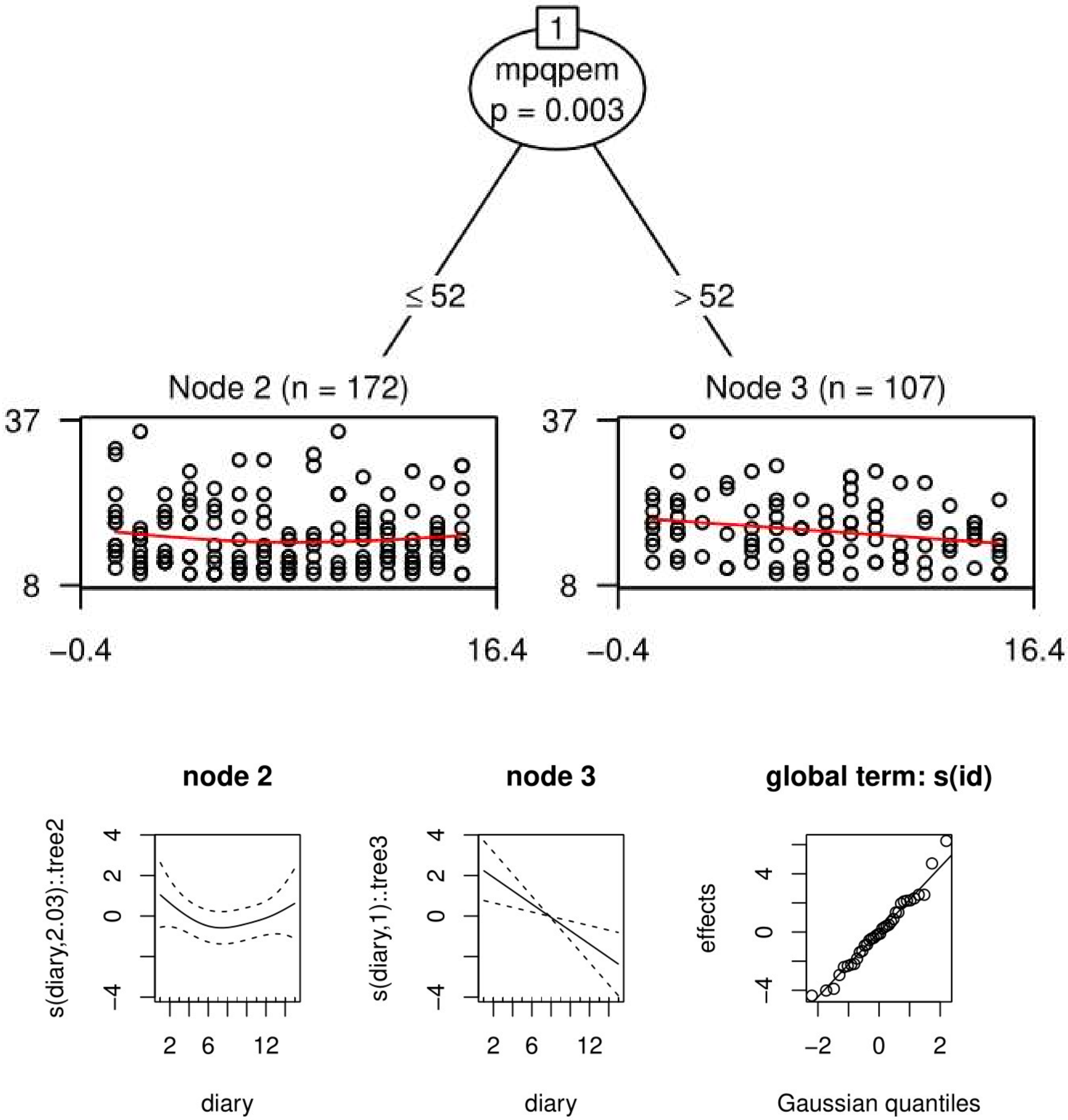


1
peer
p < 0.001
≤ 0.894
> 0.894
Node 2 (n = 138)
Node 3 (n = 108)
3
0
−0.2
2.2
node 2
node 3
global term: s(id)
s(age,1):tree2
s(age,1.19):tree3
−0.4
0.0
0.4
0.0
1.0
2.0
age
effects
−1.0
0.0
1.0
−2
0
2
Gaussian quantiles

GAM trees: Stage fright

```
gamt1 <- gamtree(na ~ s(diary) | audience + s(id, bs = "re") | gender +
                 instrument + mpqab + mpqpem + mpqnem + mpqcon, data = music,
                 verbose = FALSE, cluster = music$id)
```





1
mpqpem
p = 0.003
≤ 52
> 52
Node 2 (n = 172)
Node 3 (n = 107)
37
8
–0.4
16.4
node 2
node 3
global term: s(id)
s(diary,2.03):tree2
s(diary,1):tree3
effects
diary
Gaussian quantiles