

# metacart 3.0

## Classification and regression trees for Exploratory Moderator Analysis in Meta-Analysis

Juan Claramunt Gonzalez, Xinru Li, Elise Dusseldorp, Xiaogang Su,  
and Jacqueline Meulman



Universiteit  
Leiden  
The Netherlands



July 2026

- Meta-analysis: summarize results reported in multiple studies on the same topic and analyze which predictors have an effect.
- Common approach: Meta-regression.
- Statistical problem: Linear model is often not suitable (too many interactions are possible) or interaction effects are ignored.
- Solution: Use a tree algorithm! MetaCART.

### Problems:

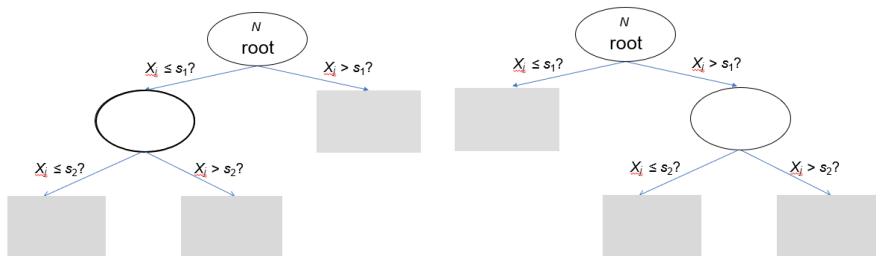
- 1 The split may be based on a local optimum

### Solutions:

- 1 Splitting using look ahead

# Tree construction, convergence and stability

```
REtree_lookahead <-REMrt(form_Levine, vi = vi, c.pruning = 0,  
  data = SpermCon, lookahead = TRUE)
```



- Find the best scenario with two or more split points on the same or different moderators.
- Maximize  $Q_B^*$ , the heterogeneity between subgroups.

### Problems:

- 1 The split may be based on a local optimum
- 2 The algorithm might favor continuous study characteristics to categorical ones

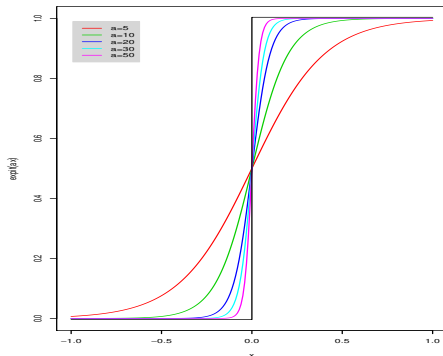
### Solutions:

- 1 Splitting using look ahead
- 2 Use smooth sigmoid surrogate strategy

# Tree construction, convergence and stability

```
REtree_sss <- REMrt(form_Levine, vi = vi, c.pruning = 0,  
                    data = SpermCon, sss = TRUE)
```

Transform step functions into spline functions that resemble the step functions.



### Problems:

- 1 The split may be based on a local optimum
- 2 The algorithm might favor continuous study characteristics to categorical ones
- 3 Subgroups are identified and tested using the same data

### Solutions:

- 1 Splitting using look ahead
- 2 Use smooth sigmoid surrogate strategy
- 3 Permutation test of  $Q_B^*$

## Permutation procedure

$Q_B^*$  obtained via permutation replaces chi-square to determine the statistical significance of the subgroup heterogeneity.

```
set.seed(111)
REtree_perm <-REmrt(form_Levine, vi = vi, c.pruning = 0, data = SpermCon,
                    lookahead = TRUE, sss = TRUE, perm = TRUE)
summary(REtree_perm)
```

Test for Between-Subgroups Heterogeneity under RE assumption:

$Q_b = 61.371$  (df = 2), Permutation p-value 0.001996;

The estimate without bootstrap for the residual heterogeneity  $\tau^2 = 227.914$

Random Effects Meta-analysis Results without Bootstrap:

	K	est	se	zval	pval	ci.lb	ci.ub	
2	69	76.530	2.021	37.875	0.000	72.570	80.490	***
4	87	90.627	1.900	47.701	0.000	86.904	94.351	***
5	88	70.764	1.739	40.700	0.000	67.357	74.172	***
---								

### Problems:

- 1 The split may be based on a local optimum
- 2 The algorithm might favor continuous study characteristics to categorical ones
- 3 Subgroups are identified and tested using the same data
- 4 CIs of summary effect sizes in subgroups are too optimistic

### Solutions:

- 1 Splitting using look ahead
- 2 Use smooth sigmoid surrogate strategy
- 3 Permutation test of  $Q_B^*$
- 4 Bootstrap-based confidence intervals

## Bias correction bootstrap procedure

New bootstrap procedure to reduce bias in the estimate of the confidence intervals in the subgroups.

```
set.seed(111)
Results_boot <- BootCI(REplustree, nboot = 50)

summary(Results_boot)
```

Random Effects Meta-analysis Results with Bootstrap:

	K	est	se	ci.lb	ci.ub
2	69	77.378	2.635	72.213	82.542
4	87	91.154	2.435	86.381	95.926
5	88	71.029	2.290	66.540	75.519

Compare with previous result:

Random Effects Meta-analysis Results without Bootstrap:

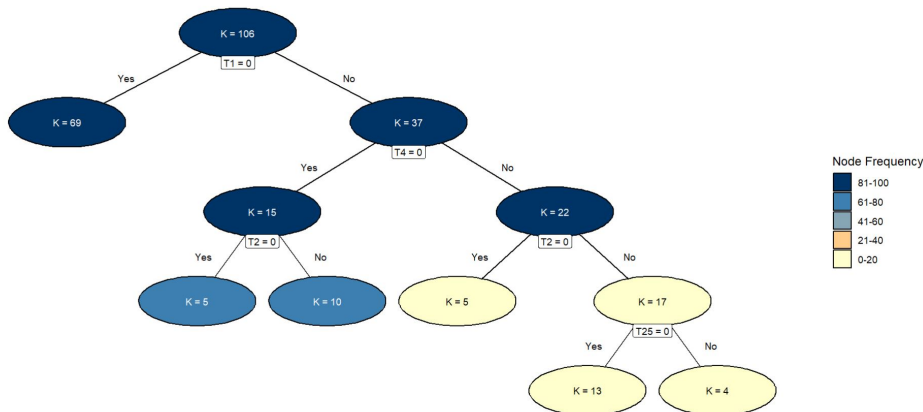
	K	est	se	zval	pval	ci.lb	ci.ub	
2	69	76.530	2.021	37.875	0.000	72.570	80.490	***
4	87	90.627	1.900	47.701	0.000	86.904	94.351	***
5	88	70.764	1.739	40.700	0.000	67.357	74.172	***

---

# Visualization tree stability

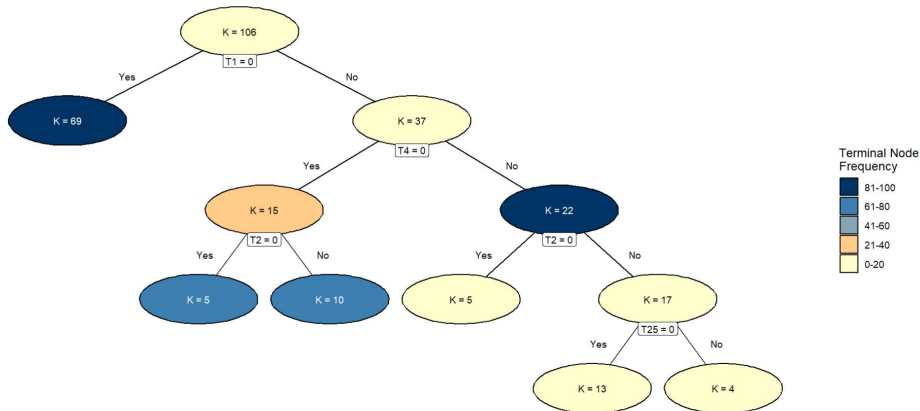
Check stability of the tree using Cross Validation:

```
PLOT_PV<-plotPV(REtree, iter = 10, c.pruning = 0)
```



# Visualization tree stability

Check the stability of the tree using Cross Validation:



Thank you for your attention!

<https://cran.r-project.org/package=metacart>

