Selective Randomization Inference for Adaptive Experiments

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- Inference without modelling- or i.i.d. data- assumptions

Fisher (1935), Pitman (1937), Zhang & Zhao (2023)

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2	7	7		0
3	-3	-3		0
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Randomization Inference

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- Test statistic: $T(Z, Y(\cdot))$, e.g. average outcome of treated minus control

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- P-value:

$$\mathbb{P}(\, T(Z^*, Y(\cdot)) \leq T(Z, Y(\cdot)) \mid Y(\cdot), Z),$$

where $\quad Z^* \stackrel{D}{=} Z$ and $Z^* \perp\!\!\!\perp Z \mid Y(\cdot)$

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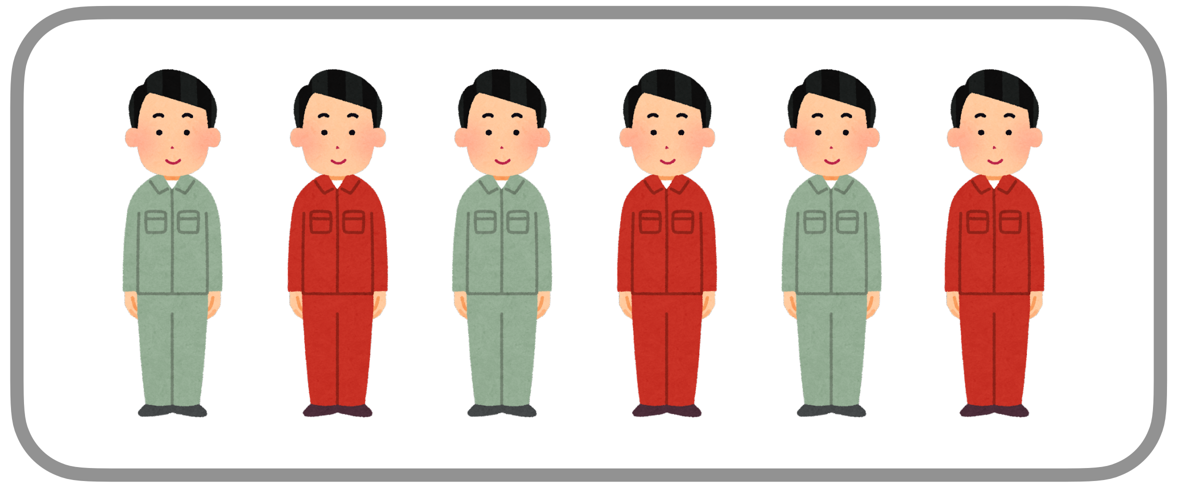


High genetic risk


Low genetic risk

FOURIER trial: Marston et al. (2020)

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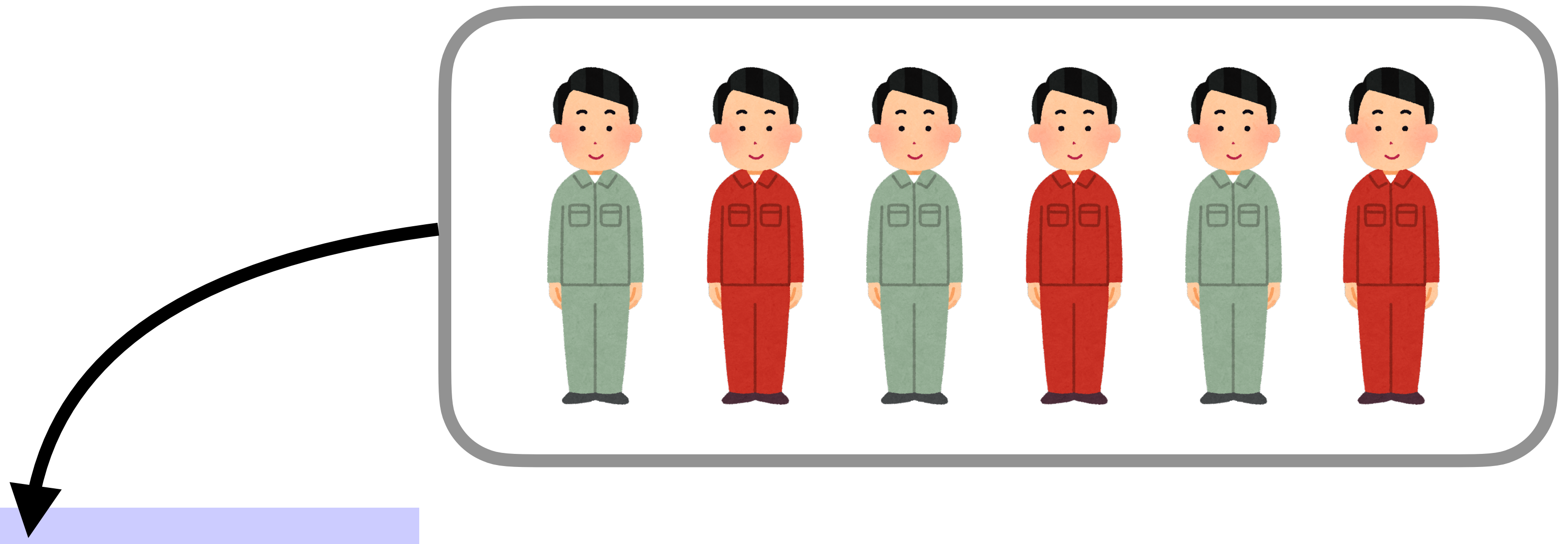

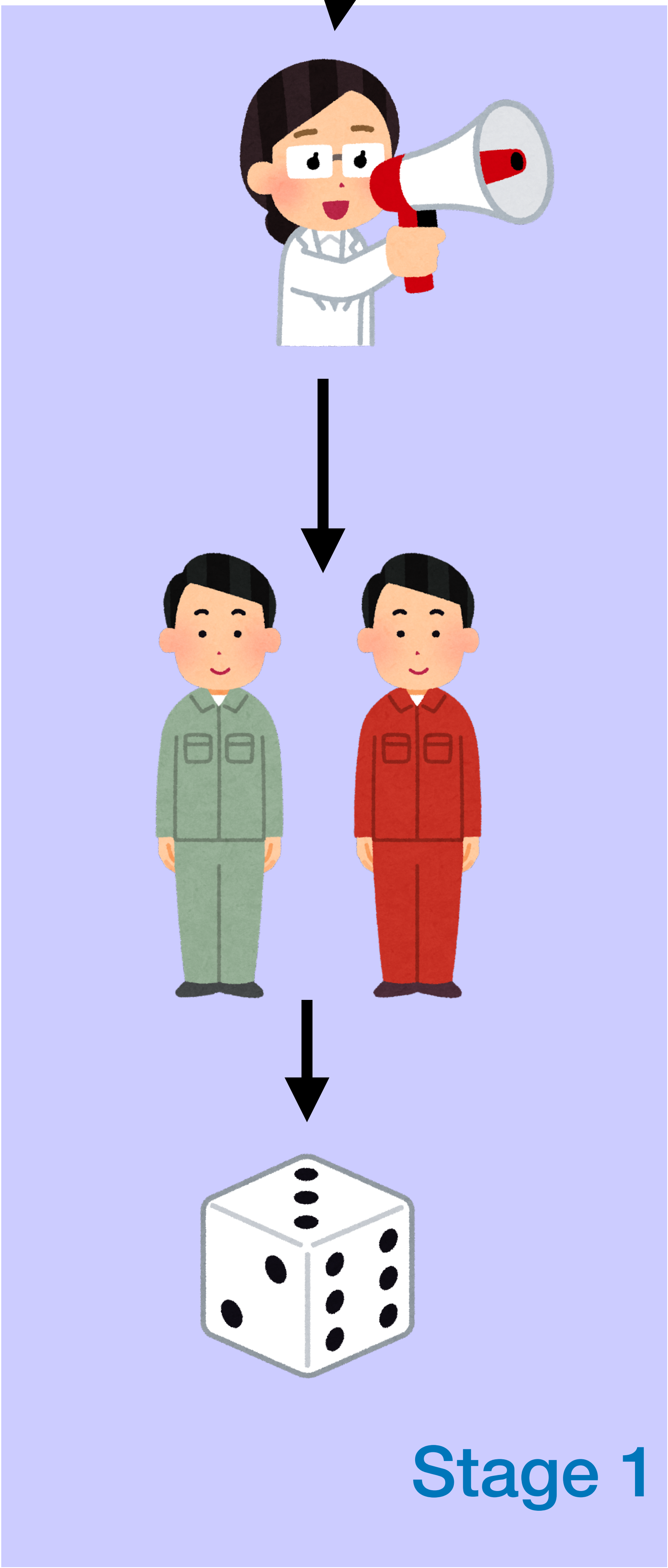

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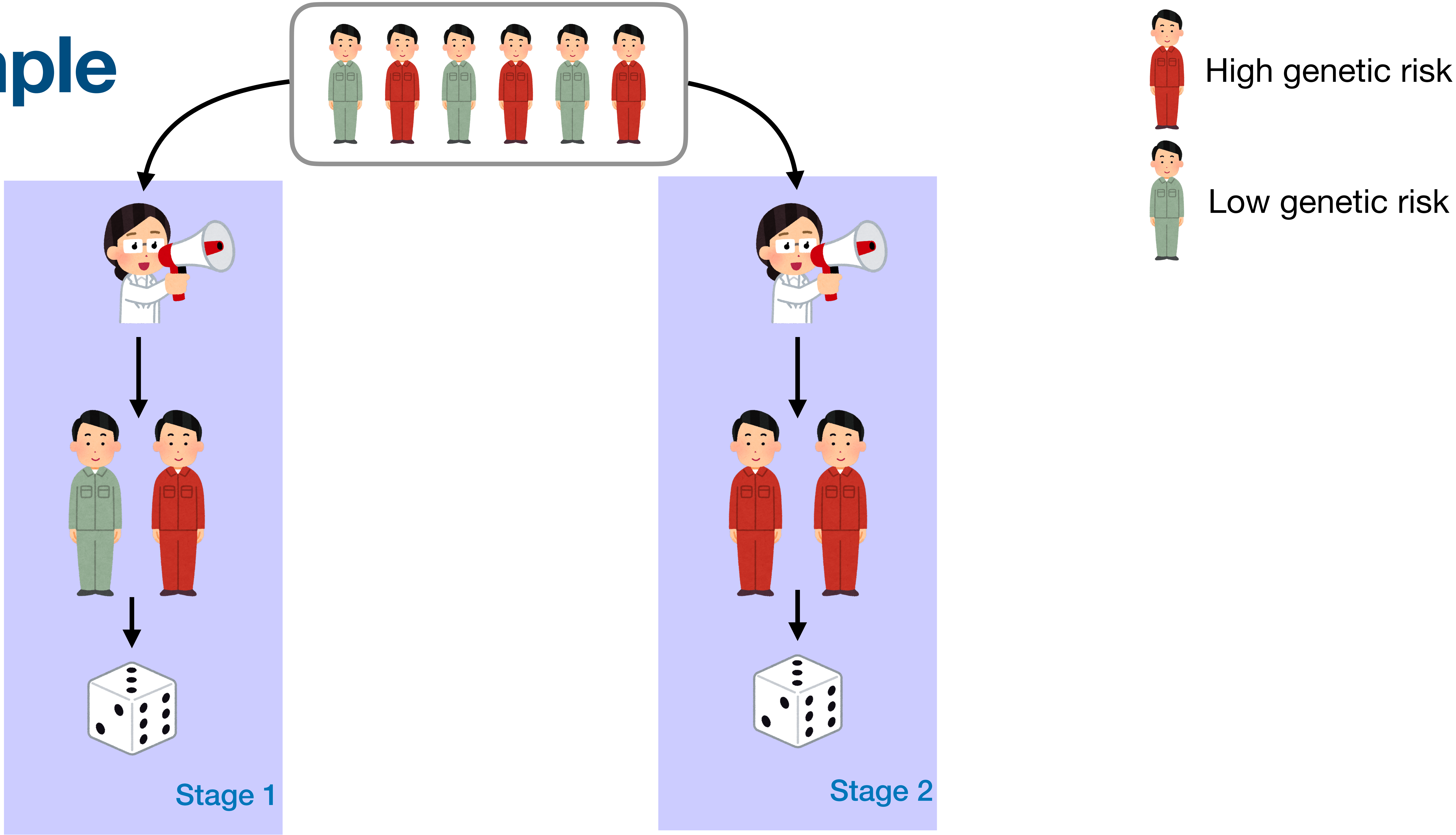

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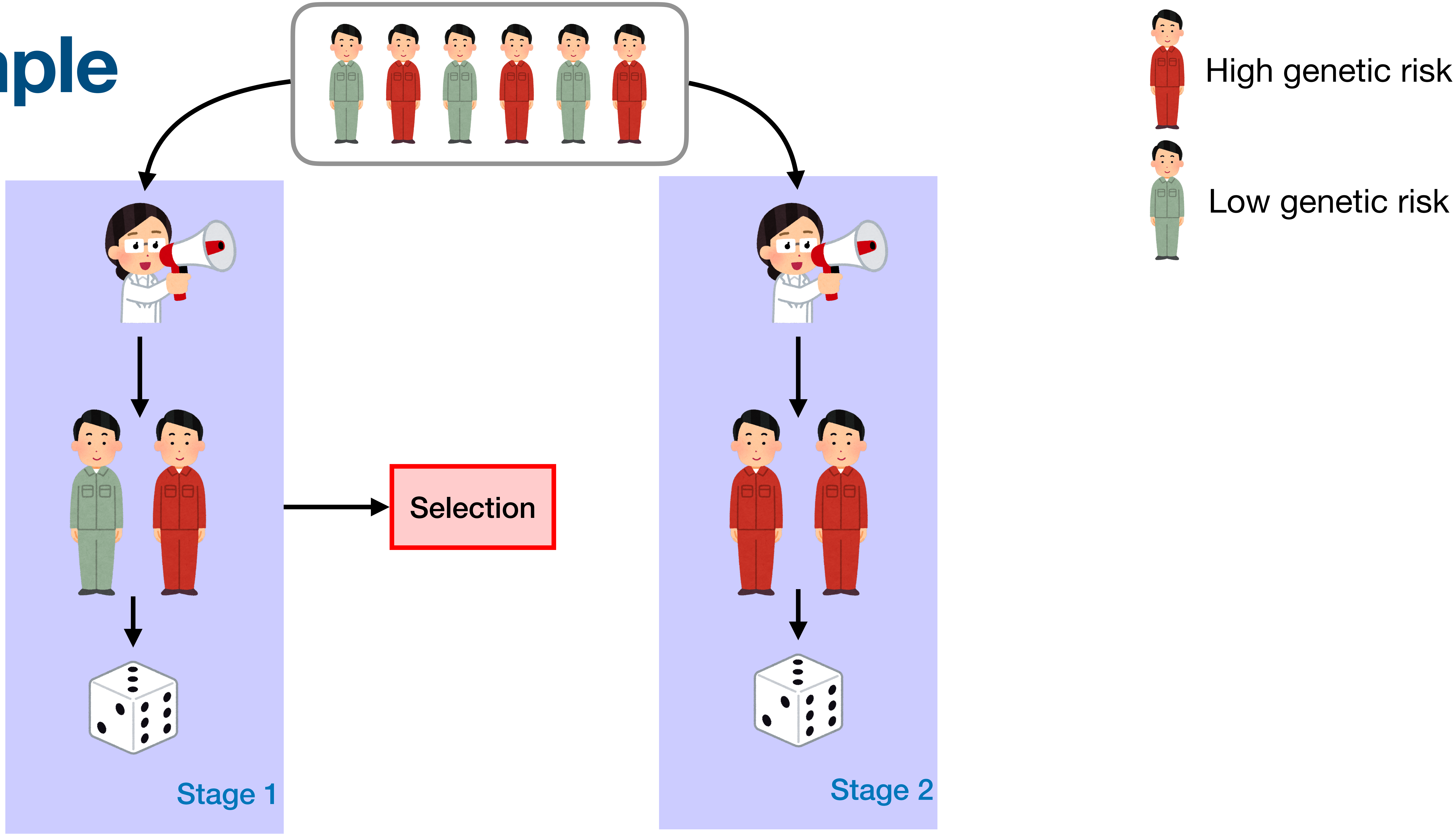

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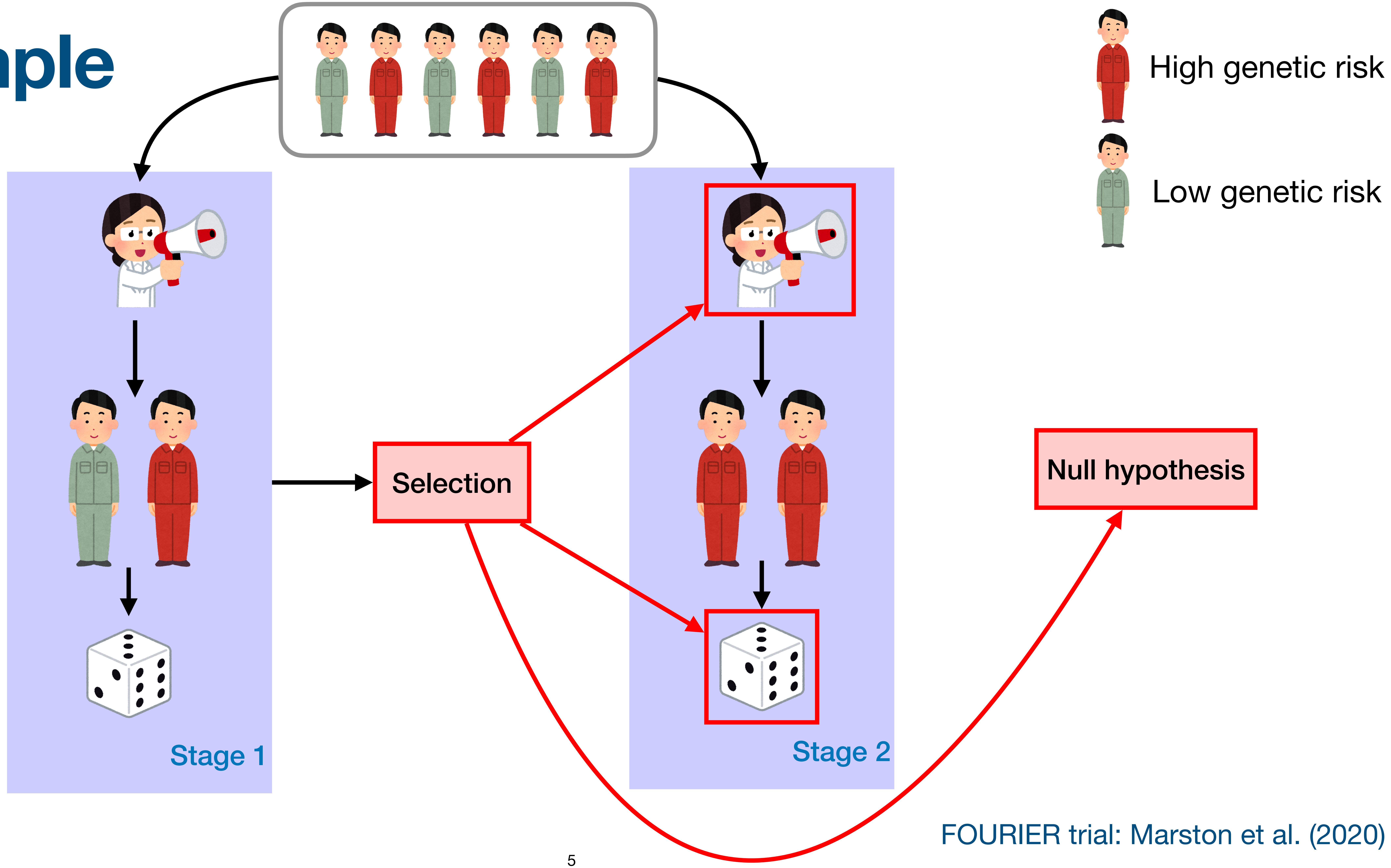

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- Potential outcomes: $Y(\cdot)$

$$\boxed{X, Y(\cdot)}$$

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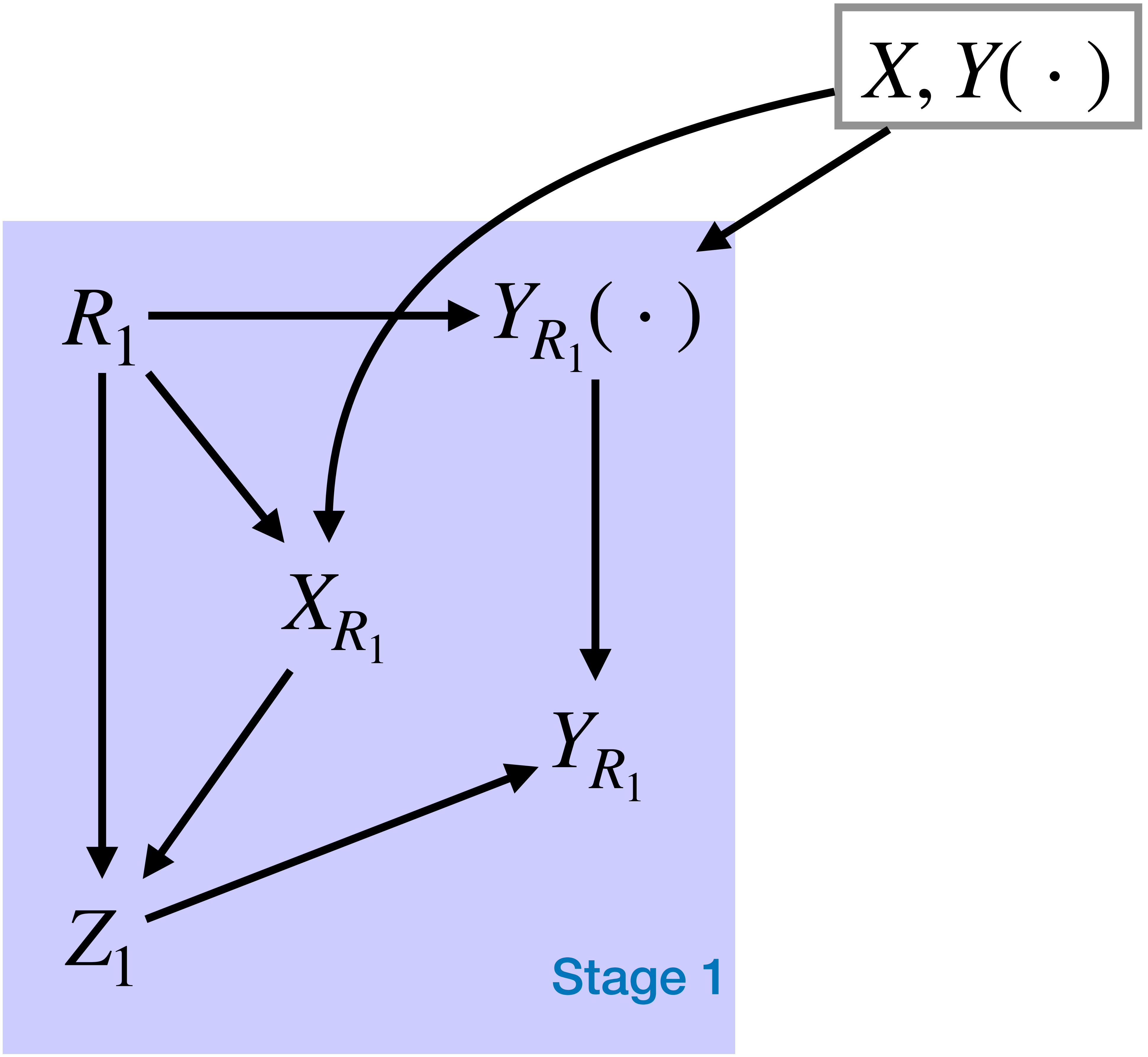

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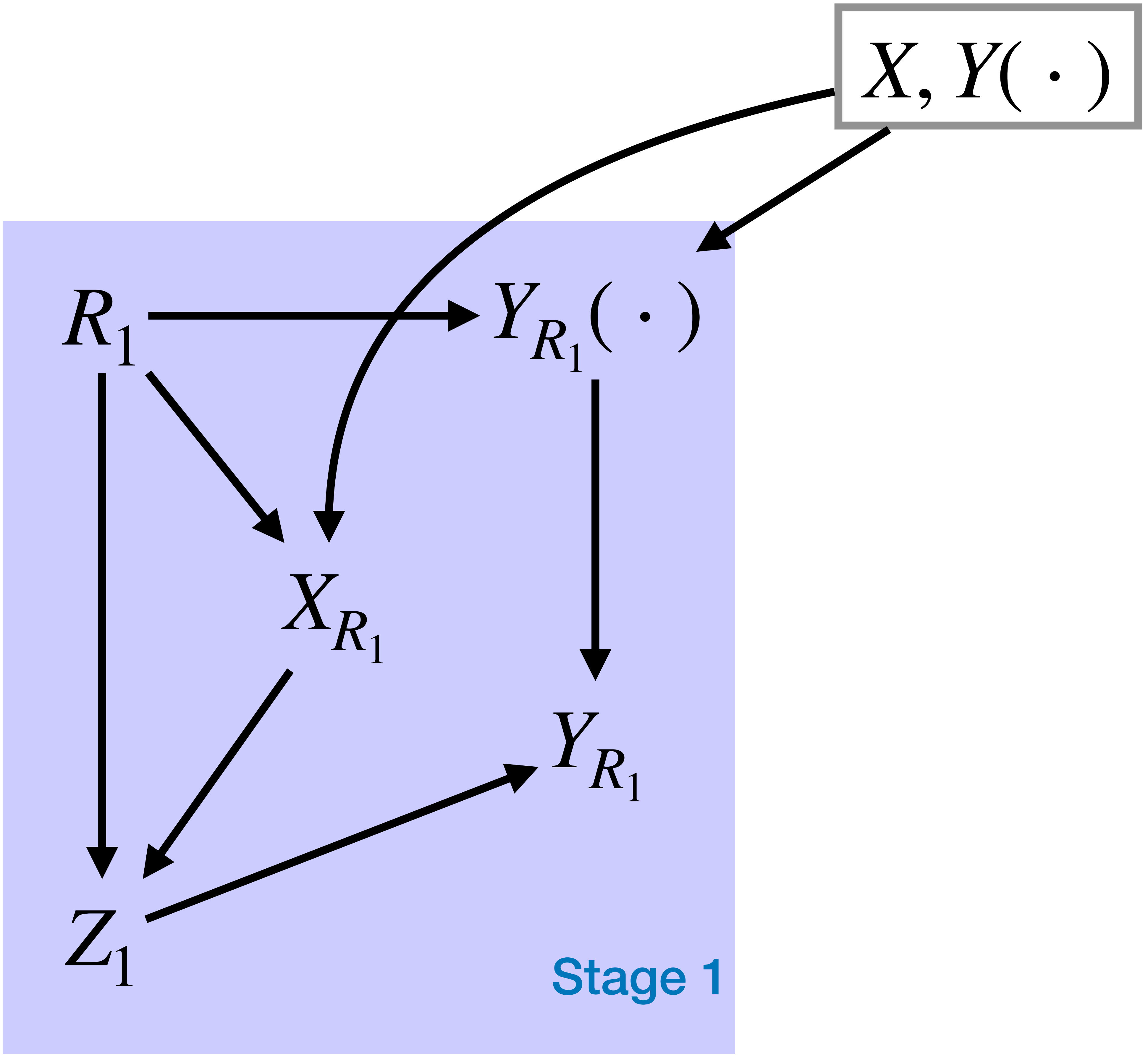

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- Treatments: Z_k
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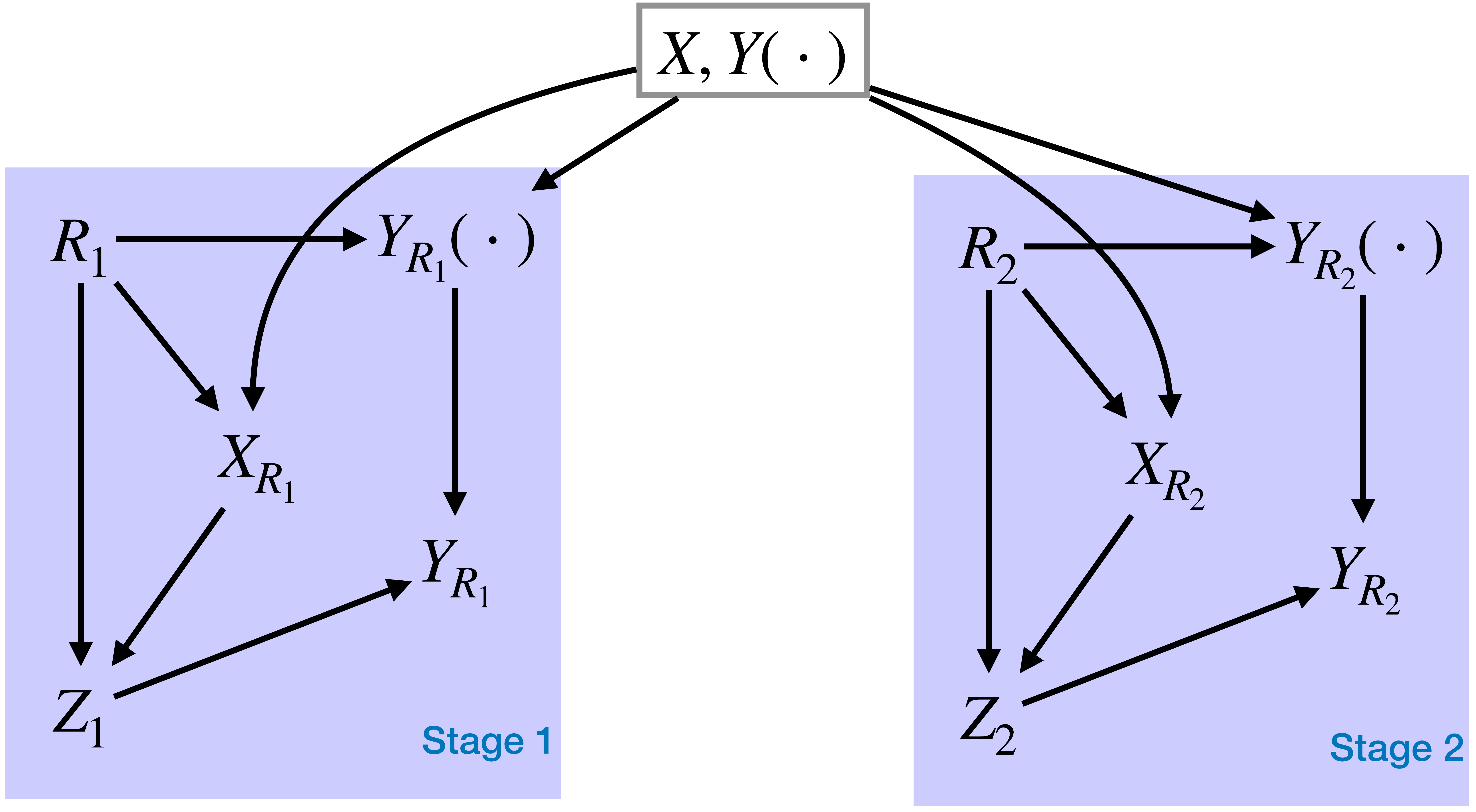

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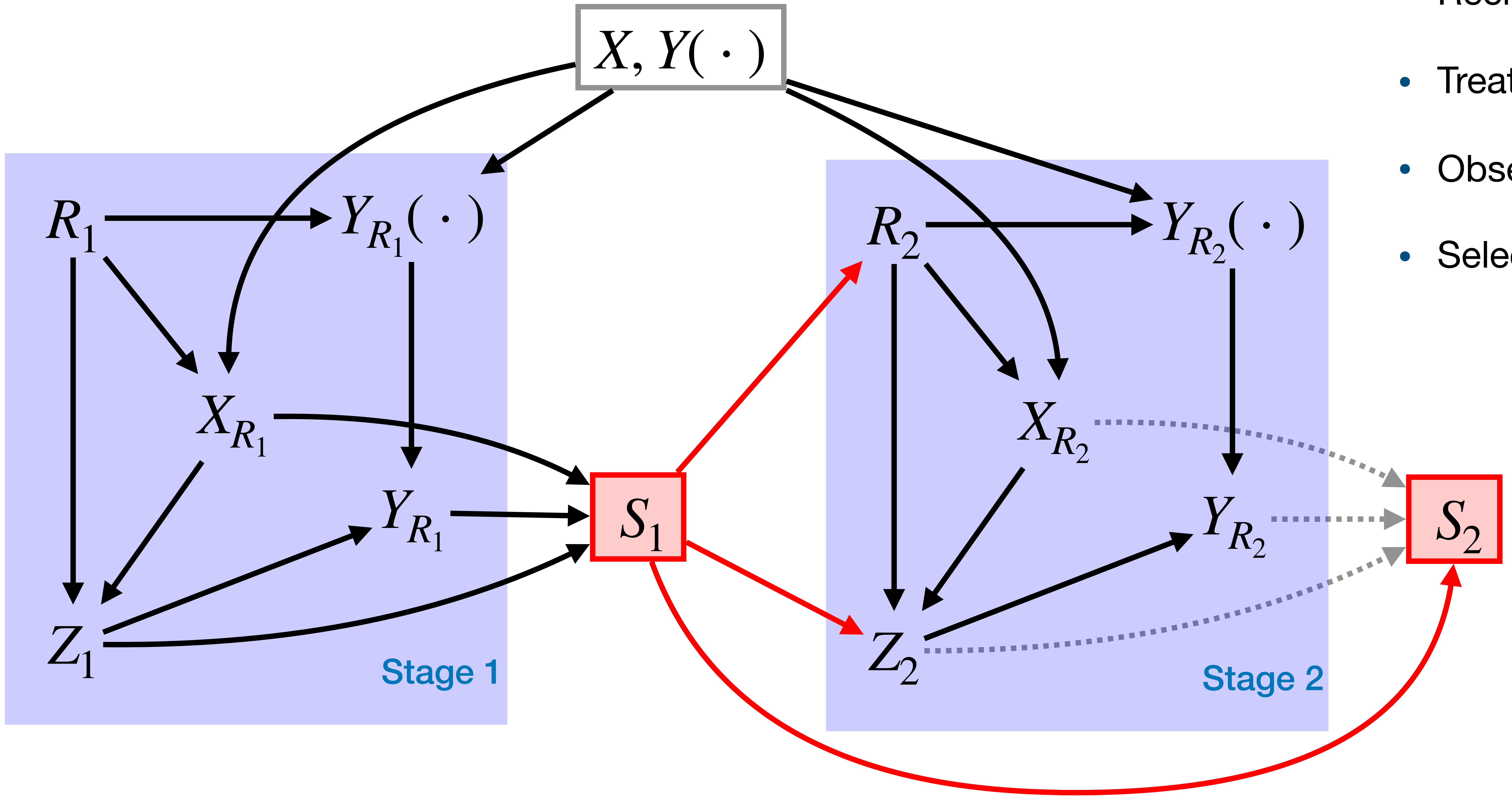

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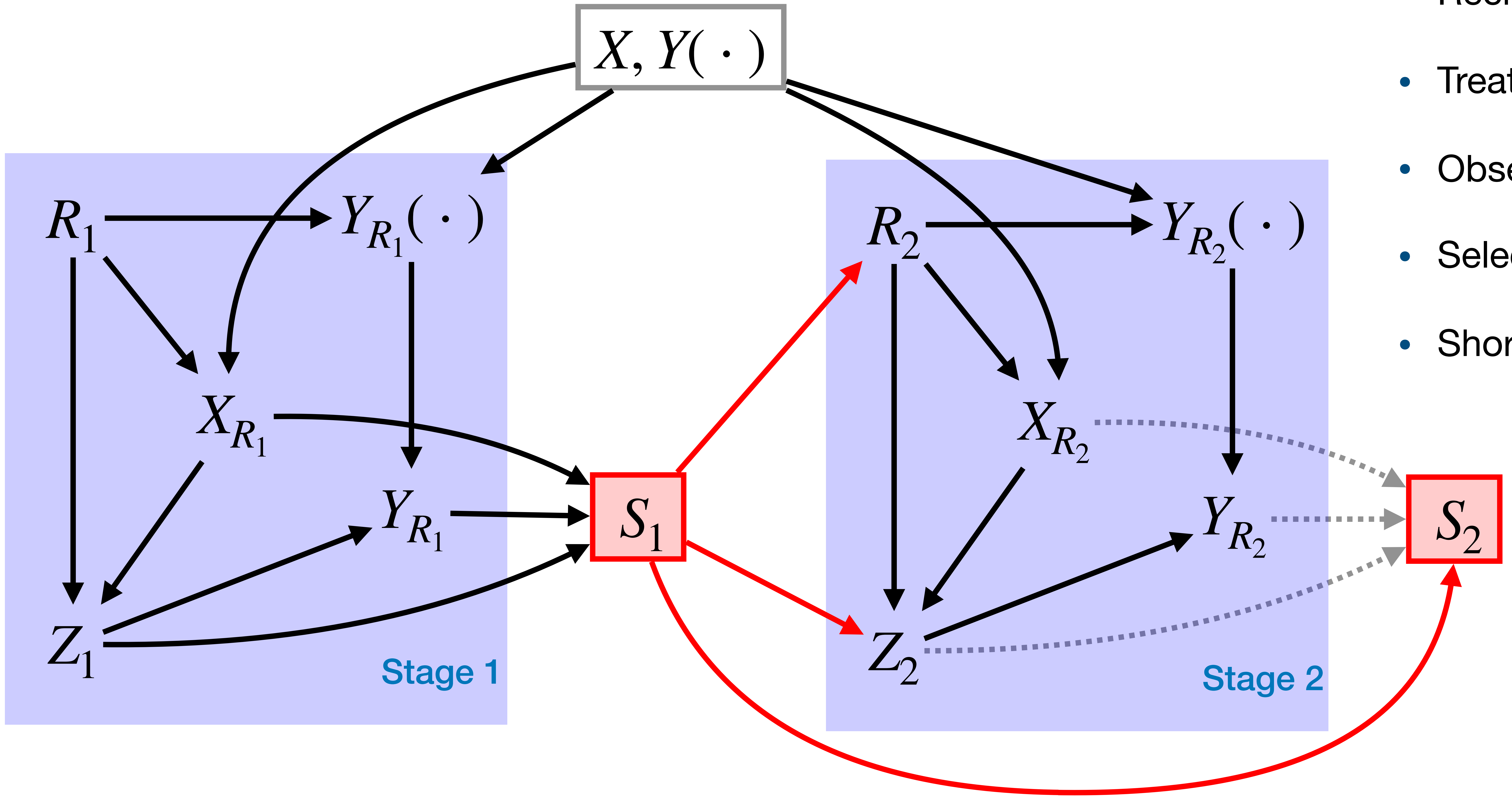

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- Selective choice: S_k
- Short-hand: $W = (R, X_R, Y_R(\cdot))$

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  - Bandit algorithms: exploration and exploitation
  - Reinforcement learning

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- Different overlapping fields:
  - Response-adaptive randomization: trade off statistical power and patient benefit
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  - Reinforcement learning
- Analysing data from adaptive experiments despite the **dependence** between different data points

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

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- Is there a problem when the experiment is adaptive?

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  - Selective randomization inference:

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- Rejection sampling, Markov Chain Monte Carlo (MCMC)

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  - test $Y_i(1) - Y_i(0) = \tau$ for different τ
  - $(1 - \alpha)$ confidence interval: $C_{1-\alpha} = \{\tau : P_{sel}(\tau) \geq \alpha\}$

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- Estimation: τ such that $P_{sel}(\tau) = 0.5$

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- 2 stages, 2 treatments $Z_i \in \{0,1\}$, 2 groups $X_i \in \{\text{low, high}\}$
- Potential outcomes: $Y_i(0) = Y_i(1) \sim N(0,1)$ i.i.d.
- First stage: 100 patients, Second stage: 40 patients

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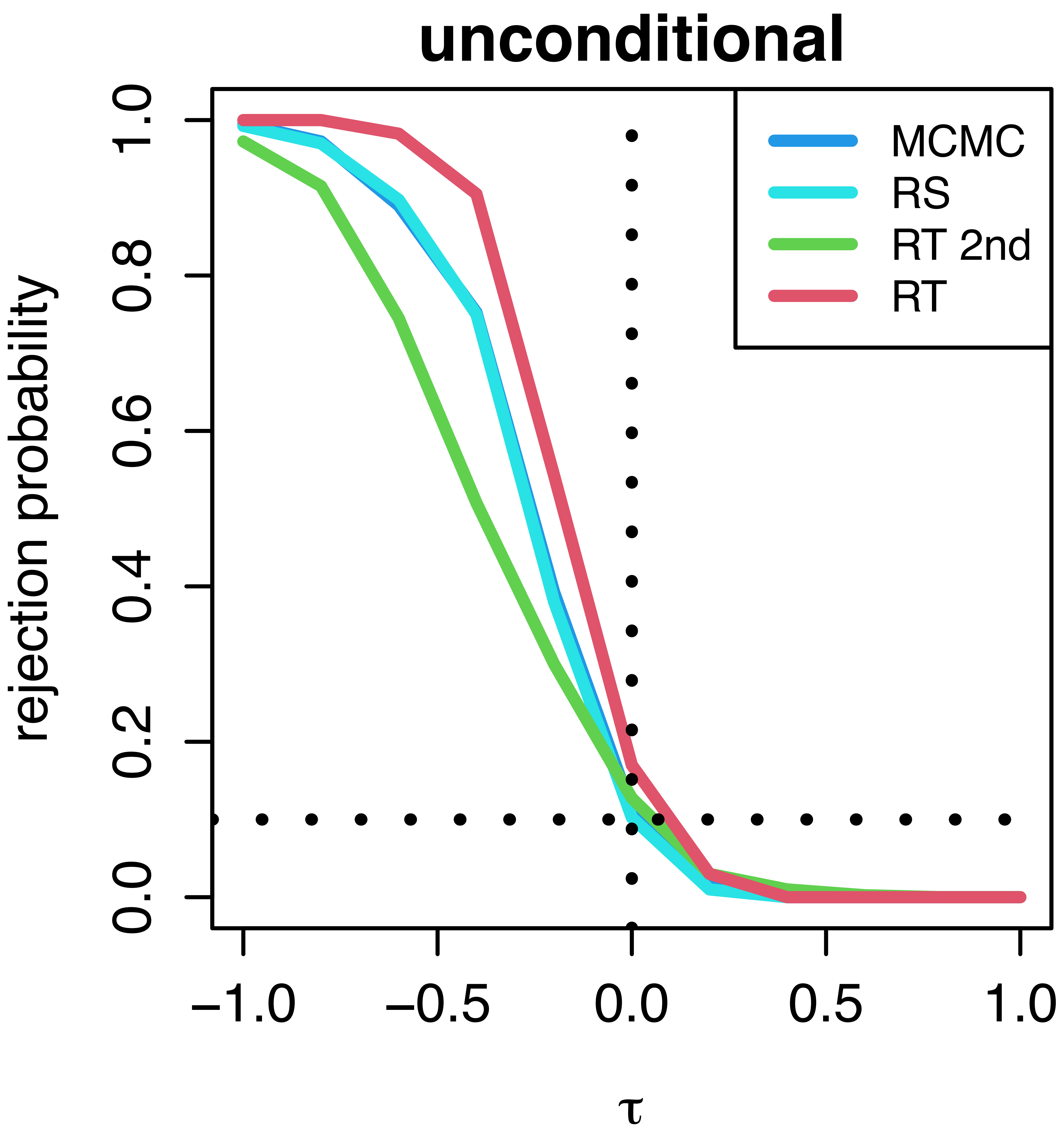
- Selection variable:

$$S = \begin{cases} \text{only low,} & \Delta < \Phi^{-1}(0.2), & \text{recruit 40 from group } X_i = \text{low} \\ \text{only high,} & \Delta > \Phi^{-1}(0.8), & \text{recruit 40 from group } X_i = \text{high} \\ \text{both,} & \text{otherwise,} & \text{recruit 20 from each group} \end{cases}$$

Power Analysis



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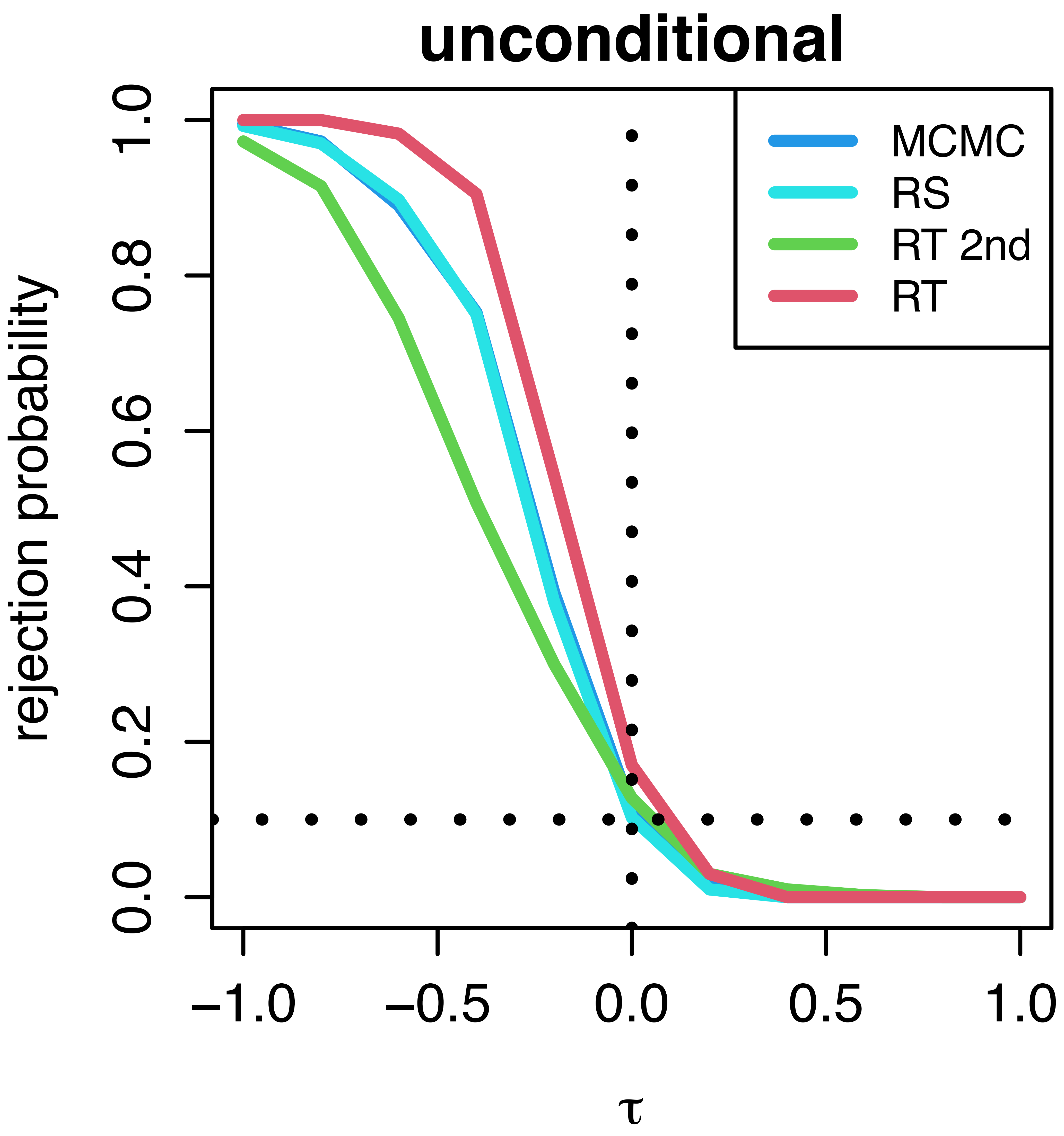

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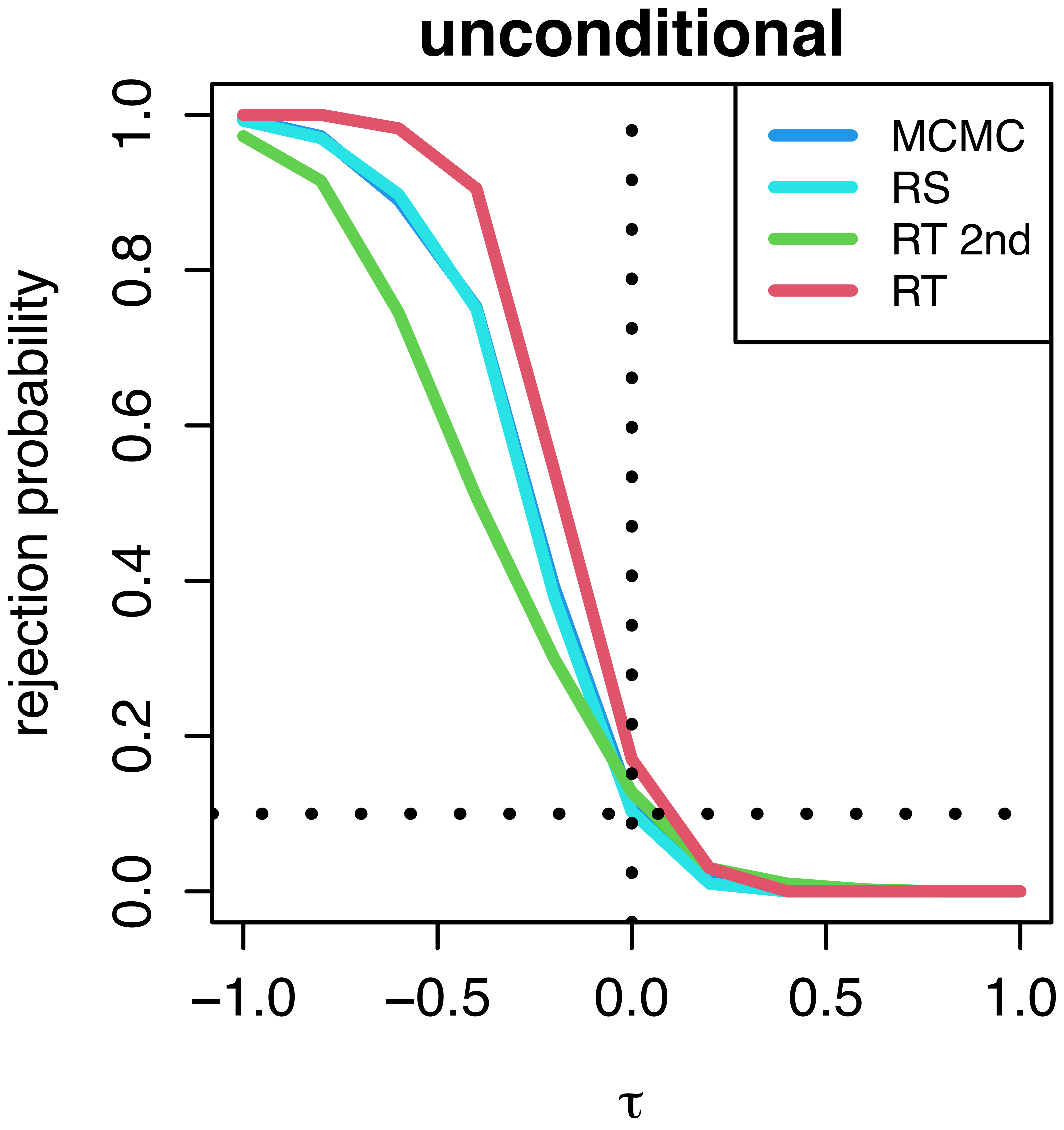

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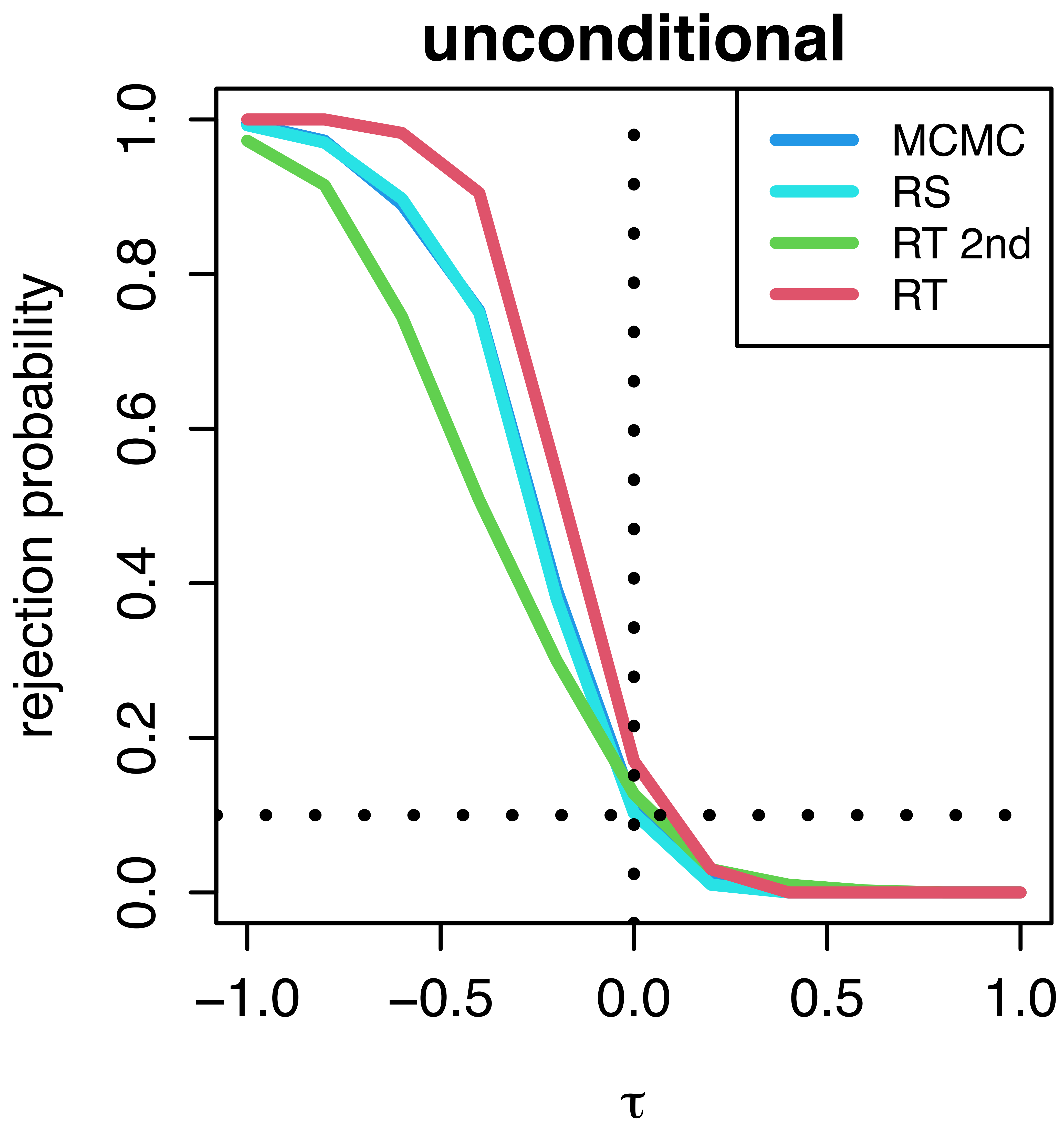

- RT: **no type-I error control**
- RT 2nd: valid but has **low power**
- Selective RT: **valid and more powerful**
- Rejection sampling and MCMC lead to very similar approximations.

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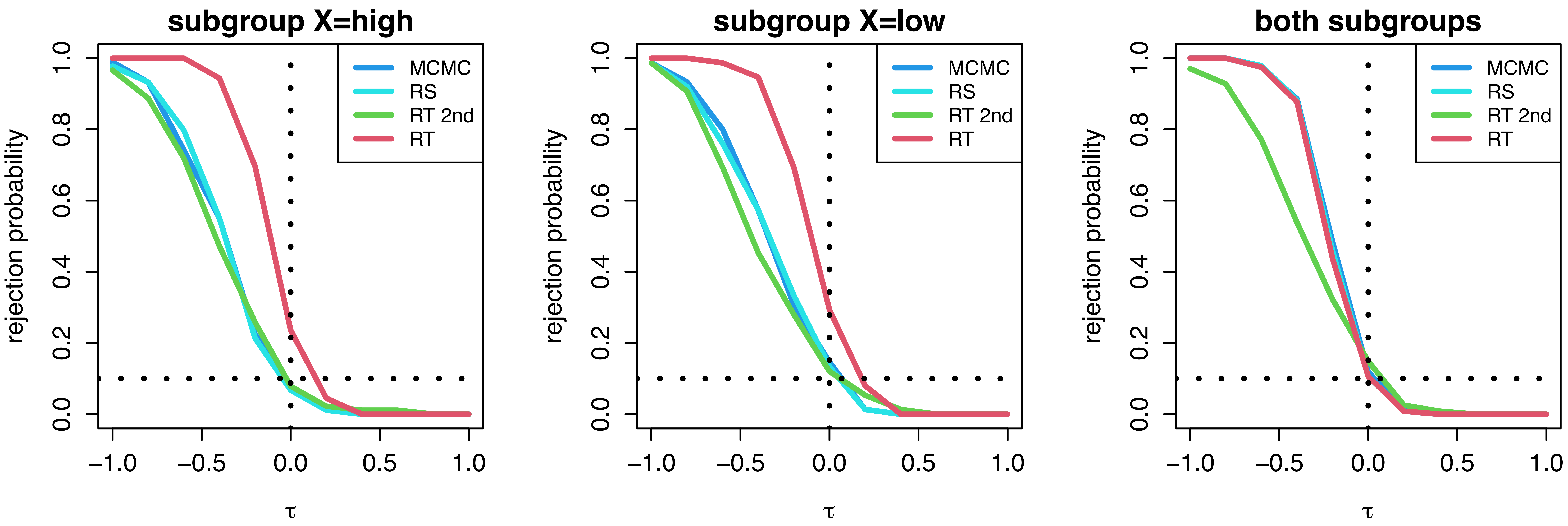

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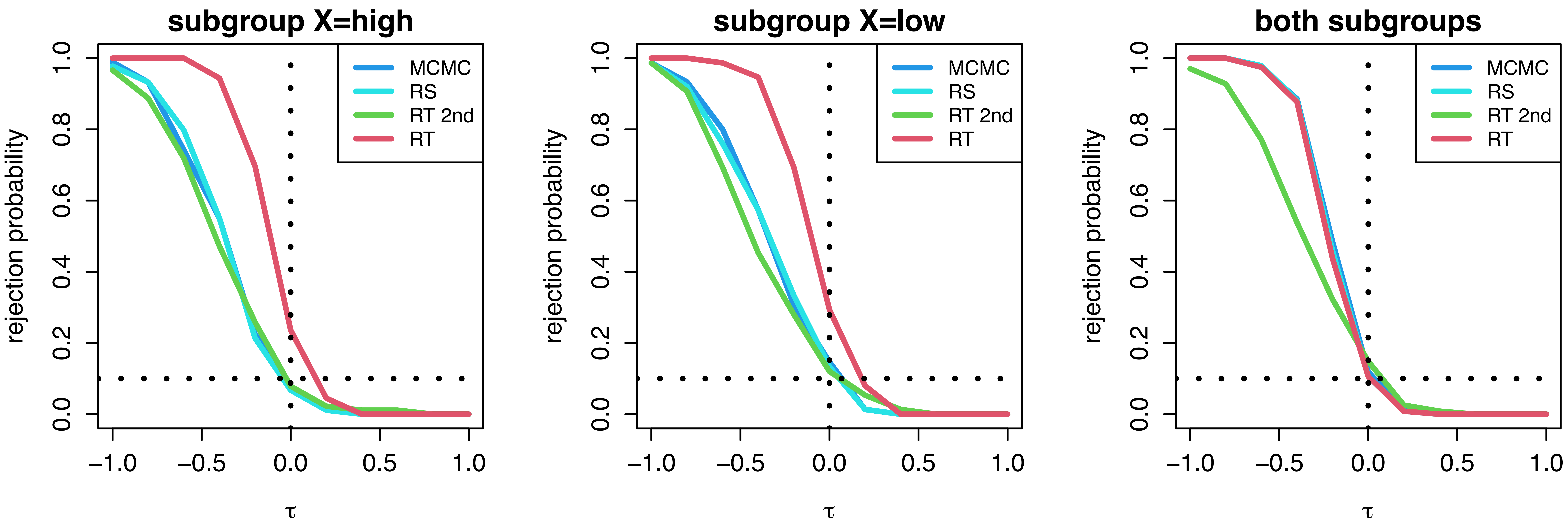

- Type-I error control in every subgroup

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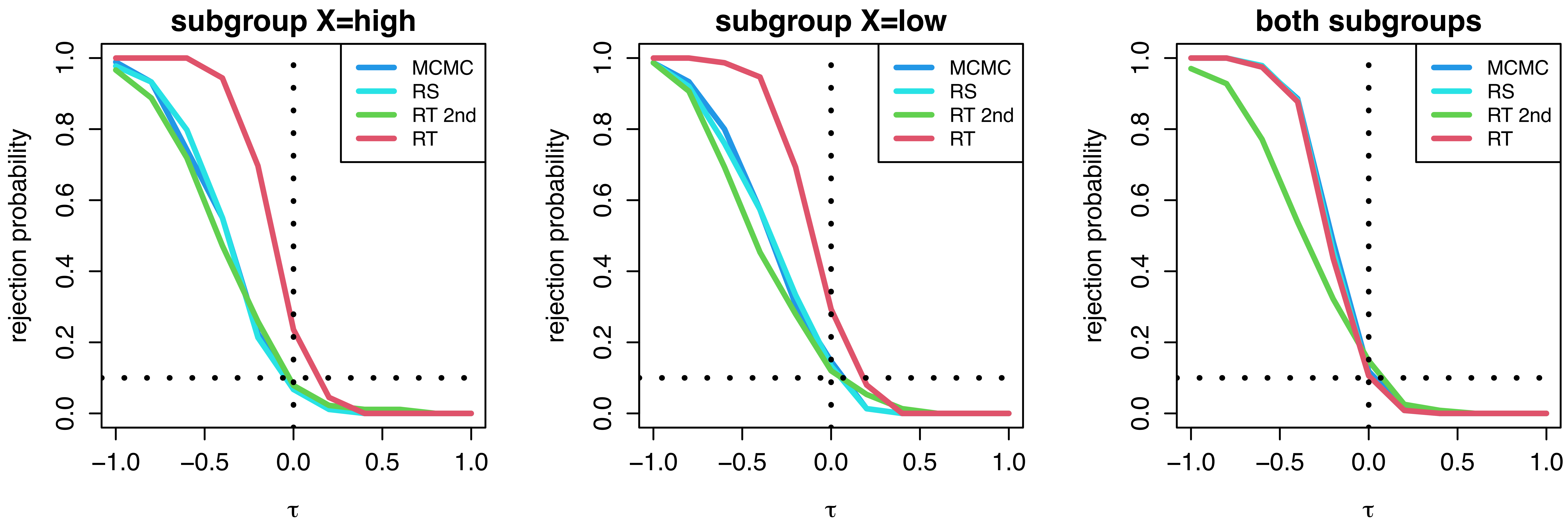

- Type-I error control in every subgroup
- Gain in power when there is a lot of “randomness left”

Conclusion

- Experiments with adaptive treatments, recruitment and null hypothesis
- Visualization via DAGs
- **Key idea: Conditioning randomization p-value on the selection information**
- Computability under general assumptions
- Approximation via rejection sampling or MCMC

Thanks for your attention!

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Hold-out Units