Selective Randomization Inference for Adaptive Experiments

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Randomization Inference

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- Randomized controlled trial

Fisher (1935), Pitman (1937), Zhang & Zhao (2023), Imbens & Rubin (2015)

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- Distribution of Z is **known** and $Z \perp\!\!\!\perp Y(\,\cdot\,) \mid X$

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Randomization Inference

i	Y	Y(0)	Y(1)	Z
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2	7	7		0
3	-3	-3		0
4	0		0	1
…	…	…	…	…

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Randomization Inference

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- P-value:

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

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

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Example

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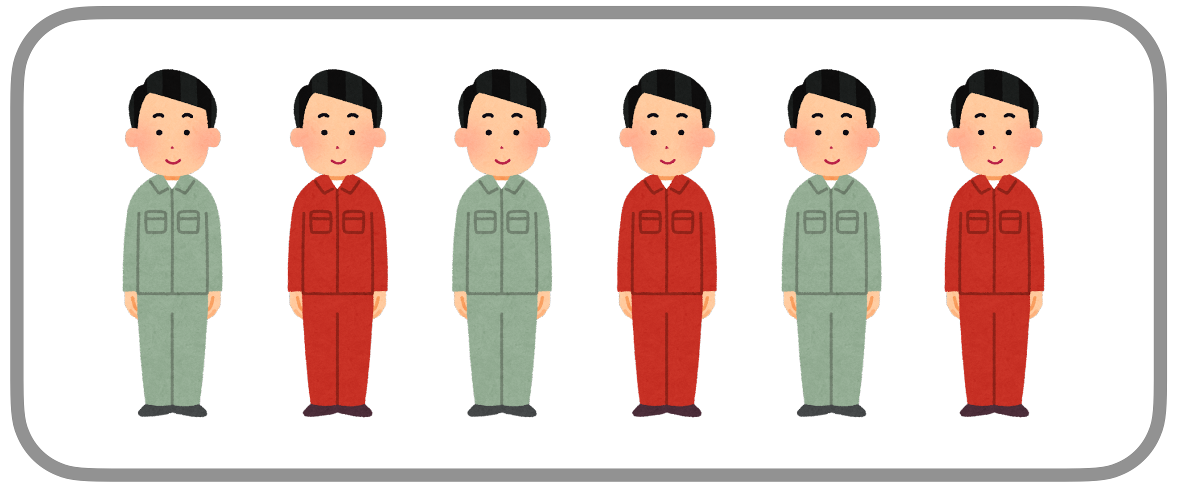
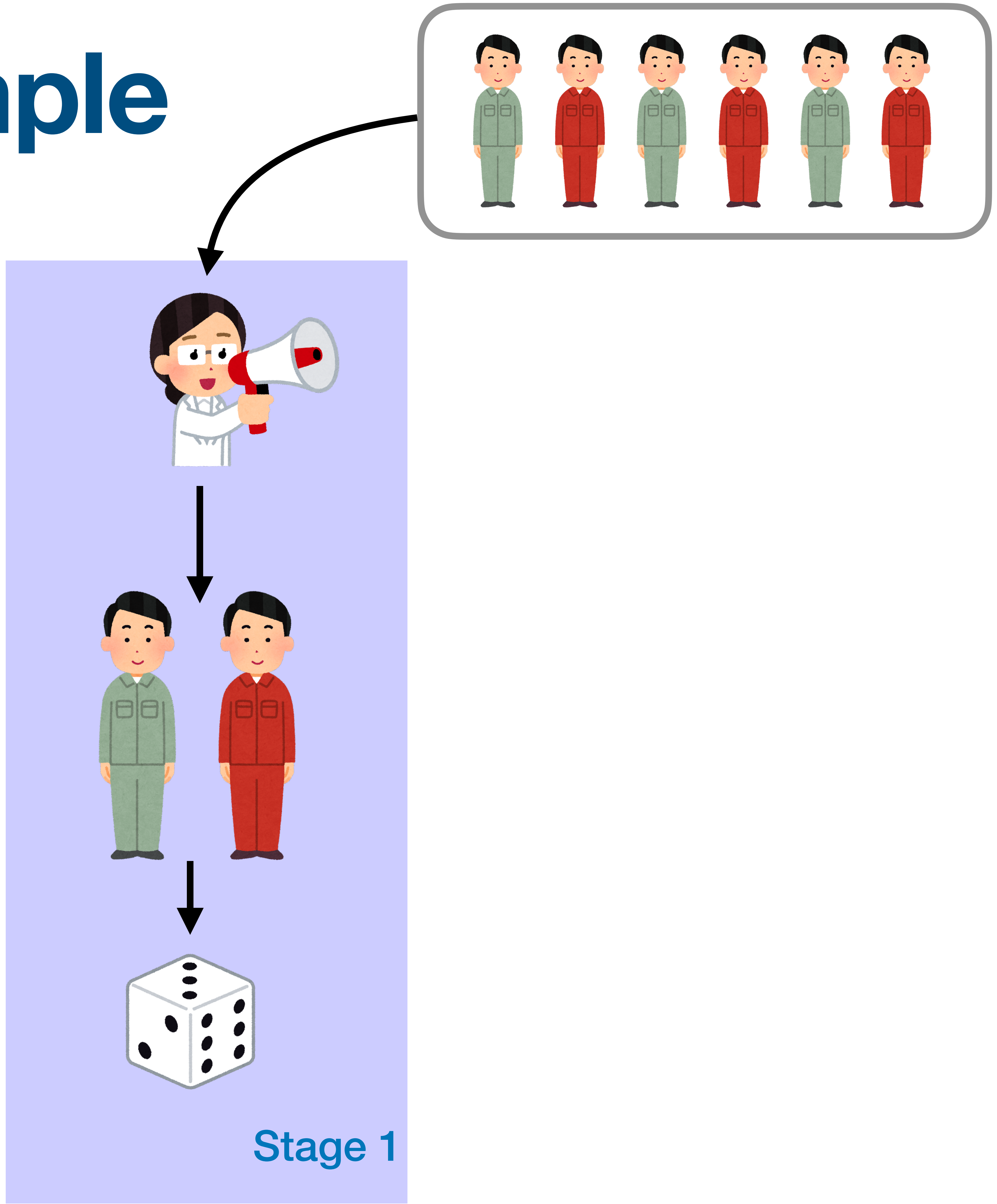



High genetic risk


Low genetic risk

FOURIER trial: Marston et al. (2020)

Example



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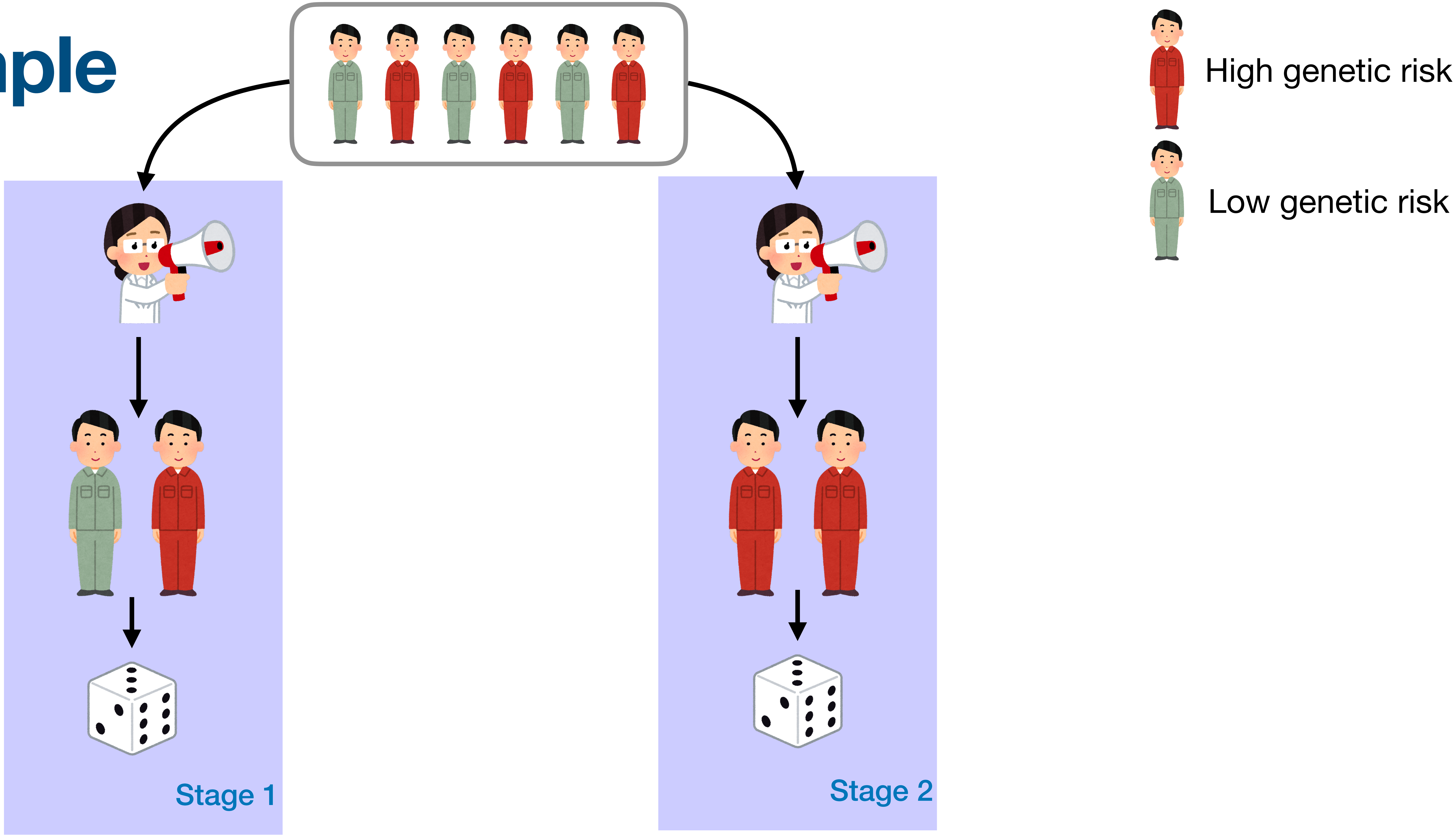

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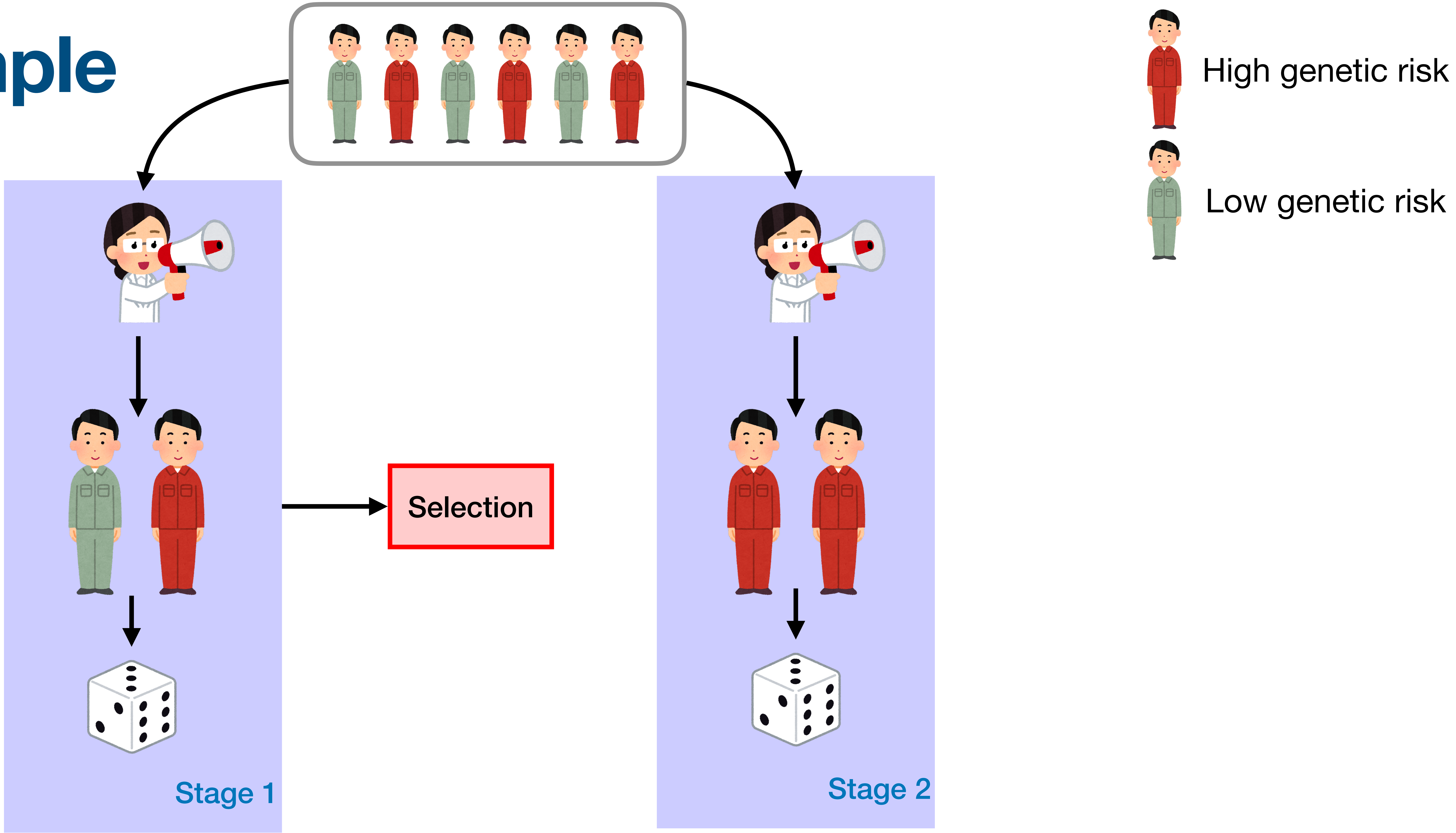

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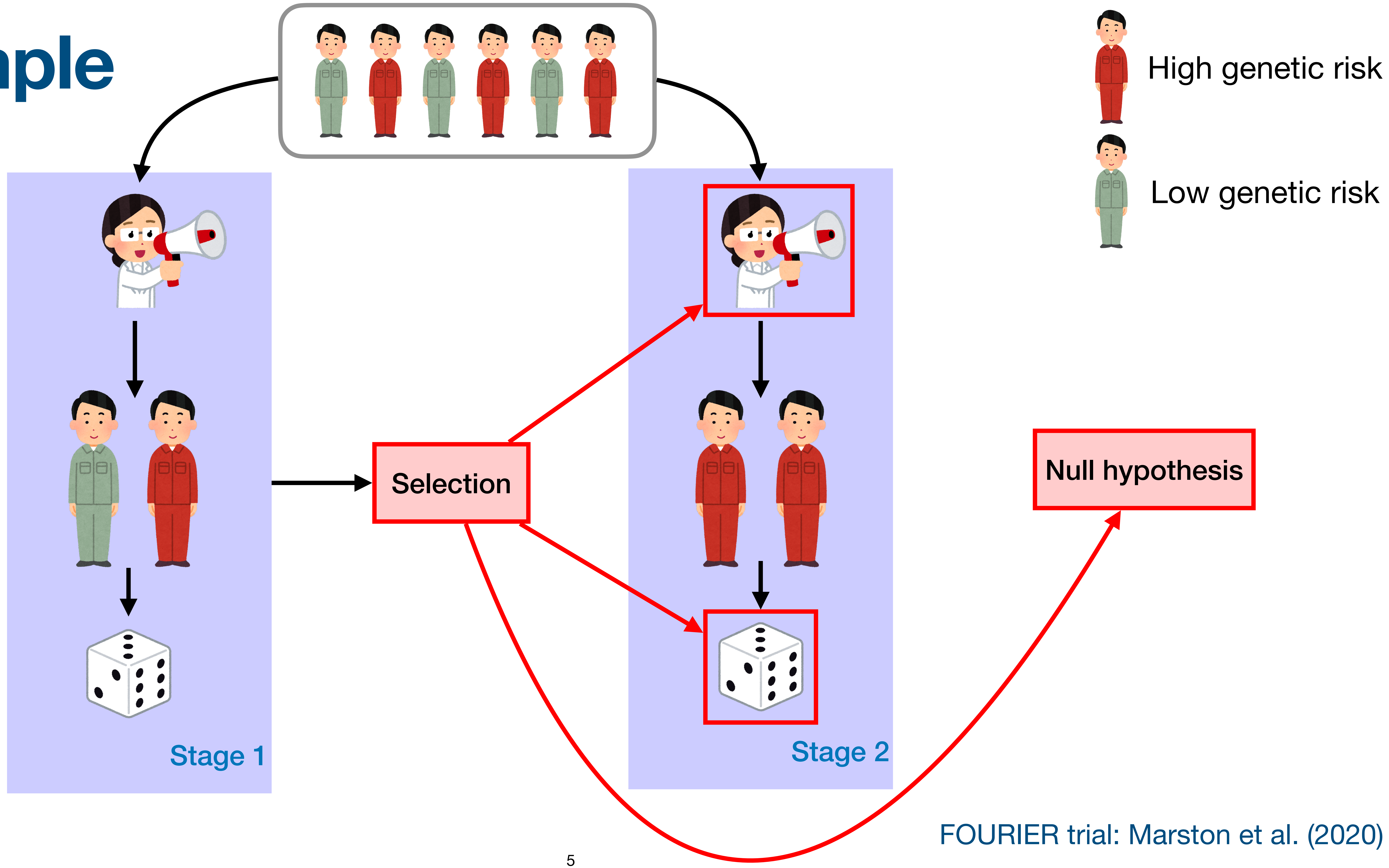

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Graphical Model

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Pearl (2009)

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

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

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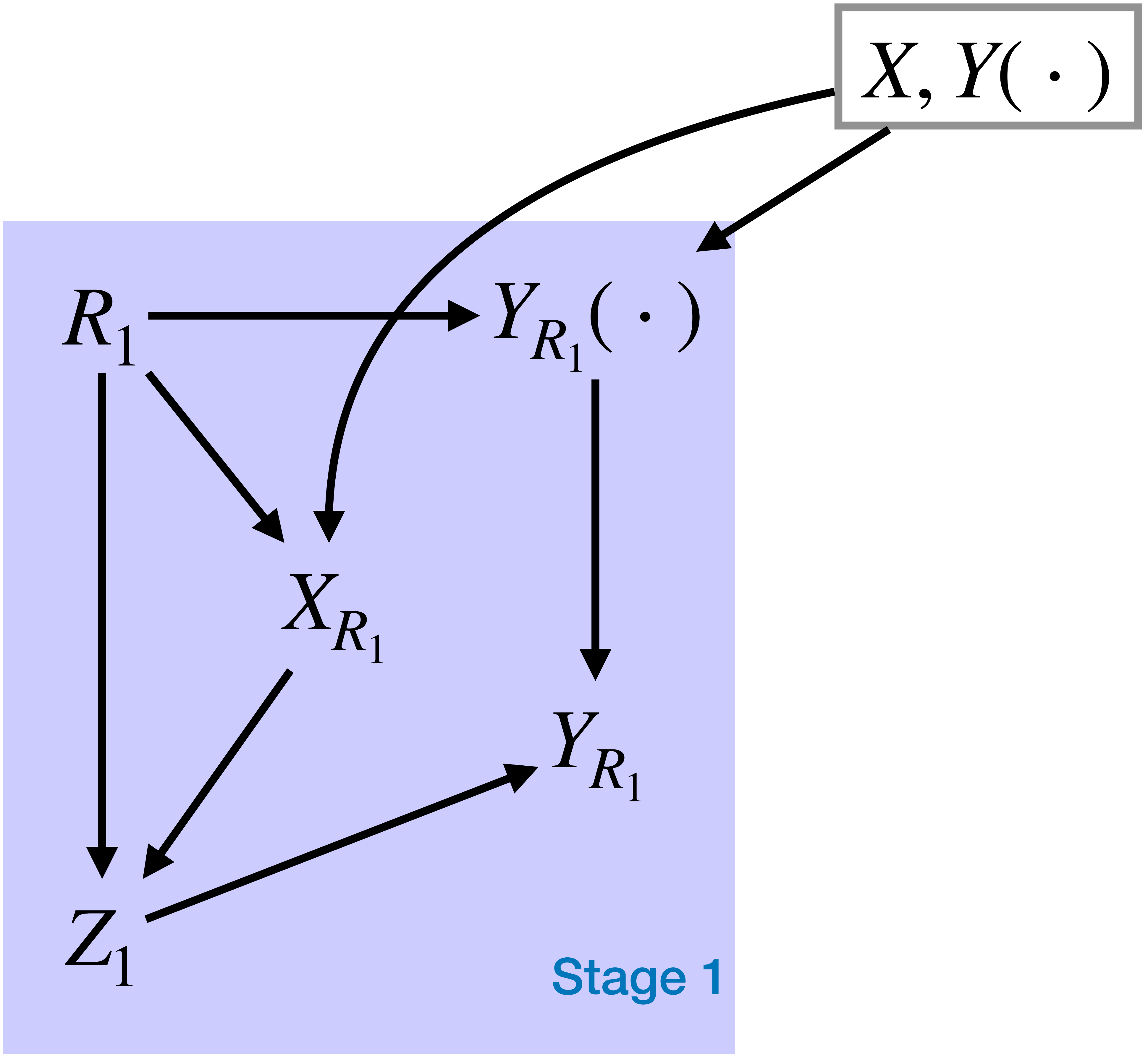

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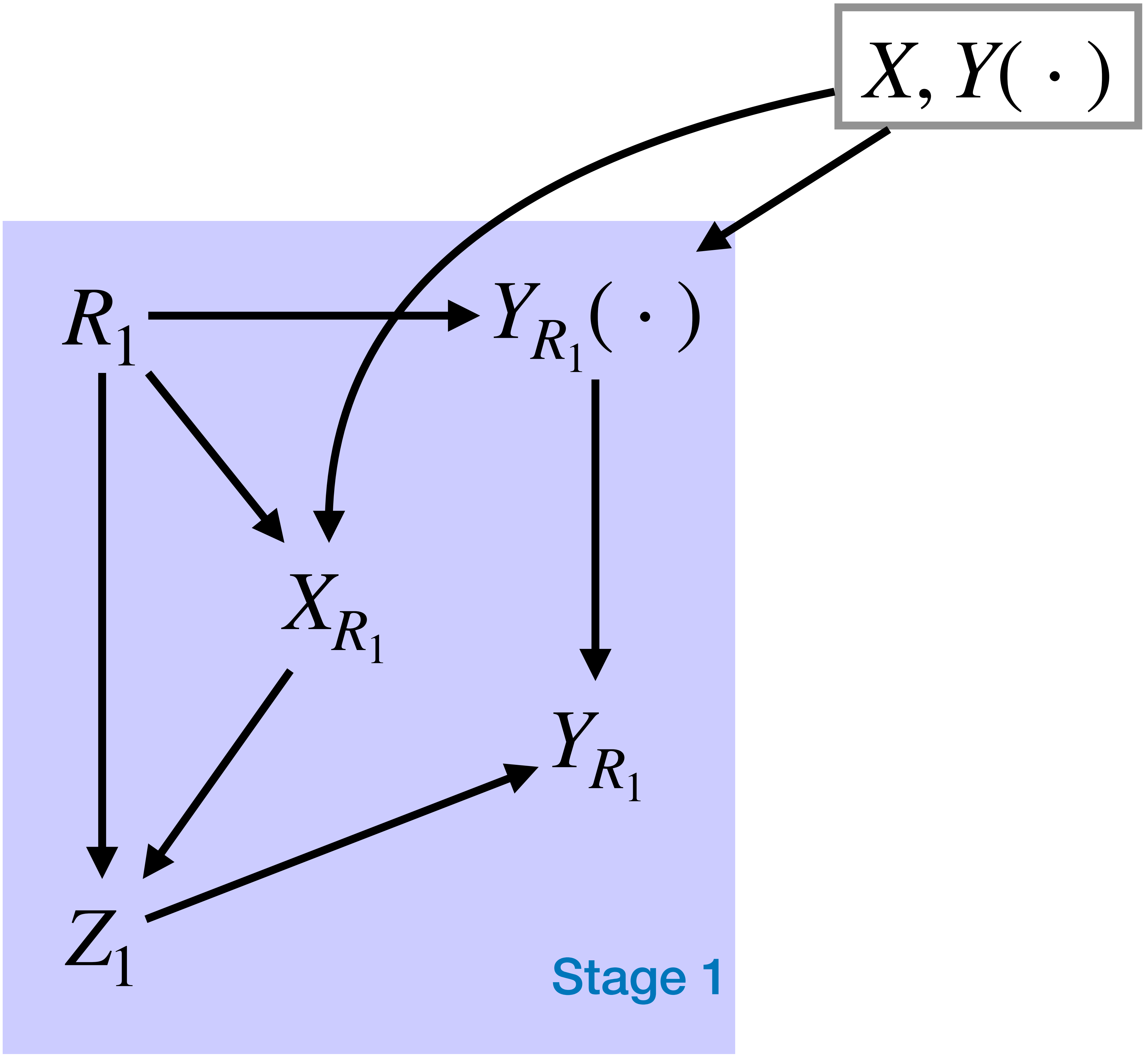

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- Potential outcomes: $Y(\cdot)$
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- Treatments: Z_k
- Observed outcomes: $Y = Y(Z)$

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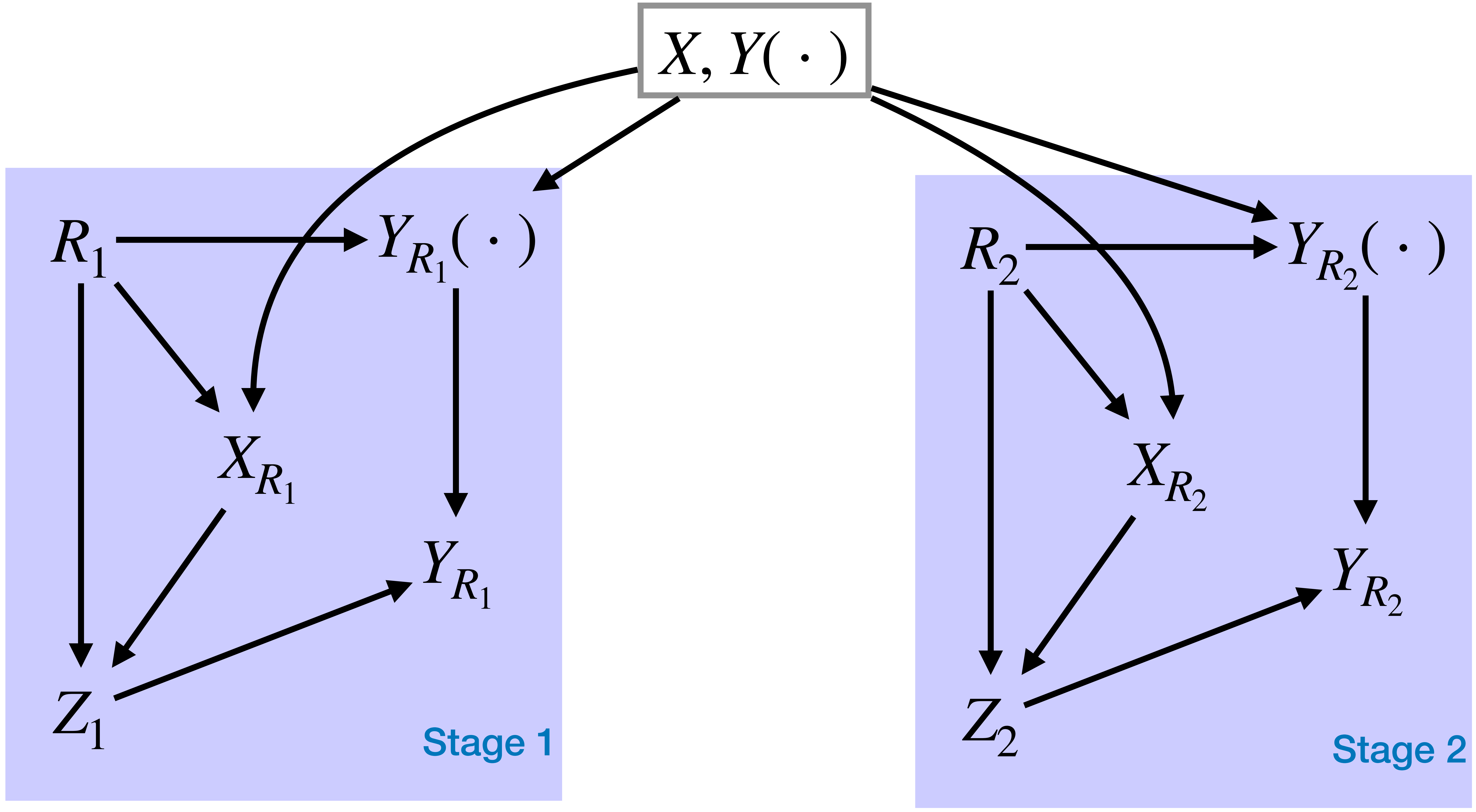

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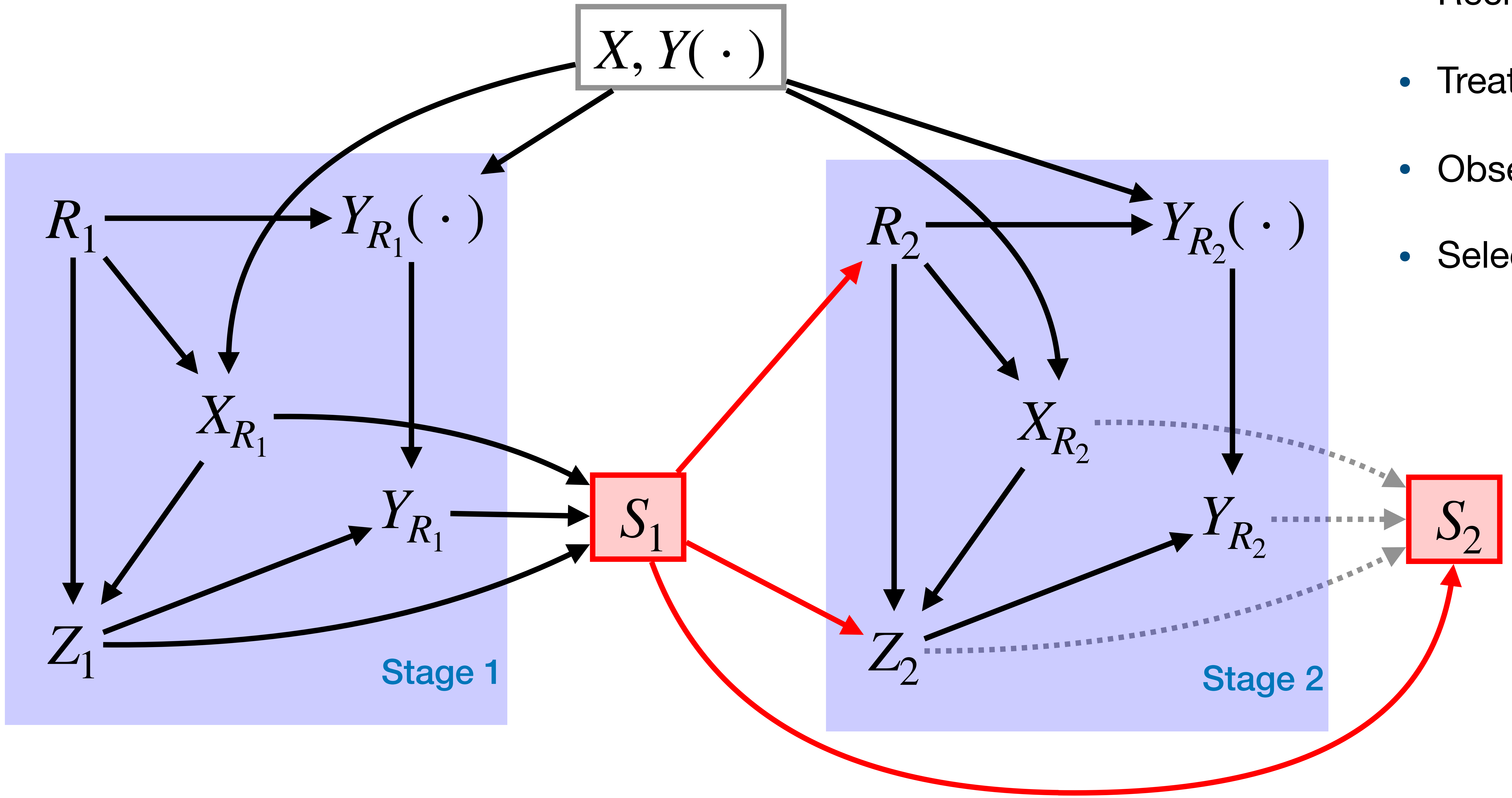

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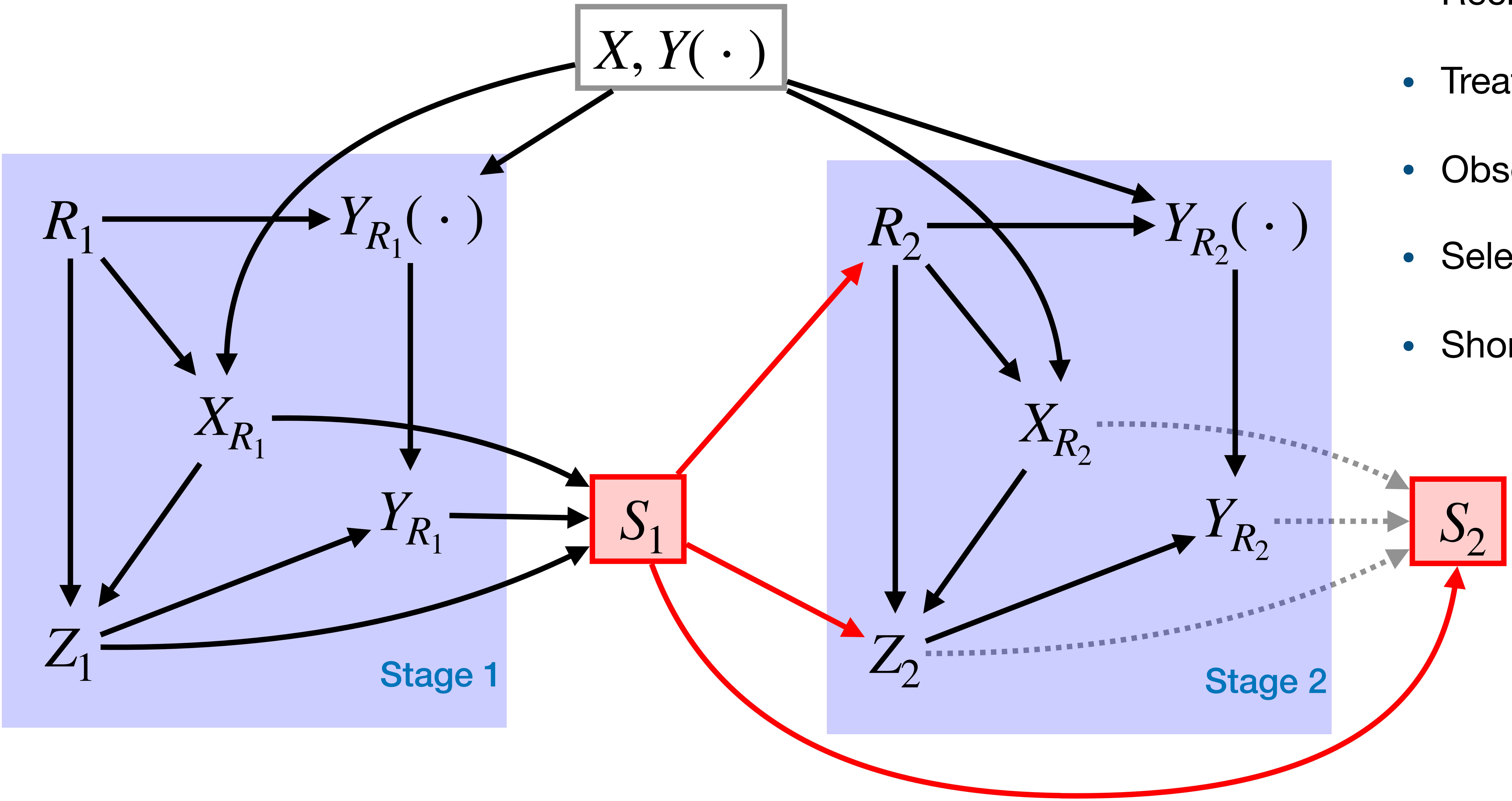

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- Short-hand: $W = (R, X_R, Y_R(\cdot))$

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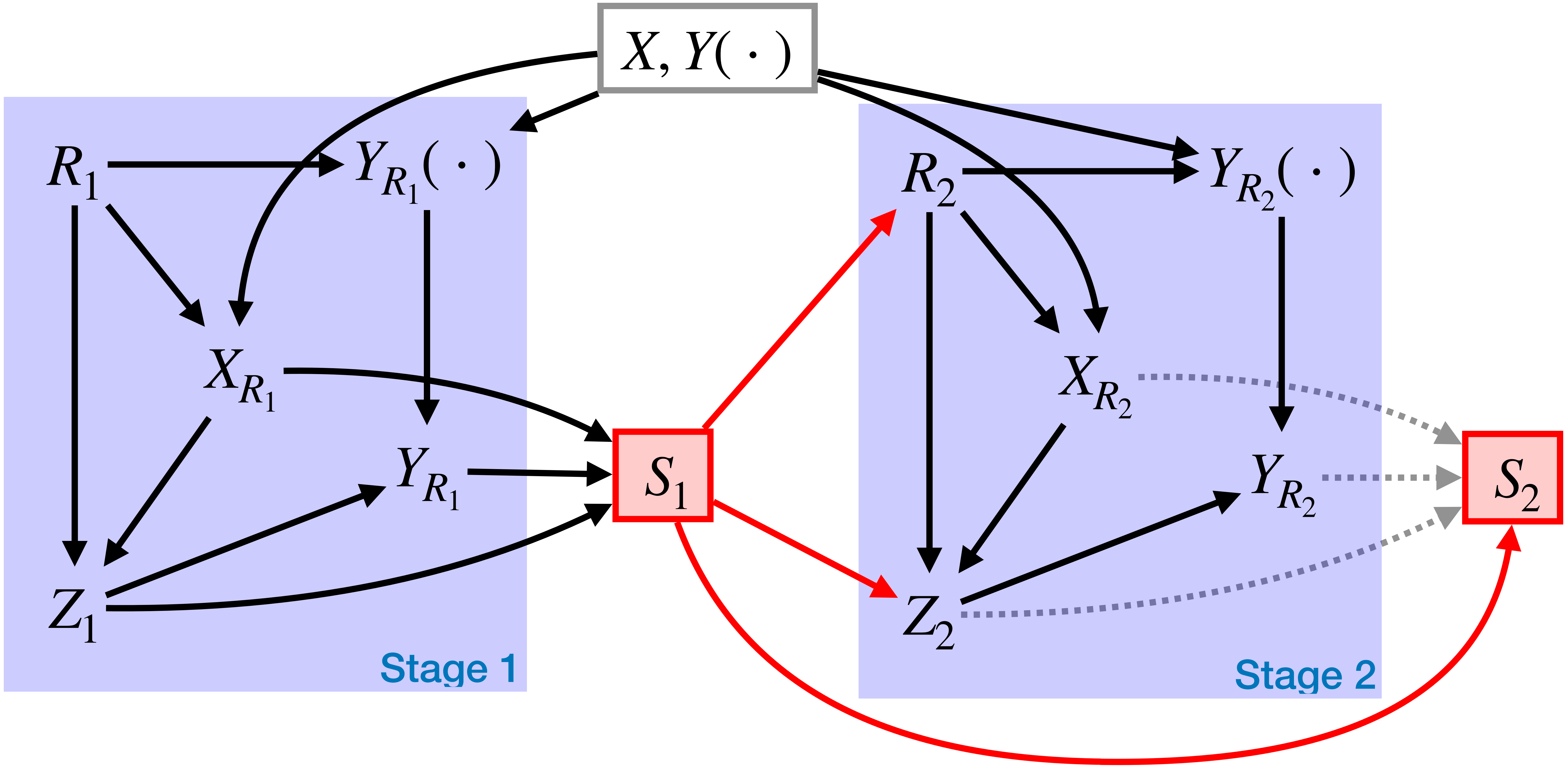
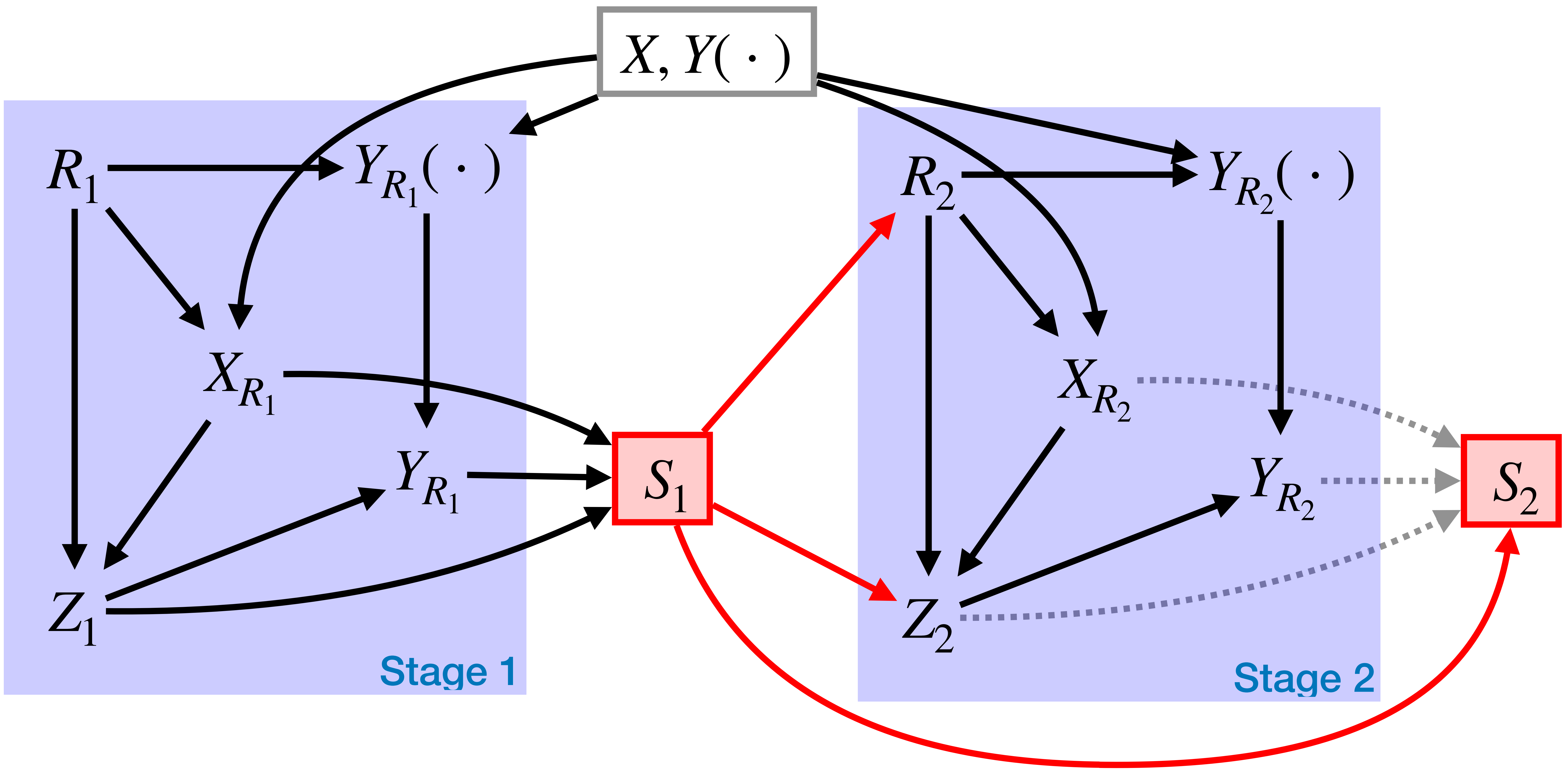
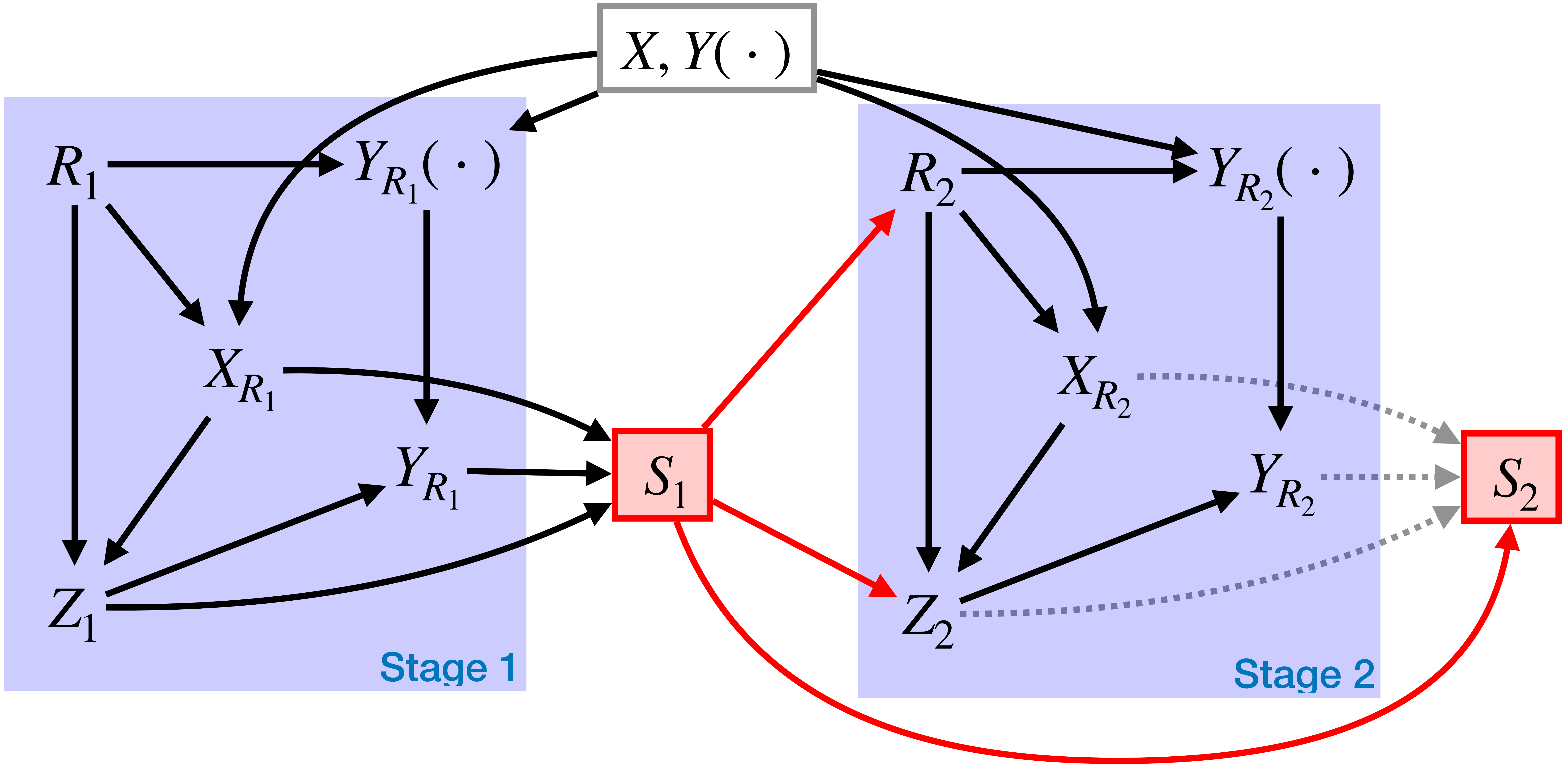

$X, Y(\cdot)$
R_1
$Y_{R_1}(\cdot)$
X_{R_1}
Y_{R_1}
Z_1
Stage 1
S_1
R_2
$Y_{R_2}(\cdot)$
X_{R_2}
Y_{R_2}
Z_2
Stage 2
S_2



- **Assumption (A1):** Distribution of $Z = (Z_1, \ldots, Z_K)$ is known



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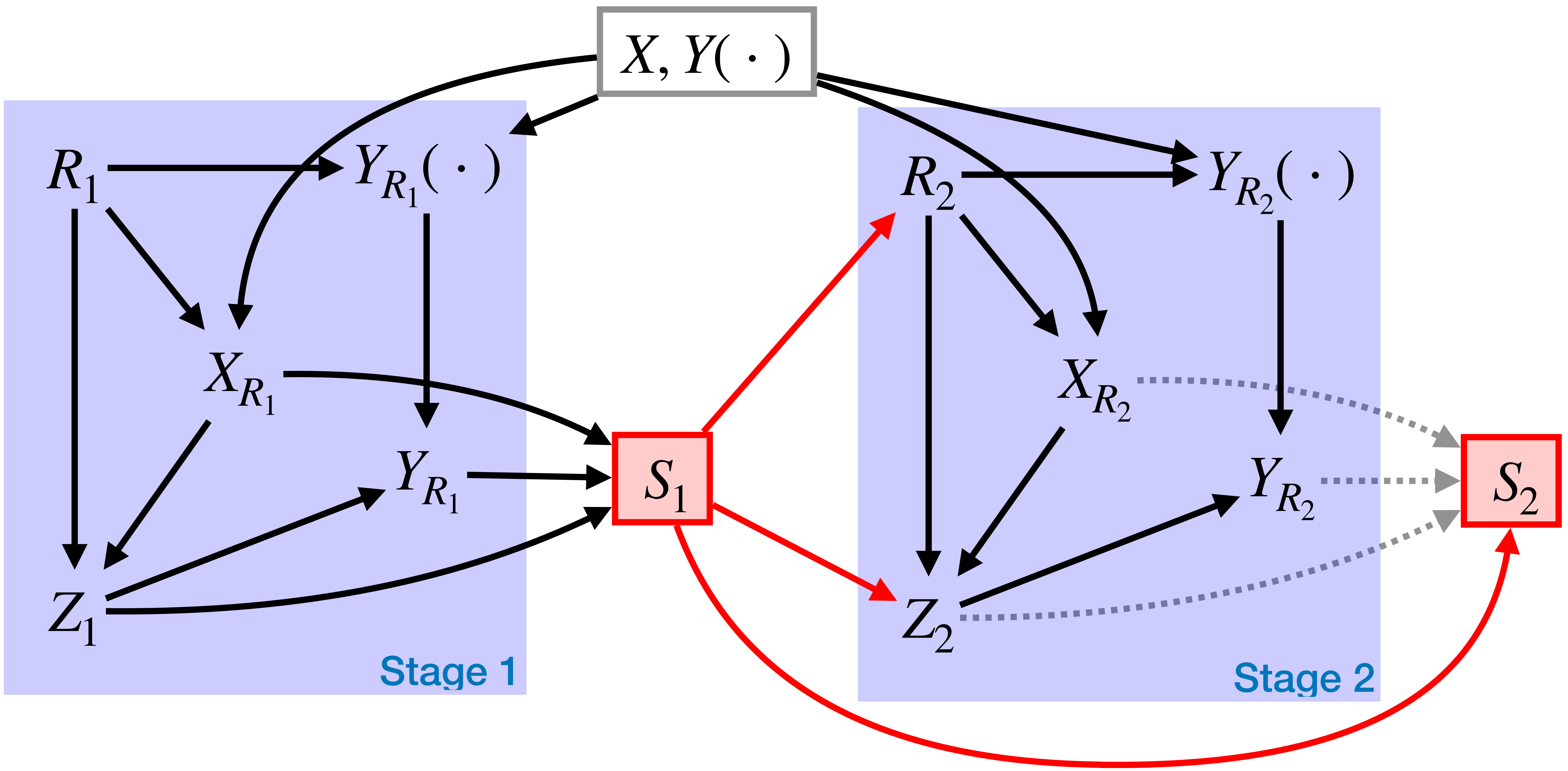
- **Assumption (A2):** Conditional independence of present and post potential outcomes

$$Z_k \perp\!\!\!\perp Y_{R_{[k]}}(\cdot) \mid R_{[k]}, X_{R_{[k]}}, Y_{R_{[k-1]}}, Z_{[k-1]} \quad \forall k \in [K]$$



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- **Assumption (A3):** S_k captures all the information that is passed on

  $R_k, X_{R_k}, Y_{R_k}(\cdot) \perp\!\!\!\perp Z_{[k-1]} \mid W_{[k-1]}, S_{k-1} \quad \forall k \in [K]$

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- Comparing to $Z*$ that choose different stage-II design or null hypothesis than Z

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  - Selective randomization inference:

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- Formula for p-value: $P_{sel} = \dfrac{\sum_{z^*} \mathbf{1}\{T(z^*, W) \leq T(Z, W)\}\ \mathbf{1}\{S(z^*) = S(Z)\}\ q\left(z^* \mid W\right)}{\sum_{z^*} \mathbf{1}\{S(z^*) = S(Z)\}\ q\left(z^* \mid W\right)}$

- $q(z \mid w) = \prod_{k=1}^{K} \mathbb{P}(Z_k = z_k \mid R_k = r_k, X_{R_k} = x_{R_k}, S_{k-1} = s_{k-1})$ under slightly stronger assumptions

Computation

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

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- Rejection sampling, Markov Chain Monte Carlo (MCMC)

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Inference

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- Confidence intervals:
  - test $Y_i(1) - Y_i(0) = \tau$ for different τ
  - $(1 - \alpha)$ confidence interval: $C_{1-\alpha} = \{\tau : P_{sel}(\tau) \geq \alpha\}$
- Estimation: τ such that $P_{sel}(\tau) = 0.5$

Simulation Study

Simulation Study

- 2 stages, 2 treatments $Z_i \in \{0,1\}$, 2 groups $X_i \in \{\text{low}, \text{high}\}$
- 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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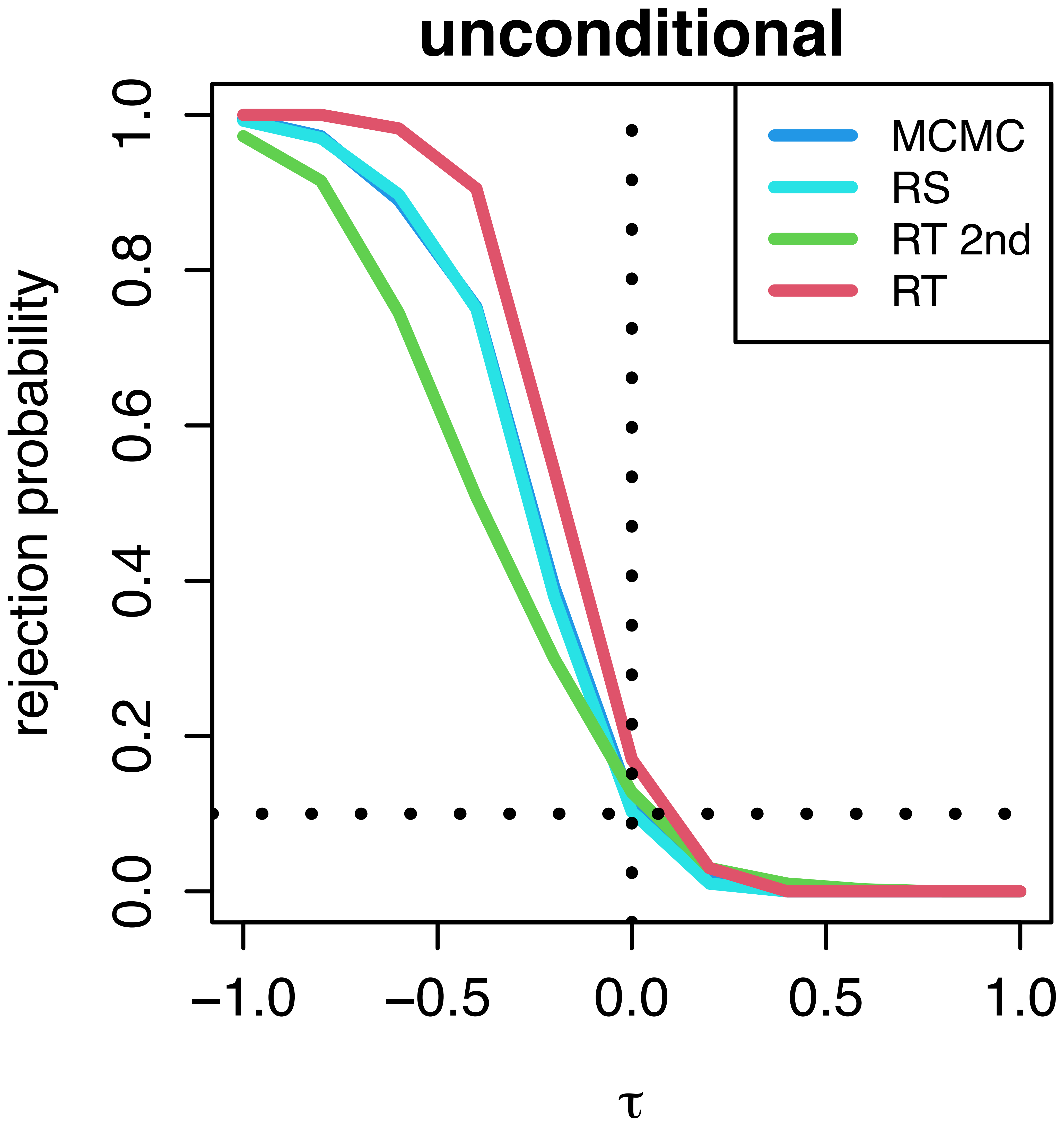
- First stage: 100 patients, Second stage: 40 patients
- $\Delta =$ standardized difference in SATEs between groups
- Selection variable:

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

Power Analysis



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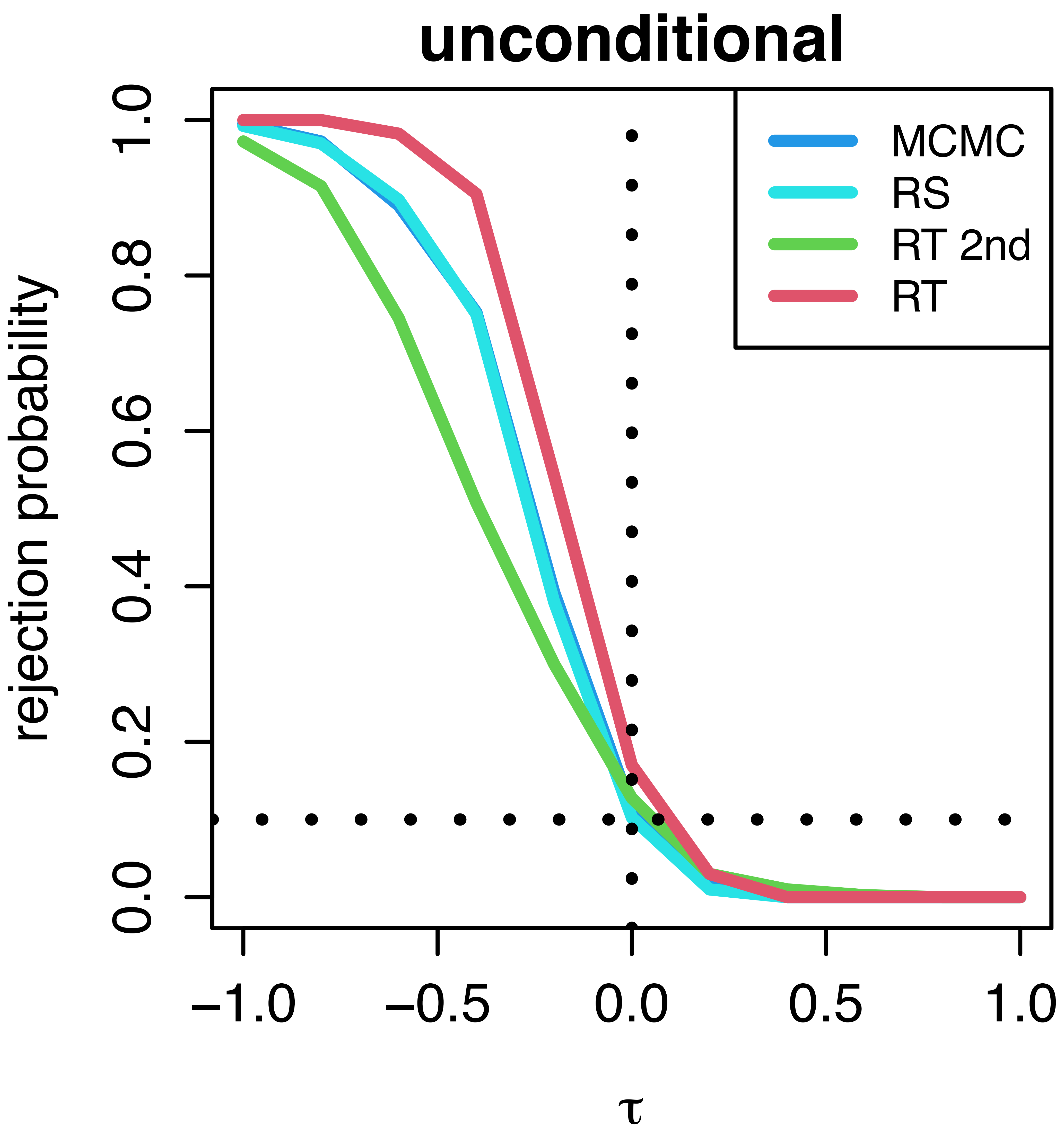

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- RT 2nd: valid but has **low power**

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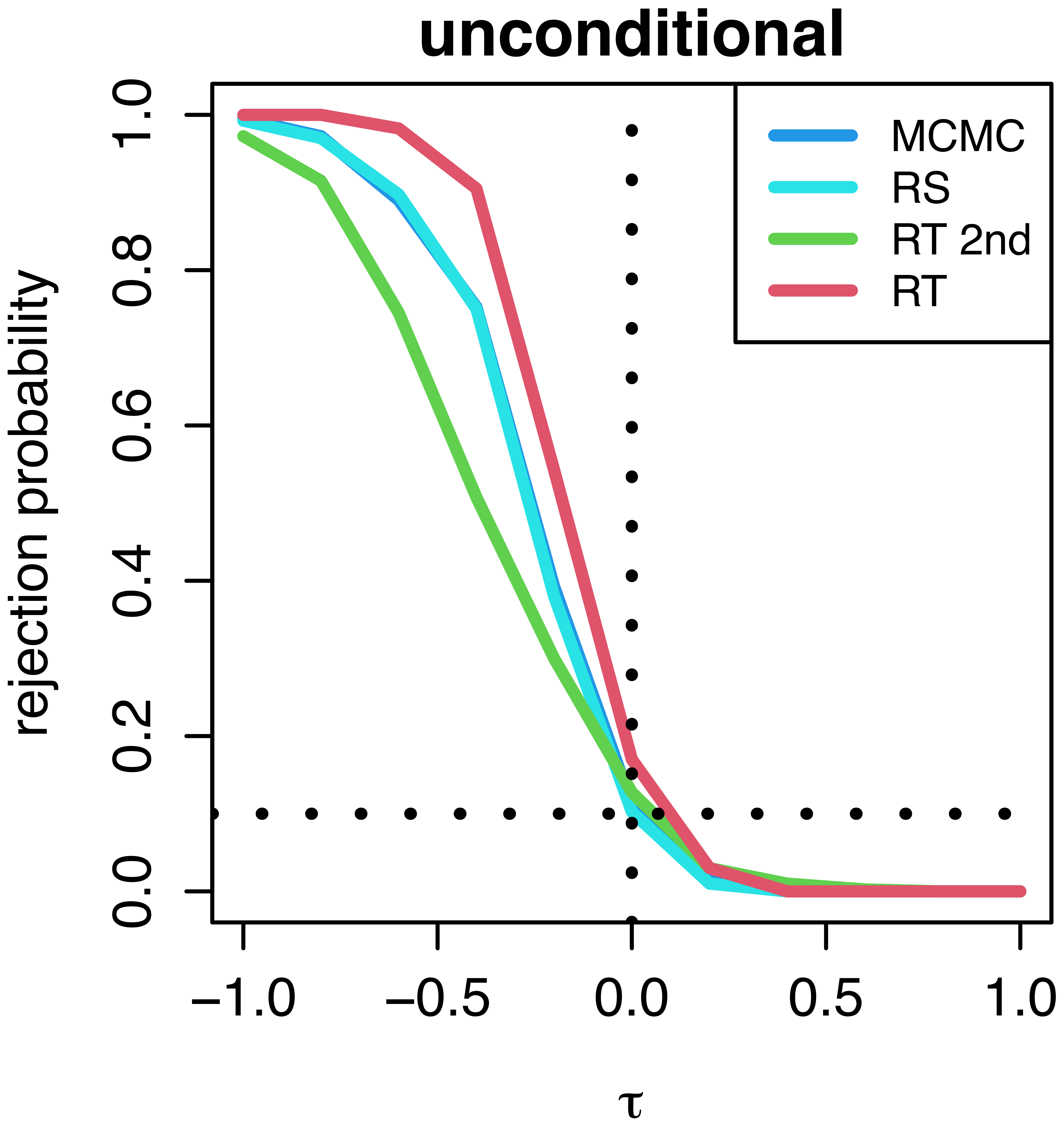

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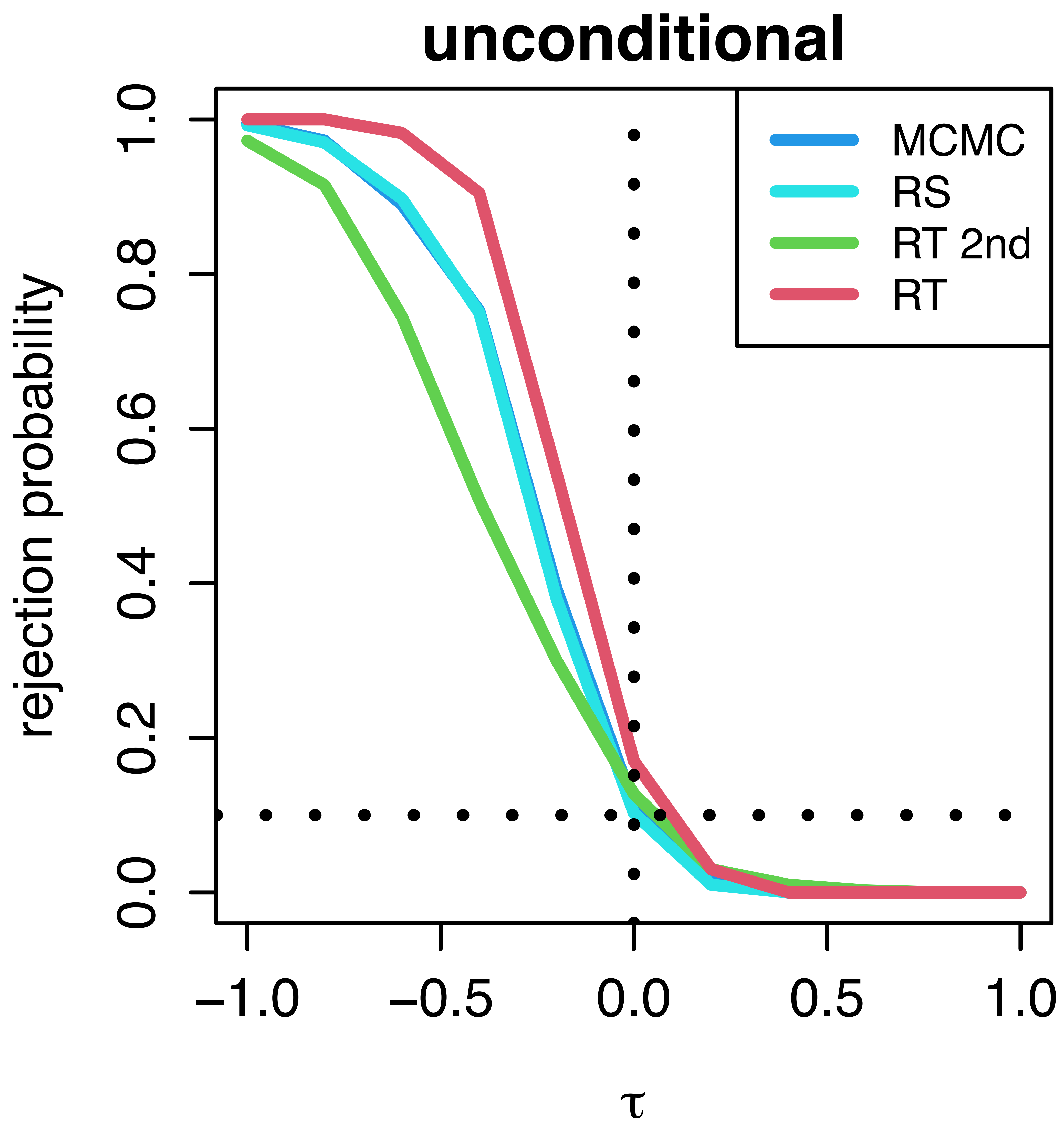
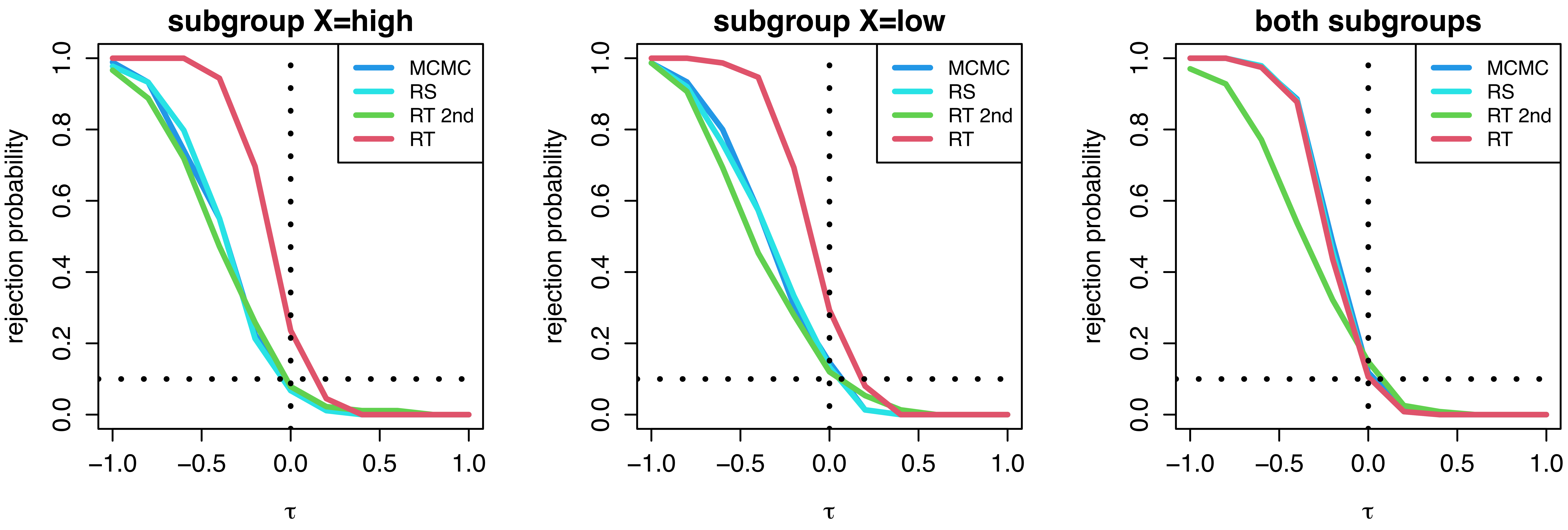


- RT: **no type-I error control**
- RT 2nd: valid but has **low power**
- Selective RT: **valid and more powerful.**
- Rejection sampling and MCMC lead to very similar approximations.

Power Analysis



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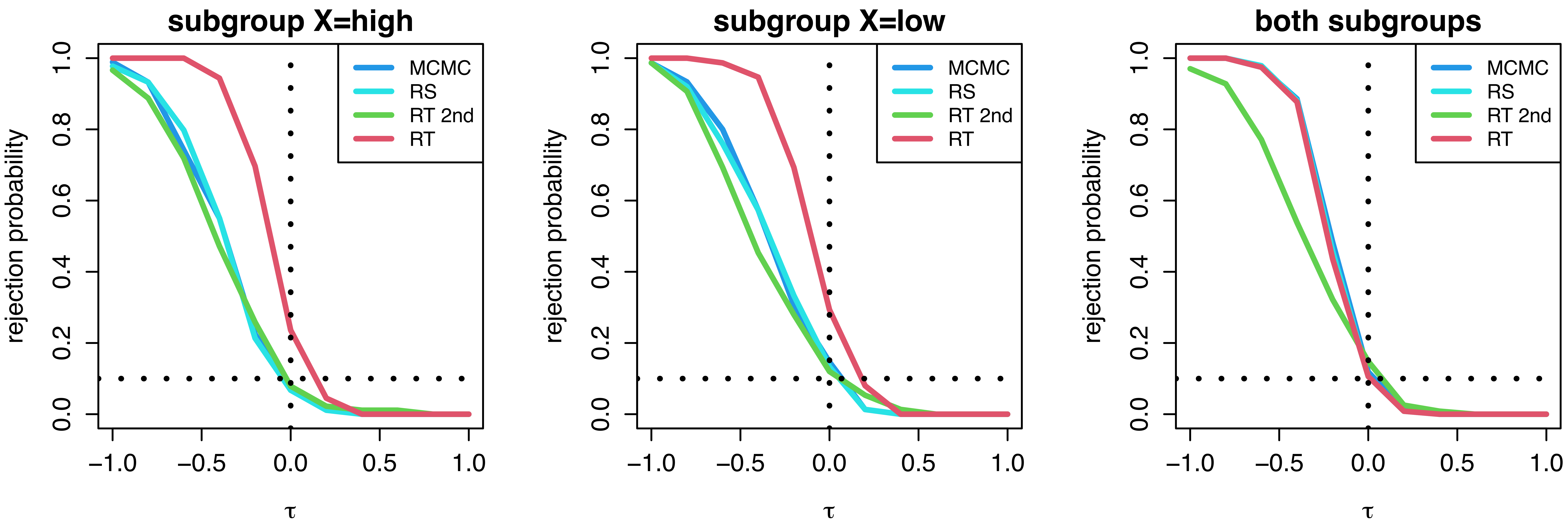

- Type-I error control in every subgroup

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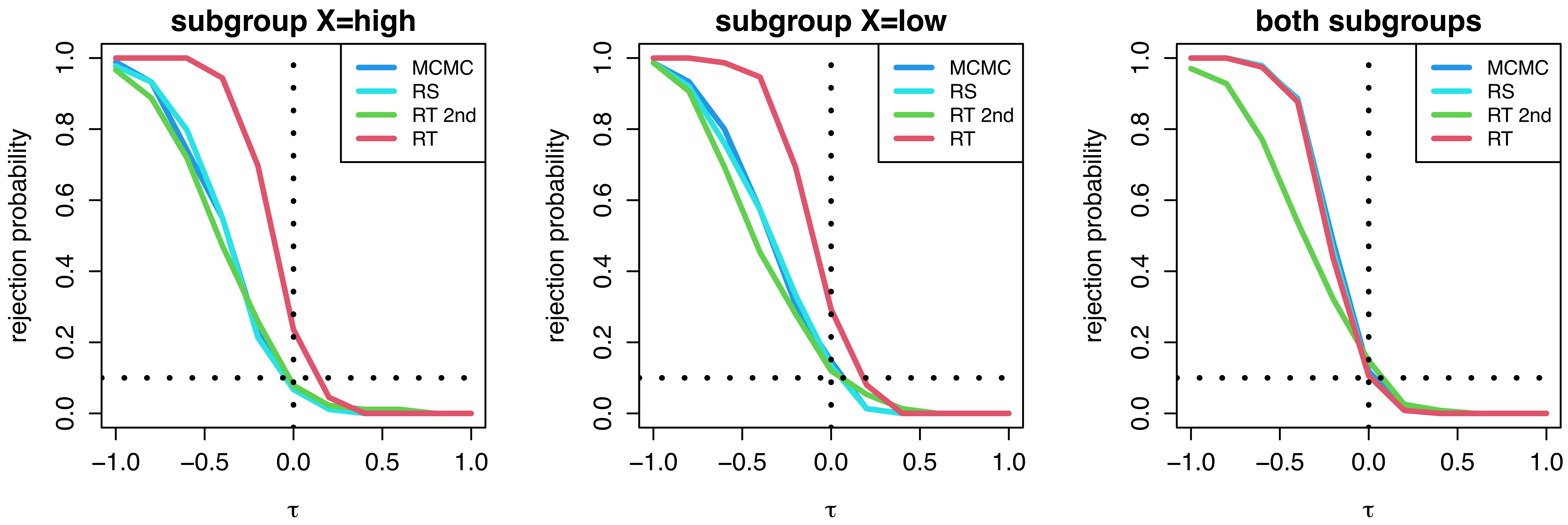

- Type-I error control in every subgroup
- Gain in power when there is a lot of “randomness left”

Conclusion

- Robust inference in randomized controlled trials
- Experiments with adaptive treatments, recruitment and null hypothesis
- Visualization via graphs
- **Key idea: Conditioning randomization p-value on the selection information**
- Approximation via rejection sampling or MCMC

Thanks for your attention!

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Hold-out Units