

Using causal trees to explore the heterogeneity of effects

INTRODUCTION

Causal tree allows to explore the complex relationships between treatments and clinical outcomes, by identifying possible heterogeneous effects of treatments in specific subgroups of patients. This methodology will be used to compare the effectiveness of a remote monitoring system according to patient characteristics in SNDS data.

METHODS

Patients treated by treatment A (cases) were matched to patients treated by treatment B (controls) to compare the occurrence of adverse events since the inclusion.

Causal trees were constructed using the following characteristics: gender, age, year of inclusion, comorbidities, treatment history, social deprivation index and history of hospitalizations of interest.

Several parameters were explored and their impact on the structure of tree was studied, in particular the size of the leaves. Honest causal tree were also implemented.

The effect of treatment within each leaf was assessed using a generalized linear model with a binomial distribution and a logit link and results were expressed in Odds-Ratios (OR) and their confidence interval (CI). All analyses were weighted according to the weight of cases and controls.

Definitions

Treatment effect: Let i be the individual, T_i the treatment indicator (1 = treated, 0 = control), Y_i the outcome, and X_i the covariates:

- Counterfactual under treatment a for individual: $Y_i(a)$
- Individual treatment effect: $Y_i(1) - Y_i(0)$
- Average treatment effect (ATE): $\mathbb{E}[Y_i(1) - Y_i(0)]$
- Conditional average treatment effect (CATE): $\tau(x) = \mathbb{E}[Y_i(1) - Y_i(0) | X_i = x]$

	Causal tree	
	Adaptative method	Honest method
Training sample	Training set	Training set and estimation set
Fit criterion	$EMSE = \mathbb{E}[(Y_i^* - \hat{\tau}(X_i))^2 - Y_i^{*2}]$	
	$\tau(X_i)$ calculated from training set	$\tau(X_i)$ calculated from estimation set

MSE : Mean squared error ; EMSE : Expected mean squared error of the treatment effects

Construction steps¹

1 Causal tree initialization

The tree is built using recursive partitioning, selecting splits that minimize a fit criterion.

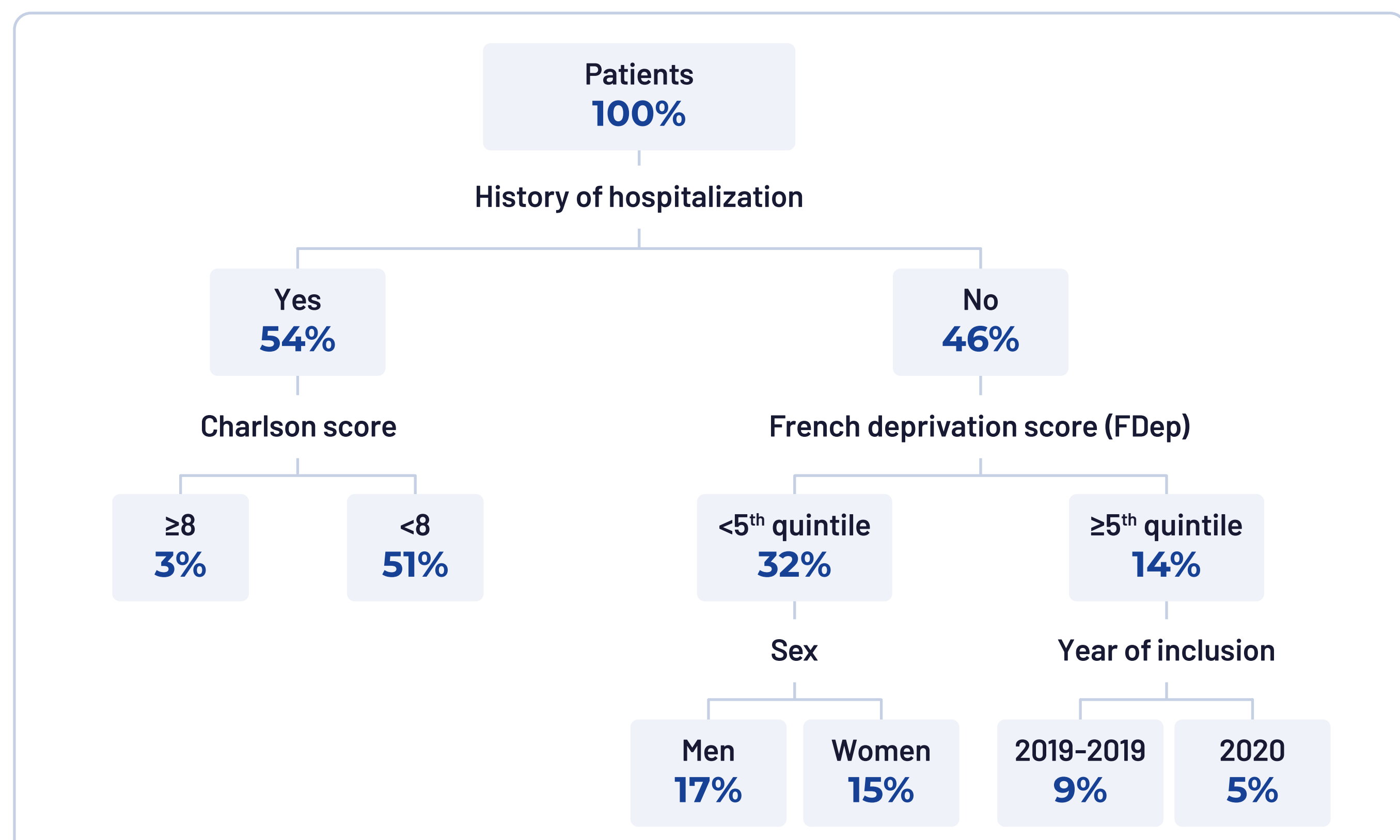
In the case of causal trees, this fit criterion is specifically designed to capture treatment heterogeneity and includes the following component:

- uses an auxiliary variable Y_i^* representing the individual treatment effect:

$$Y_i^* = \frac{Y_i}{D_i \cdot p(X_i) - (1 - D_i) \cdot (1 - p(X_i))}$$

- includes a penalty for tree depth to avoid overfitting,
- enforces minimum treated/control sample sizes in each leaf

Figure: Initial causal tree structure



2 K-fold Cross-Validation

This validation method is used to select a complexity parameter for tree pruning. A new tree is built to determine the optimal depth, i.e., the depth that minimizes the fit criterion.

3 Tree pruning

The trained tree is then pruned to the optimal depth determined by cross-validation.

4 Estimation of treatment effects

Conditional means are computed for each tree leaf.

5 Significativity of effects

A generalized linear model is applied to estimate the treatment effect within each leaf.

Practical implementation in R

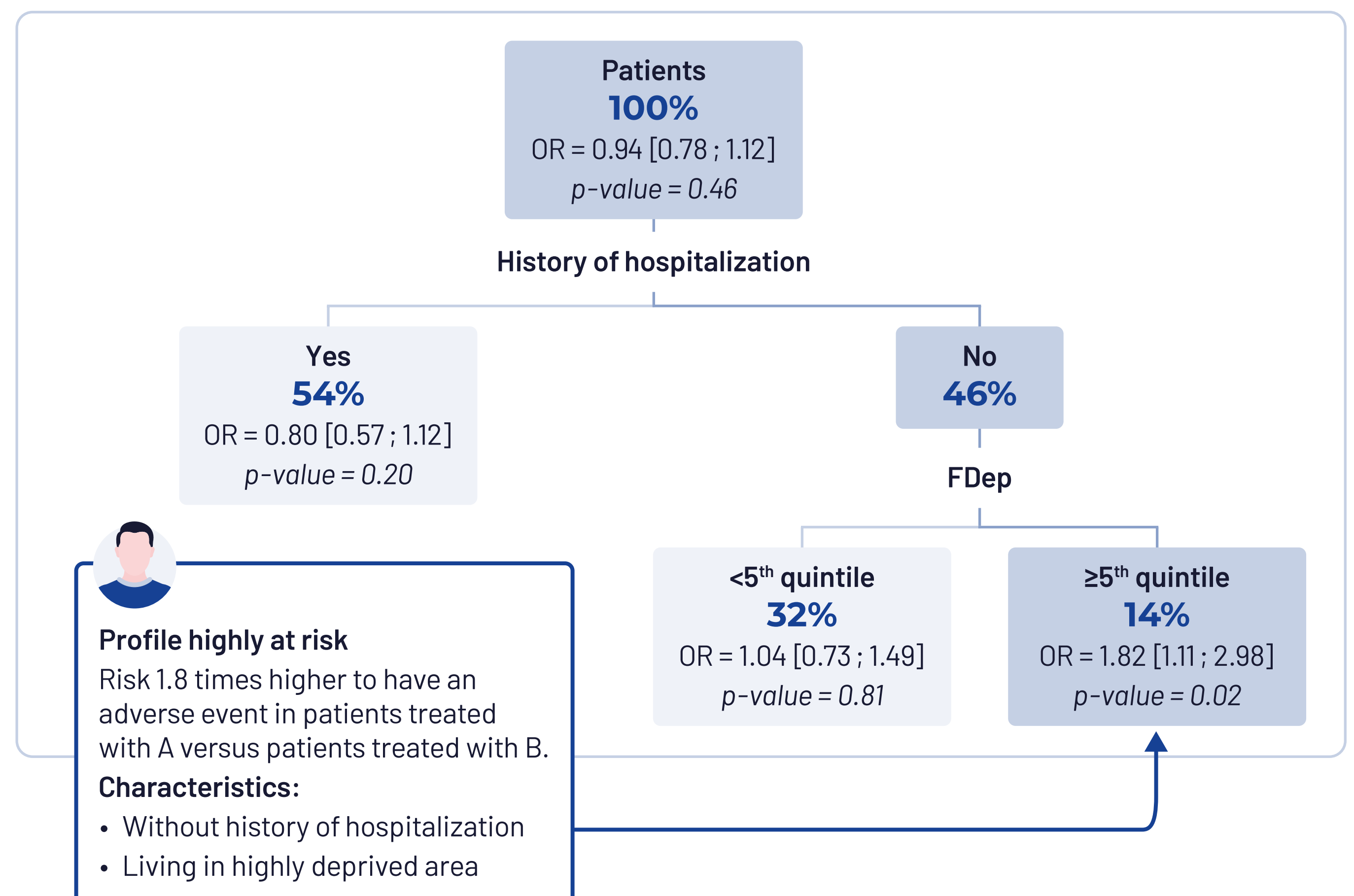
```
formula = as.formula(Y ~ Q5 + sexe + annee + score_Charlson + top_FDiabet_ind + top_comor1 + top_comor2 + top_atcd_trt1 + top_atcd_trt2 + top_atcd_trt3 + top_atcd_trt4 + top_atcd_trt5 + top_sej_lan + classe_age)
```

Causal tree calculation

Adaptative method	Honest method
<pre>tree= causalTree(formula, data=data.frame(Y=Y, X), treatment=T, weights=W, #paramètre de division split.Rule = "CT", split.Honest = F, split.alpha = 1, split.Bucket = T, #paramètre de validation croisée cv.option = "CT", cv.Honest = F, minsize = 80)</pre>	<pre>tree= honest.causalTree(formula, #1er échantillon data=data.frame(Y=Y1,X1), treatment=T1, weights=W1, #2e échantillon est_data = data.frame(Y=Y2,X2), est_treatment= T2, est_weights=W2, #paramètre de division split.Rule = "CT", split.Honest = T, split.alpha = 0.5, #paramètre de validation croisée cv.option = "CT", cv.Honest = T, cv.alpha = 0.5, split.Bucket = F, HonestSampleSize = nrow(est_data), minsize = 10)</pre>

RESULTS

Figure: Causal tree with adaptative method



The leaf size had no significant impact on the results in the adaptative method. The honest trees were highly unstable in small sample size contexts and are not presented here.

CONCLUSION

Causal trees highlight subgroups where heterogeneous treatment effects exist.

	Causal tree	
	Adaptative method	Honest method
Strength	Works with all sample sizes	Uses two independent samples for partition and estimation
Limitation	Overfitting possible without separation of training and validation set	Loss of power and high instability in small sample size

Using causal trees on a limited sample size enabled exploration of subgroup analyses that would have been difficult to perform manually.

This methodology uncovers crucial causal factors, enabling a better understanding of underlying mechanisms and fostering the development of tailored therapeutic strategies.

References

¹ Athey S, Imbens G. Recursive partitioning for heterogeneous causal effects. Proc Natl Acad Sci U S A. 5 juill 2016;113(27):7353-60.

Acknowledgments

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