Selective Randomization Inference for Adaptive Clinical Studies

Tobias Freidling, Qingyuan Zhao, Zijun Gao

Response-Adaptive Randomisation in Clinical Trials Workshop 29/02/2024

Example

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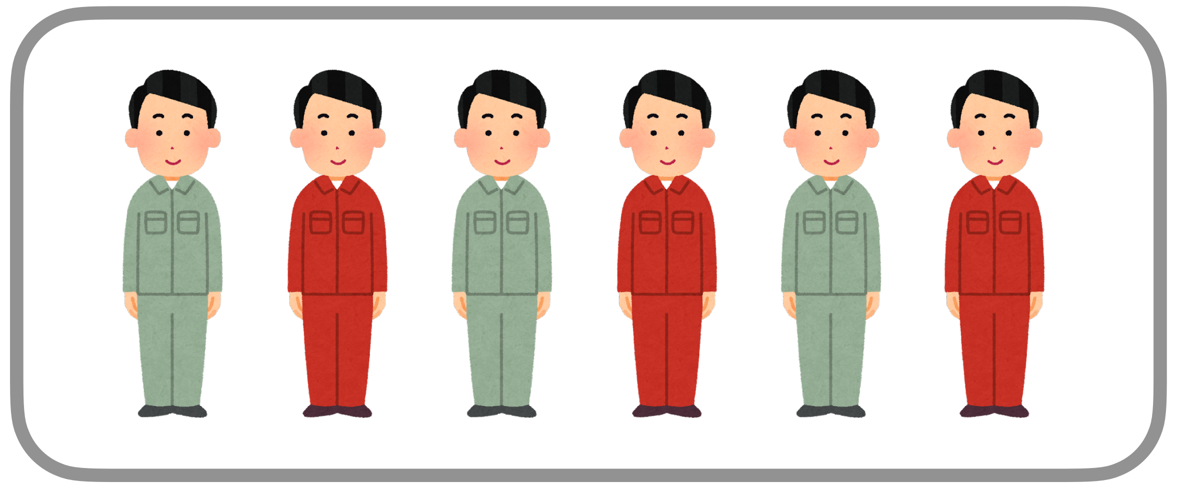

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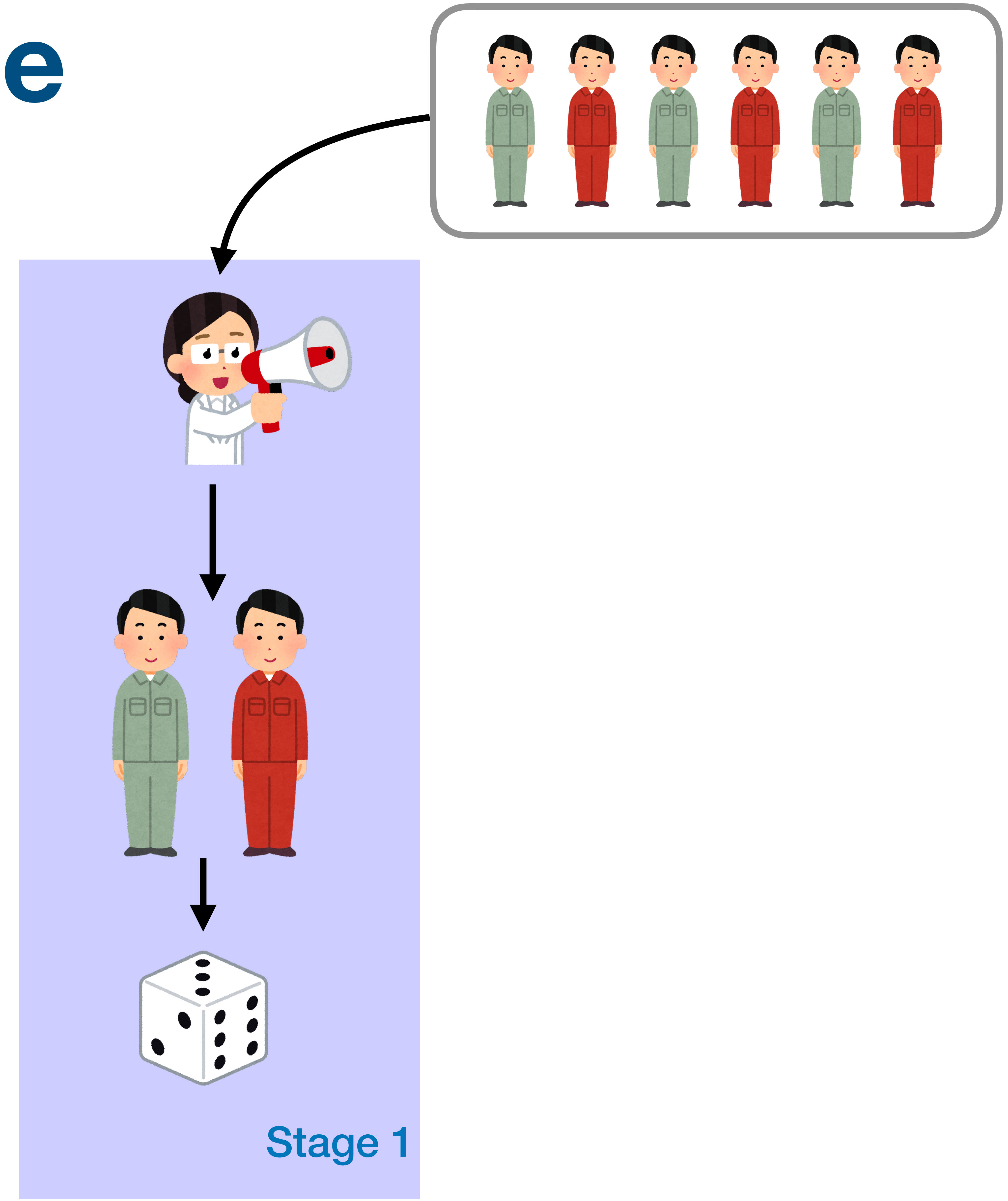

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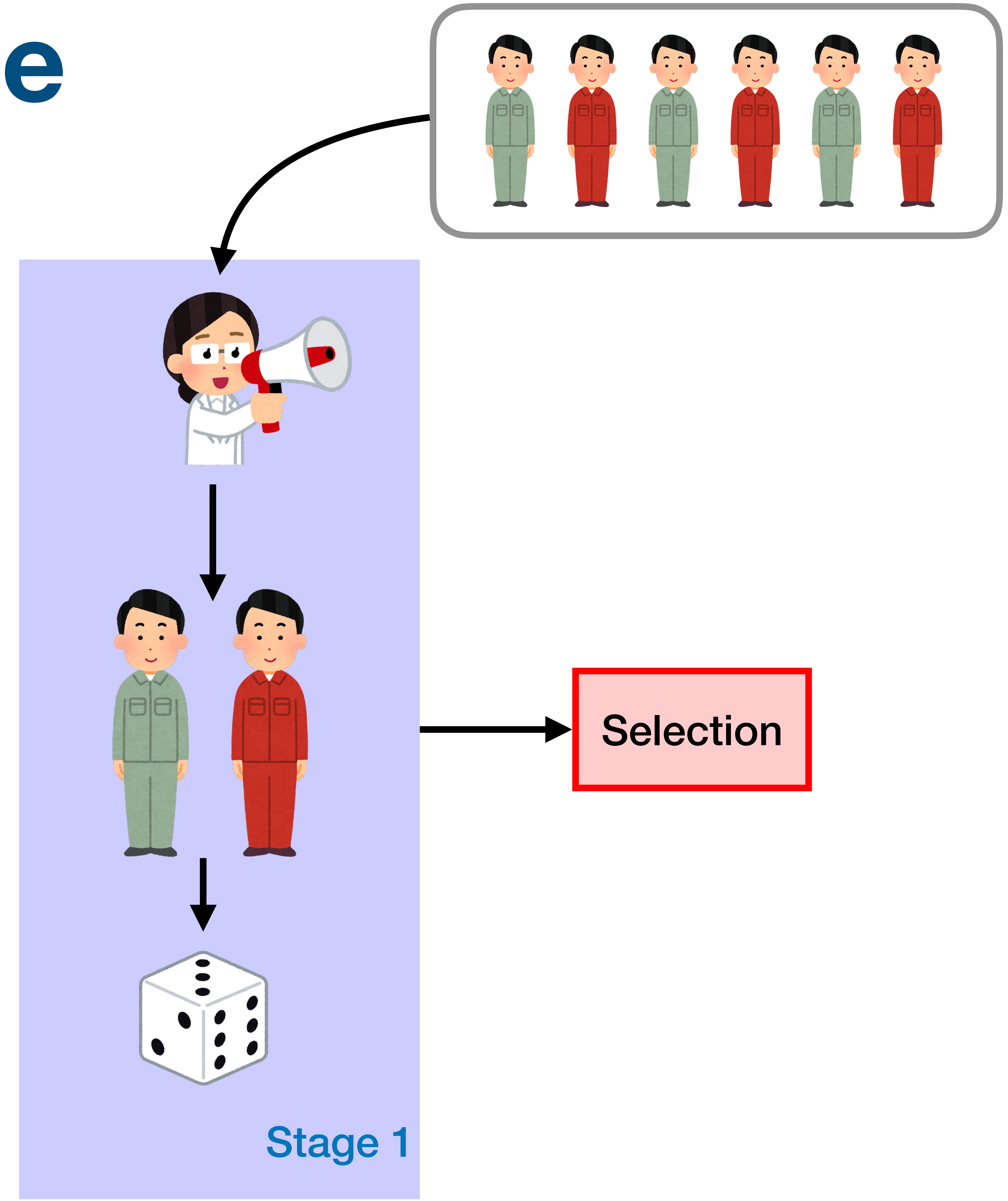

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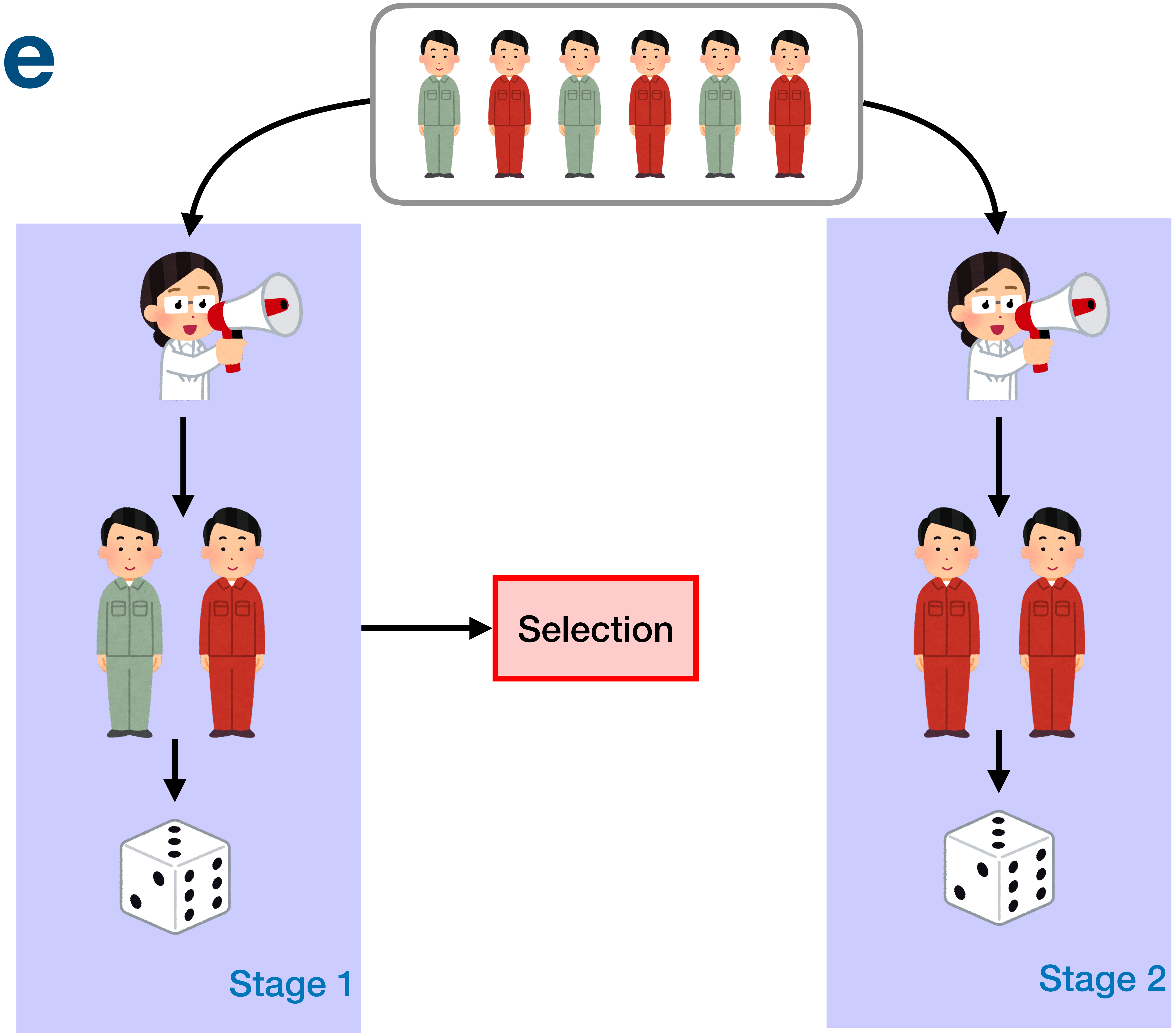

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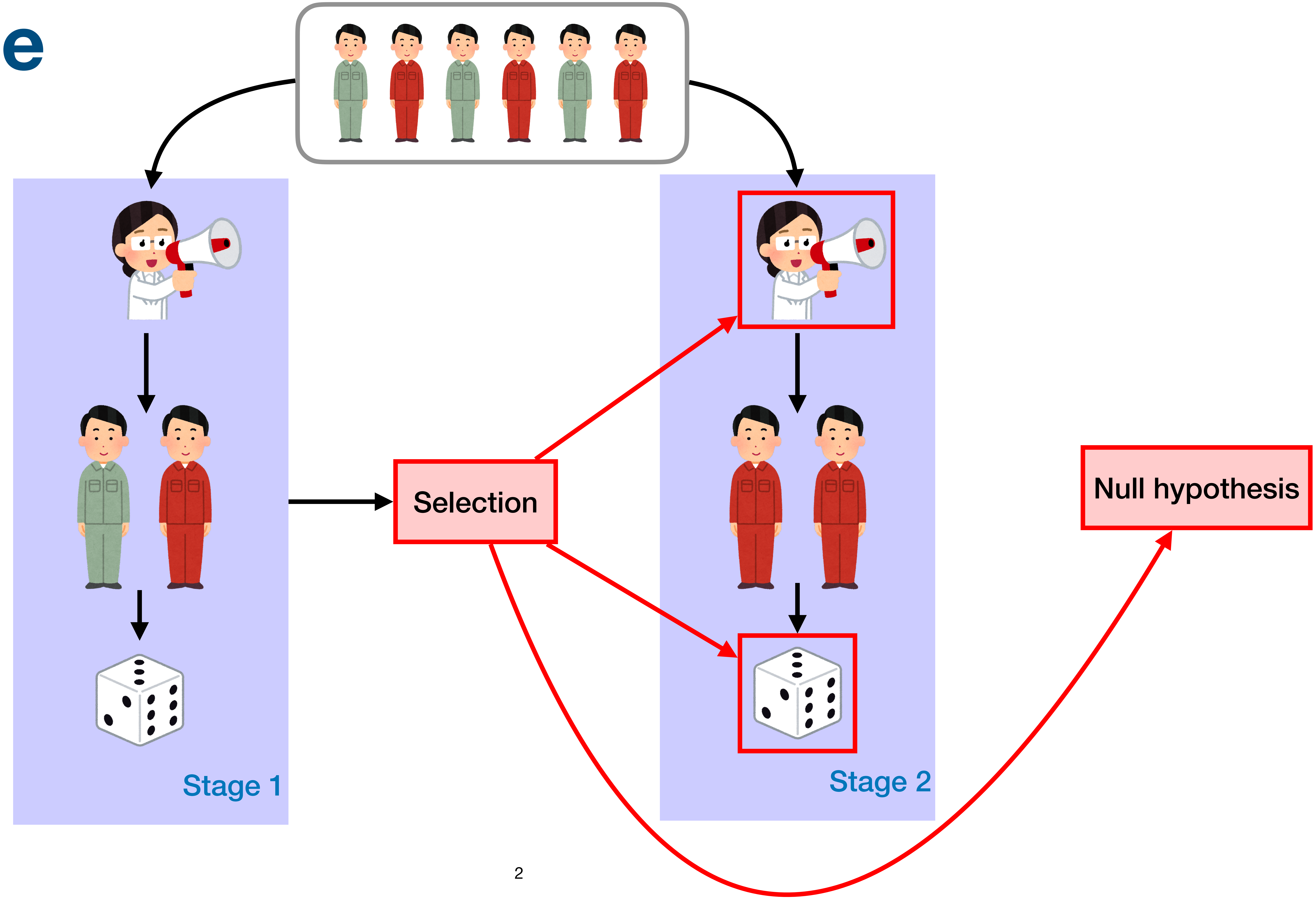

Graphical Model

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$X, Y(\cdot)$

- Covariates: X
- Potential outcomes: $Y(\cdot)$

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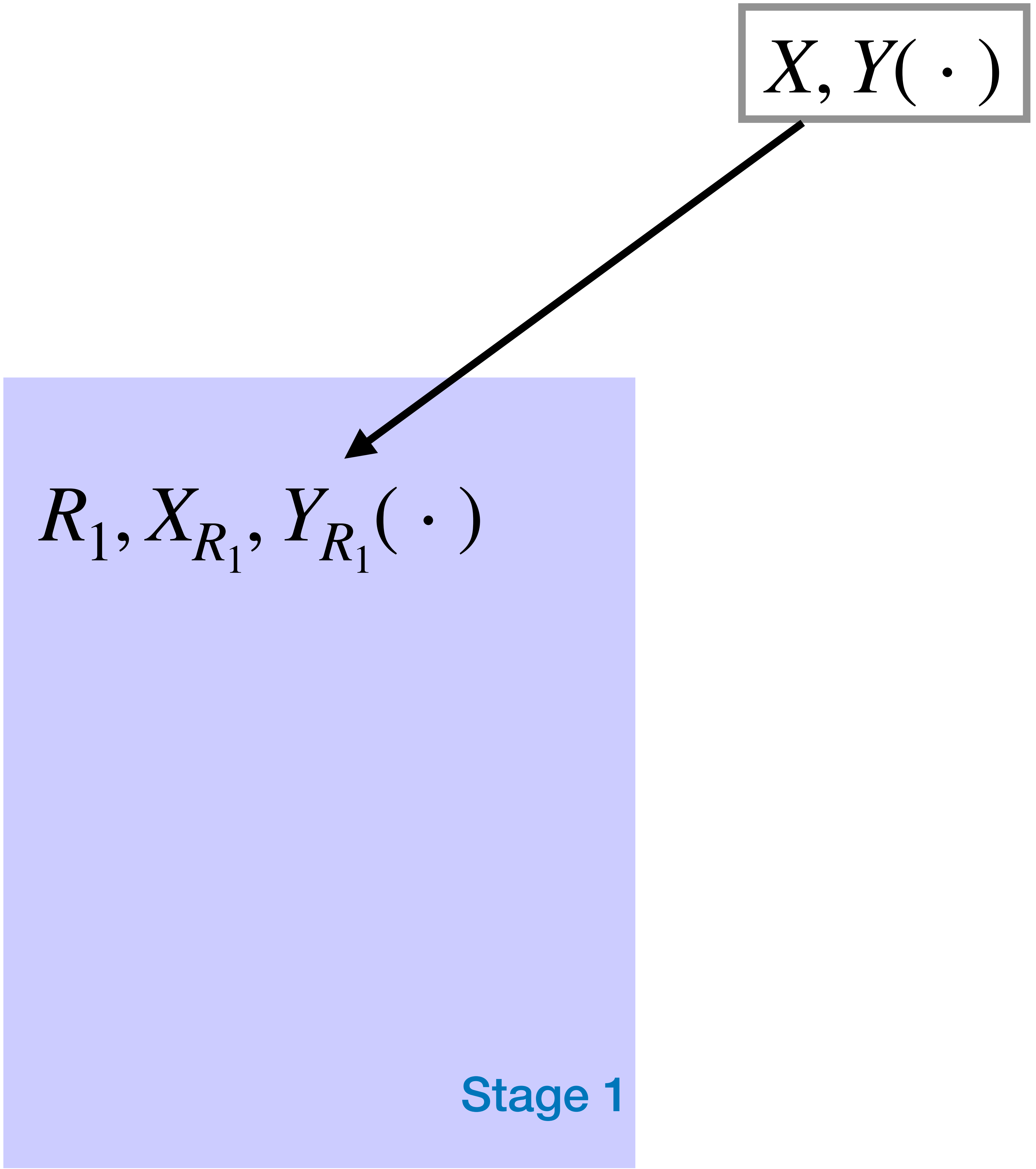

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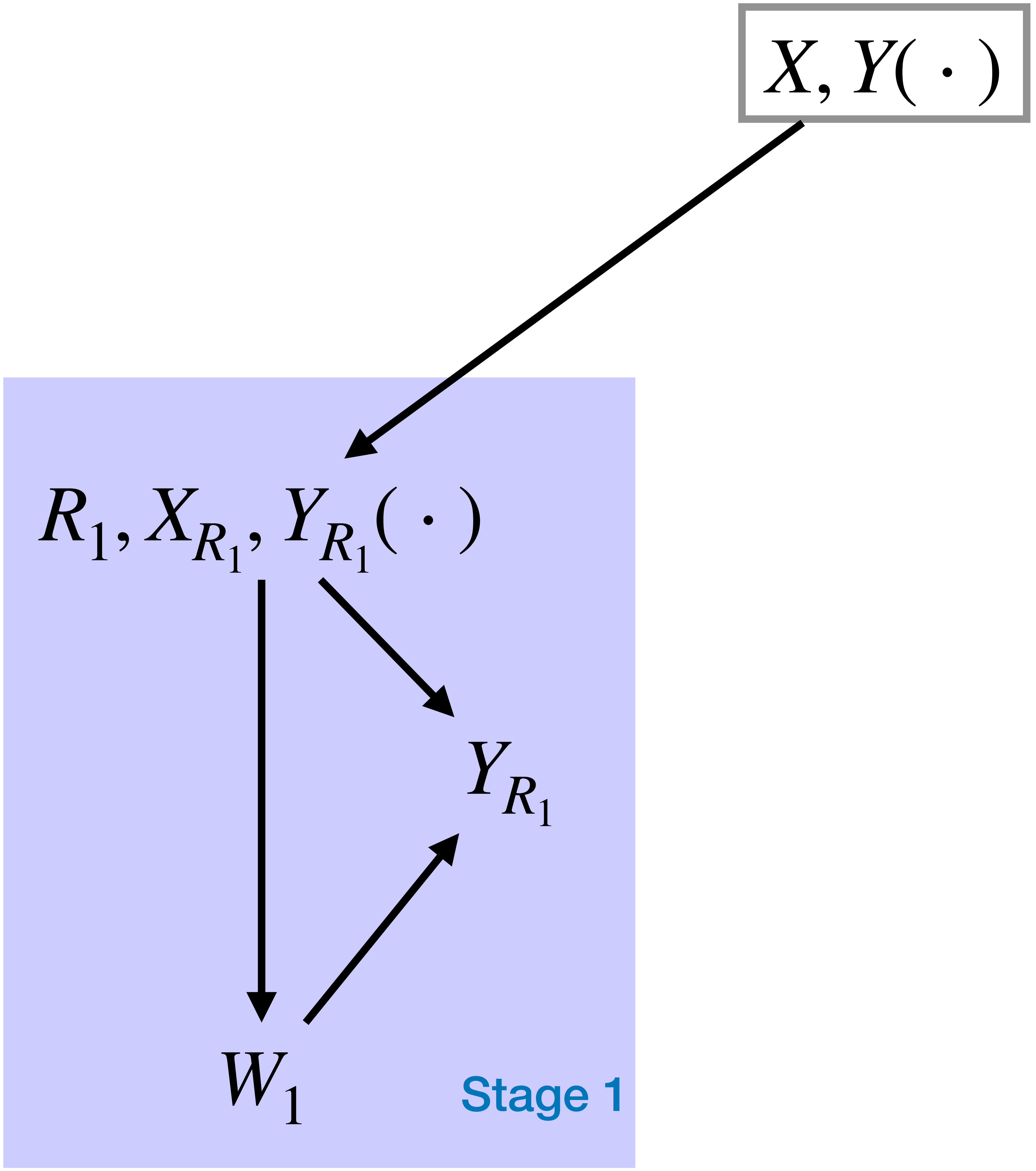

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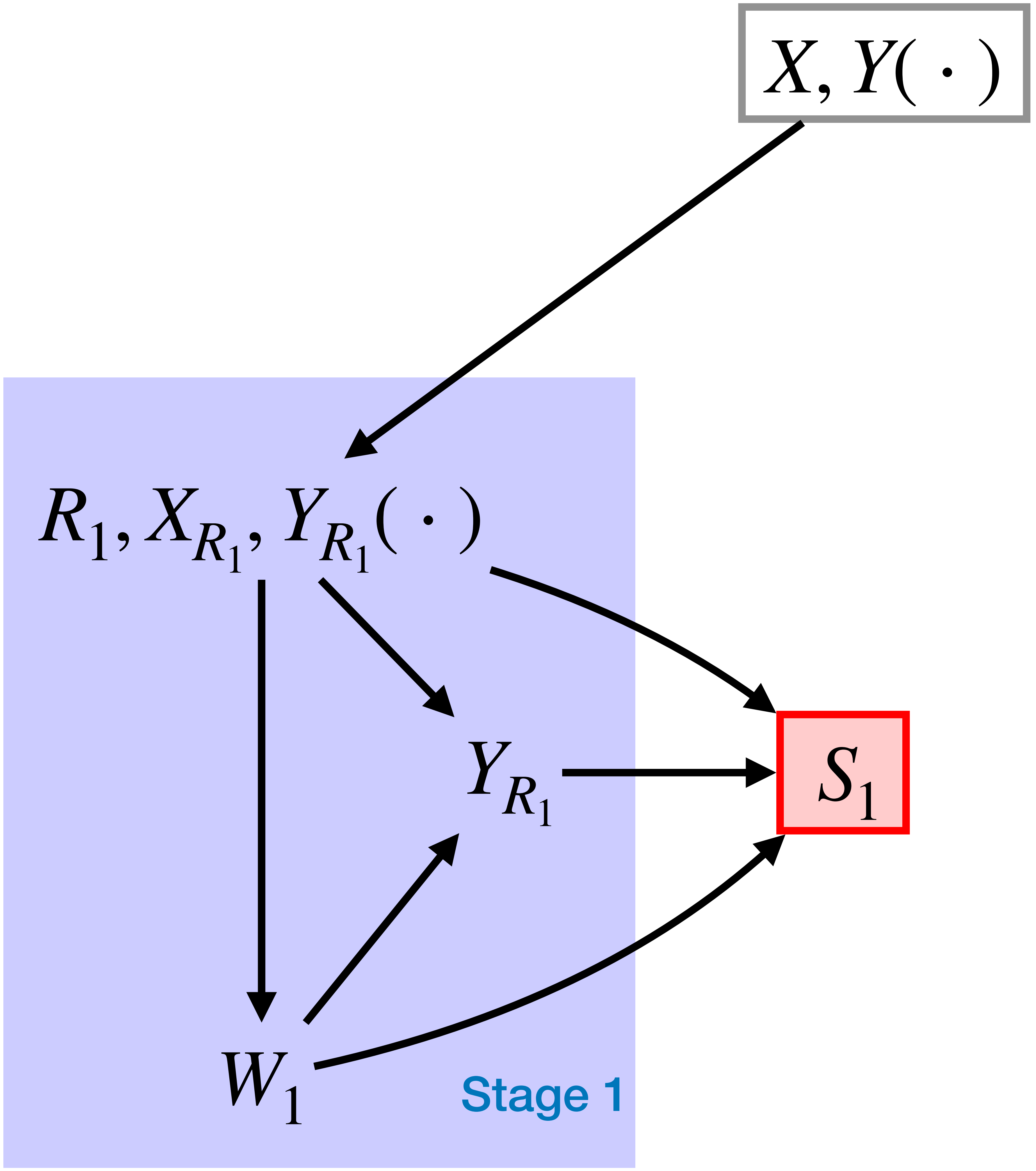

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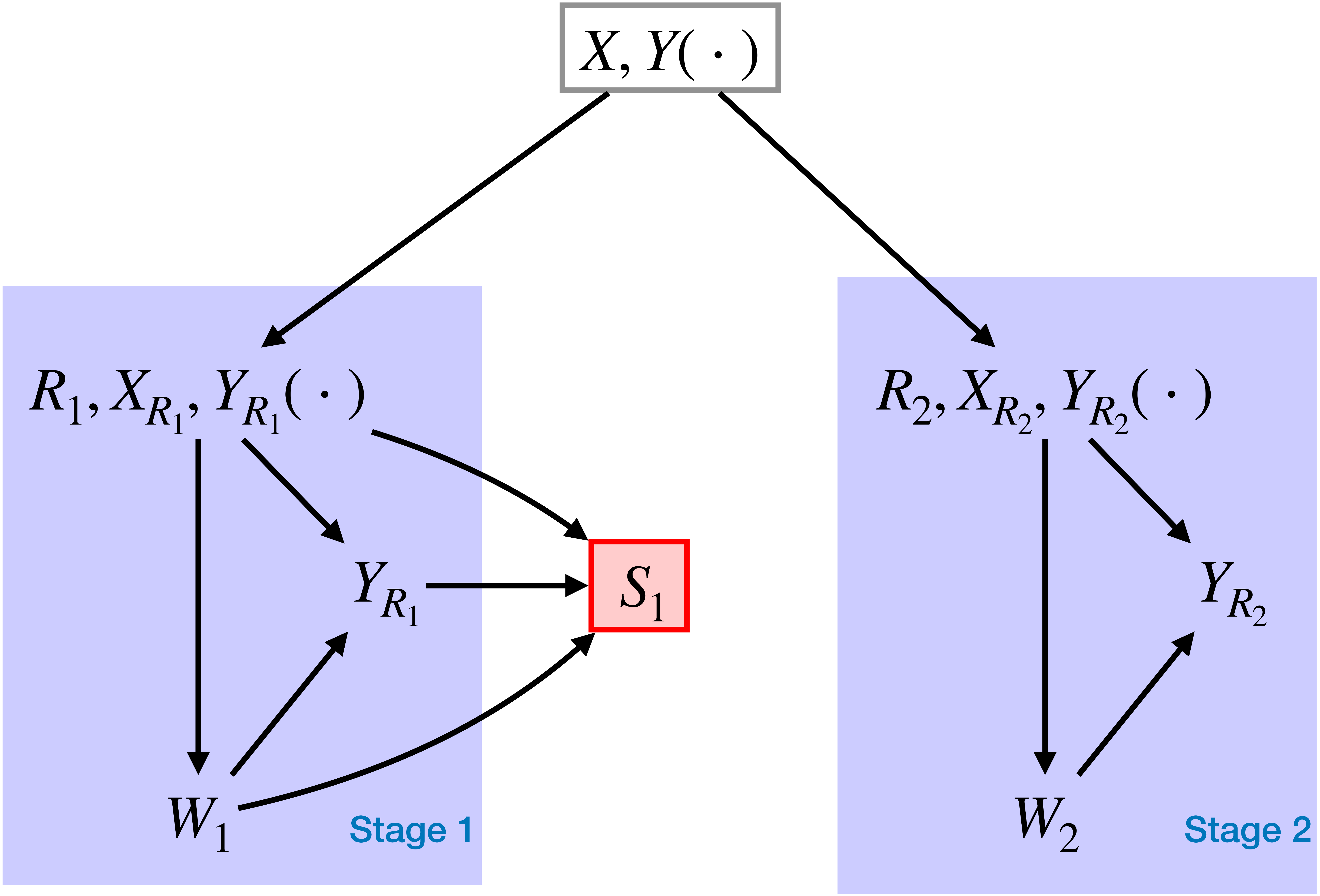

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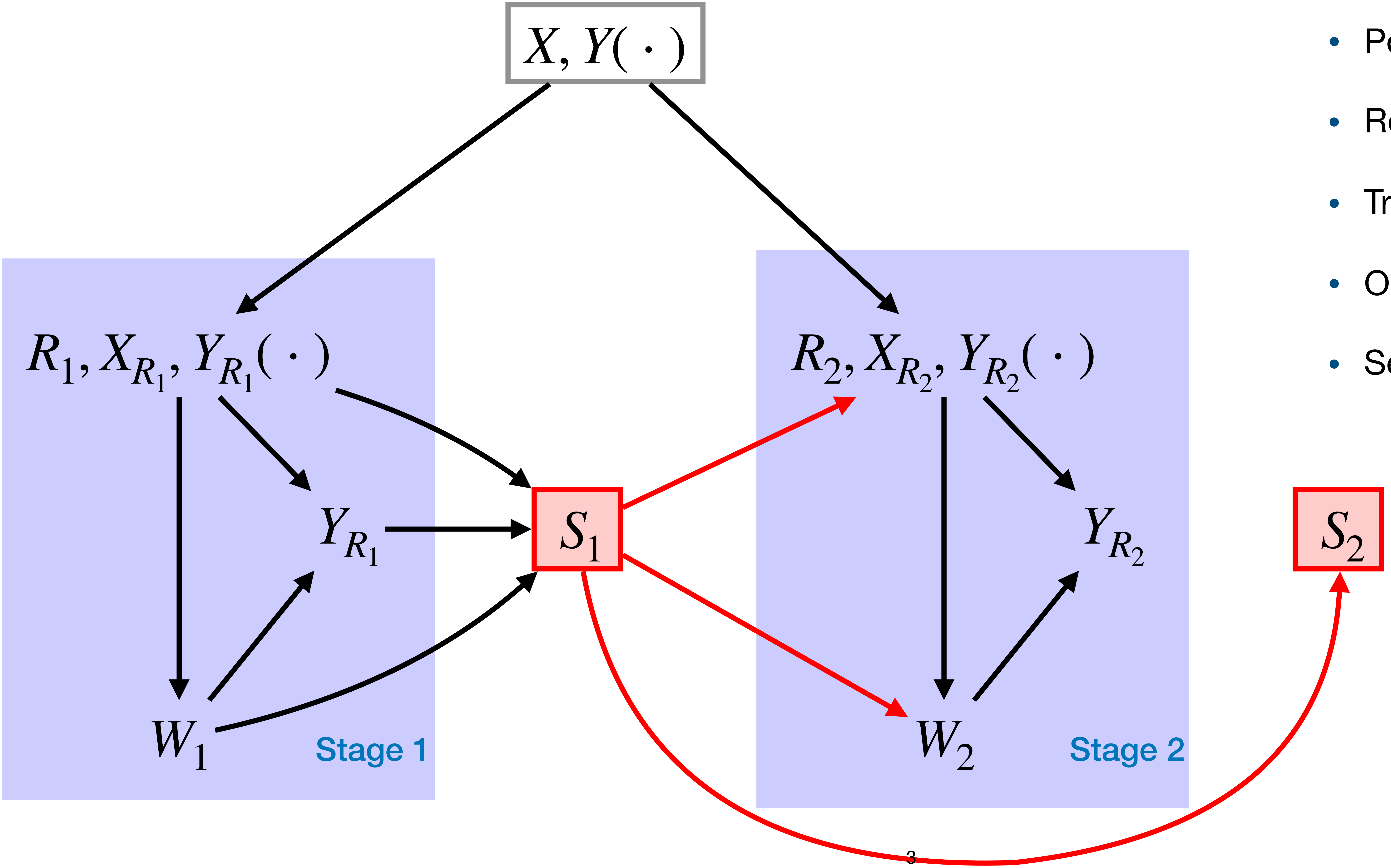

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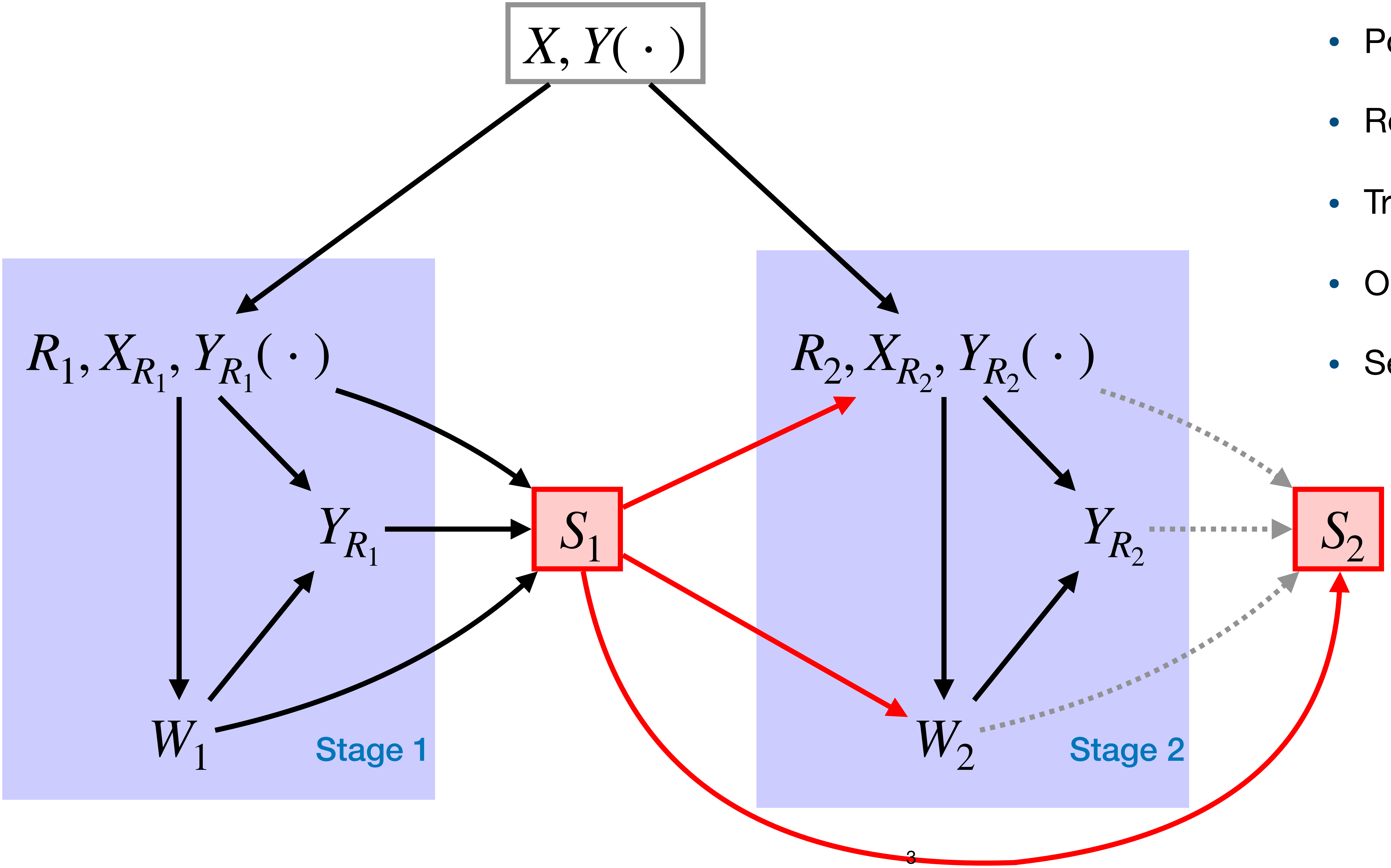

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- Condition on $Z = (R, X_R, Y_R(\,\cdot\,))$ and compare observed value of statistic $T(W, Z)$ against values $T(W^*, Z)$ under alternative treatment assignments W^*.
- $\mathbb{P}^*(\ T(W^*, Z) \leq T(W, Z) \mid W, Z)$ $\qquad W^* \stackrel{D}{=} W$ and $W^* \perp\!\!\!\perp W \mid Z$

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- Problem: double dipping

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    - Selective randomization inference:

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- Data carving: non-adaptive hold out units

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- Monte Carlo approximation: Generate m feasible samples $(w_j^*)_{j=1}^m$, i.e. $S(w) = S(w_j^*)$, and compute

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- Rejection sampling, Markov Chain Monte Carlo (MCMC)

Simulation Study

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- 2 stages, 2 treatments $W_i \in \{0,1\}$, 2 groups $X_i \in \{0,1\}$
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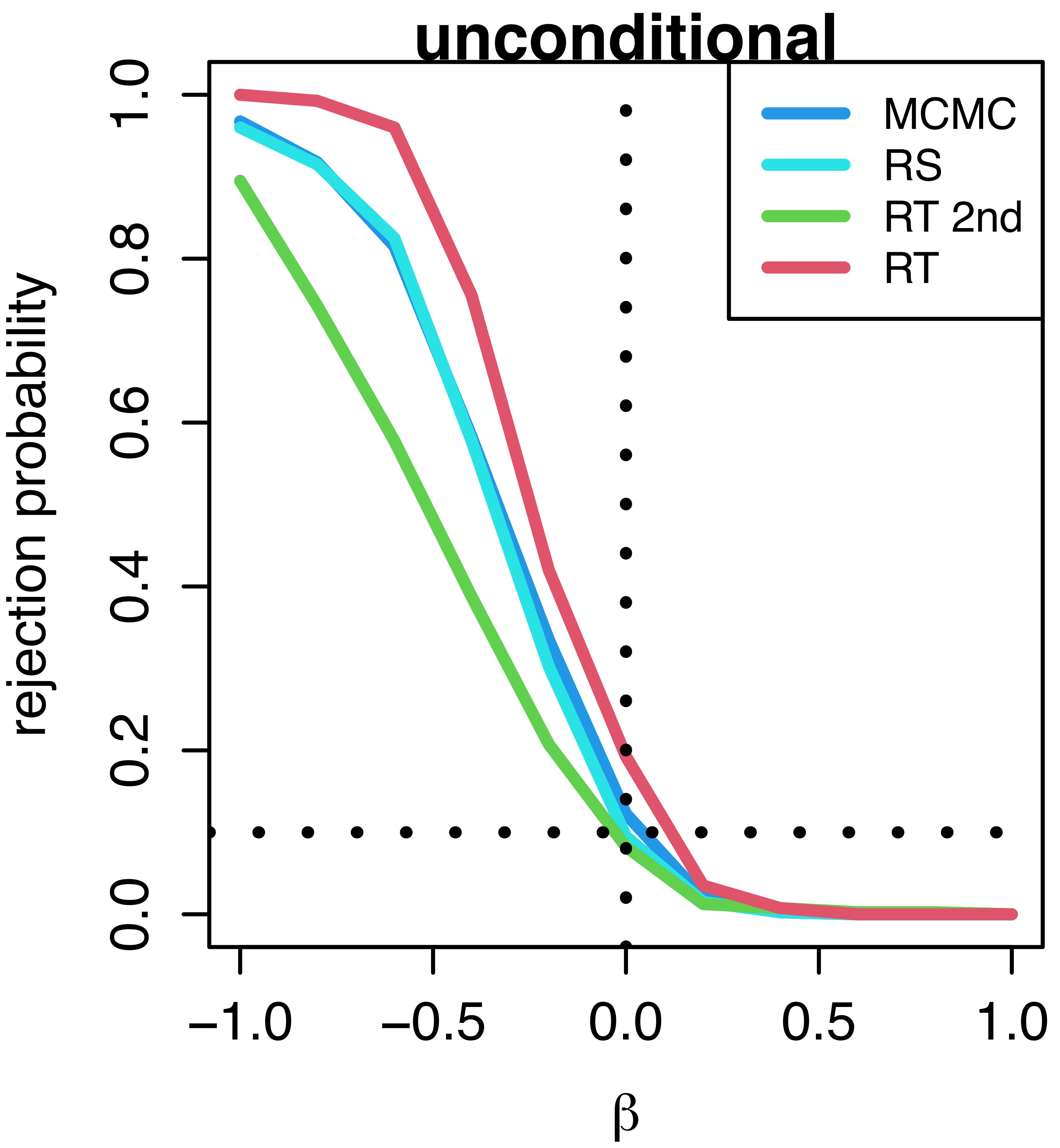
- First stage: 50 patients
- $\Delta =$ standardized difference in SATEs between groups
- Selection variable:

$$S = \begin{cases} 0, & \Phi(0.2) \leq \Delta \leq \Phi(0.8), & \text{recruit 13/12 in stage II,} \\ 1, & \Delta < \Phi(0.2), & \text{recruit 25 from group 1 in stage II,} \\ 2, & \Delta > \Phi(0.8), & \text{recruit 25 from group 2 in stage II.} \end{cases}$$

Power Analysis



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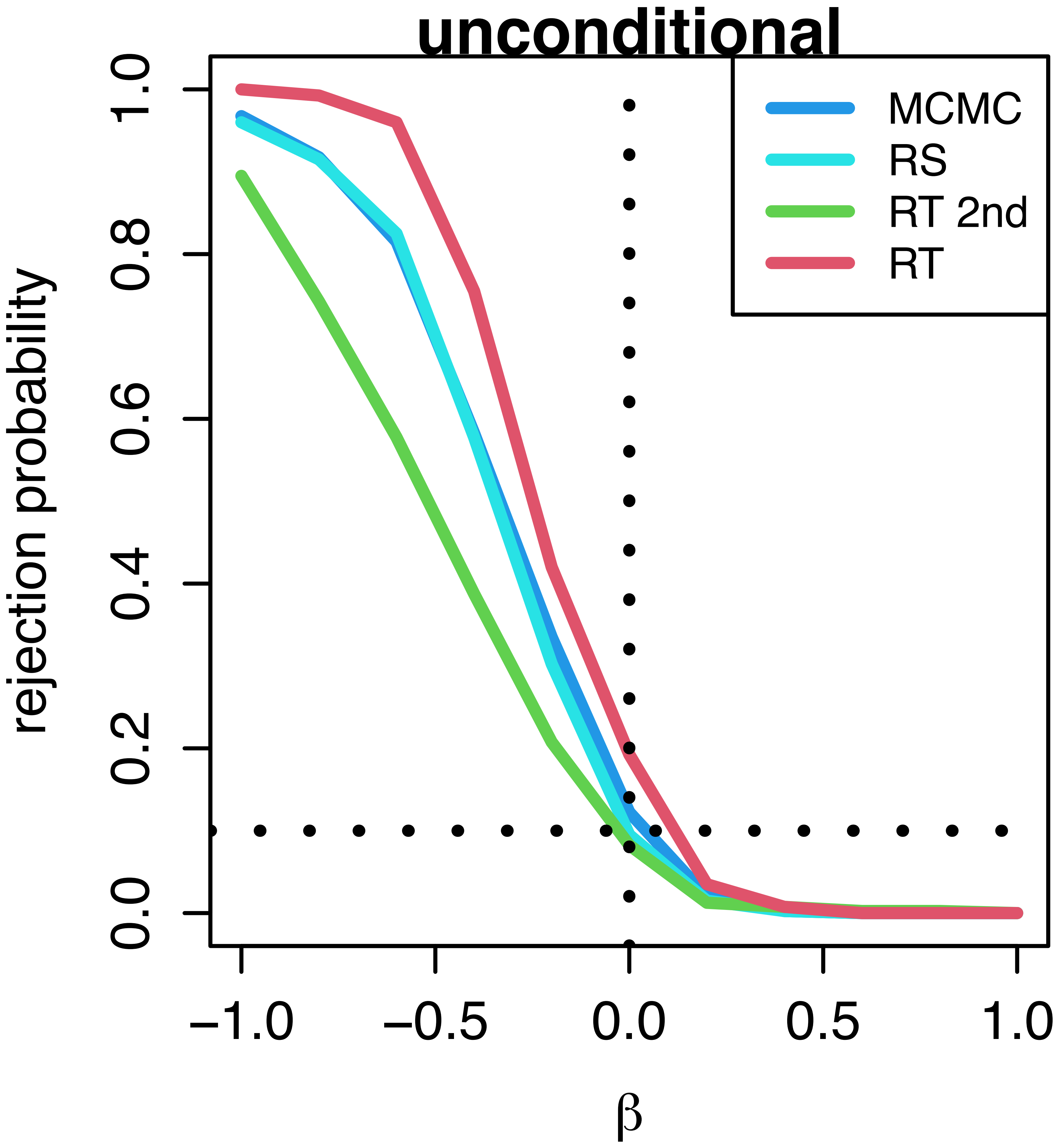

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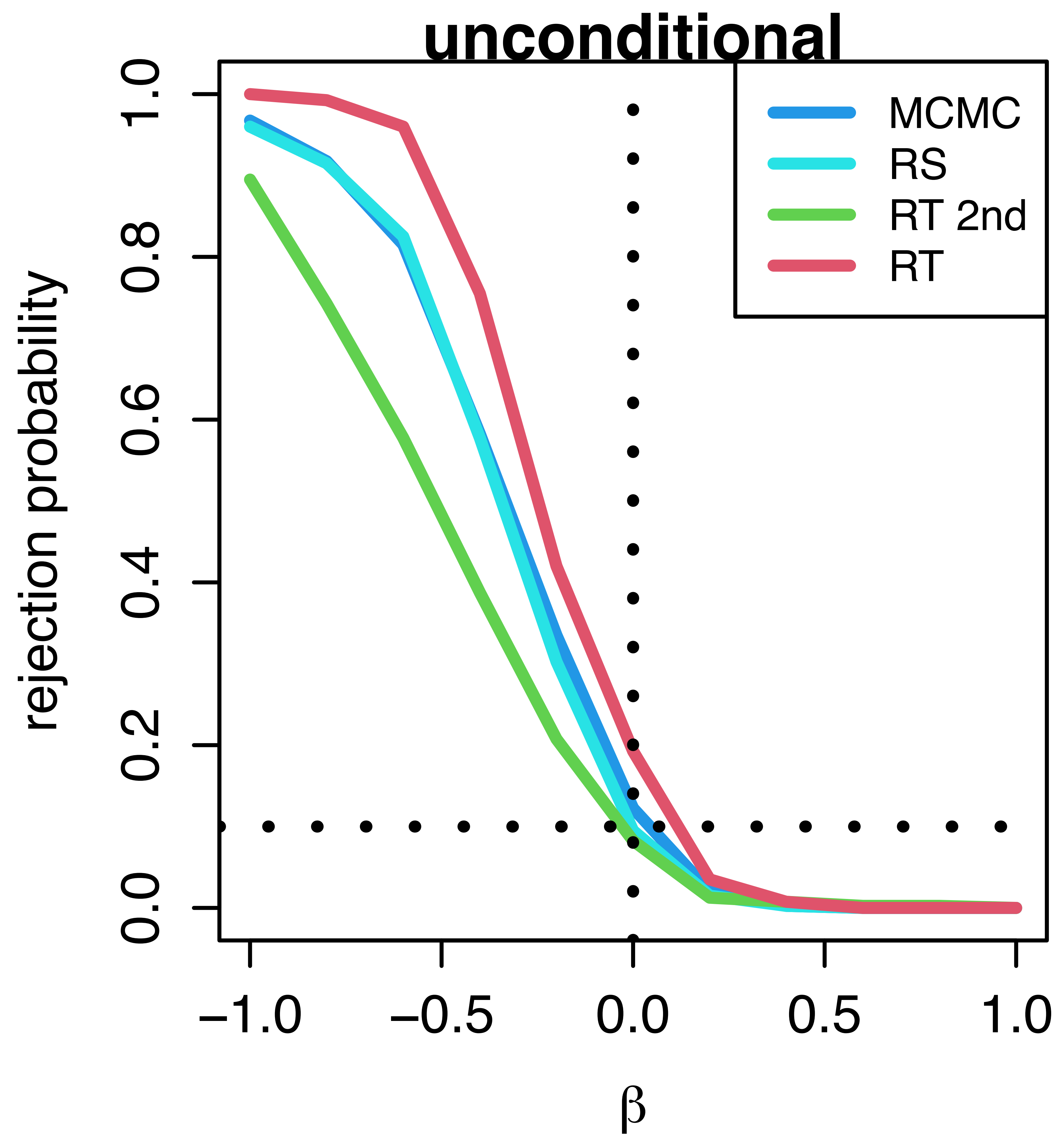

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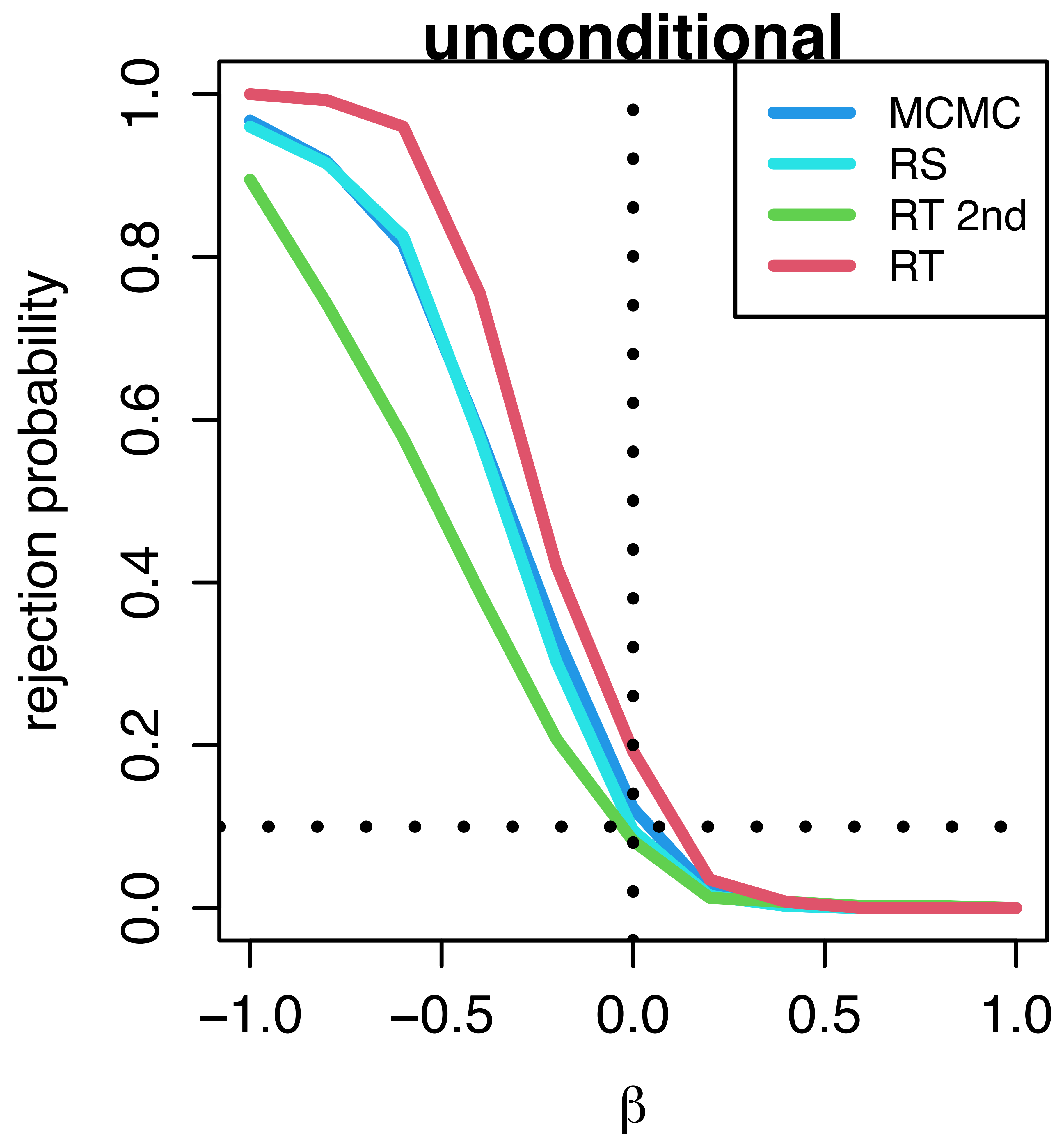

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- Rejection sampling and MCMC lead to very similar approximations.

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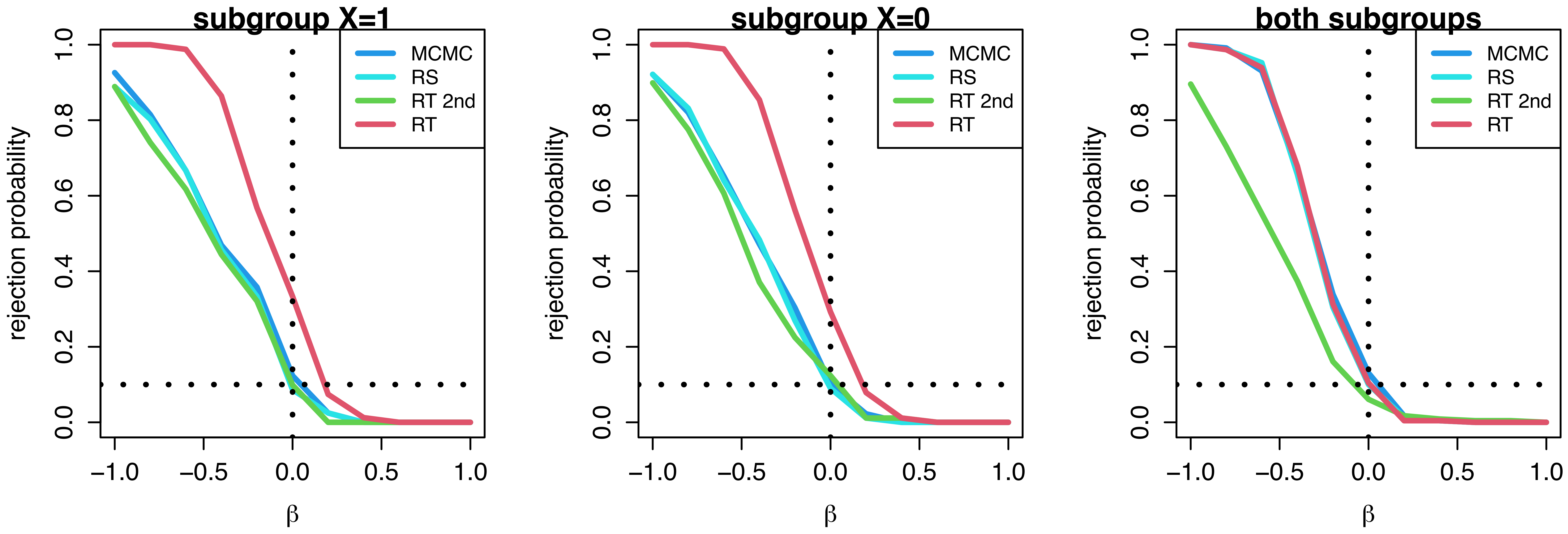

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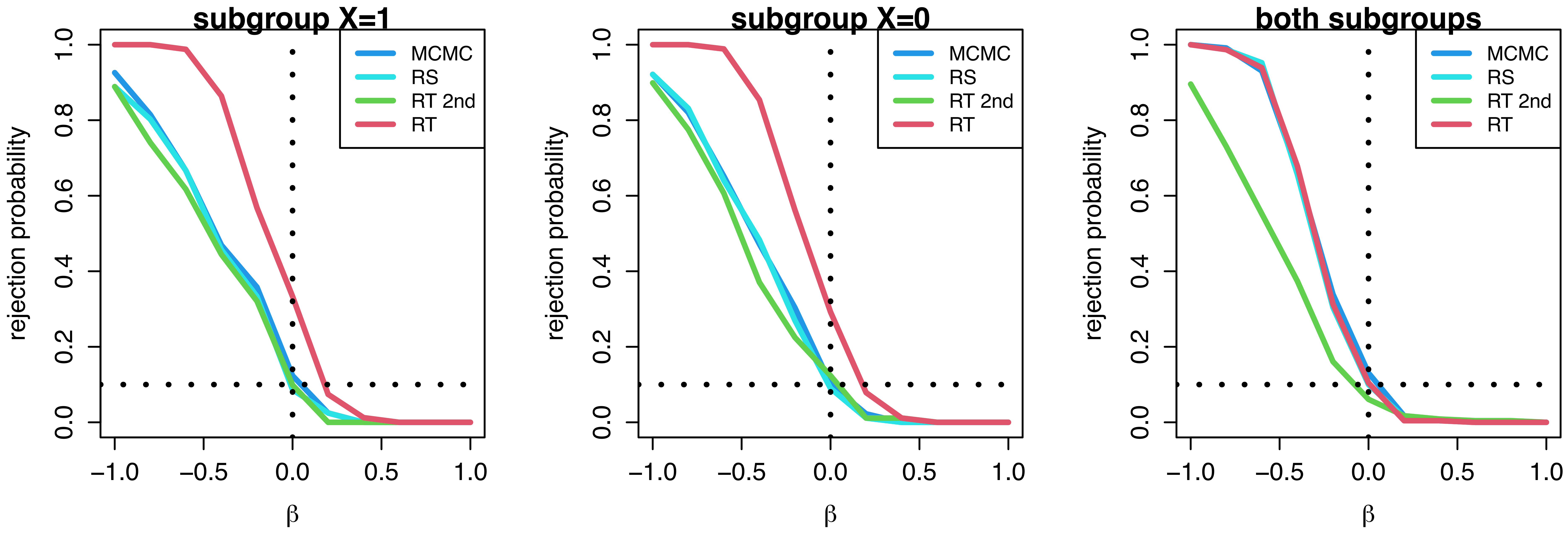

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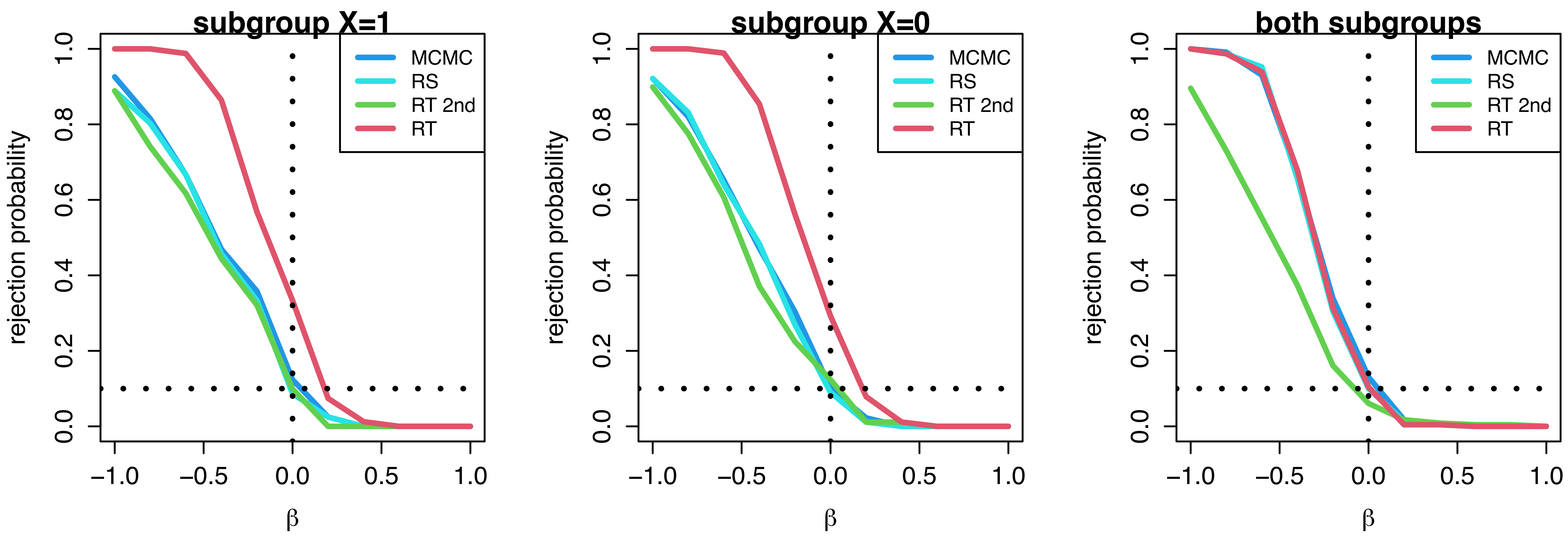

- Type-I error control in every subgroup
- Gain in power when there is a lot of “randomness left”

Thanks for your attention!

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References

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