Bayesian Approaches to Predicting Individual Treatment Effects in Precision Medicine

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April 11, 2025

Motivation

- Not all participants will react equally to an intervention
- Characterizing this heterogeneity in intervention effects is key to improving patients outcomes

Goal

To assess the performance of Bayesian inference across diverse data conditions, with an emphasis on their capacity to handle heterogeneity, non-linearity, and high-dimensionality in the estimation of individual treatment effects.

The predicted individual treatment effects (PITE) framework

- PITE estimates individual treatment effects.
- PITE consists of the difference between experimental(E) and control (C) **prediction** for each individual (Jaki et al. 2024).

$$\text{PITE}_i = f_E(X_i) - f_C(X_i), \qquad f(\cdot) \text{ is a predictor}$$

! Challenge

- PITE is unobserved.
- The best method to estimate the PITE is not necessarily the best fitted model.

Bayesian approches

Dimensionality

Bayesian Ridge Regression ("bridge"), Spike and Slab Regression ("spikeslab"), The Bayesian Lasso ("blasso").

Complex outcomes

Bayesian Generalized Linear Model ("bayesglm"), Bayesian Regularized Neural Networks ("brnn").

Tree Regression

Bayesian Additive Regression Trees ("bartMachine") (Lamont et al. 2016)

Regressions approches applied

Metrics

- The risk (% Expected Prediction Squared Error)

$$\frac{1}{n}\sum_{i=1}^{i=n}(\text{tPITE}_i - \text{PITE}_i)^2$$

- Sensitivity (Detect PITE direction)

$$\text{Same Direction}_i = 1, \quad \text{if} \quad \text{tPITE}_i \times \text{PITE}_i > 0$$

true tPITE_i and estimate PITE_i.

Data generation mechanism 1

- Sample size $n = 40$, 70, 100, 300, 400, **500**, **1000**,1200,1500 with allocation ratio 1:1 ($n_C = n_T = n/2$).

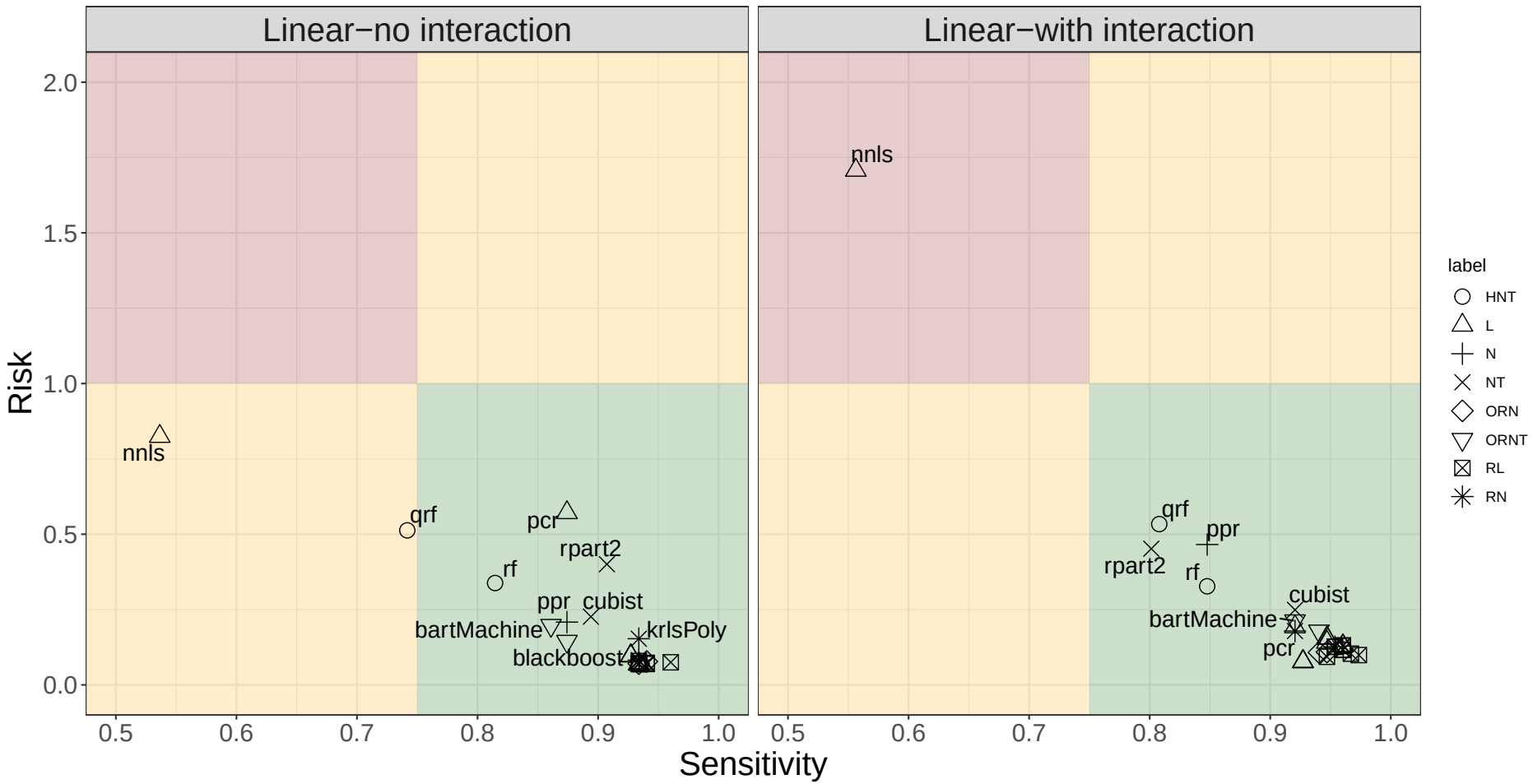
$$y = X\beta + tZ\gamma + \epsilon, \quad \epsilon \sim N(0, 1)$$

- $t \in (0, 1) \Rightarrow$ benefit $Z\gamma$

Leave-one-out cross-validation for validation

- Normal, Linear, Independent
- Normal, Linear, Interactions

$n = 500$


Linear−no interaction
Linear−with interaction
Risk
Sensitivity
2.0
1.5
1.0
0.5
0.0
0.5
0.6
0.7
0.8
0.9
1.0
nnls
grf
pcr
rpart2
rf
ppr
cubist
bartMachine
krlsPoly
blackboost
label
HNT
L
N
NT
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ORNT
RL
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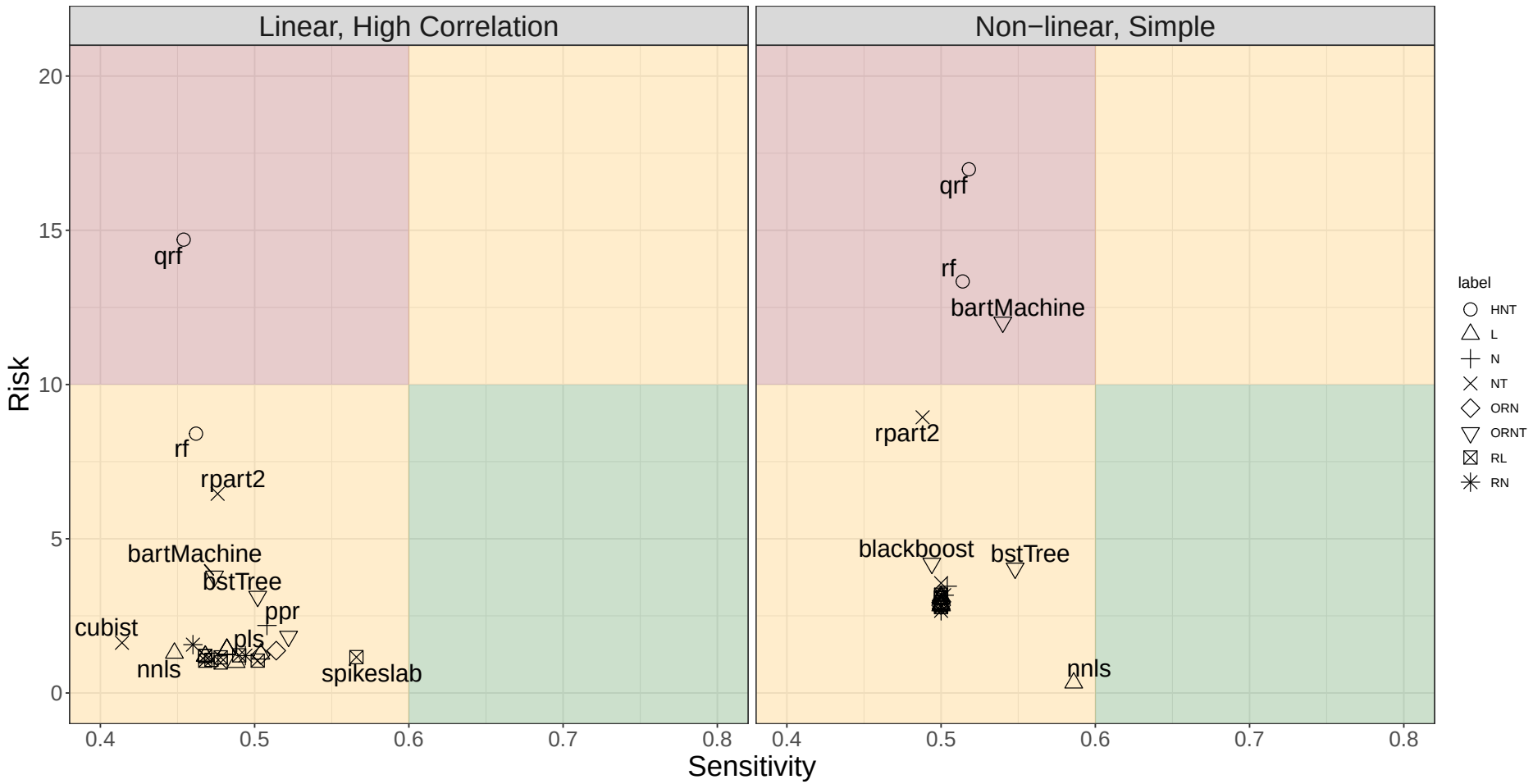
Data generation mechanism 2

- Z Normal, Linear, High correlations **(up to 0.5)**
- Z Normal, Linear, Low correlations **(up to 0.3)**
- $Z \sim U[0.1, 0.5]$, Non-linear. Benefit: $Z_1\gamma_1/(Z_2 + \gamma_2)$
- $Z \sim U[0.1, 0.5]$, Non-linear. Benefit: $\frac{\log(Z_1)\gamma_0}{{Z_1}^{\gamma_2} - \gamma_3\sqrt{Z_2+2}}$

$n = 500$


Linear, High Correlation
Non−linear, Simple
Risk
Sensitivity
0
5
10
15
20
0.4
0.5
0.6
0.7
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qrf
rf
rpart2
bartMachine
bstTree
ppr
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pls
nnls
spikeslab
blackboost
label
HNT
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ORNT
RL
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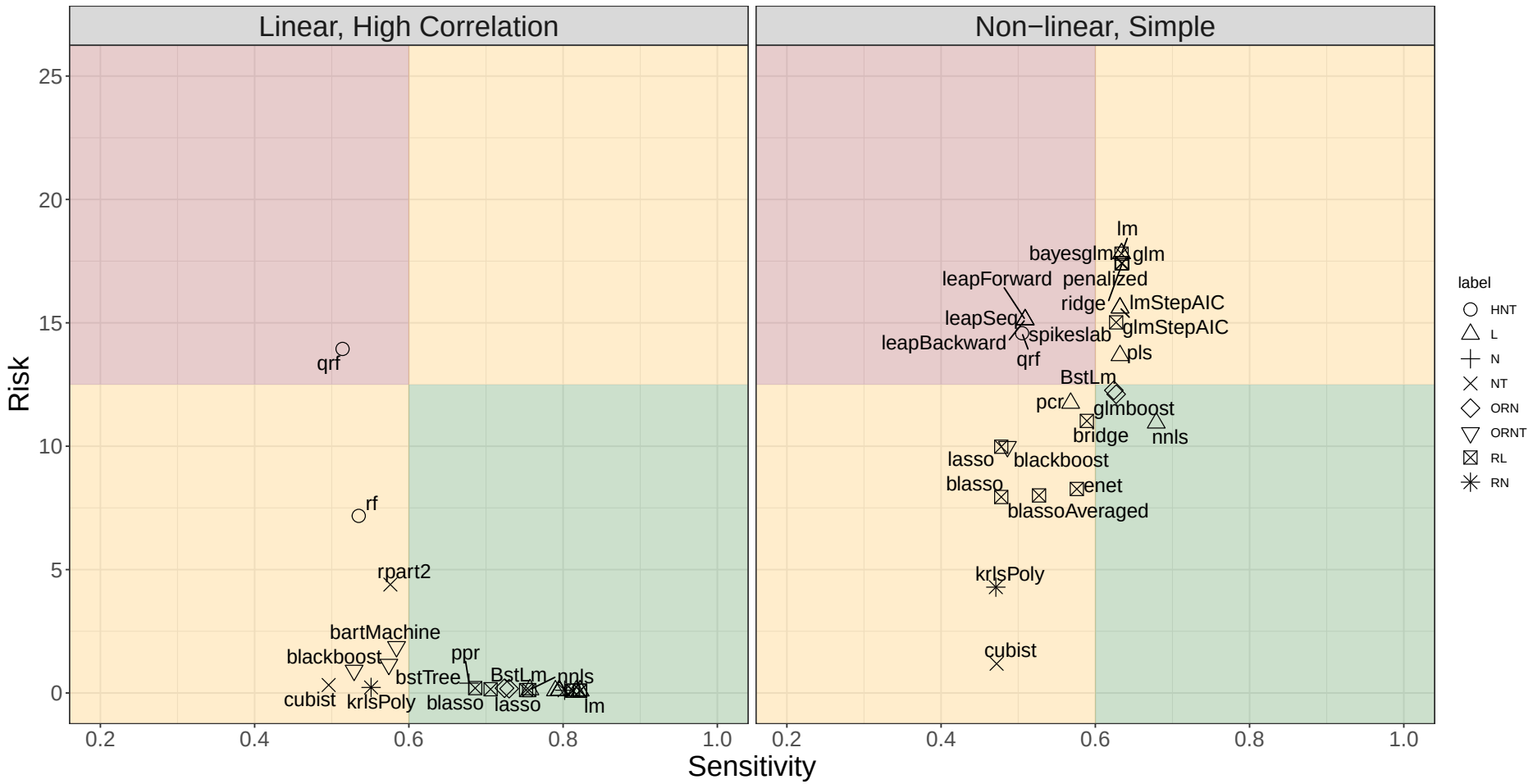
$n = 1000$


Linear, High Correlation
Non−linear, Simple
Risk
Sensitivity
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20
25
0.2
0.4
0.6
0.8
1.0
qrf
rf
rpart2
bartMachine
blackboost
ppr
bstTree
BstLm
nnls
cubist
krlsPoly
blasso
lasso
lm
bayesglm
glm
leapForward
penalized
ridge
lmStepAIC
leapSeq
glmStepAIC
leapBackward
spikeslab
qrf
pls
BstLm
pcr
glmboost
bridge
nnls
lasso
blackboost
blasso
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blassoAveraged
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Conclusions

- This work evidences potential approaches for different contexts.
- An analyst should know what characteristics their dataset presents.
- For each situation sensitivity varies little for different methods.
- Risk is more variable.
- Some methods benefit more from smaller sample size.
- Leave complex methods for large sample size.

References

- Jaki, Thomas, Chi Chang, Alena Kuhlemeier, and M. Lee Van Horn. 2024."Predicting Individual Treatment Effects: Challenges and Opportunities for Machine Learning and Artificial Intelligence."KI - KünstlicheIntelligenz, January.https://doi.org/10.1007/s13218-023-00827-4.
- Lamont, Andrea, Michael D Lyons, Thomas Jaki, Elizabeth Stuart, DanielJ Feaster, Kukatharmini Tharmaratnam, Daniel Oberski, HemantIshwaran, Dawn K Wilson, and M Lee Van Horn. 2016. "Identificationof Predicted Individual Treatment Effects in Randomized ClinicalTrials."Statistical Methods in Medical Research27 (1): 142–57.https://doi.org/10.1177/0962280215623981.

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