Identification conditions for the effect of treatment in the treated

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The average treatment effect (ATE) and the average treatment effect in the treated (ATT) are oft-targeted parameters of interest in causal inference.

This presentation will:

1. Provide an example where the ATE and ATT differ.
2. Describe conditions sufficient to point-identity the ATE and the ATT.
3. Demonstrate a simulation study where we vary the identification conditions.

Motivation: tPA effect heterogeneity

Results of Multivariable Logistic Regression, Propensity Matching, Propensity Adjustment, and Propensity-based Weighting under Conditions of Nonuniform Effect[1]

Tobias Kurth, Alexander M. Walker, Robert J. Glynn, K. Arnold Chan, J.Michael Gaziano, Klaus Berger, and James M. Robins

Kurth et al. (2006) Background

Investigated the effect of tissue-type plasminogen activator (tPA) therapy on in-hospital ischemic stroke mortality

- tPA is the gold standard for ischemic stroke patients
- Often contraindicated

Data source

- The Stroke Registry of Northwest Germany (2000 - 2001)

Compared 5 methods of treatment effect estimation

1. Multivariable logistic regression adjustment
2. PS matching
3. PS regression adjustment
4. IPTW
5. SMR weights

Bootstrapped for (weighted) standard error estimates.

2006 Results: Propensity Scores

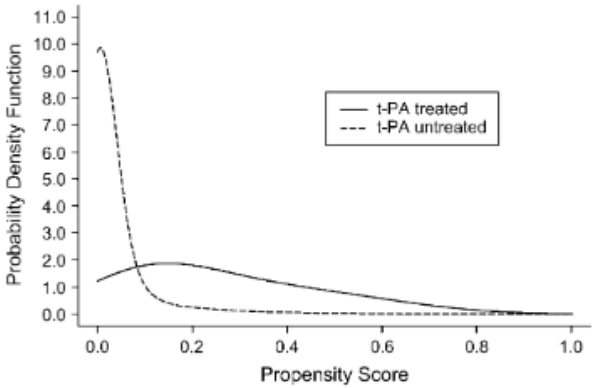

Figure 1: Probability density function of the propensity score for the 212 tissue plasminogen activator (t-PA)-treated and the 6,057 t-PA untreated ischemic stroke patients registered in a German stroke regisry between 2000 and 2001

2006 Results: Propensity Scores

Percentile	Treated (n = 212)				Not treated (n = 6,057)				Empirical OR*
	Score†	No.	Deaths		Score†	No.	Deaths		
			No.	%			No.	%	
99 to 100	0.5809	36	3	8.3	0.5474	26	7	26.9	0.25
95 to <99	0.3143	73	13	17.8	0.2912	178	27	15.2	1.21
90 to <95	0.1393	55	8	14.6	0.1363	258	19	7.4	2.14
75 to <90	0.0585	31	3	9.7	0.0459	910	82	9.0	1.08
50 to <75	0.0115	10	4	40.0	0.0084	1,558	87	5.6	11.27
25 to <50	0.0017	5	2	40.0	0.0014	1,561	54	3.5	18.60
10 to <25	0.0004	2	1	50.0	0.000267	940	36	3.8	25.11
5 to <10		0	0	0	0.000066	313	6	1.9	
1 to <5		0	0	0	0.000027	251	8	3.2	
0 to <1		0	0	0	0.000007	62	1	1.6	
Overall	0.2521	212	34	16.0	0.0262	6057	327	5.4	3.35

* Propensity-stratum-specific-treatment–mortality odds ratio.
† Mean propensity score in percentile.

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2006 Results: Comparison of effect estiamtes

Untrimmed

	No.	OR*	95% CI*
Crude model	6,269	3.35	2.28, 4.91
Multivariable model†	6,269	1.93	1.22, 3.06
Matched on propensity score	406	1.17	0.68, 2.00
Regression adjusted with propensity score			
Propensity score, continuous	6,269	1.53	0.95, 2.48
Multivariable†	6,269	1.85	1.13, 3.03
Propensity score, deciles	6,269	1.76	1.13, 2.72
Multivariable†	6,269	1.96	1.20, 3.20
Weighted models			
IPTW*	6,269	10.77	2.47, 47.04
SMR* weighted	6,269	1.11	0.67, 1.84

Trimmed

	No.	OR*	95% CI*
Crude model	978	1.36	0.84, 2.19
Multivariable model†	978	1.30	0.74, 2.31
Matched on propensity score	338	0.89	0.49, 1.63
Regression adjusted with propensity score			
Propensity score, continuous	978	0.99	0.58, 1.68
Multivariable†	978	1.29	0.73, 2.29
Propensity score, deciles	978	1.24	0.75, 2.03
Multivariable†	978	1.31	0.74, 2.33
Weighted models			
IPTW*	978	1.09	0.62, 1.93
SMR* weighted	978	0.82	0.47, 1.44

2006: Conclusion

- Low propensity patients different from others wrt death under treatment.
- Treatment effects are sensitive to the (implicit or explicit) weighting system in the presence of hetereogeneity.
  - And answer different questions.

Motivating Example: 2024 (in-progress)

We updated the analysis using 2020-2021 data from the same stroke registry.

Updates:

1. Focused on risk ratios
2. SMR & IPT weighted effect estimates.
3. Utilized M-estimation. (WHY?)

2024 Analysis

- Estimated propensity score using logistic regression.
  - *Some changes to variables.*
- IPT weights to target ATE
- SMR weights to target ATT
- Hajek & Horvitz Thompson estimators for the IPT weighted risks.

2024 Analysis: Hajek vs. Horvitz-Thompson

Horvitz-Thompson

$$\hat{Pr}(Y^a = 1) = \frac{1}{n}\sum_{i=1}^{n} I(A_i = a) Y_i \hat{w}_i$$

Hajek

$$\hat{Pr}(Y^a = 1) = \frac{\sum_{i=1}^{n} I(A_i = a) Y_i \hat{w}_i}{\sum_{i=1}^{n} \hat{w}_i I(A_i = a)}$$

Why both?

2024 Results: Analysis Sample

- 150,029 ischemic stroke patients
- Sampled 6,000
- 20% recieved t-PA treatment.
- 5% overall mortality

2024 Results: Propensity Scores

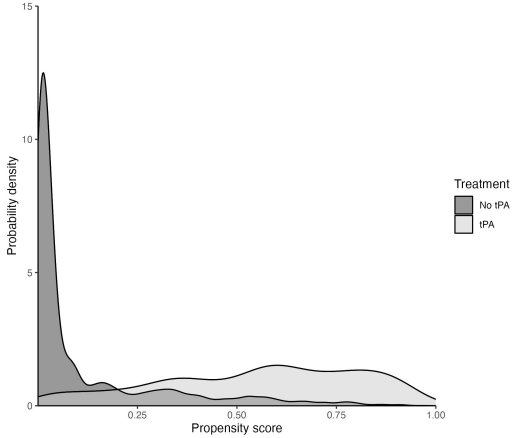

Figure 2: Probability density function of the propensity score by treatment status

Table 1: tPA treatment effect on in-hospital mortality by propensity score percentile.

Percentile	RR
95 to 100	0.67
90 to <95	0.63
75 to <90	0.71
50 to <75	1.24
25 to <50	1.04
10 to <25	3.08
5 to <10	13.59
0 to <5	

2024 Results: Comparison of Effect Estimates

Table 2: Estimated treatment effect of tPA on in-hospital stroke mortality

	Risk Ratio	95% CI
Crude	1.51	1.17, 1.95
IPT	2.27	0.89, 5.76
SMR	0.82	0.55, 1.21

2024 Conclusions

- Effect of tPA on in-hospital mortality shows considerable treatment effect heterogeneity.
- The effect estimate targeting the ATE indicates tPA harm
- The effect estimate targeting the ATT indicates tPA benefit

What's the right question?

What's identifiable?

Identification conditions

A = treatment (1: treated, 0: untreated), W = set of measured confounders, Y^a = potential outcome under treatment $A = a$

Average treatment effect (ATE)[2]

1. Causal consistency: If $A_i = a, Y_i = Y_i^a$
2. Conditional exchangeability: $Y^a \perp A|W$
3. Positivity: $Pr(A = a|W = w) > 0$, for all w where $f(w) > 0$

Average treatment effect in the treated (ATT)

1. Causal consistency: If $A_i = a, Y_i = Y_i^a$
2. Partial conditional exchangeability: $Y^{a=0} \perp A|W$
3. Partial positivity: $Pr(A = a|W = w) > 0$, for all w where $f(w|A = 1) > 0$

Simulation

- Three populations, with confounder W prevalence: 0.25, 0.5, 0.75
- Treatment assignment scenarios (marginal 0.2):
  - Complete positivity:

$$0 < P(A = 1|W = w) < 1$$

  - Partial positivity (in treated):

$$0 < P(A = 1|W = 1) < 1$$

$$P(A = 1|W = 0) = 0$$

Simulation

- Treatment effect: risk ratio of 0.8.
- Untreated outcome incidence 0.01 (W=0) to 0.08 (W=1).
- Estimated the ATE and ATT.
  - Hajek and Horvitz-Thompson estimators for the ATE
  - *Why?*
- Utilized M-estimation
- Simulation performance measures: bias, ASE, ESE, MSE, 95% CI coverage

Simulation Results (Hajek)

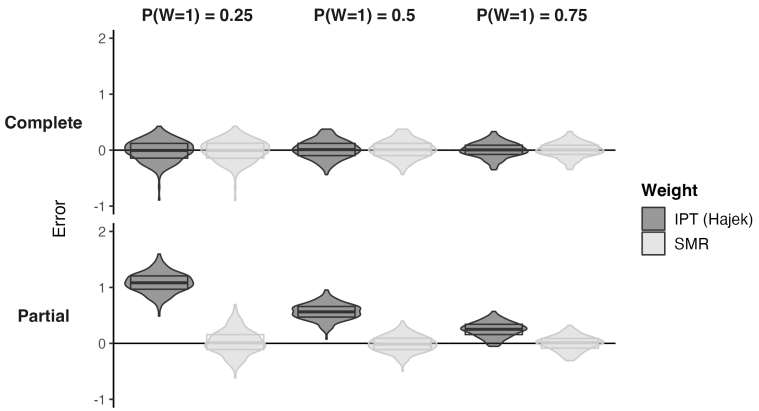

Figure 3: Bias of the log risk ratio in simulated populations under complete exchangeability and partial exchangeability with varying marginal distributions of W.

Simulation Results (Horvitz-Thompson)

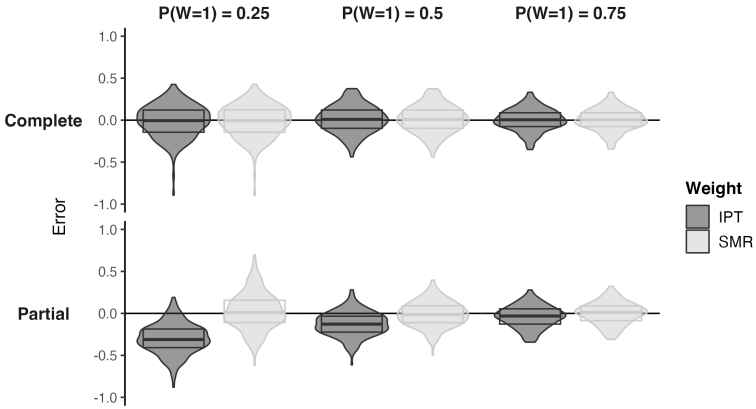

Figure 4: Bias of the log risk ratio in simulated populations under complete exchangeability and partial exchangeability with varying marginal distributions of W.

Conclusions

- Targeting the ATE when causal identification conditions are not met results in biased effect estimates.
- The direction and magnitude of the bias depends on the selected IPT weighted estimator.
- If partial causal identification conditions are met in one group, can consistently estimate the treatment effect for that group.

Still working on:

- Articulating discrepancies by weighted risk estimators (Hajek vs. Horvitz-Thompson)
- Running all 5,000 simulations

Bonus slide

$$\psi(O_i, \hat{\theta}) = \begin{bmatrix} A_i - expit(\hat{\theta}_1 + \hat{\theta}_2 W_i) \\ (A_i - expit(\hat{\theta}_1 + \hat{\theta}_2 W_i))W_i \\ A_i Y_i \ \widehat{w}_{IPT,i} - \hat{\theta}_3 \\ (1 - A_i) Y_i \ \widehat{w}_{IPT,i} - \hat{\theta}_4 \\ A_i \ \widehat{w}_{IPT,i}(Y_i - \hat{\theta}_5) \\ (1 - A_i)\widehat{w}_{IPT,i}(Y_i - \hat{\theta}_6) \\ A_i \widehat{w}_{SMR,i}(Y_i - \hat{\theta}_7) \\ (1 - A_i)\widehat{w}_{SMR,i}(Y_i - \hat{\theta}_8) \\ ln\left(\frac{\hat{\theta}_3(1 - \hat{\theta}_4)}{\hat{\theta}_4(1 - \hat{\theta}_3)}\right) - \hat{\theta}_9 \\ ln\left(\frac{\hat{\theta}_3}{\hat{\theta}_4}\right) - \hat{\theta}_{10} \\ ln\left(\frac{\hat{\theta}_5(1 - \hat{\theta}_6)}{\hat{\theta}_6(1 - \hat{\theta}_5)}\right) - \hat{\theta}_{11} \\ ln\left(\frac{\hat{\theta}_5}{\hat{\theta}_6}\right) - \hat{\theta}_{12} \\ ln\left(\frac{\hat{\theta}_7(1 - \hat{\theta}_8)}{\hat{\theta}_8(1 - \hat{\theta}_7)}\right) - \hat{\theta}_{13} \\ ln\left(\frac{\hat{\theta}_7}{\hat{\theta}_8}\right) - \hat{\theta}_{14} \end{bmatrix}$$

References

1. Kurth T, Walker AM, Glynn RJ, et al. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of nonuniform effect. *American Journal of Epidemiology*. 2006;163(3):262-270. doi:10.1093/aje/kwj047
2. Hernán MA, Robins JM. Estimating causal effects from epidemiological data. *Journal of Epidemiology and Community Health*. 2006;60(7):578-586. doi:10.1136/jech.2004.029496