Dynamic Treatment Regimes and Interference: Recent Developments in Estimation and Implementation

Michael Wallace
Associate Professor
University of Waterloo

Slide deck available at: `mpwallace.github.io`

Motivating example:

- Goal: Reduce cigarette dependence.
- Intervention: e-cigarette use.
- Method: Personalized decision-making.
- Challenge: Interference.

A personalized treatment rule example:

"If age $\geq$ 35, recommend e-cigarettes, otherwise recommend alternative therapy."

- Question: How do we choose the best decision rule?

  Should age cut-off be 25, 35, 45?

The Data

Some hypothetical data:

Participant	Age	e-cigarette use?	Dependence at 3 months
1	53	No	57
2	25	Yes	35
3	28	Yes	40
4	41	Yes	21
5	27	No	42
...	...	...	...

Goal: Identify treatment A that optimizes $E[Y|X, A]$

$$\underbrace{E[Y|X,A]}_{\substack{\text{Expected outcome}\\ \text{(to be maximized)}}} \qquad A \in \{0,1\}$$

- We might propose the following model

$$E[Y|X,A;\beta,\psi] = \beta_0 + \beta_1 X + A(\psi_0 + \psi_1 X)$$

"Recommend e-cigarettes ($A = 1$) if $\psi_0 + \psi_1 X > 0$"

- More generally:

$$\overbrace{E[Y|X,A;\beta,\psi]}^{\substack{\text{Expected outcome}\\ \text{(to be maximized)}}} = \overbrace{G(X;\beta)}^{\text{Treatment-free}} + \overbrace{\gamma(X,A;\psi)}^{\text{Blip}}$$

- Simplifies focus: choose A that maximizes $\gamma(X,A;\psi)$.

- Suppose the true outcome model is:

$$E[Y|X,A;\beta,\psi] = \beta_0 + \beta_1 X + \beta_2 X^2 + A(\psi_0 + \psi_1 X)$$

- But we propose:

$$E[Y|X,A;\beta,\psi] = \beta_0 + \beta_1 X + A(\psi_0 + \psi_1 X)$$

- Problem: A depends on $X \implies \psi_0, \psi_1$ mis-estimated.
- Solution: Account for this dependency.

$$E[Y|X, A; \beta, \psi] = G(X; \beta) + \gamma(X, A; \psi)$$

- Three models to specify:
    1. Treatment-free model: $G(X; \beta)$.
    2. Blip model: $\gamma(X, A; \psi)$.
    3. Treatment model: $P(A = 1|X; \alpha)$.
- Estimate ψ via WOLS of Y on covariates in blip and treatment-free models, with weights $w = |A - P(A = 1|X; \hat{\alpha})| = |A - \pi(X)|$.

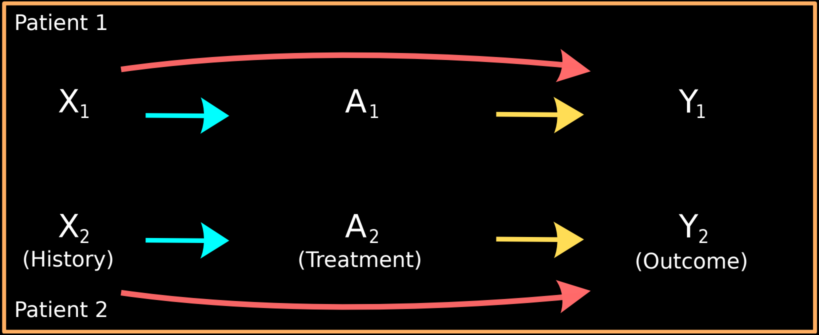
- Suppose the true outcome model is:

$$E[Y|X,A;\beta,\psi] = \beta_0 + \beta_1 X + \beta_2 X^2 + A(\psi_0 + \psi_1 X)$$

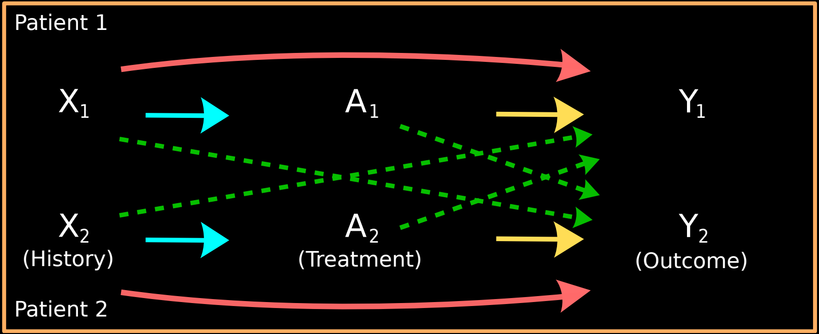
- But we propose:

$$E[Y|X,A;\beta,\psi] = \beta_0 + \beta_1 X + A(\psi_0 + \psi_1 X)$$

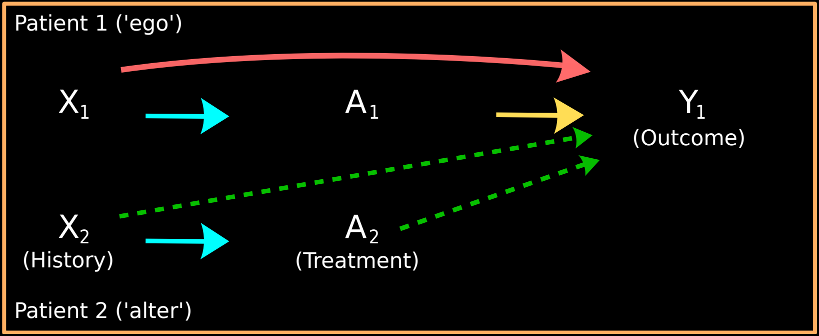
- WOLS with weights $w = |A - P(A=1|X;\hat{\alpha})| = |A - \pi(X)|$ will still yield consistent estimators of ψ_0, ψ_1.
- Estimators are "doubly robust": consistent if at least one of treatment-free or treatment components correctly specified.
- The blip must always be correct.



Challenge: Account for others.



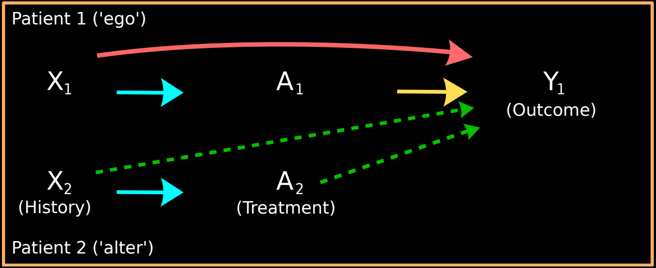
Challenge: Interference between neighbours.



Approach: Identify study unit ('ego') and neighbours ('alters').

- We might propose the following model

$$E[Y_1|X_1, X_2, A_1, A_2; \beta, \psi] = \beta_0 + \beta_1 X_1 + \beta_2 A_2 + A_1(\psi_0 + \psi_1 X_1 + \psi_2 A_2)$$



- More generally, let $\mathcal{N}_i$ denote neighbours of ego i.
- Let $t(A_{\mathcal{N}_i})$ = some function of neighbours' treatments, e.g.:
  - The number or proportion of treated neighbours.
  - The existence of a treated neighbour.
- Then can generalize outcome model to:

$$E[Y_i|\cdot] = \beta_0 + \beta_1 X_i + \beta_2 t(A_{\mathcal{N}_i}) + A_i(\psi_0 + \psi_1 X_i + \psi_2 t(A_{\mathcal{N}_i}))$$

Network propensity function for individual i with neighbours $\mathcal{N}_i$ and treated neighbours $S_{i,A}$:

$$\pi_{i,A_i,S_{i,A}}(X_i, \mathcal{N}_i, X_{\mathcal{N}_i}) = P(A_i \cap S_{i,A} | X_i, \mathcal{N}_i, X_{\mathcal{N}_i})$$

$$= \overbrace{\pi_i(X_i)^{A_i}(1 - \pi_i(X_i))^{1-A_i}}^{\text{Individual } i} \cdot \overbrace{\prod_{j \in S_{j,A}} \pi_j(X_j)}^{\substack{\text{Treated} \\ \text{neighbours}}} \cdot \overbrace{\prod_{j \in \mathcal{N}_i \setminus S_{i,a}} (1 - \pi_j(X_j))}^{\substack{\text{Untreated} \\ \text{neighbours}}}$$

dWOLS may be extended using the network propensity function, for example, WOLS for the outcome model

$$E[Y_i|X_i, X_{\mathcal{N}_i}, A_i, A_{\mathcal{N}_j}; \beta, \psi] = \beta_0 + \beta_1 X_i + \beta_2 t(A_{\mathcal{N}_i}) + A_i(\psi_0 + \psi_1 X_i + \psi_2 A_{\mathcal{N}_i})$$

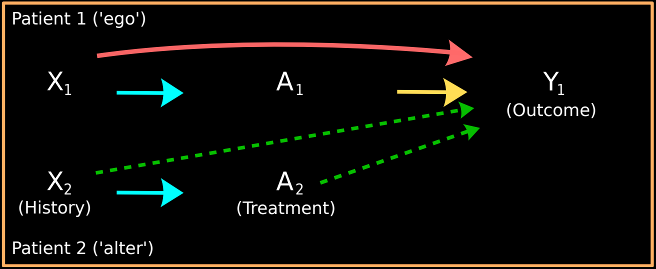
with weights

$$w_i = \overbrace{|A_i - P(A_i = 1|X_i = x_i)|}^{\substack{\text{Absolute weight} \\ \text{for unit } i}} \cdot \overbrace{\prod_{j \in \mathcal{N}_i} |A_j - P(A_j = 1|X_j)|}^{\substack{\text{Absolute weight} \\ \text{for neighbours}}}$$

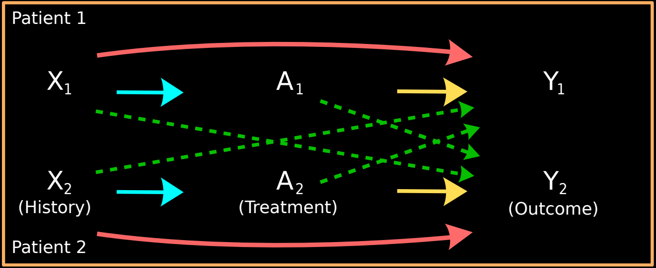
which retains the double robustness property.

Note: This is not the only viable weight function!

- Limitation: Assumes an ‘ego’ setup:



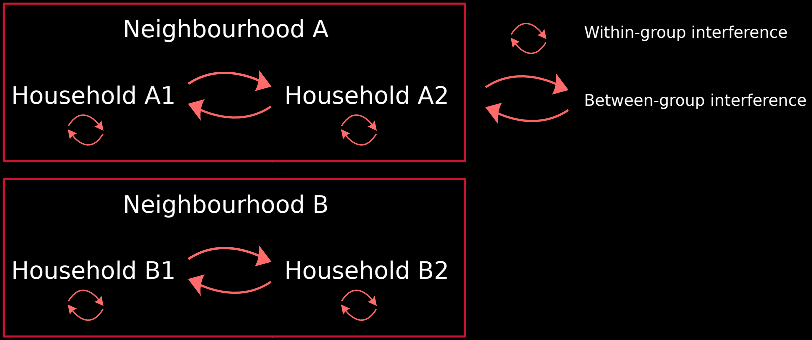
- Extension in a dyadic structure: identify and optimize a *dyad-health function*.



Extension: Ordinal Outcomes

- Limitation: Assumes a continuous outcome.
- dWOLS: Extended to numerous other outcome types in the absence of interference.
- dWPOM: A dWOLS extension for ordinal outcomes with interference, via proportional odds model.

Hierarchical structures of interference can evolve.



- **Interference** an important challenge for precision medicine.
- Progress in addressing interference for **continuous**, **ordinal**, and **utility-based** outcomes.
- Methods have been applied to the **Population Assessment of Tobacco Heatlh (PATH) Study**.
- Upcoming work to address **hierarchical structures**.
- Future work concerns logistical challenges such as **cost constraints** and **implementation of treatment regimes**.

Acknowledgments

Cong Jiang
cong.jiang@umontreal.ca
dWOLS extensions

Marzieh Mussavi Rizi
mmussavirizi@uwaterloo.ca
Dyad-health function

Alexandra Mossman
a2mossman@uwaterloo.ca
Hierarchical models

NSERC CRSNG
CIHR IRSC Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

- **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.
- **Network Propensity Weights (main result presented)**: C. Jiang, M. P. Wallace and M. E. Thompson (2023). Dynamic treatment regimes with interference. *Canadian Journal of Statistics* **51(2)** 469-502.
- **Ordinal outcomes**: C. Jiang, M. E. Thompson, and , M. P. Wallace (2024). Estimating dynamic treatment regimes for ordinal outcomes with household interference: Application in household smoking cessation. *arXiv:2306.12865, Statistical Methods in Medical Research (Accepted).*
- **Dyadic Networks**: M. Mussavi Rizi, J. A. Dubin, and M. P. Wallace (2023). Dynamic Treatment Regimes on Dyadic Networks. *Statistics in Medicine (in review, please contact me!)*.

michael.wallace@uwaterloo.ca
mpwallace.github.io