Treatment Interaction Trees (TINT)

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Aim

- Insight: For which problems can we use TINT?
- Knowledge: How does TINT work?
- Inspiration: New ways to evaluate clinical trials

Problem

Two treatments – **A** and **B** – are available for patients.
[surgery and radiotherapy for patients with prostate carcinoma]

1. Which of the two treatments is most effective? [not our focus]

2. **For whom** is **A** better than **B** and **for whom** is **B** better than **A** (and **for whom** it does not make a difference)? $\Rightarrow$ different subgroups of patients

$\Rightarrow$ Disordinal treatment-subgroup interaction

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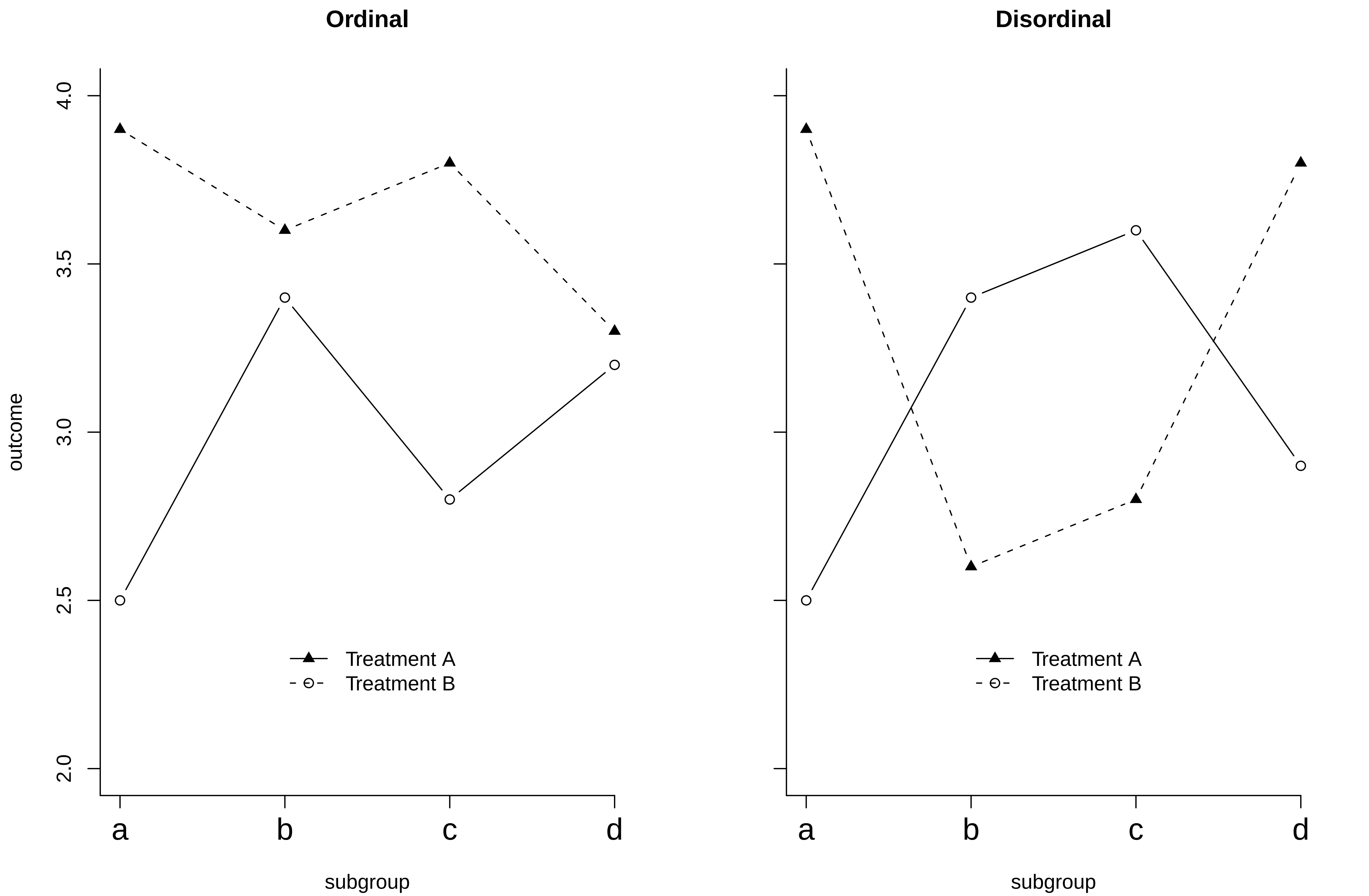
TNO



Ordinal
Disordinal
outcome
4.0
3.5
3.0
2.5
2.0
a
b
c
d
subgroup
Treatment A
Treatment B

Disordinal treatment-subgroup interaction

- **Relevance for policy-makers:** patient-tailored treatment assignment

- **Moderators or effect modifiers:** patient characteristics identifying the subgroups

- **Goal of statistical method:** identifying the patient characteristics that maximize the disordinal treatment-subgroup interaction

- **Available methods:** Moderator analysis (Baron & Kenny, 1986), Interaction Trees (Su et al, 2008), STIMA (Dusseldorp et al, 2010)

New method: TINT

- **Appropriate for complex situations**: The subgroups may comprise several types of patients defined by different (possibly nonlinear) combinations of patient characteristics

Three main subgroups / partition classes:

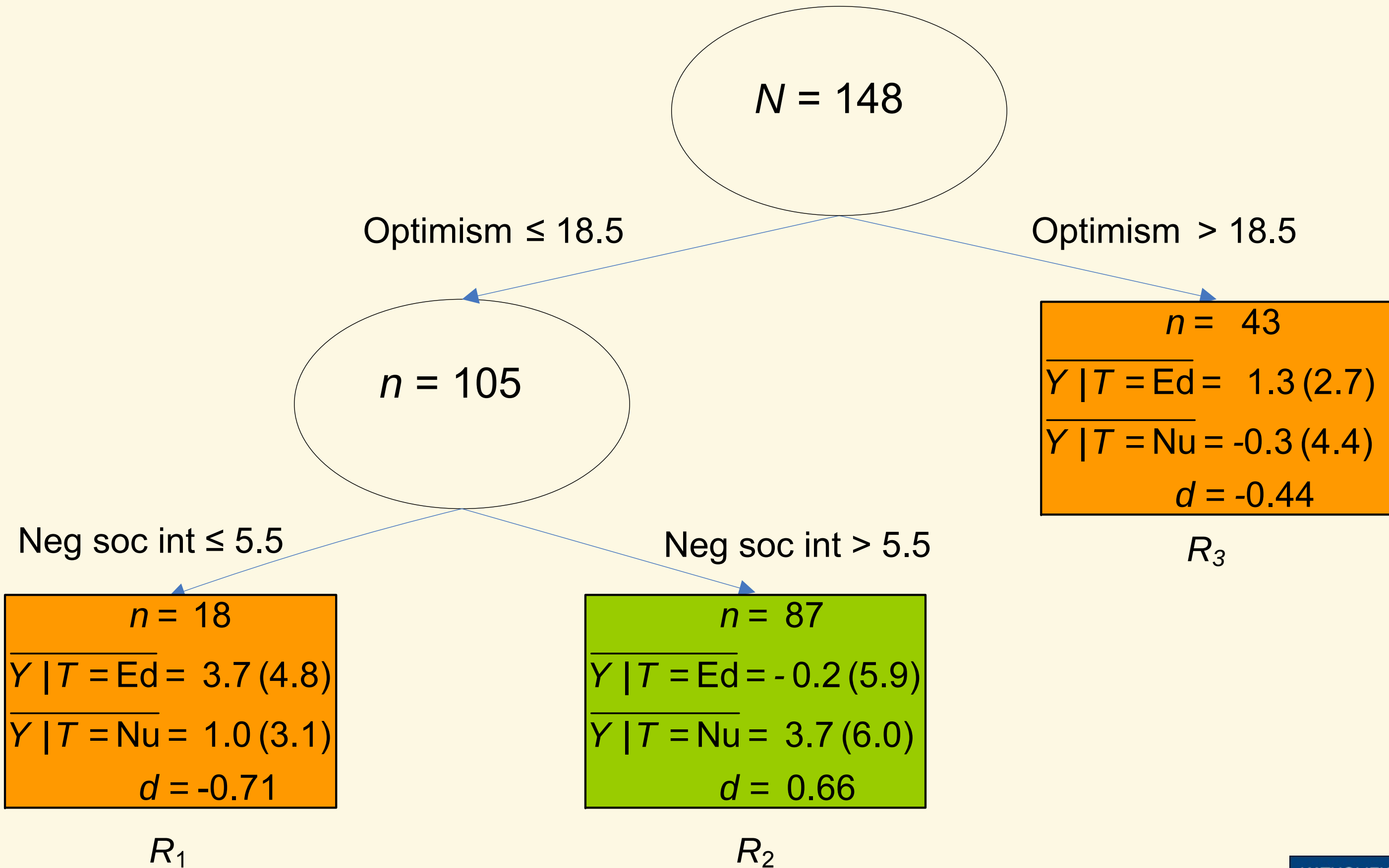
$\wp_1$: those for whom A is better than B

$\wp_2$: those for whom B is better than A

$\wp_3$: those for whom it does not make any difference

Treatment INteraction **Trees (TINT)**

Tree-based method: partitions on the basis of the patient characteristics are obtained by a binary tree



Ingredients Partitioning criterion

Difference in treatment outcome component:

Δ_1 : the weigthed average difference in mean outcome between the treatments across the leafs assigned to $\wp_1$ and

Δ_2 : the weigthed average difference in mean outcome between the treatments across the leafs assigned to $\wp_2$.

Cardinality component:

Σ_1 : the total number of patients in the leafs assigned to $\wp_1$ and

Σ_2 : the total number of patients in the leafs assigned to $\wp_2$

$$C \approx \Delta_1 * \Delta_2 * \Sigma_1 * \Sigma_2$$

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Real data: Breast Cancer Recovery Project (BCRP)
Scheier MF, Helgeson VS, et al. (JCO, 2007)

Patients:
Young women with early-stage breast cancer

Two different types of treatments:
A) Nutrition information: how to adopt a low-fat diet (n = 78; T = 1)
B) Education: provision of coping skills (n = 70; T = 0)

Design:
Pretest-posttest design with random assignment to the treatments

Outcome (Y):
Improvement in depression from pre-test to post-test (change score)

Possible moderators (X_j):
Nationality, Marital status, Age, Weight-change, Treatment extensiveness, Comorbidity, Dispositional optimism, Unmitigated communion, Negative social interaction

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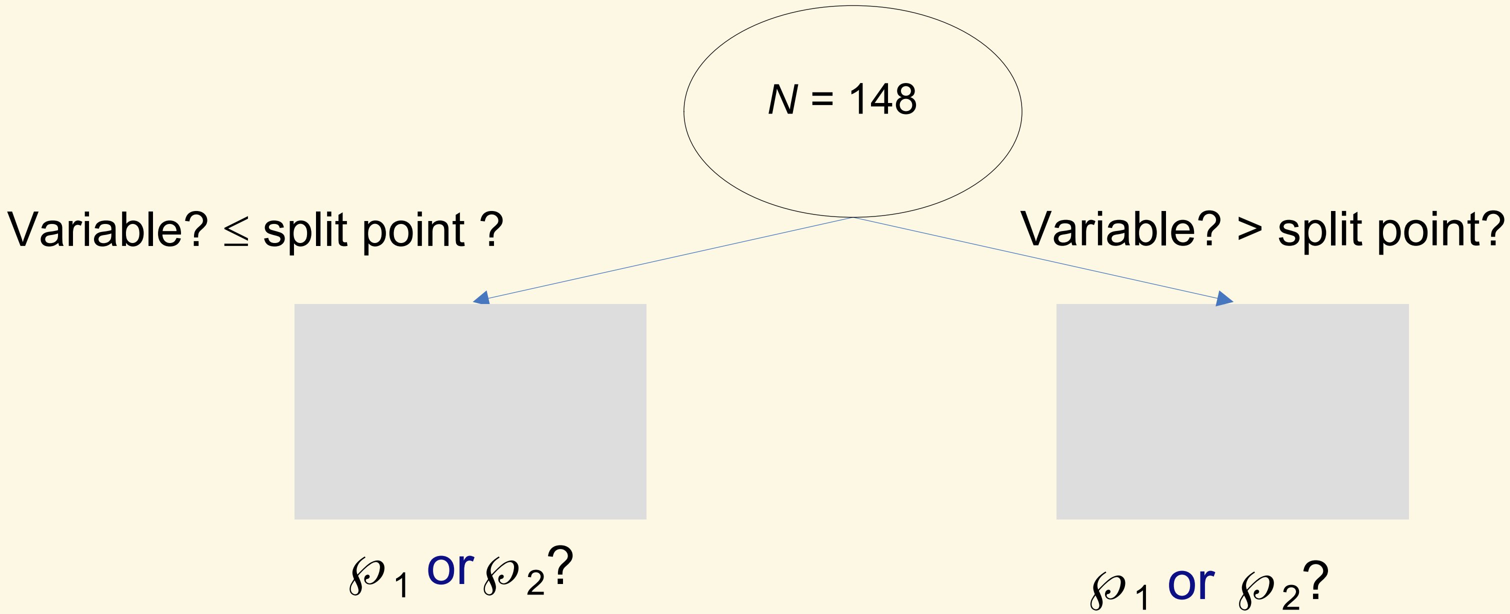
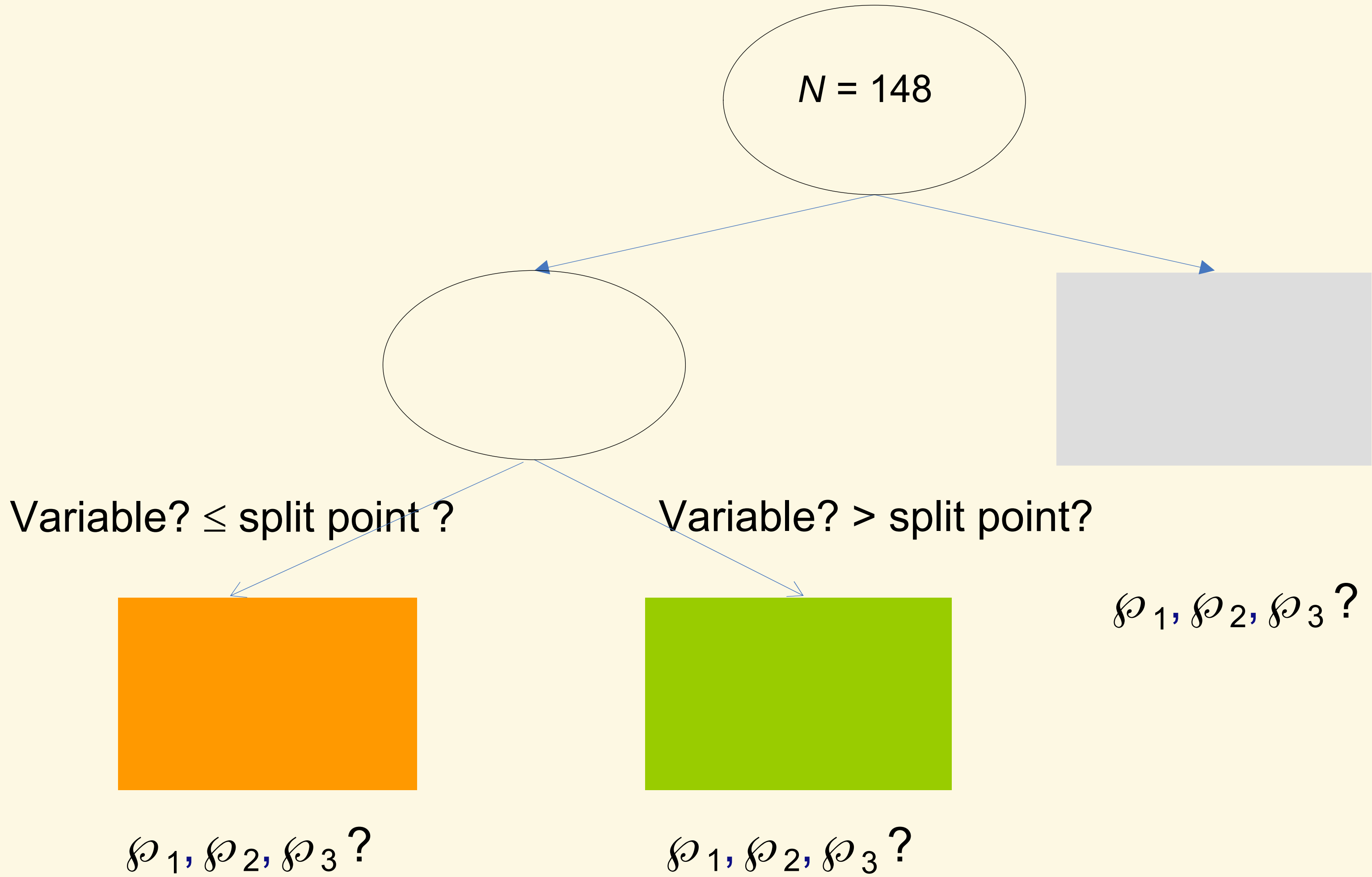
How do we grow a Treatment Interaction tree?

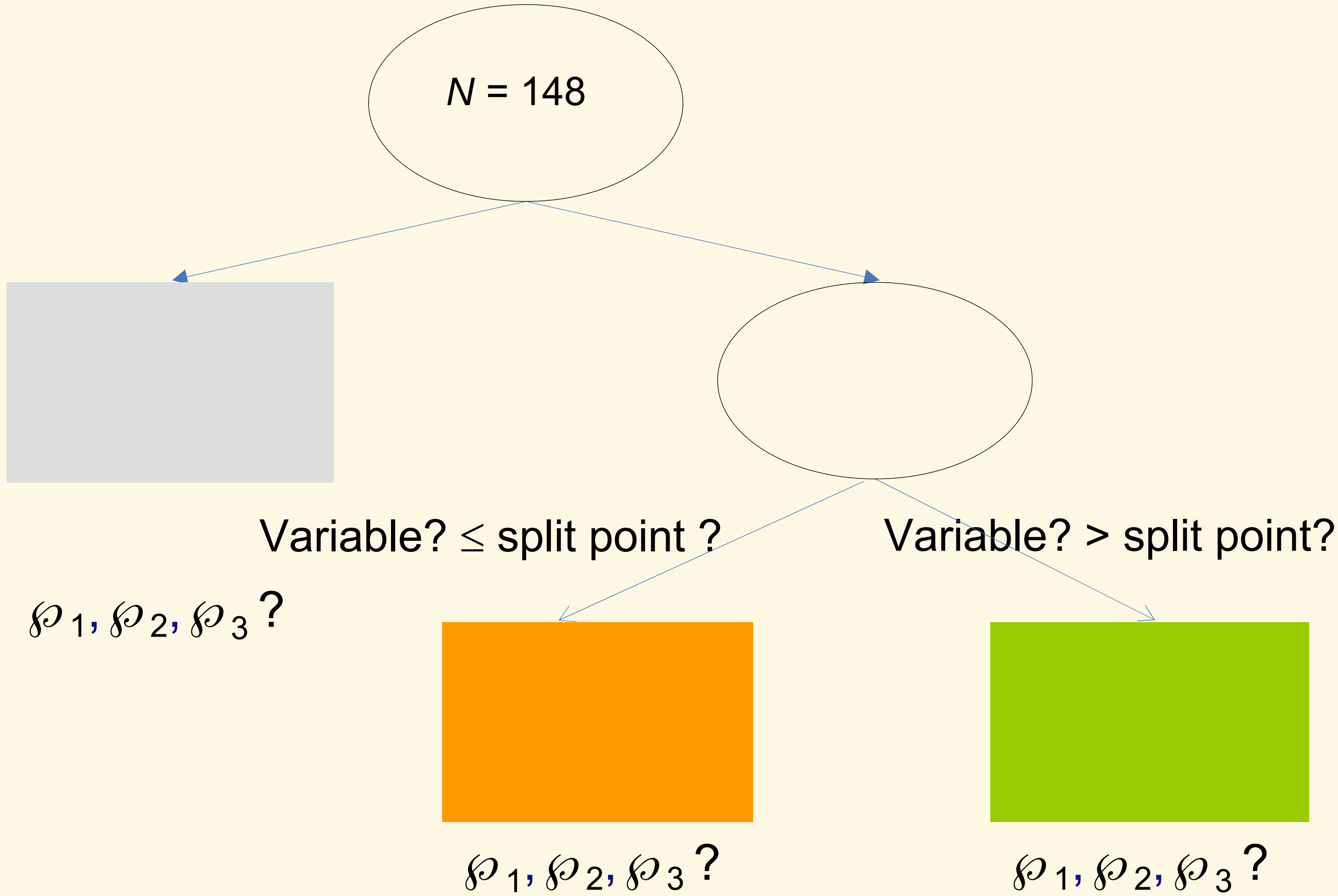
N = 148

How do we grow a Treatment Interaction tree?



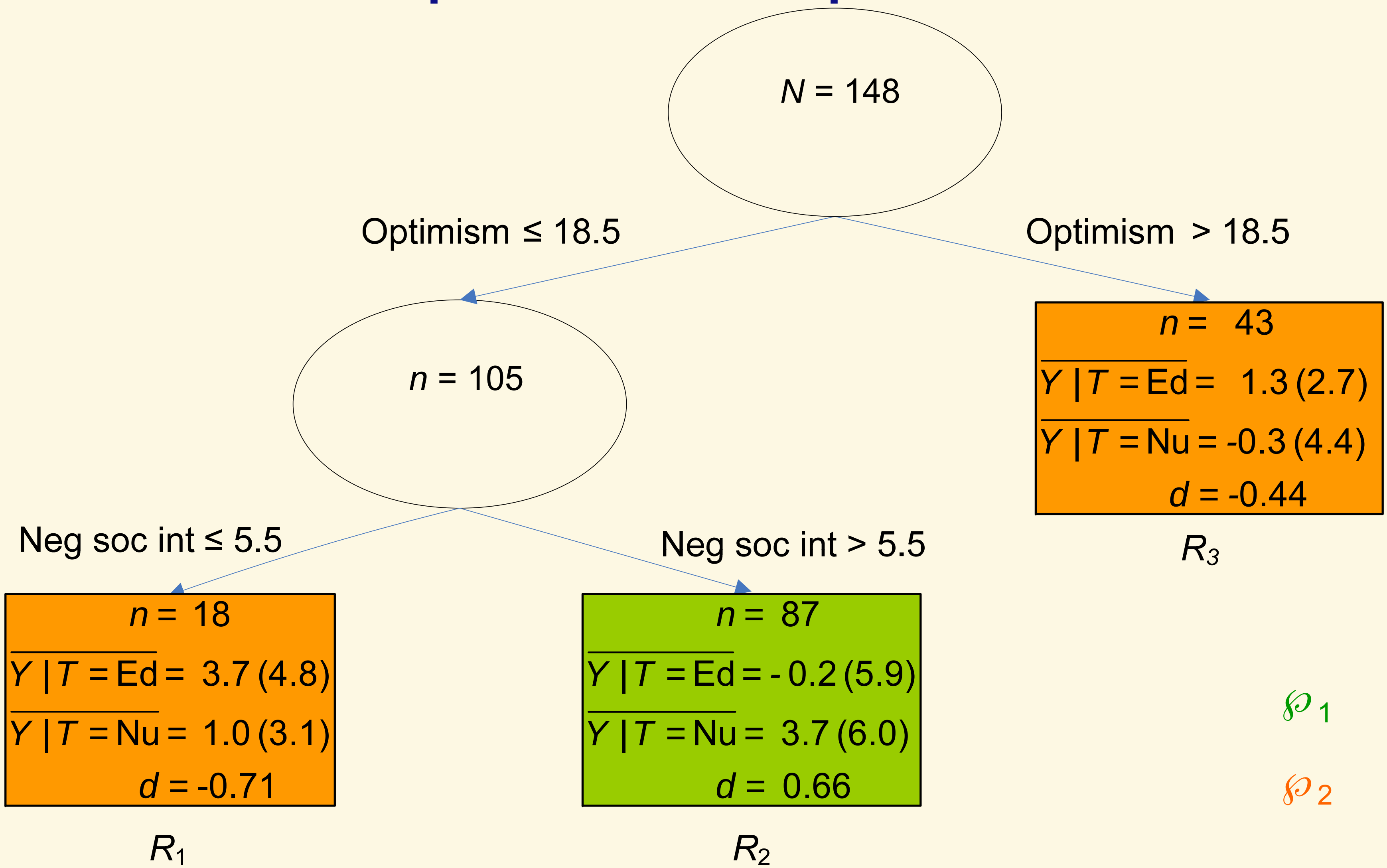
Step 1: Determine the optimal triplet (X_j, split point, assignment):
$\Rightarrow$ Select X_j (with associated optimal split point and assignment) that induces the highest C


N = 148
Variable? ≤ split point ?
Variable? > split point?
$\wp_1, \wp_2, \wp_3$?
$\wp_1, \wp_2, \wp_3$?
$\wp_1, \wp_2, \wp_3$?



Step 2: Accross all parent nodes: Select the one with the optimal triplet that implies the highest *C*

Treatment Interaction Tree for Improvement in Depression



Conclusion

- Results of TINT application to BCRP were promising
  - Large reduction of number of required analysis
  - Insightful picture of overall pattern of moderation

- Future:
  - Large-scale test with artificial data
  - Generalization to categorical outcome and patient characteristics
  - Integration of costs of the treatments
  - Optimal assignment to 1 treatment: Only Partition class 1 and 3

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