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

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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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- Null hypothesis: $Y_i(1) - Y_i(0) = 0$ for all i
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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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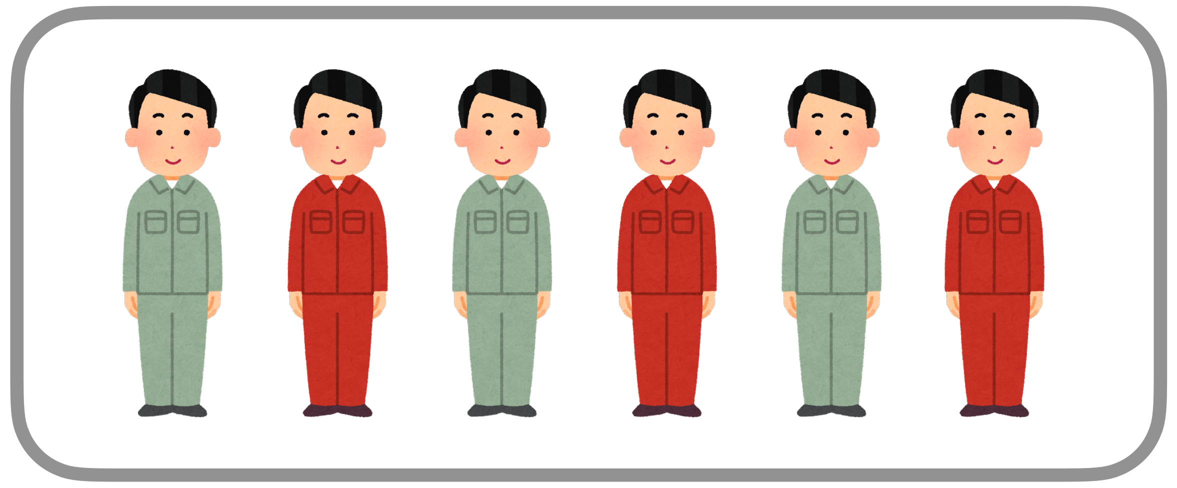

High genetic risk

Low genetic risk

FOURIER trial: Marston et al. (2020)

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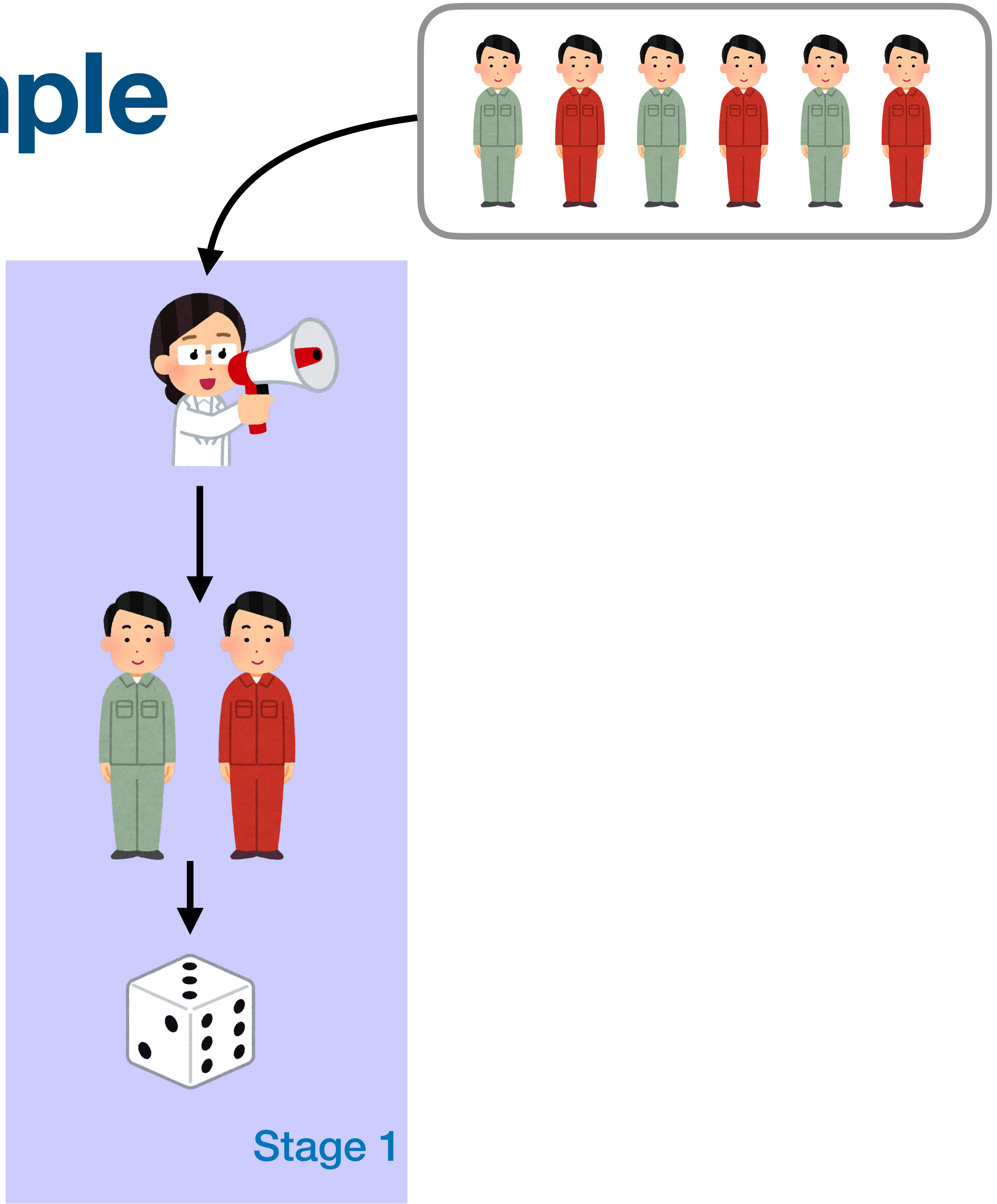

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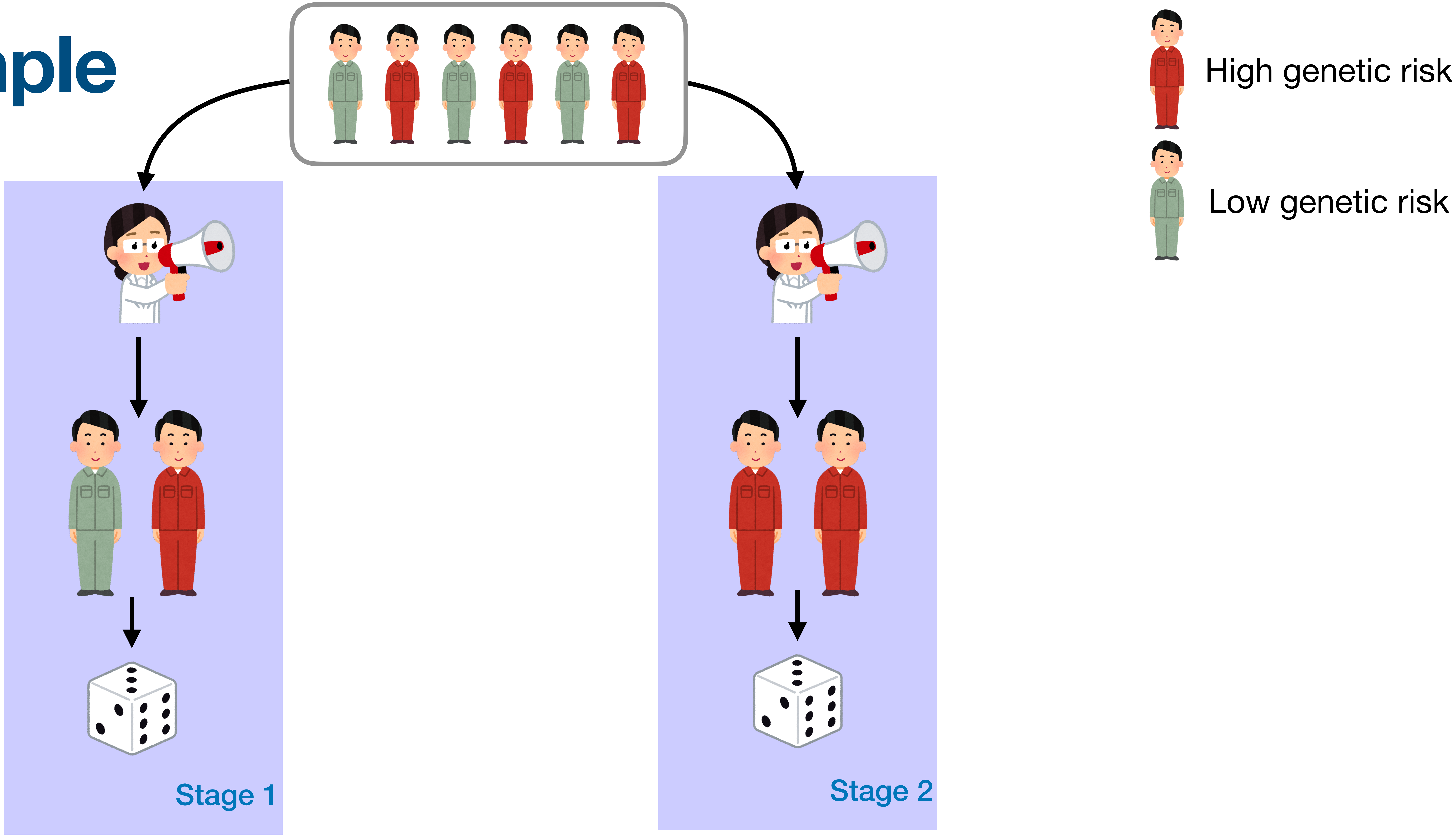

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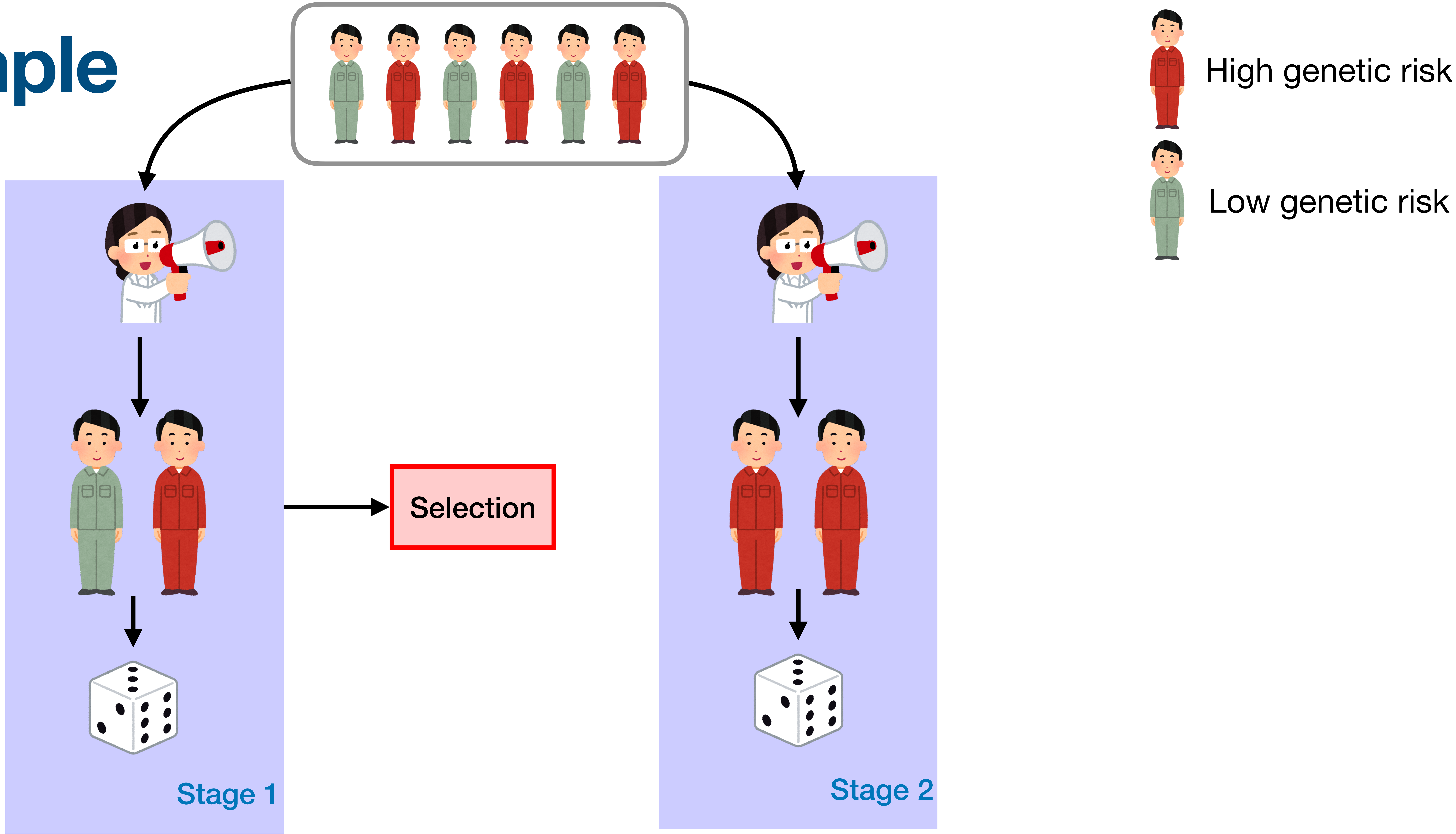

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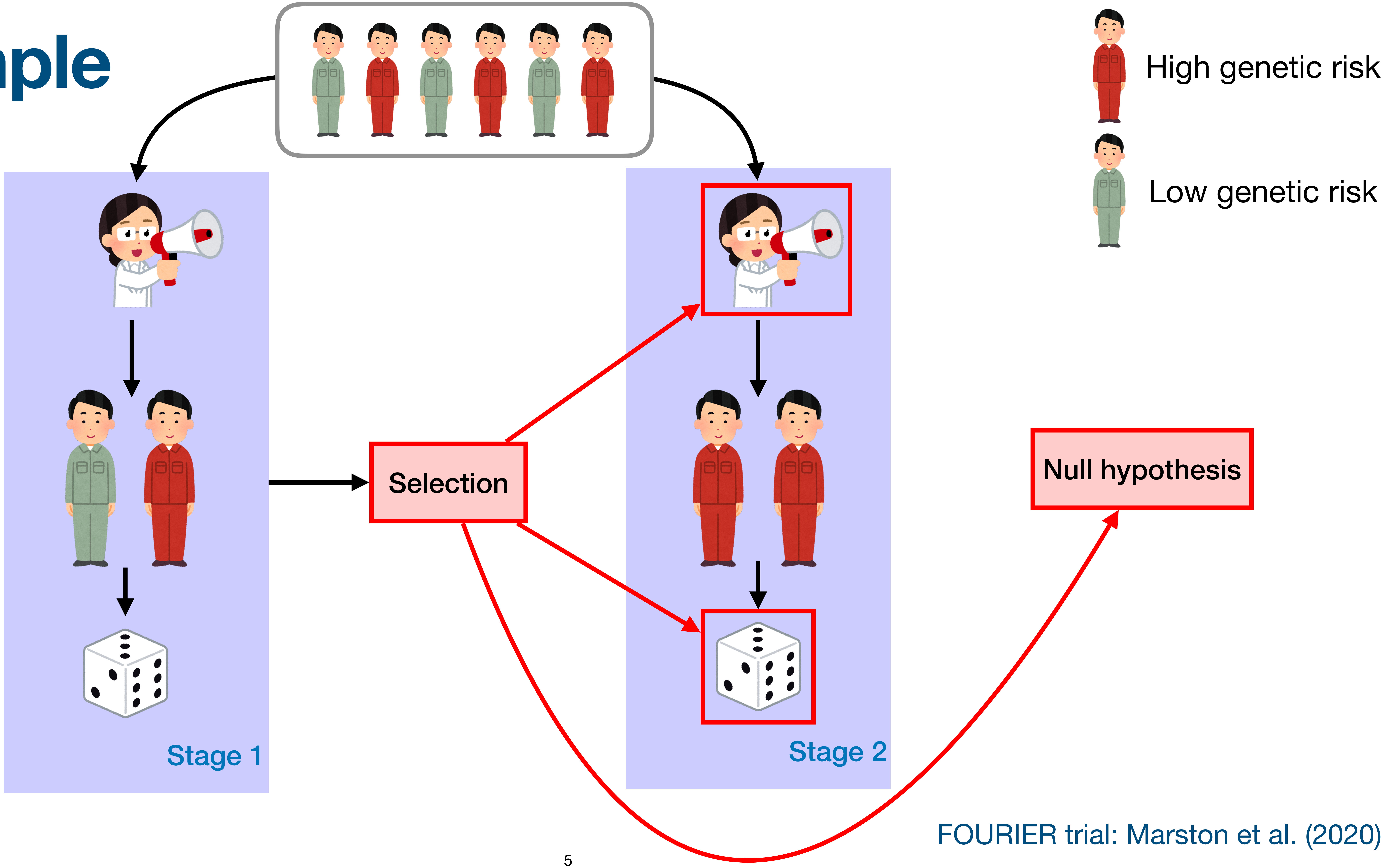

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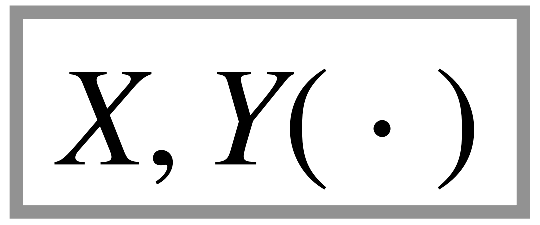
Graphical Model

Graphical Model

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



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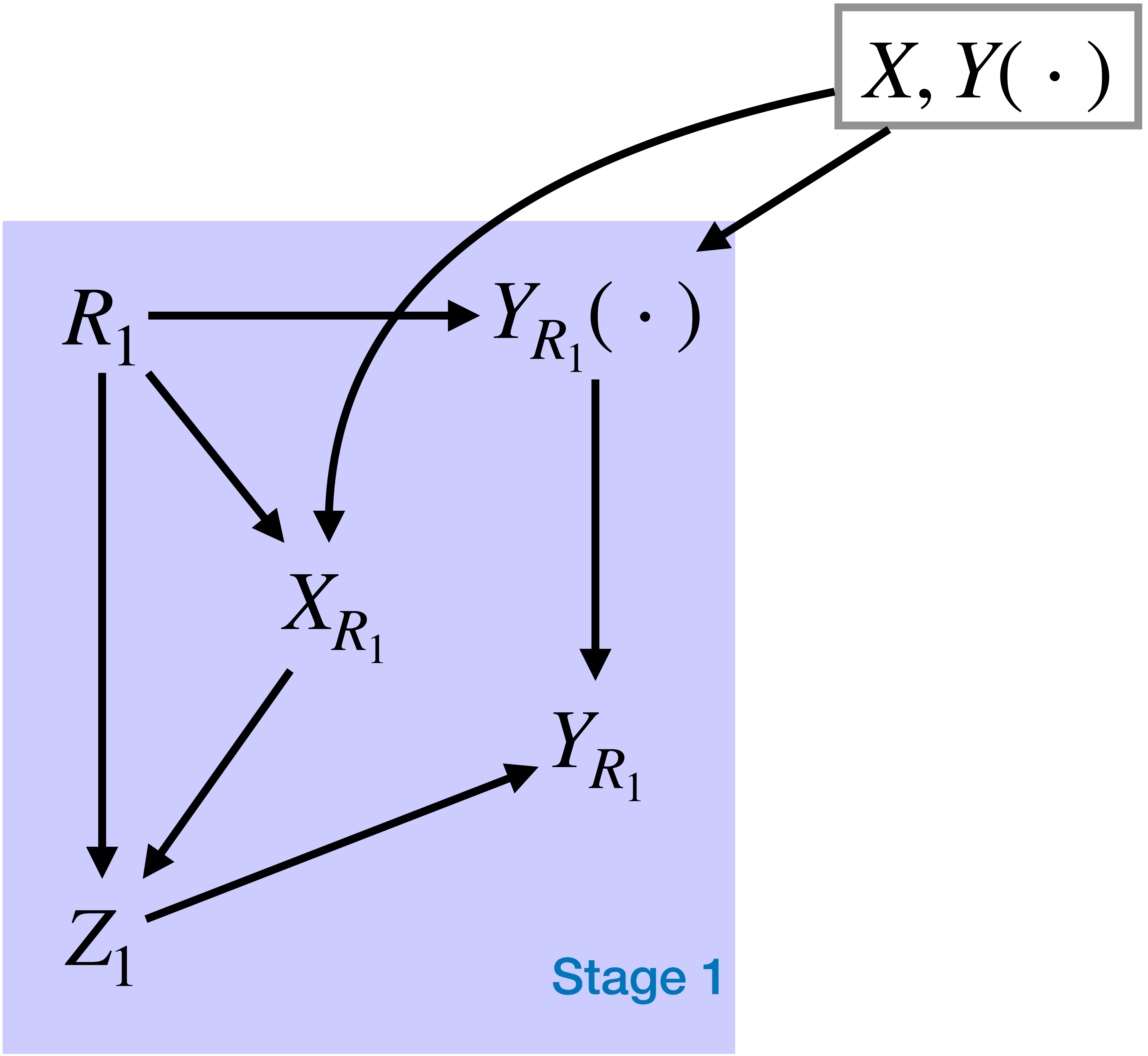

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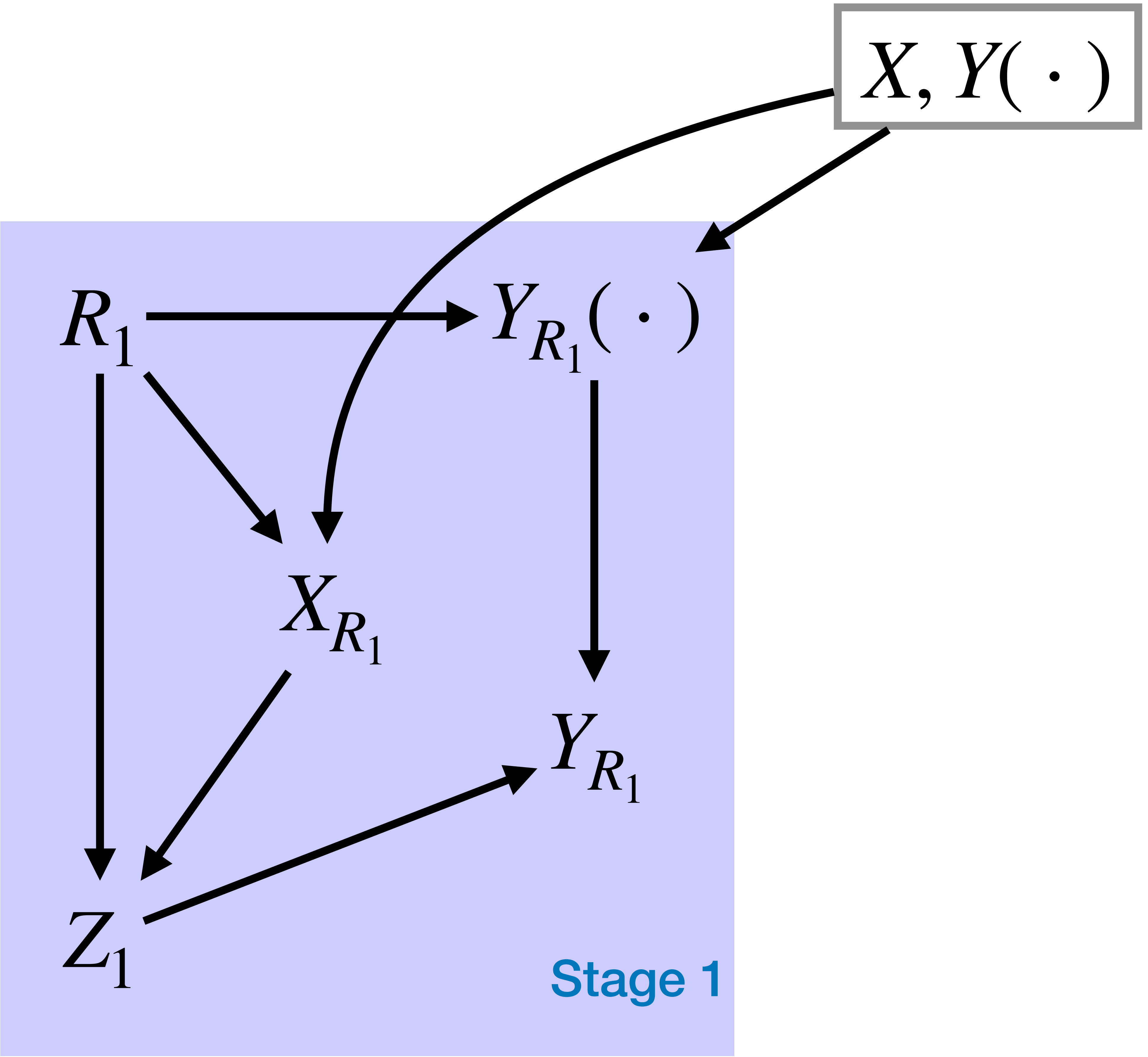

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- Treatments: Z_k
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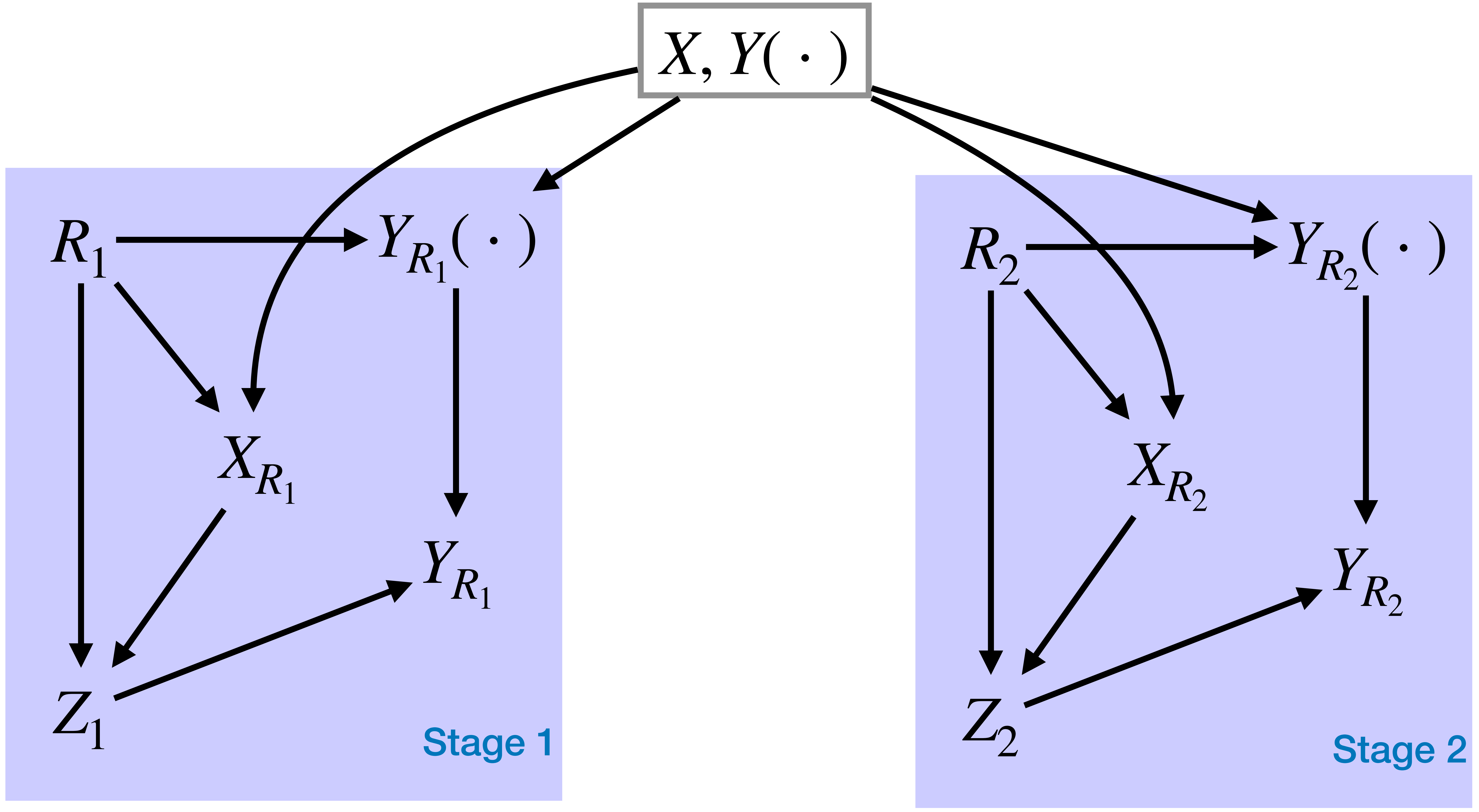

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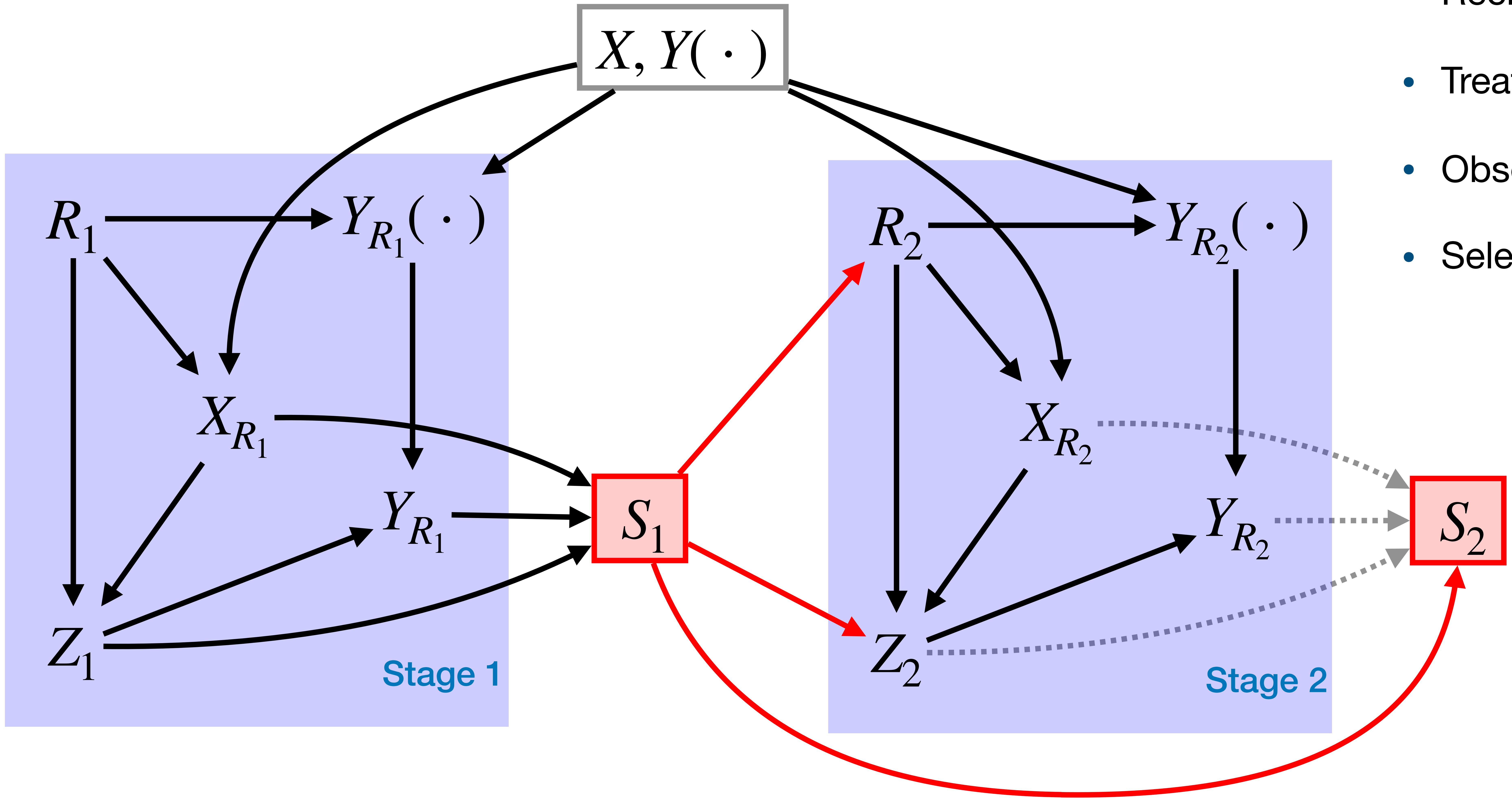

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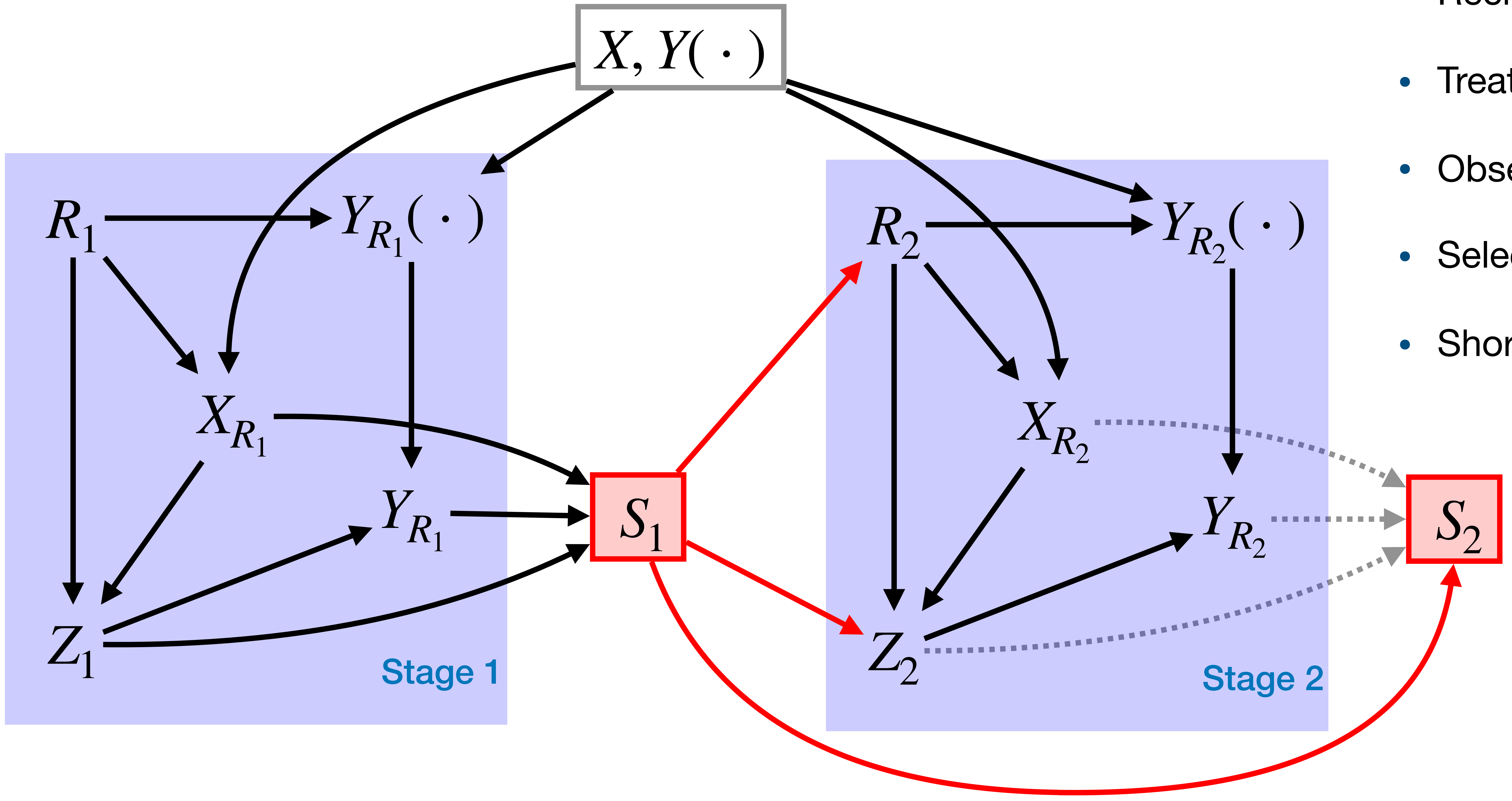

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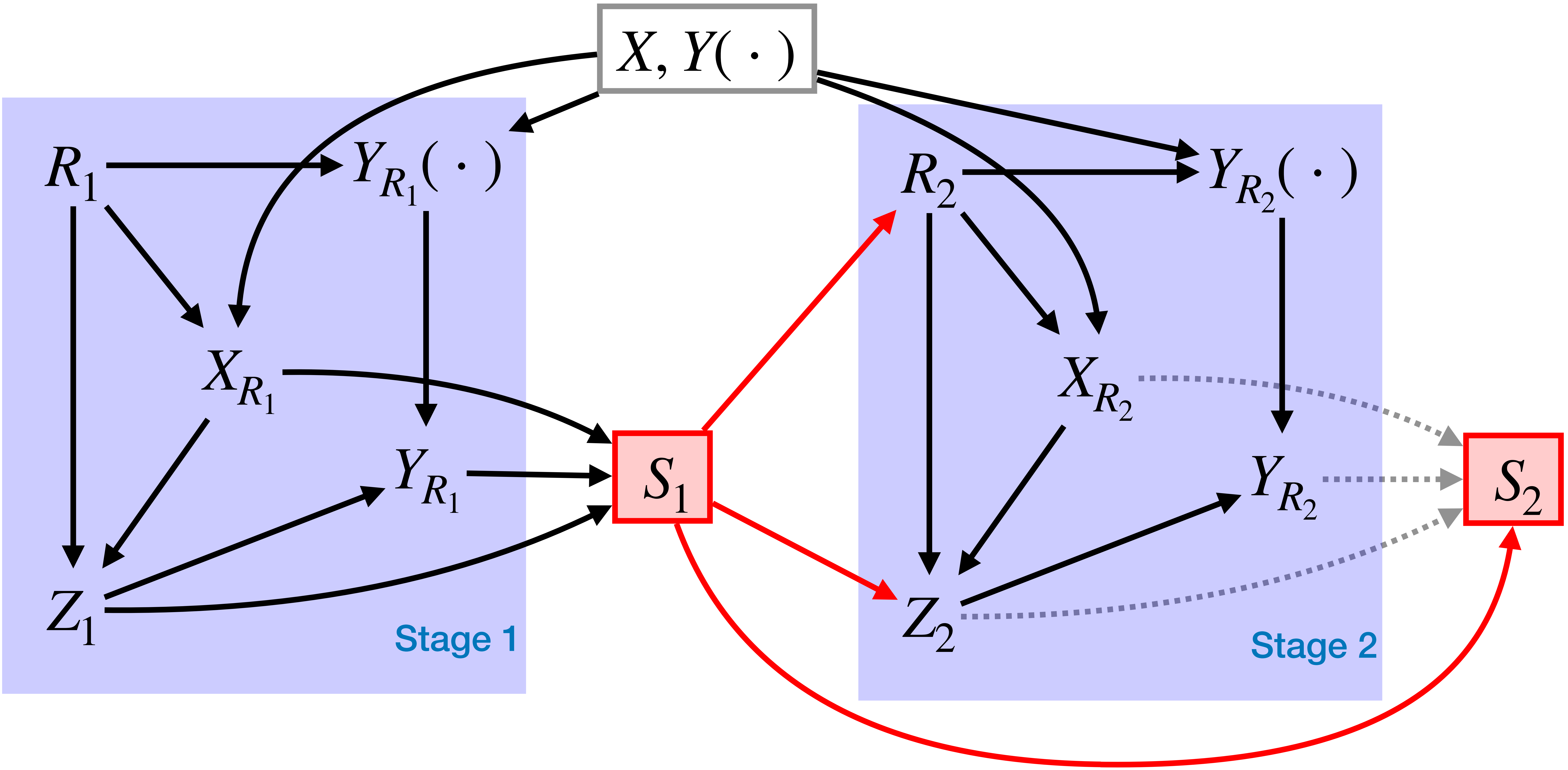
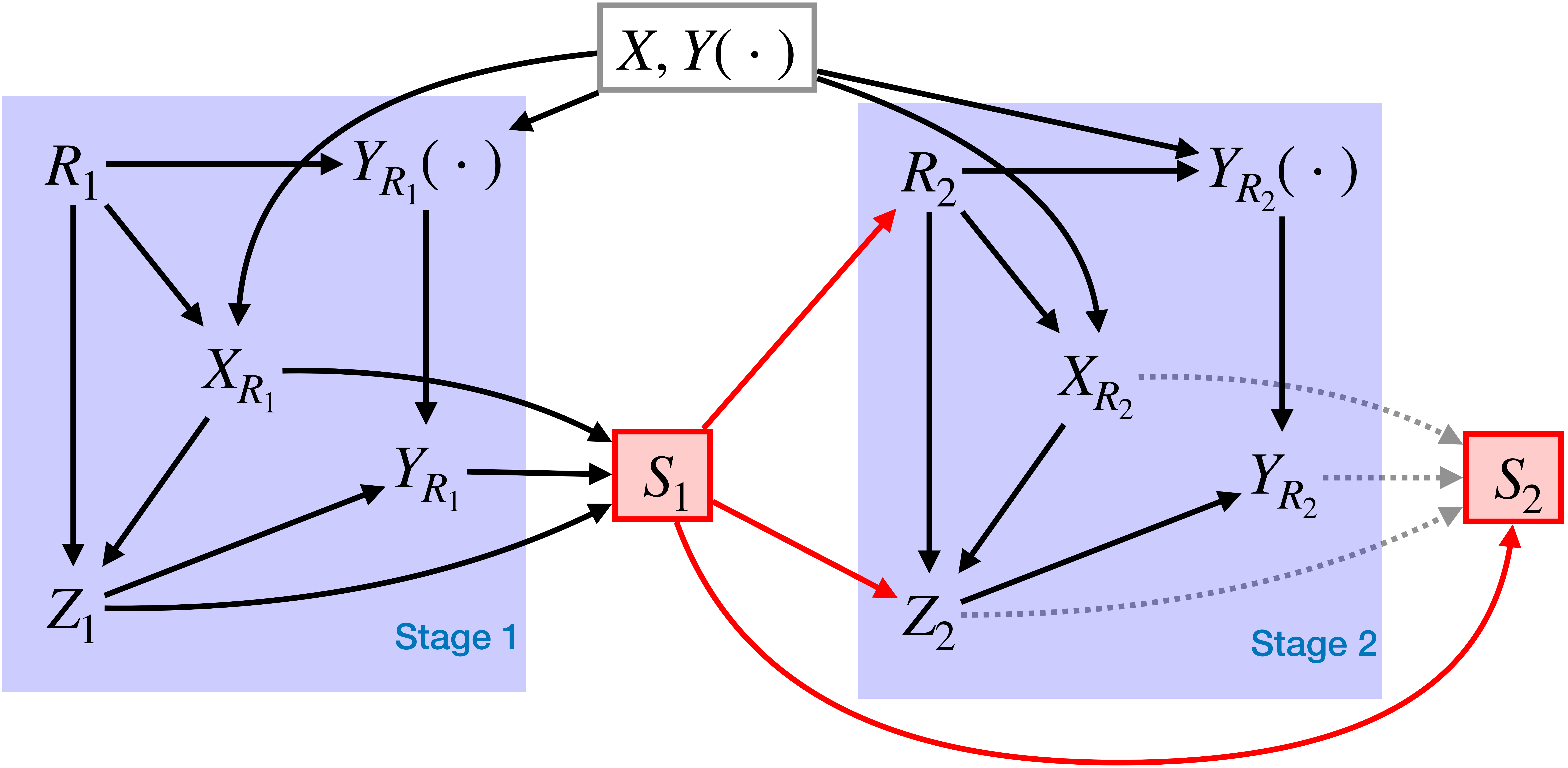
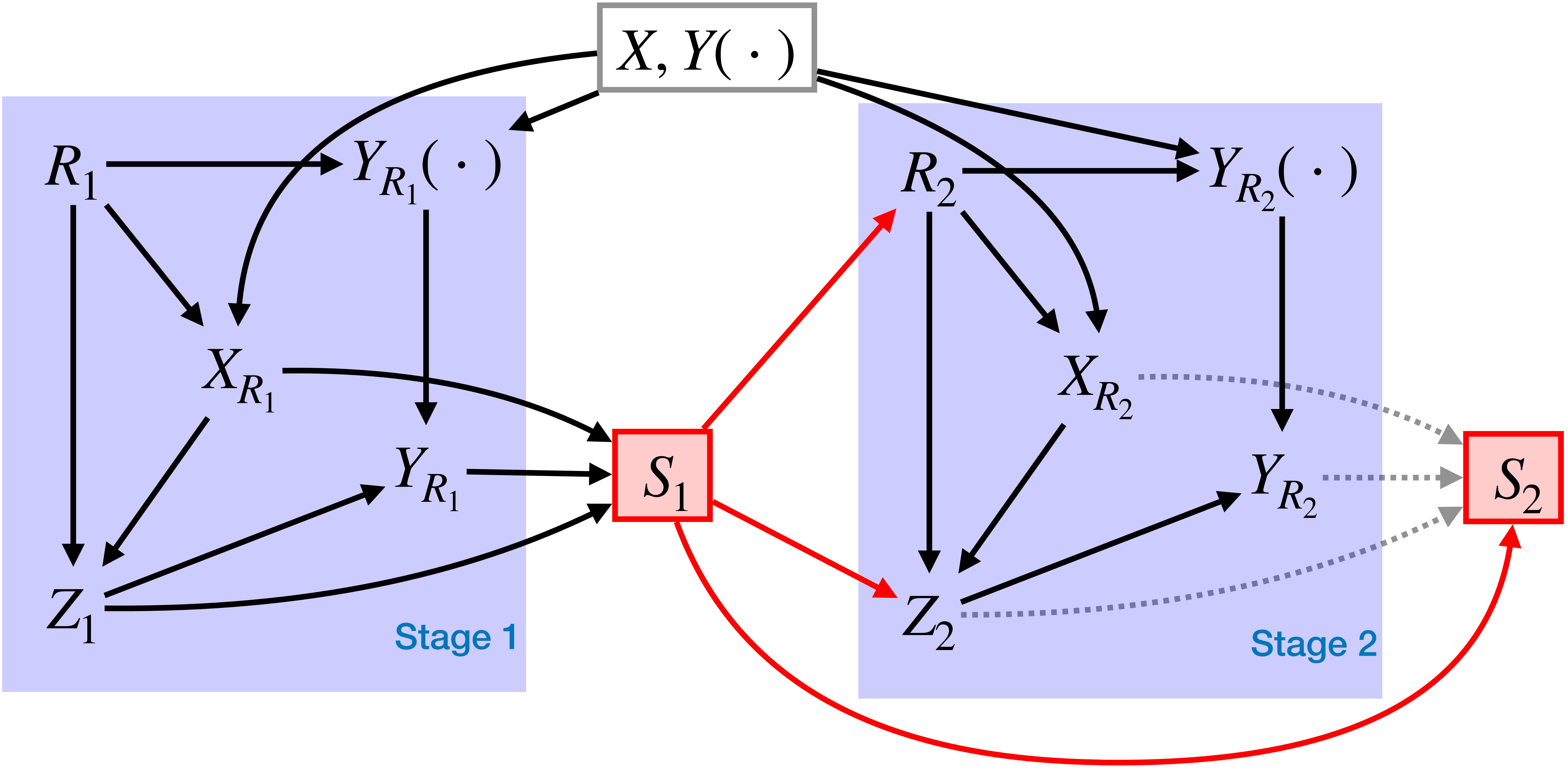
- Short-hand: $W = (R, X_R, Y_R(\cdot))$


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



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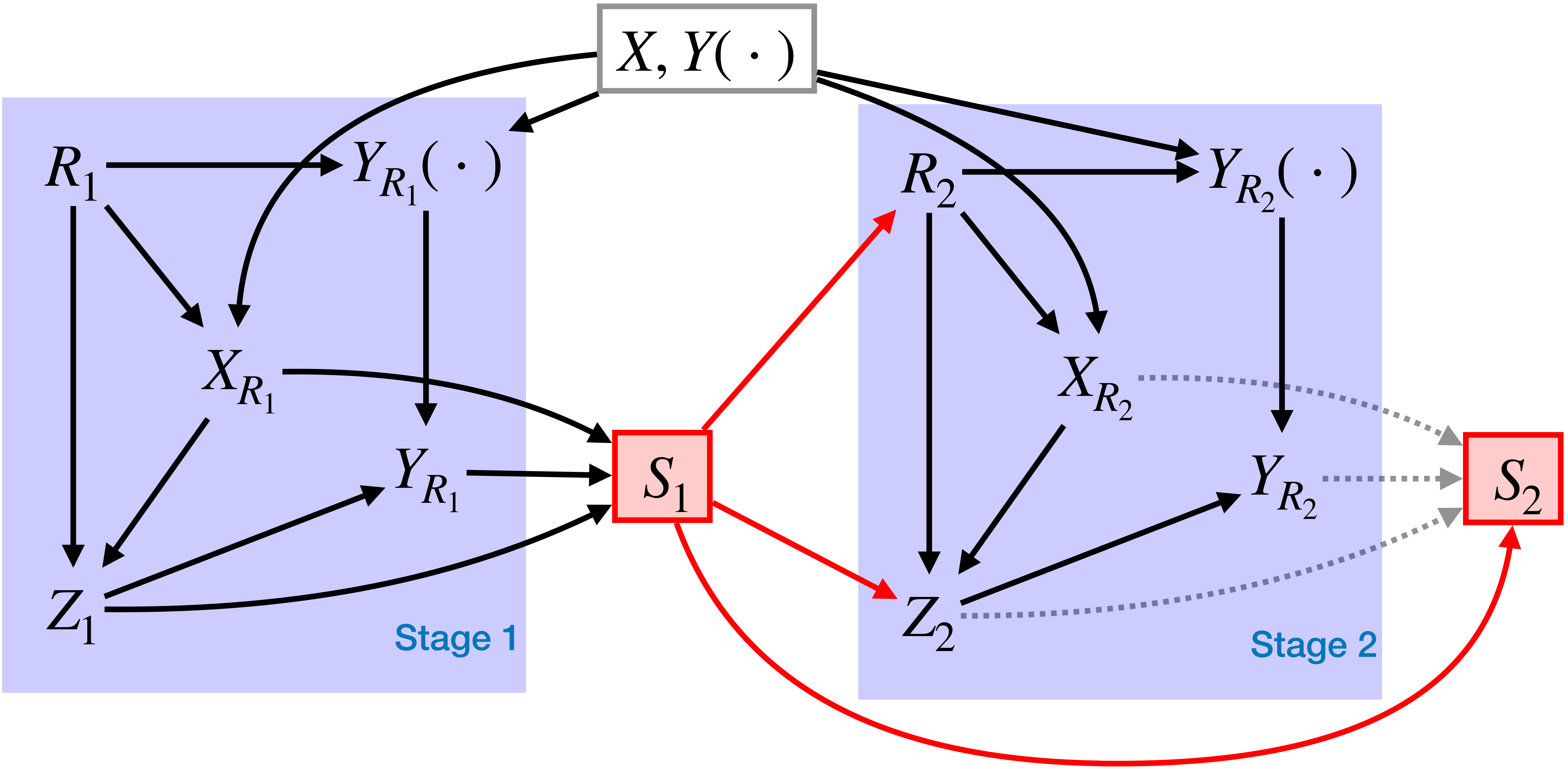

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Adaptive Treatment Strategies

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  - Response-adaptive randomization: trade off statistical power and patient benefit
  - Bandit algorithms: exploration and exploitation
  - Reinforcement learning

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- Analysing data from adaptive experiments despite the dependence between different data points

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- Is there a problem when the experiment is adaptive?

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  - Selective randomization inference:

$$P_{sel} = \mathbb{P}(\, T(Z^*, W) \leq T(Z, W) \mid W, Z,\ S(Z^*) = S(Z)\,)$$

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  - $\mathbb{P}(Z = z \mid W = w, S(Z) = s) = \dfrac{q(z \mid w, s)}{\sum_{z'} q(z' \mid w, s)}$, where

  - $q(z \mid w, s) = \mathbf{1}\{S(z) = s\} \cdot \prod_{k=1}^{K} \mathbb{P}(Z_k = z_k \mid R_k = r_k, X_{R_k} = x_{R_k}, S_{k-1} = s_{k-1})$

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

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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

$$\hat{P}_M := \frac{1 + \sum_{j=1}^M \mathbf{1}\{T(z_j^*, W) \le T(Z, W)\}}{1 + M}.$$

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- Rejection sampling, Markov Chain Monte Carlo (MCMC)

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- Confidence intervals:

Inference

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- Data carving: non-adaptive hold-out units

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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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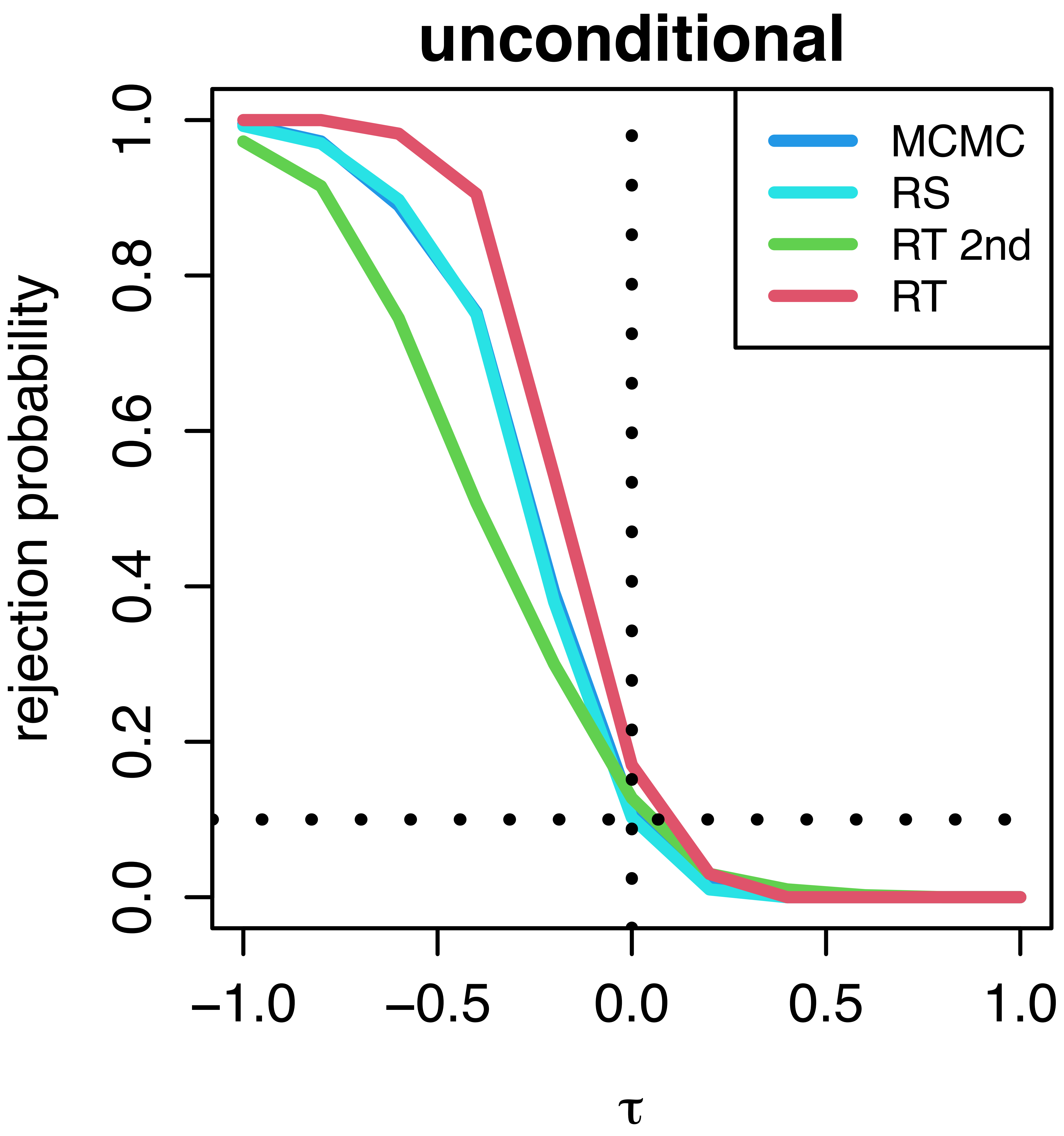
- First stage: 100 patients, Second stage: 40 patients
- $\Delta =$ standardized difference in SATEs between groups
- Selection variable:

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

Power Analysis



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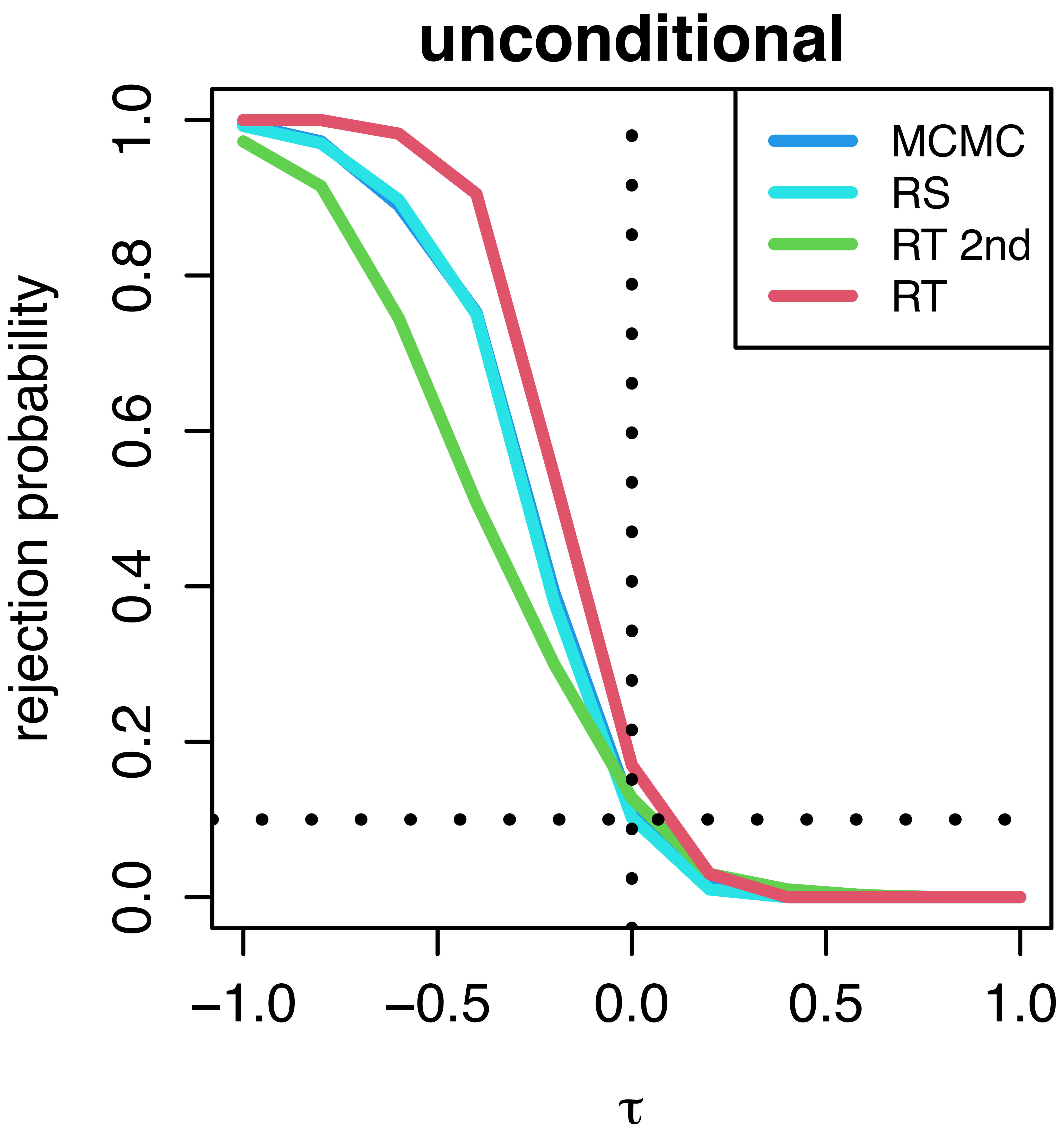

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- RT 2nd: valid but has **low power**

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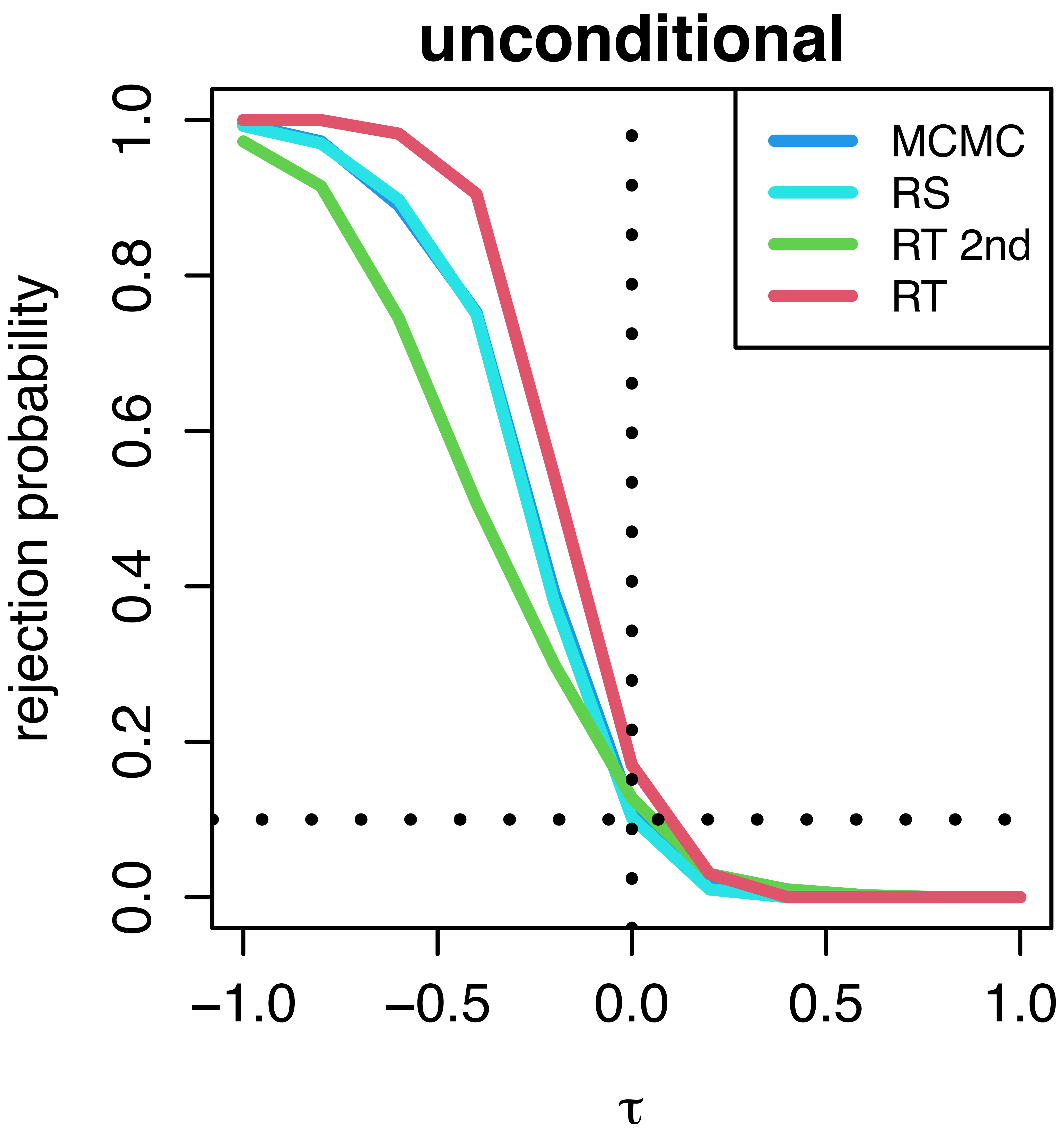

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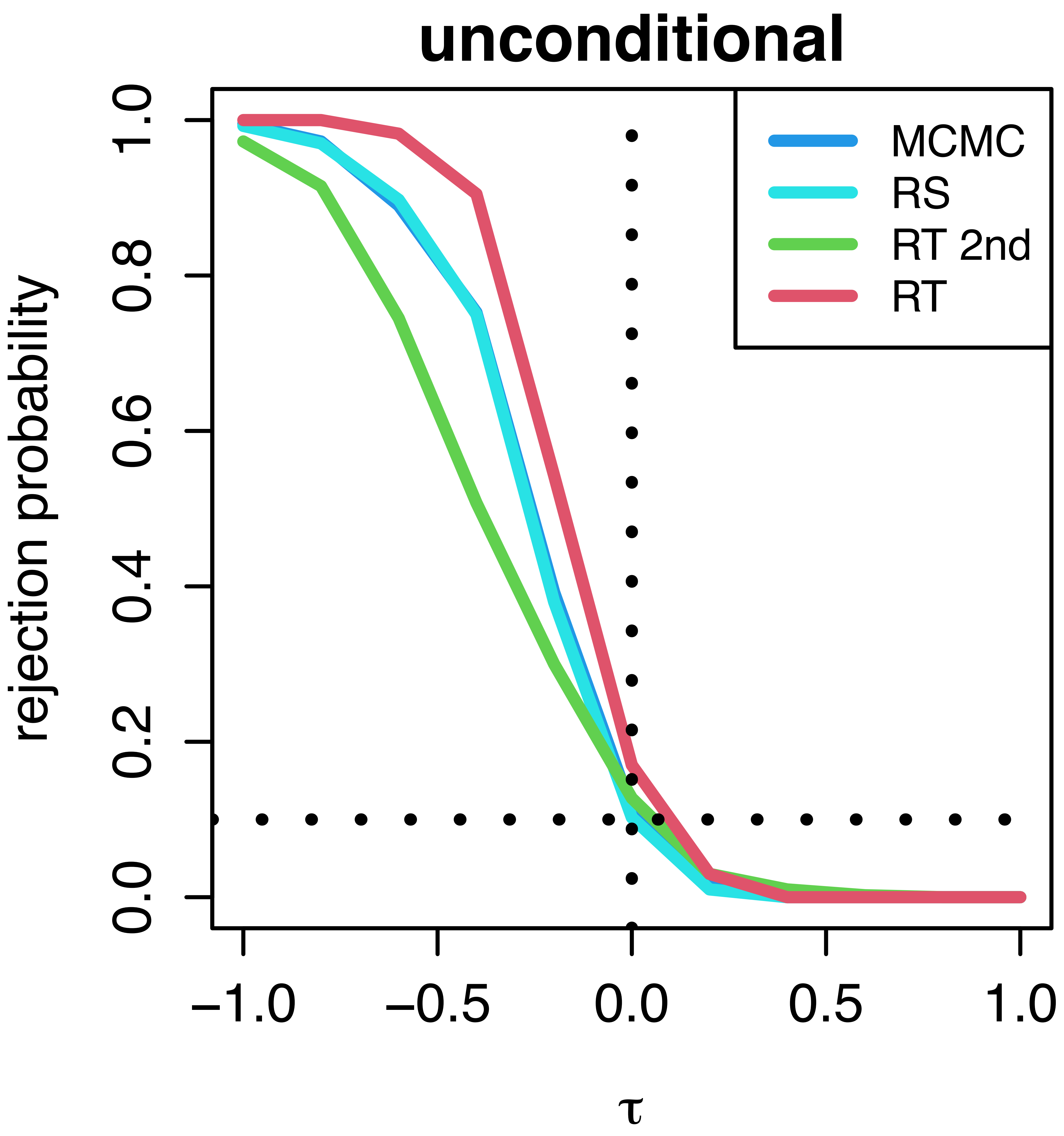

- RT: **no type-I error control**
- RT 2nd: valid but has **low power**
- Selective RT: **valid and more powerful.**
- Rejection sampling and MCMC lead to very similar approximations.

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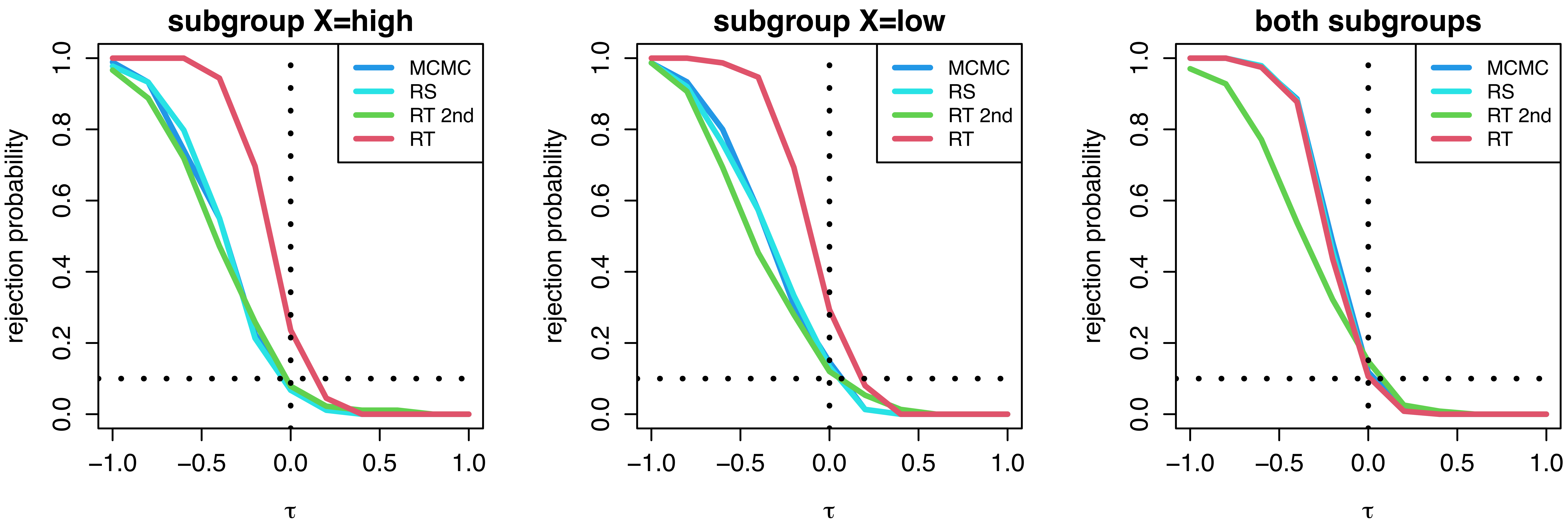

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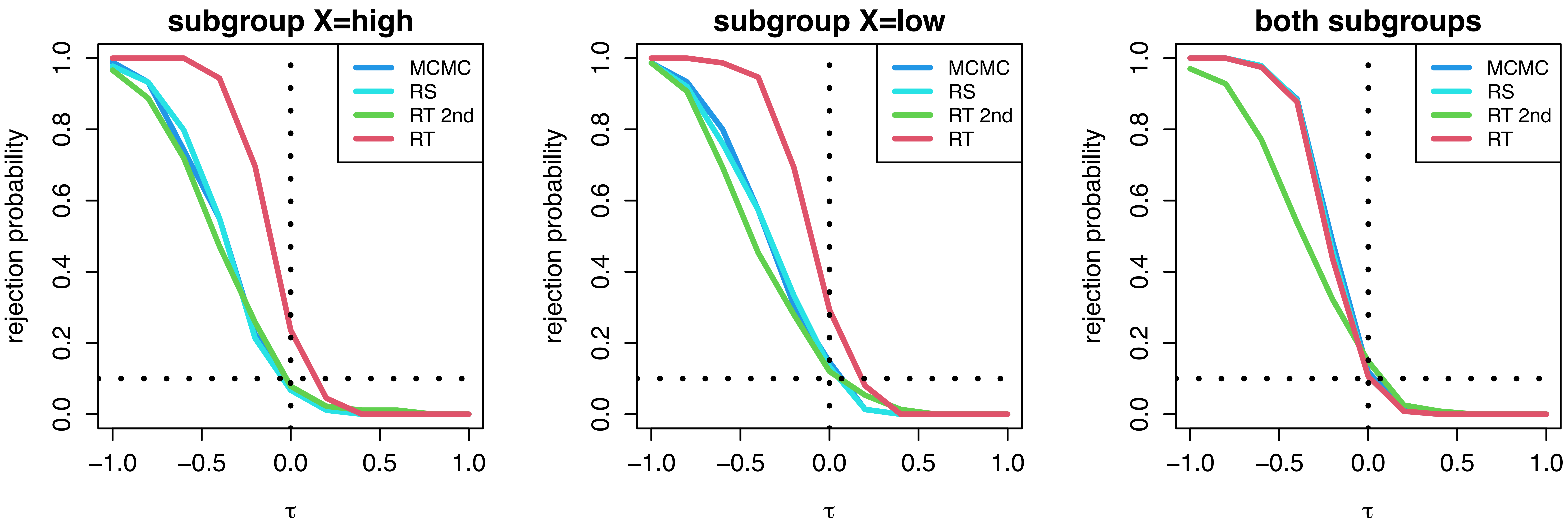

- Type-I error control in every subgroup

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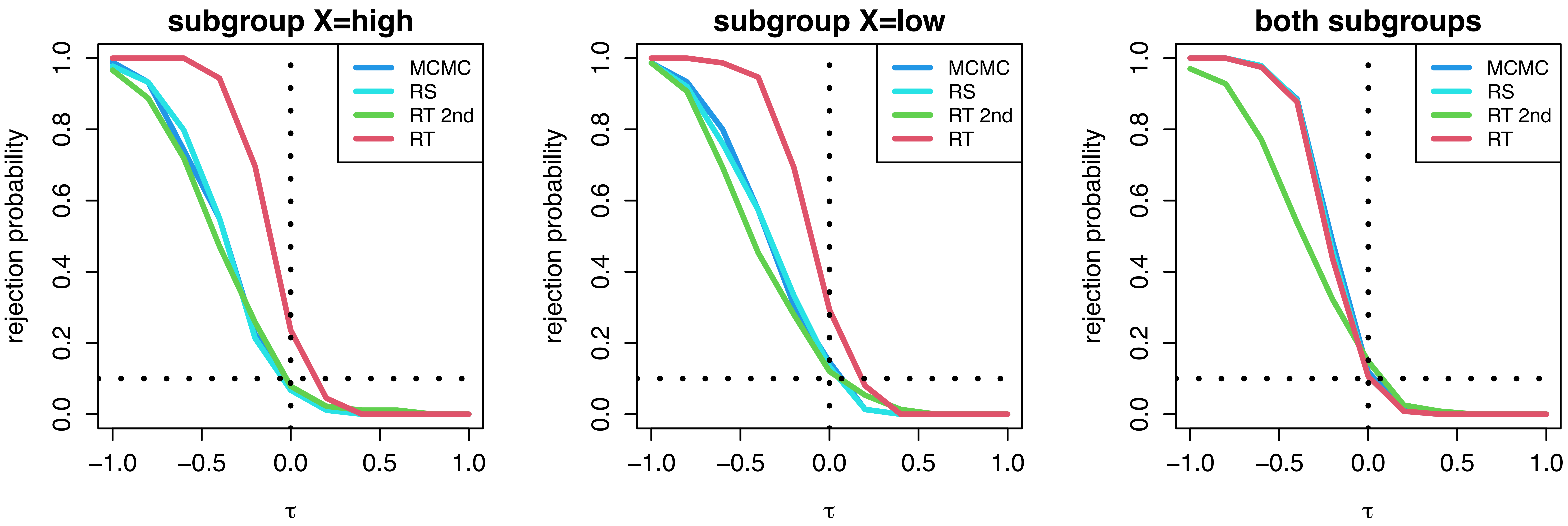

- Type-I error control in every subgroup
- Gain in power when there is a lot of “randomness left”

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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References

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Hold-out Units