Measurement Error in Precision Medicine and Dynamic Treatment Regimes

Dylan Spicker, Michael Wallace

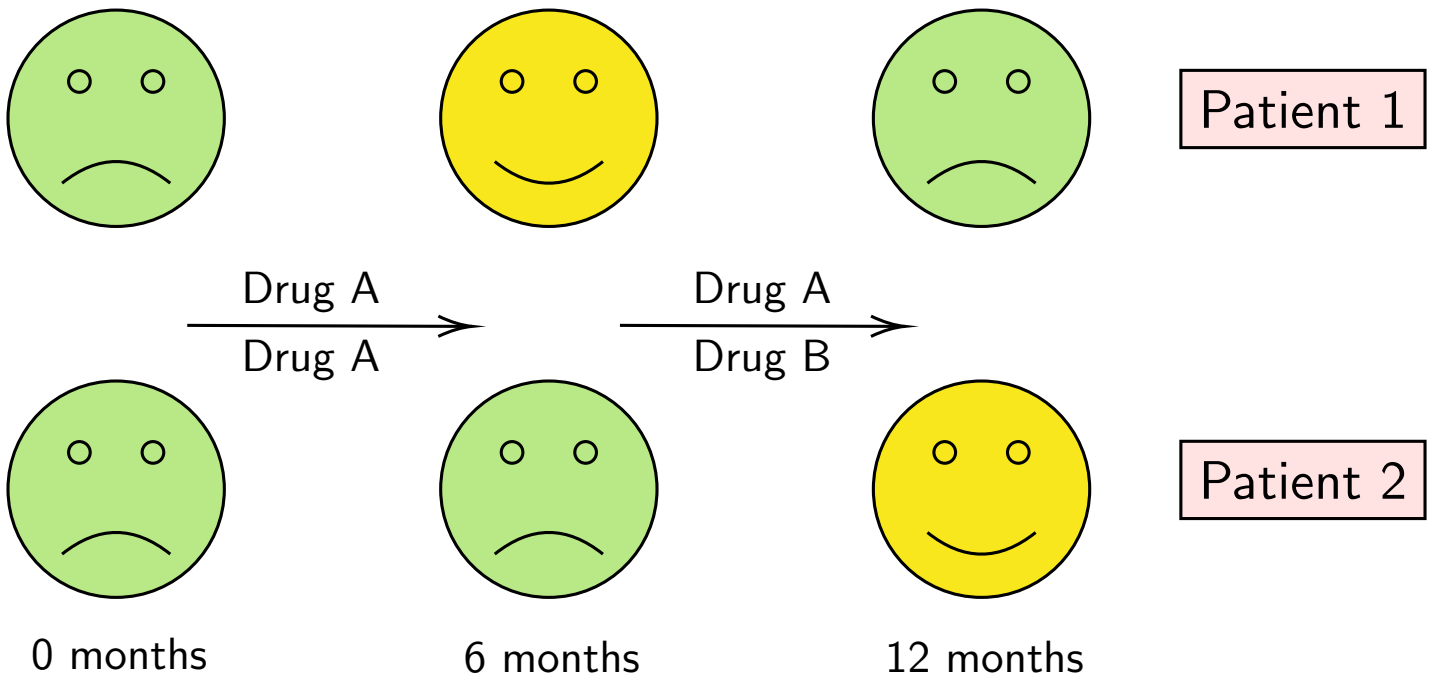
University of Waterloo

dylan.spicker@uwaterloo.ca

May 27, 2019

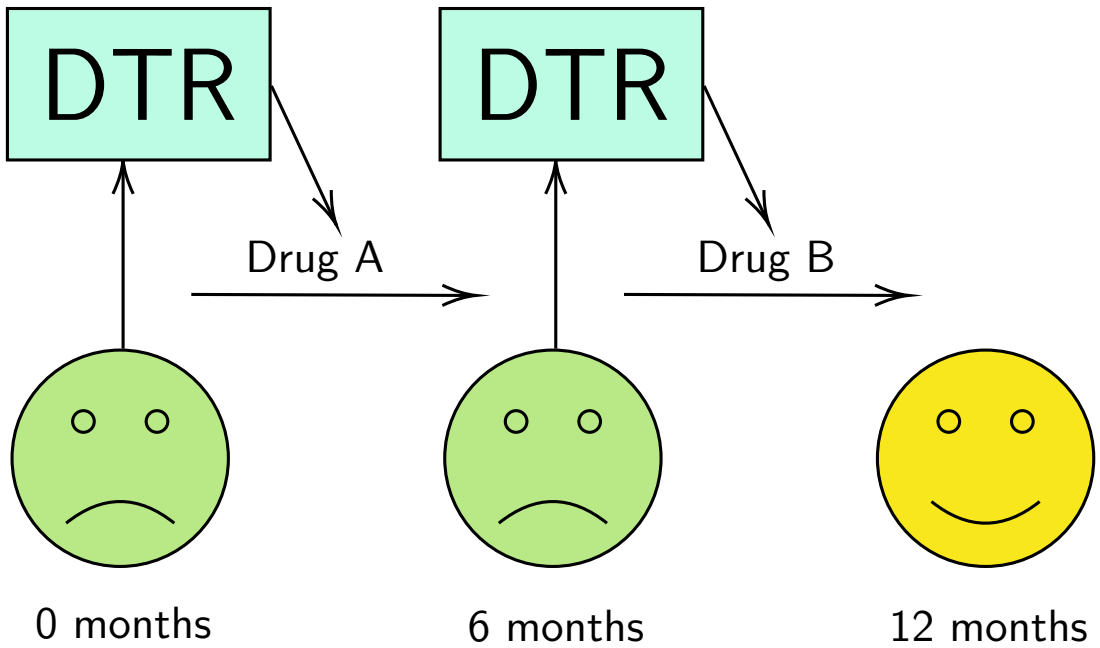
Precision Medicine

"Treat the patient, not the diagnosis."



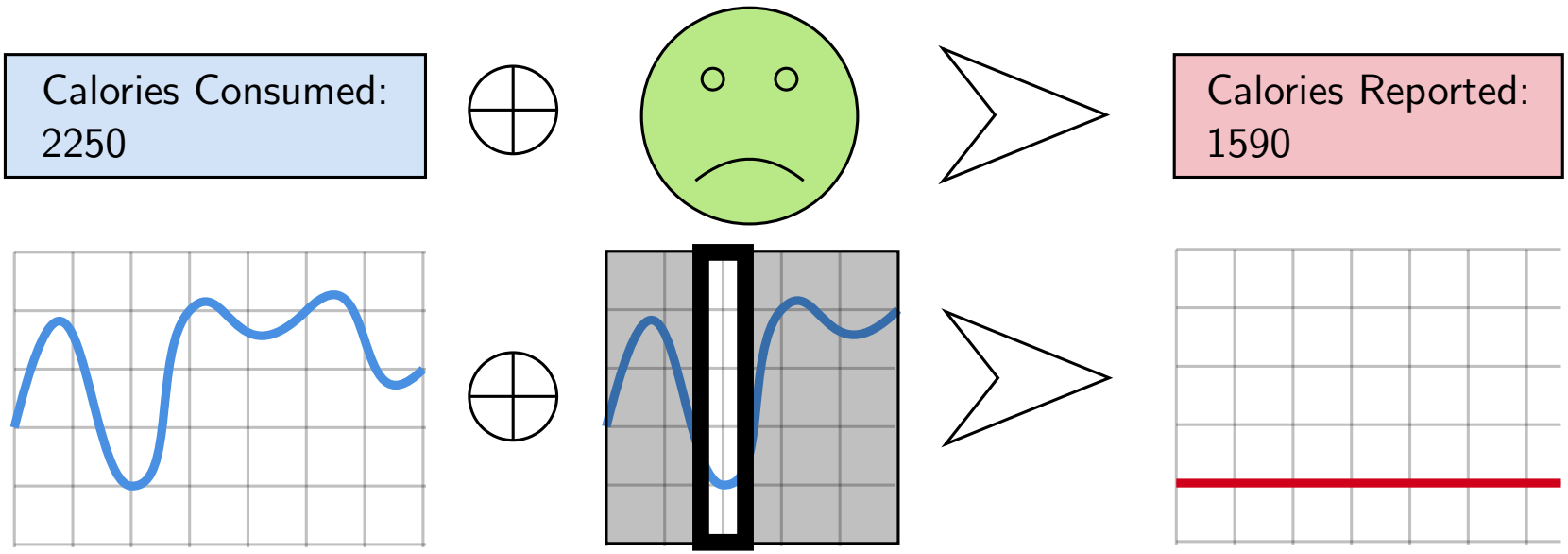
Dynamic Treatment Regimes

- DTRs provide one mechanism for formalizing precision medicine



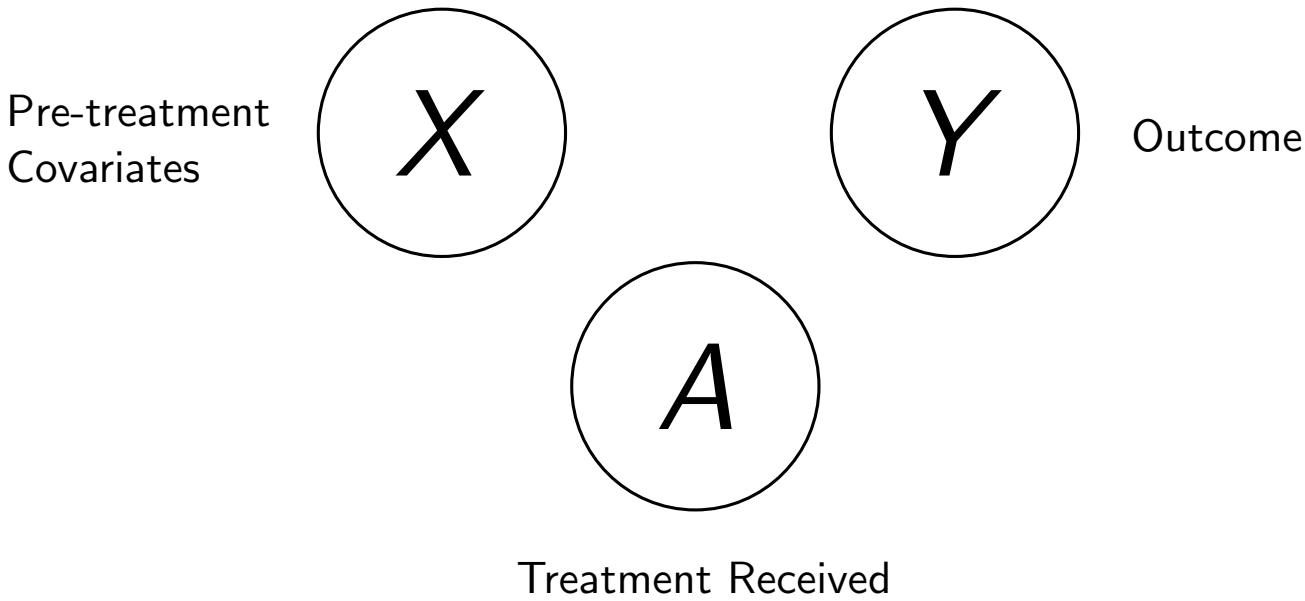
"At stage one, treat with Drug A if the patient is over 50 with a BMI greater than 30 and Drug B otherwise.
At stage two, treat with Drug A if the patient responded to stage one treatment."

Measurement Error



- Instead of observing true covariate X we observe $W = X + U$.
- $E[U] = 0$ and U is independent of everything else.

Notation and Formal Setup



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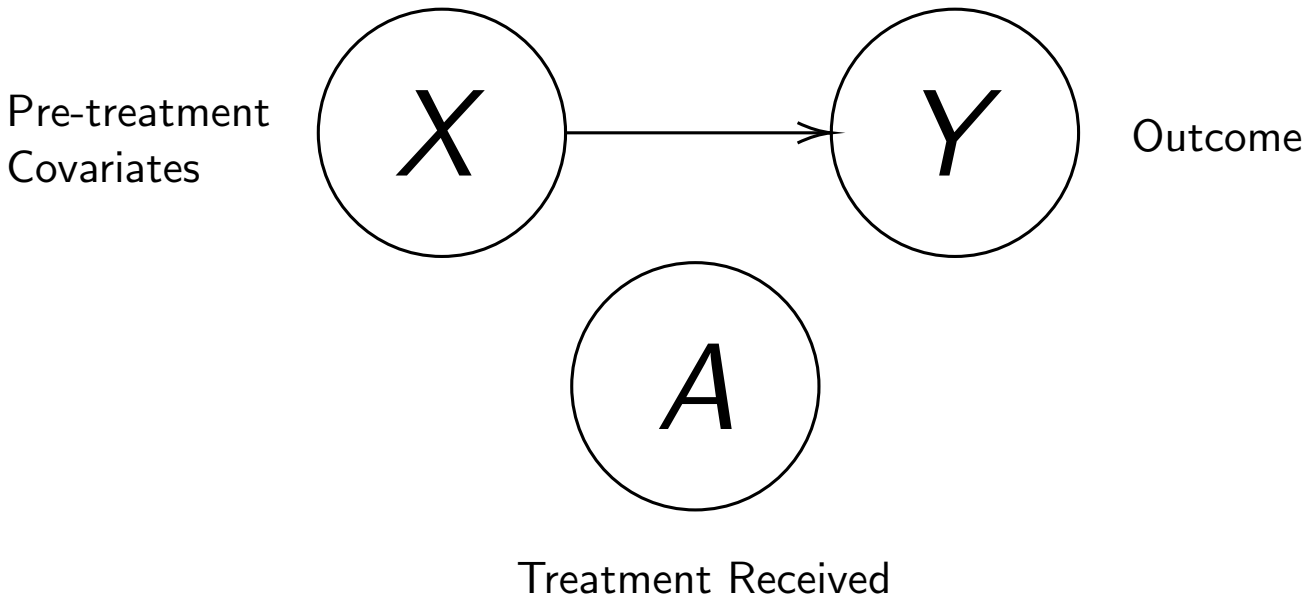

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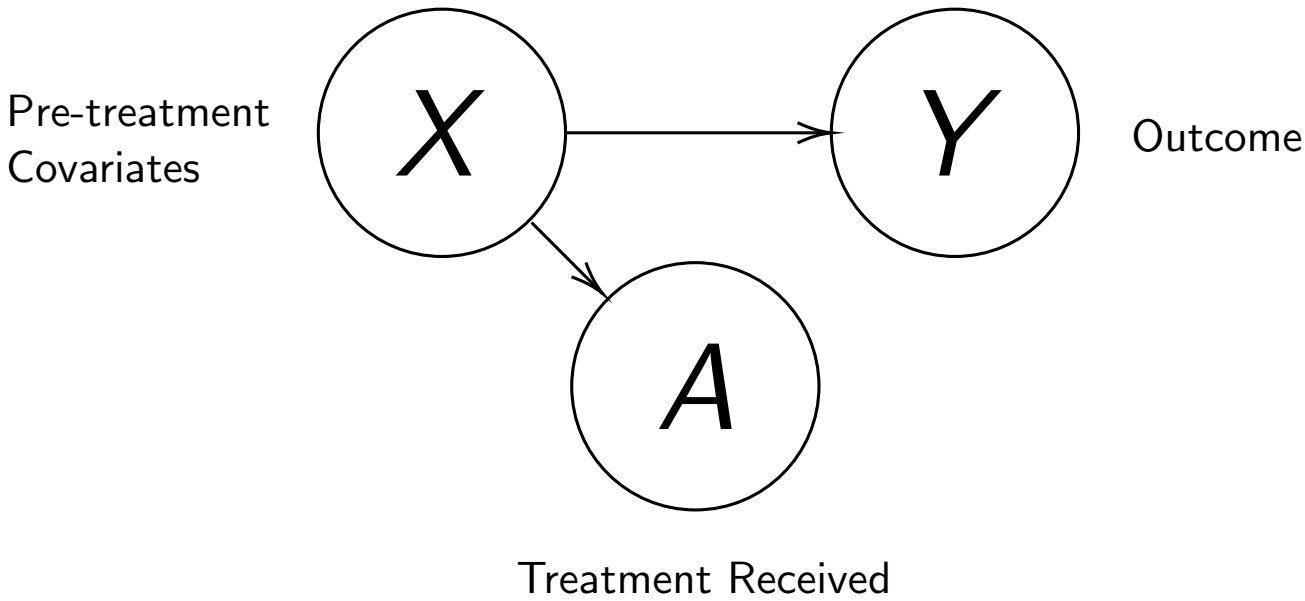

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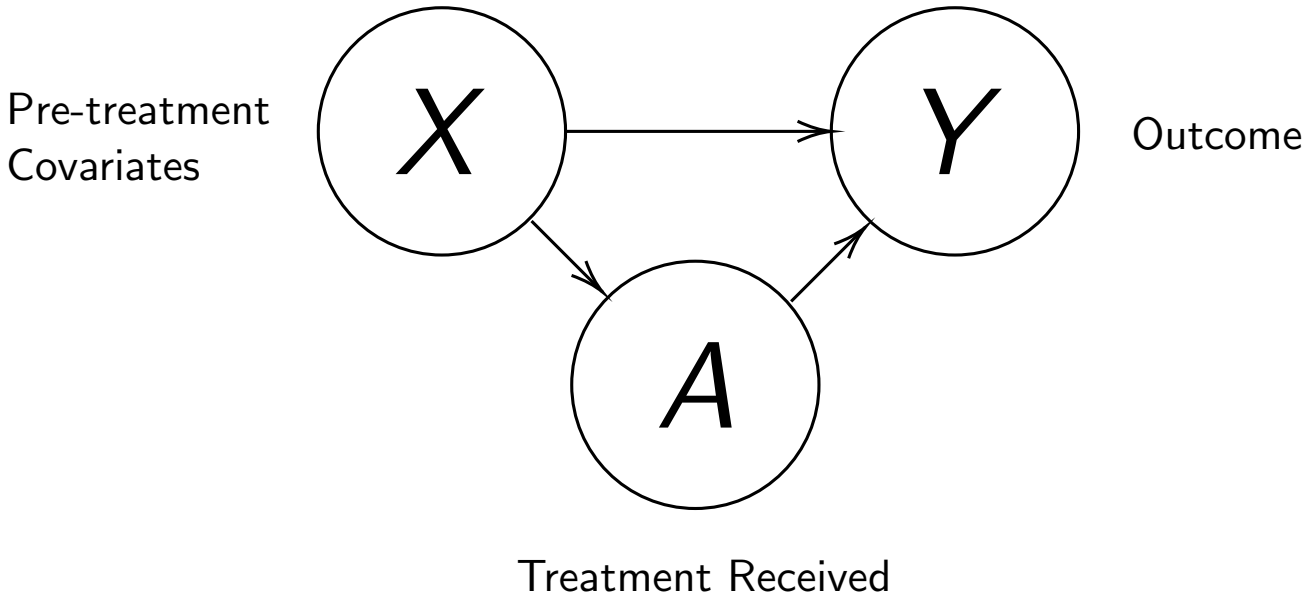
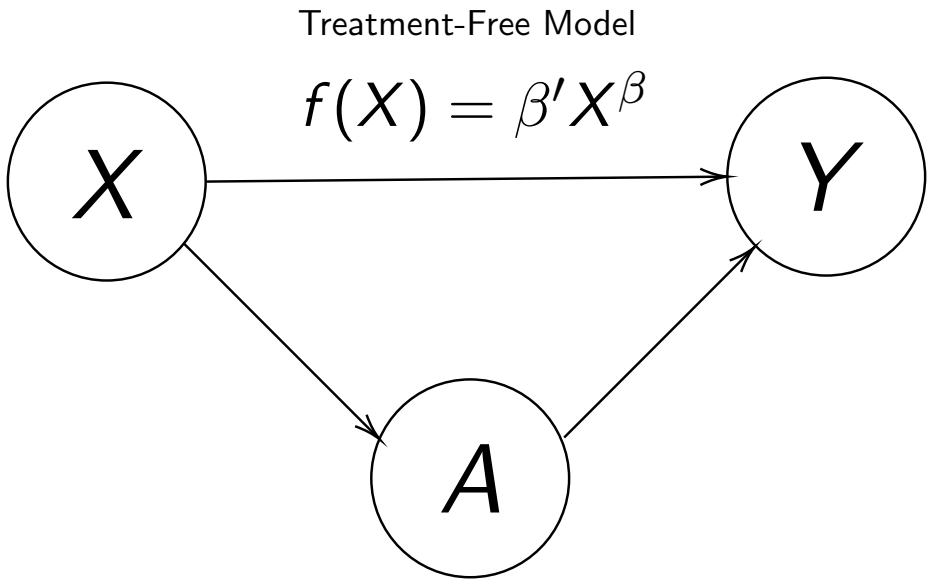


Goal

Find A^{opt} such that $E[Y|X, A^{\text{opt}}]$ is maximized.

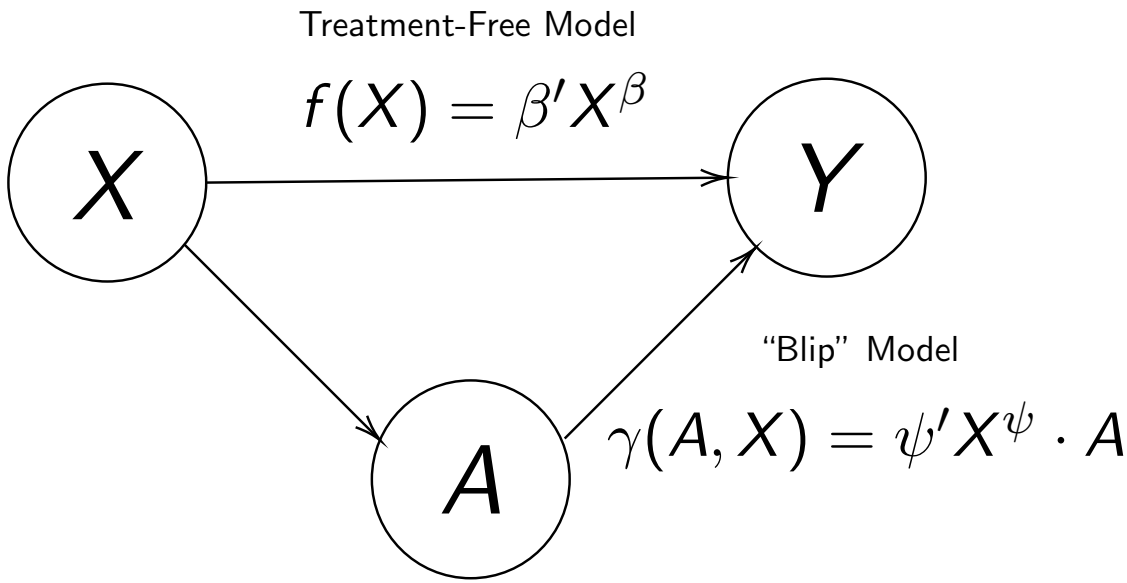
One-Stage DTR Estimation (dWOLS)

$$E[Y|X, A] = \beta' X^{\beta}$$



One-Stage DTR Estimation (dWOLS)

$$E[Y|X, A] = \beta' X^{\beta} + \psi' X^{\psi} A$$



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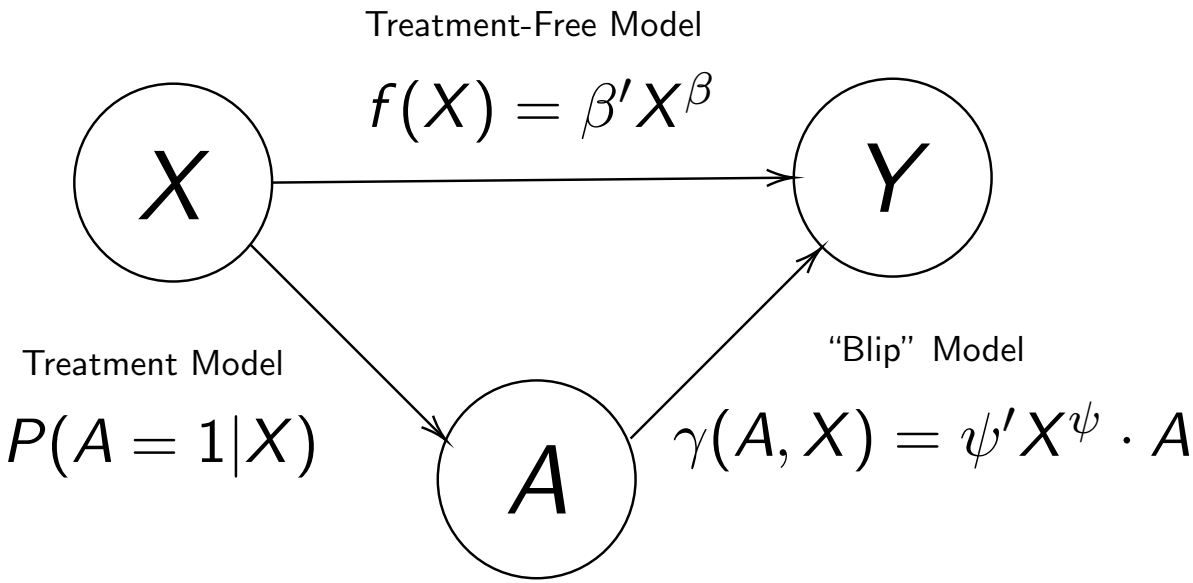

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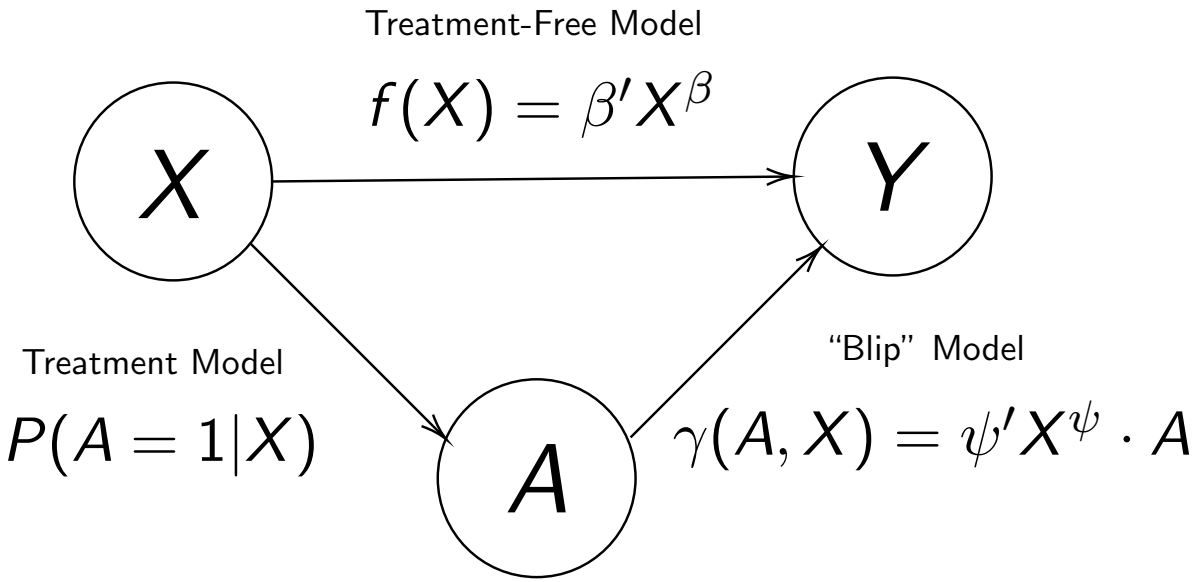


$$A^{\text{opt}} = \begin{cases} 1 & \psi' X^{\psi} > 0 \\ 0 & \text{otherwise} \end{cases}$$

One-Stage DTR Estimation (dWOLS)

$$E[Y|X, A] = \beta' X^{\beta} + \psi' X^{\psi} A$$

- Fit this using a weighted regression, with weights given by

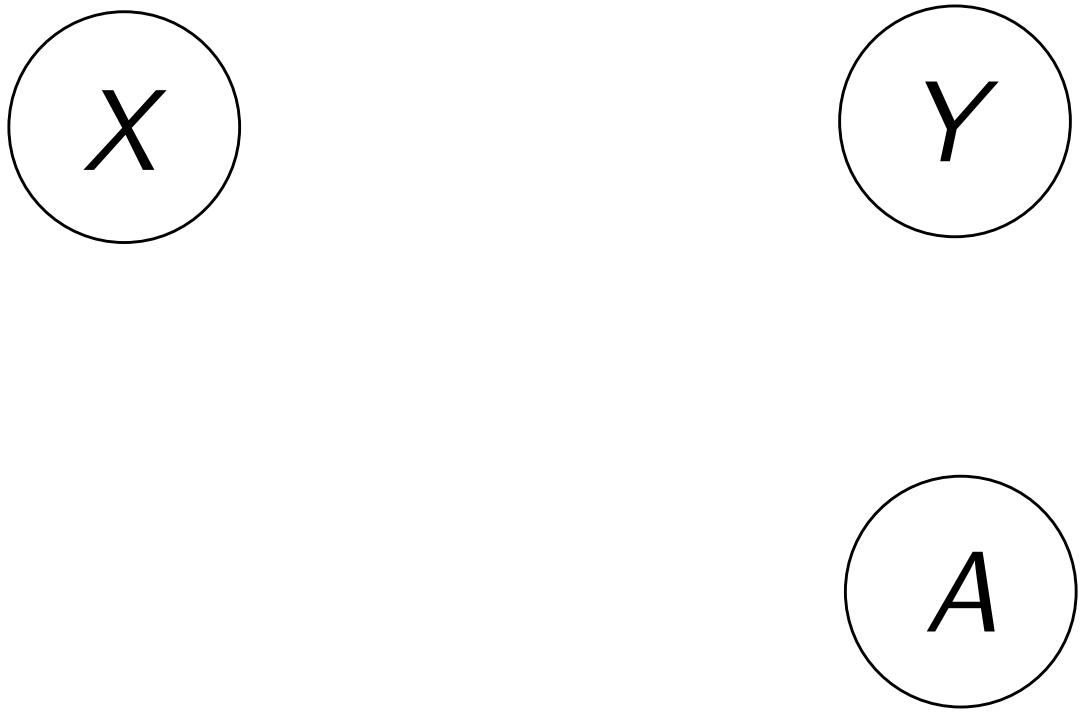
$$v(a, \mathbf{x}) = |a - P(a = 1|X = \mathbf{x})|$$

- Doubly-robust Estimator

Introduction of Measurement Error

What if we observe $W = X + U$ in place of X?

Error-prone DTRs: Biased Estimation



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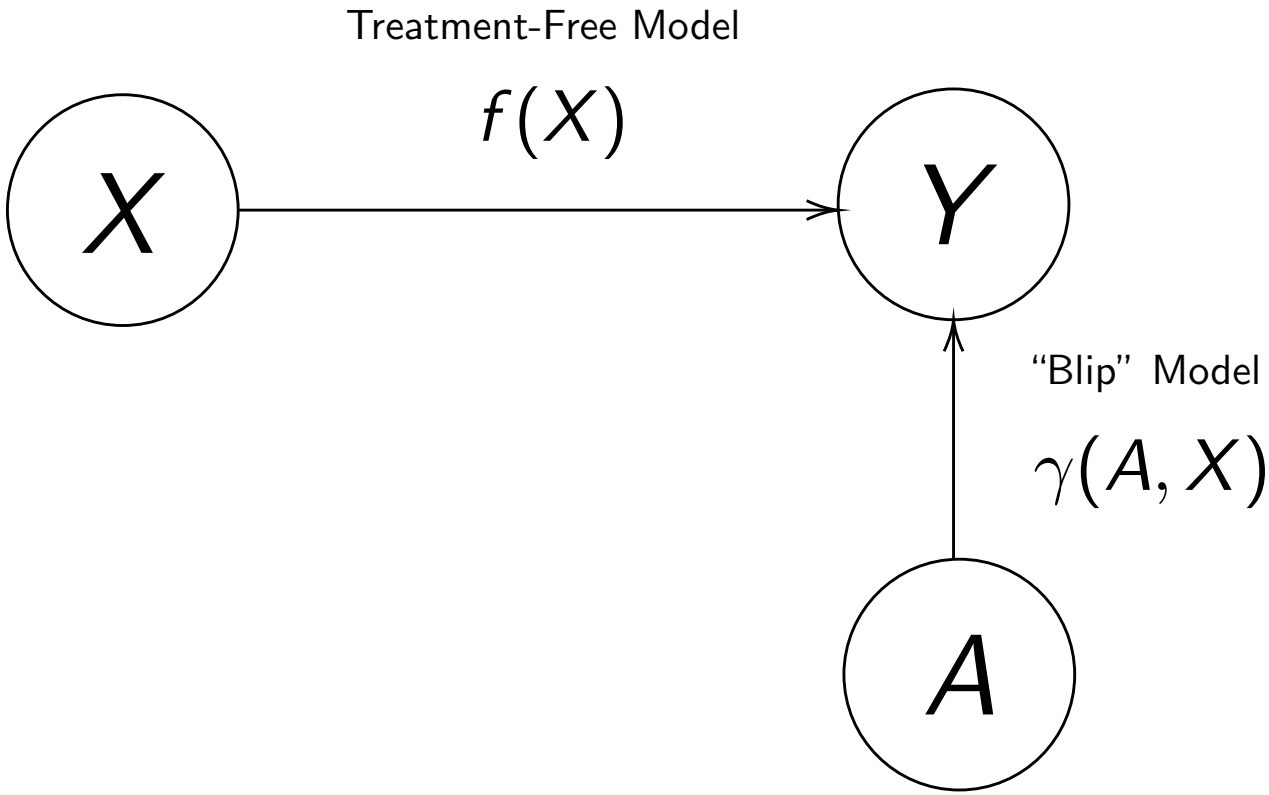

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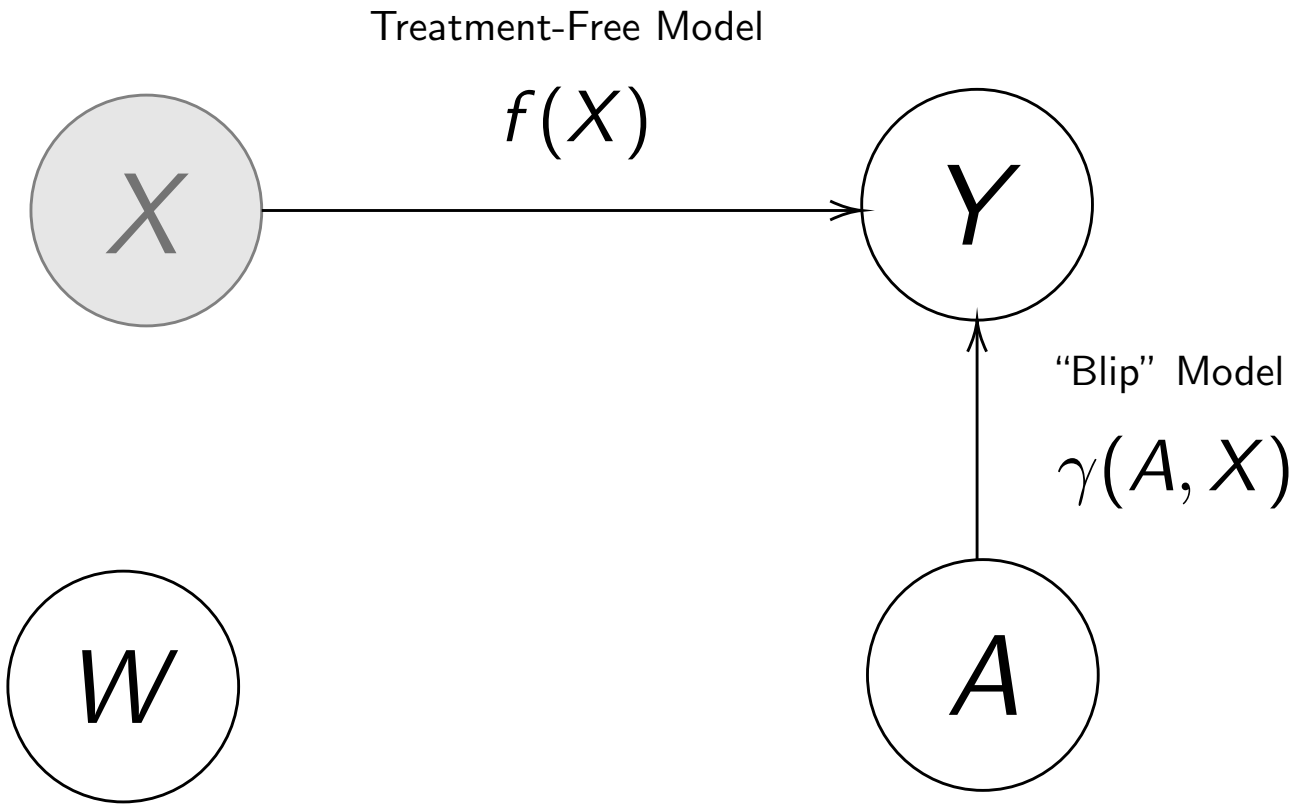

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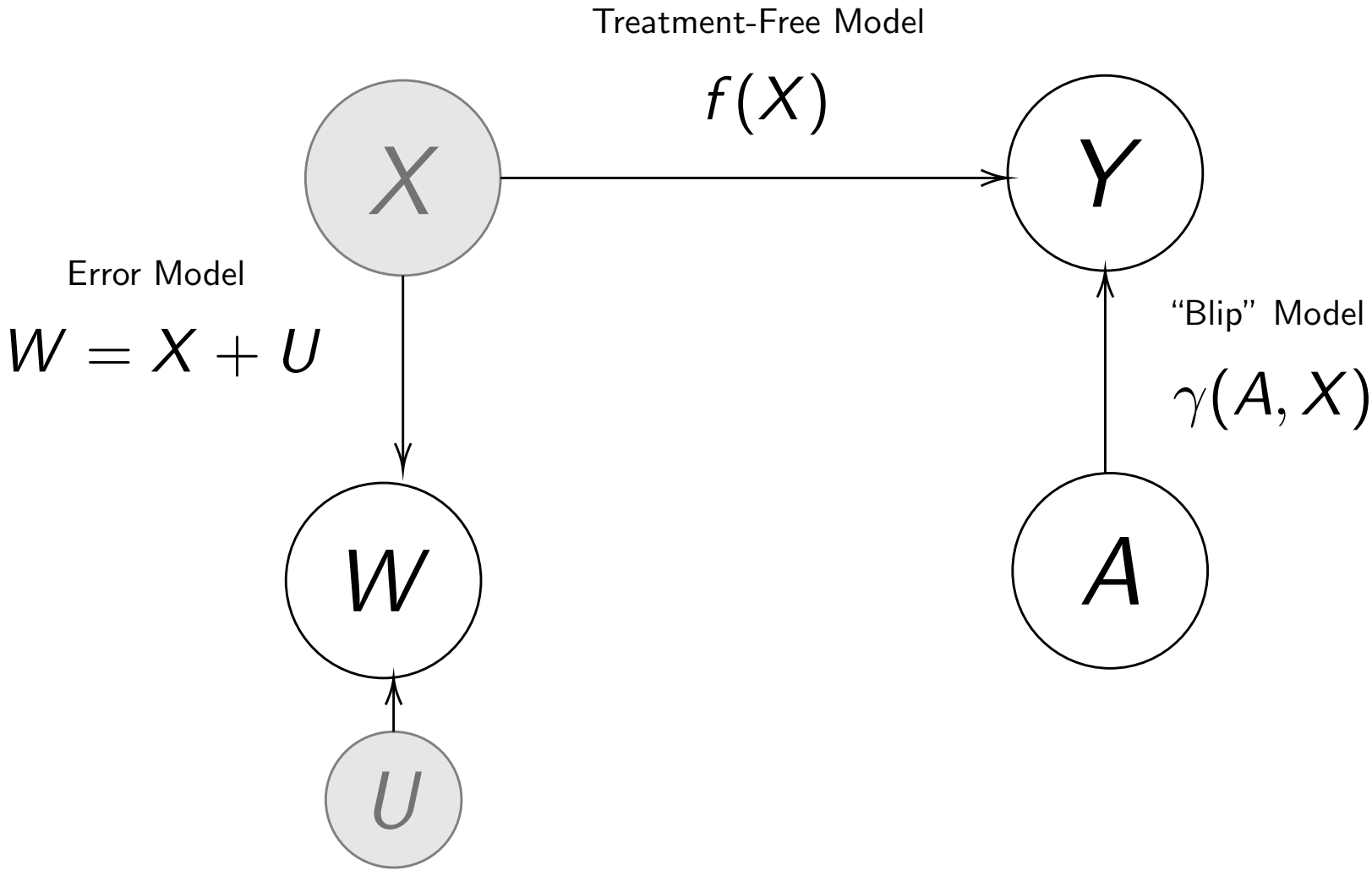

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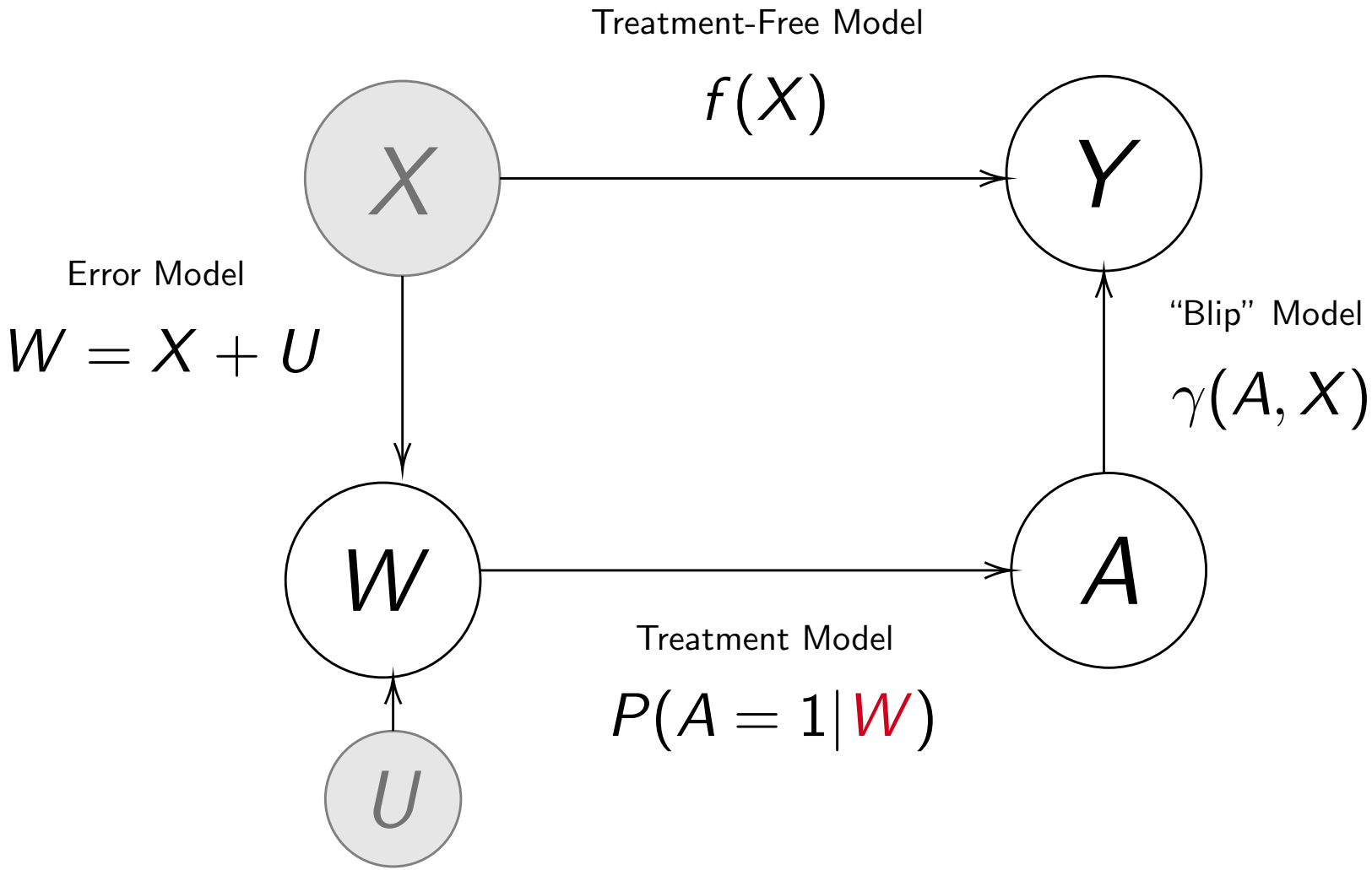

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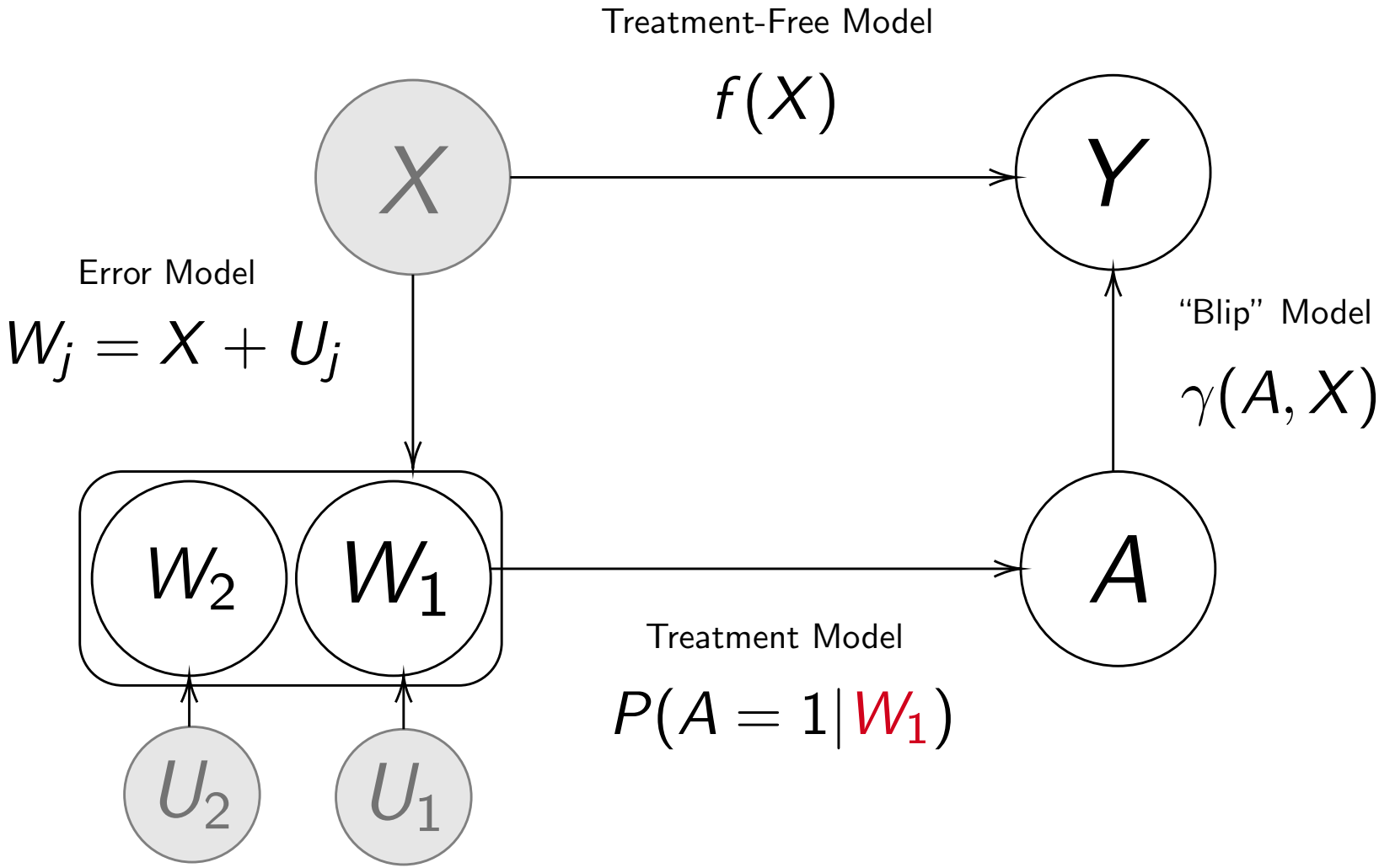
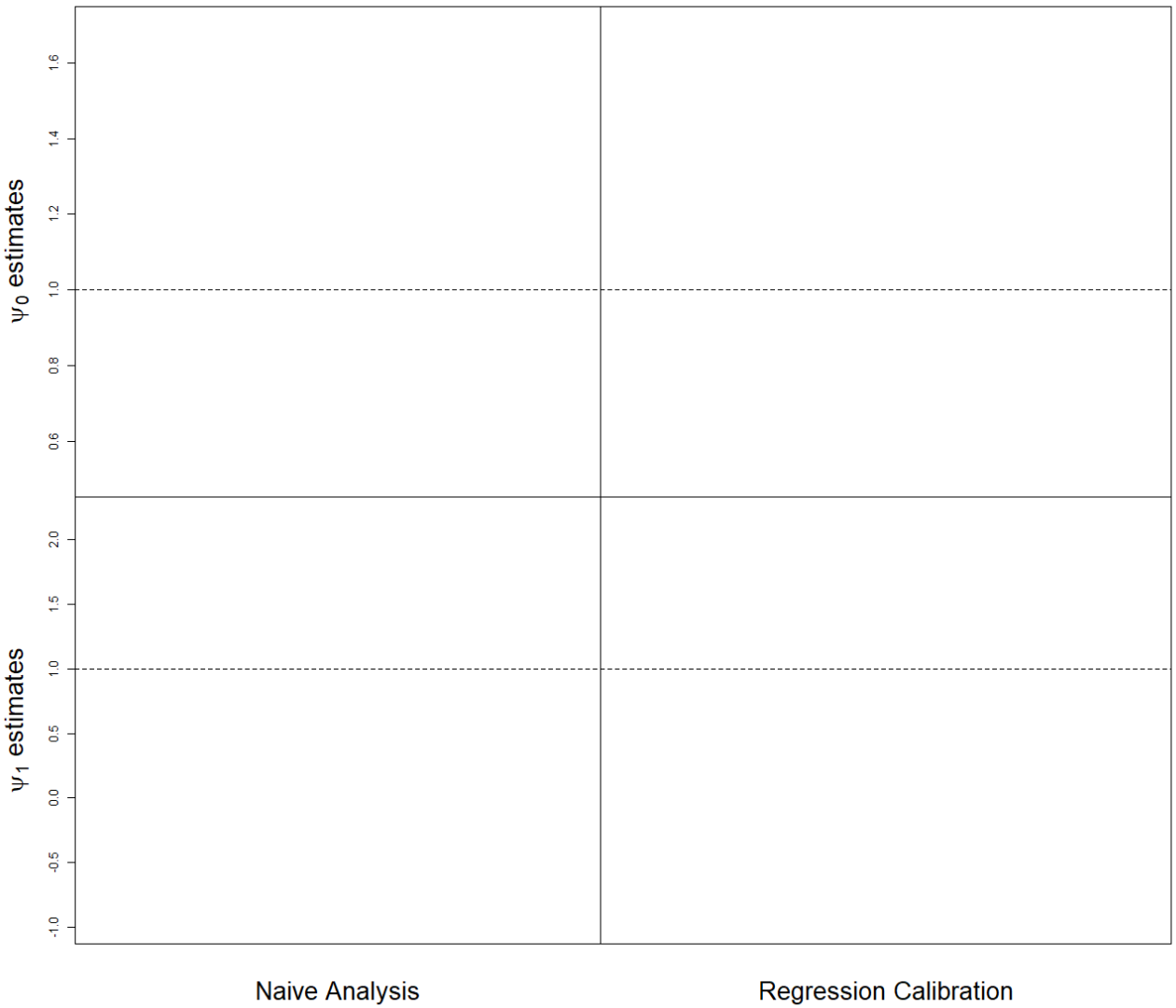


Solution: Regression Calibration

To reduce the bias, we replace X with an estimate of $E[X|W]$.

Simulation Results - Single Stage (Double Robustness)

$$Y = X - X^3 + \exp(X) + A(1 + X) + N(0, 1)$$



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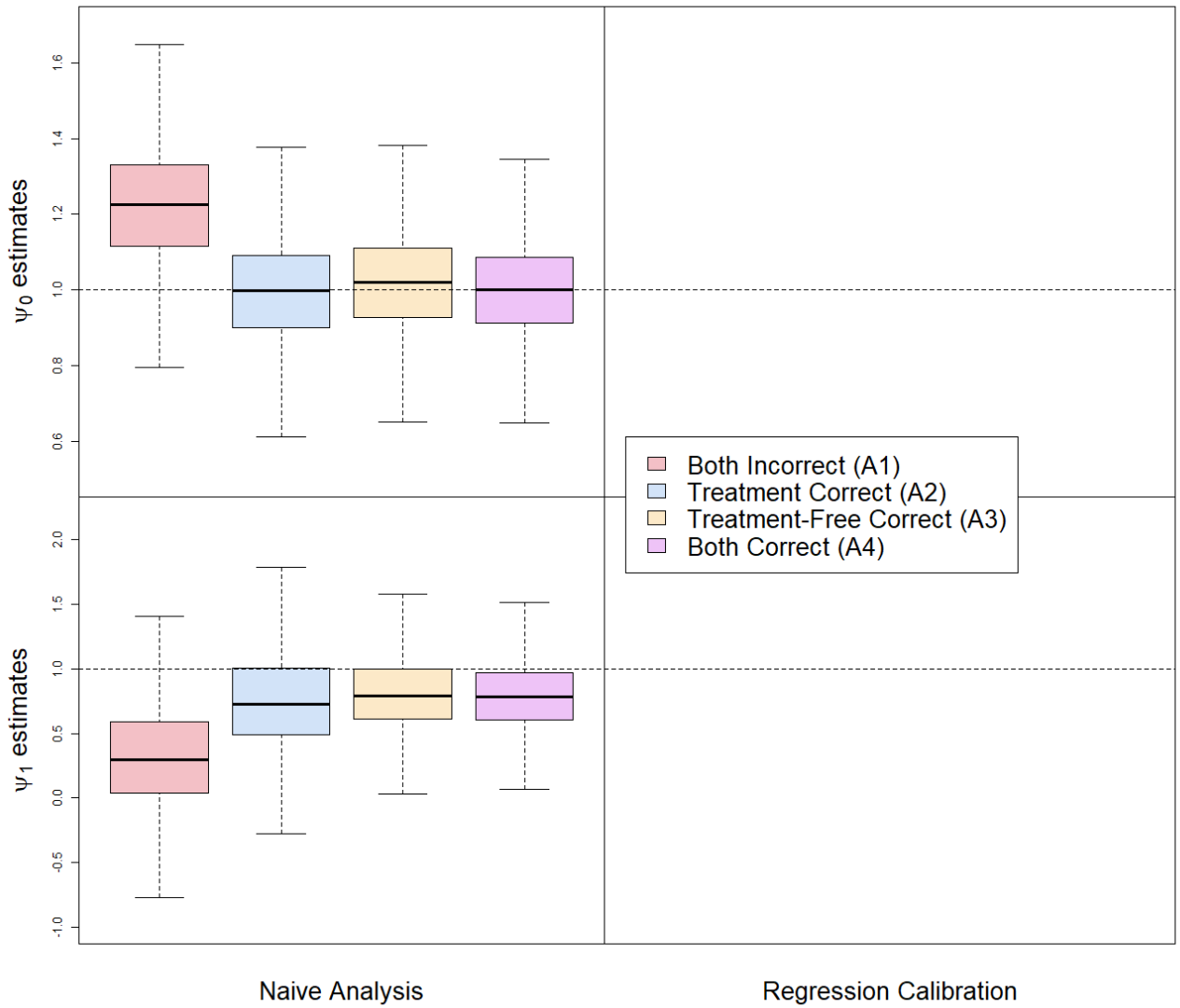

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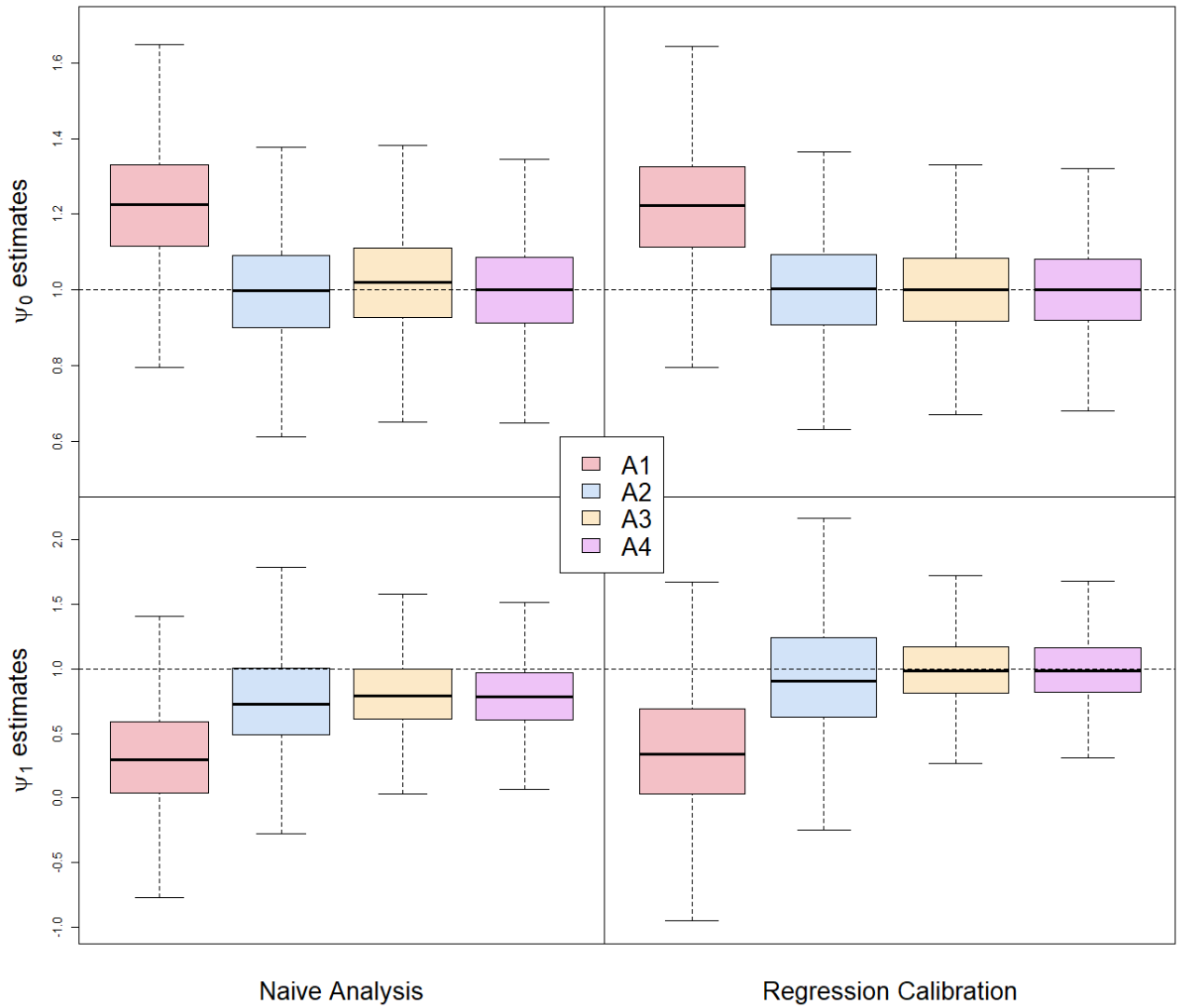
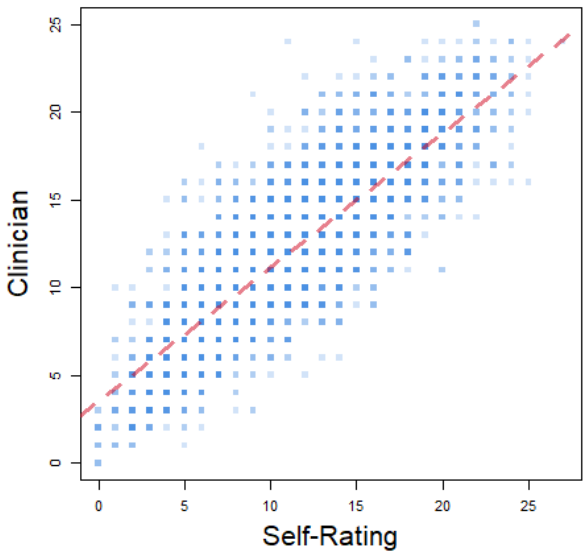
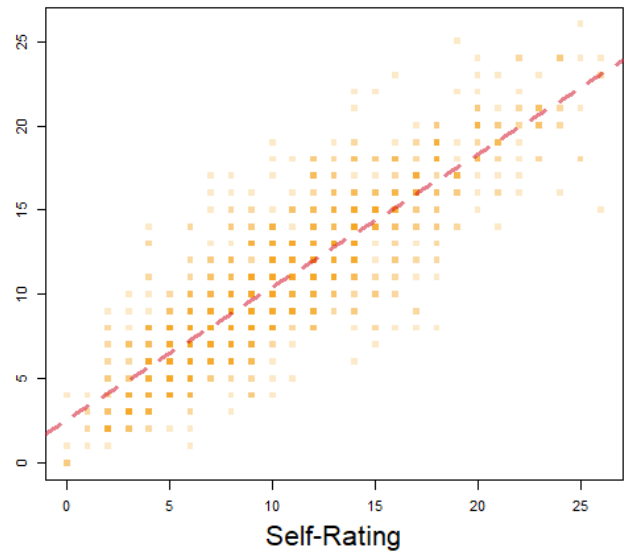


Application: STAR*D

- Sequenced Treatment Alternatives to Relieve Depression
- Multi-stage trial with treatment 'switching' or 'augmentation'
- Outcome: Quick Inventory of Depressive Symptomatology (QIDS) score (integers from 0-27)
  - Clinician measurements and self measurements are available
- Key variables: patient preference for different types of therapy, previous QIDS scores

STAR*D Results





Mean Differences

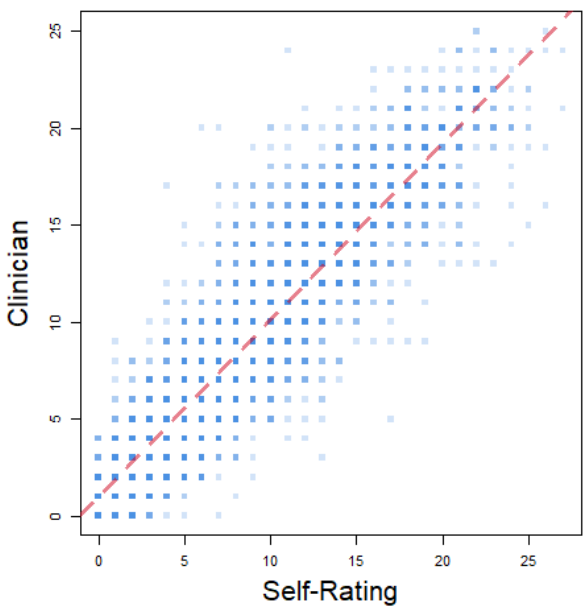
Stage 1 - Beginning: 0.9

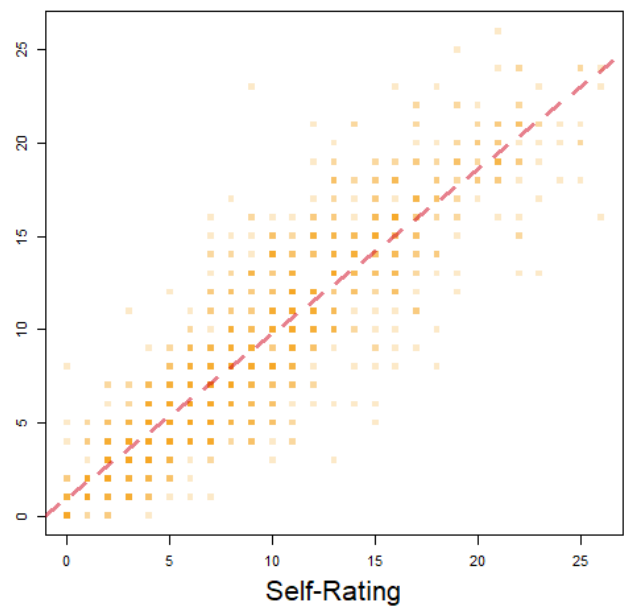
Stage 1 - End: 0.25

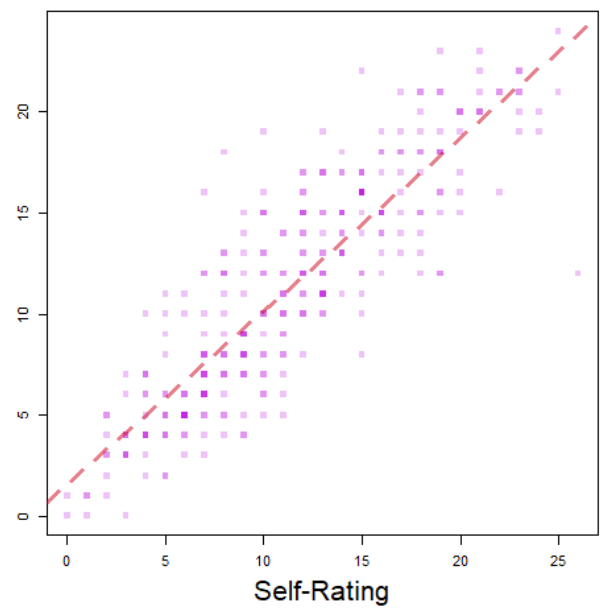
Stage 2 - Beginning: 0.32

Stage 2 - End: -0.12

Stage 3 - End: -0.03







Summary and Additional Work

- There are problems unique to the causal structure of personalized medicine in measurement error.
- In a simple one-stage DTR, comparatively simple techniques (regression calibration) effectively restore the error-free properties of estimators.

Extensions

- The same methods, with some additional considerations, also work to correct multistage estimation.

References and Acknowledgments

- **dWOLS**: M. P. Wallace and E. E. M. Moodie (2015). Doubly-robust dynamic treatment regimen estimation via weighted least squares. *Biometrics* **71(3)** 636-644.
- **RC and Measurement Error**: W. A. Fuller (1987). Measurement Error Models. *John Wiley & Sons, Inc.*

Contact: dylan.spicker@uwaterloo.ca