PQHS 500
Project Abstract

Examining the Effect of Distance to Mammography Facilities on Late-stage Diagnosis of Breast Cancer

Weichuan Dong, Uriel Kim, Siran Koroukian, Johnie Rose

Background
Women diagnosed with late-stage breast cancer (LSBC) have a greater mortality rate than those with early-stage diagnosis. The availability of screening facilities is a key factor in breast cancer stage at diagnosis. Generally, if the distance from a residential location to its nearest mammography facility is large, the difficulty of individuals from this location getting the screening increases. However, it is still unclear whether and how much does the spatial access to screening, measured as distance or travel time, contributes to LSBC diagnosis when controlling other characteristics associated with the patient. In addition, differences in individual and neighborhood characteristics often form very different groups of people, making the effect of differences in distance to screening facility on LSBC less comparable among those people if no adjustment or matching is made.

Objective
The objective of this study is to determine whether distance from a patient's residential location to the nearest mammography facility leads to LSBC diagnosis. The exposure is patients' longer distance to facility compared to shorter distance to facility. Late-stage diagnosis is the outcome compared to early-stage at diagnosis. Out researcher question is: Does a woman live farther away from the nearest mammography facility lead to the diagnosis of late-stage breast cancer?

Methods

The study population includes women who were newly diagnosed with invasive breast cancer with age between 45 to 70 in 2016 in Ohio. We identified 5 465 women from the Ohio Cancer Incidence Surveillance System (OCISS). We calculated the road distance between patient residential locations and the nearest mammography facility with ArcGIS, a geographic information system software. After defining long distant and short distance by quintile, we performed multiple propensity score strategies to match the short distance group to the long-distance group, including 1 to 1 match with and without replace, weighting by propensity score, double-robust weighting and adjusting by propensity score, and generalized boosted modeling for propensity score. We performed separate analyses for various subgroups. Finally, we found no statistically significant effect of distance to mammography facility on stage at diagnosis of breast cancer in the overall group and on any of the subgroups.

Conclusion

In a rust belt state like Ohio, people living in urban areas are more likely to be disadvantaged in many health outcomes. Urban-rural disparities are so significant that people living in different areas are hard to be matched by propensity scores. Even with good quality of matching, the model is still easy to be biased by unmeasured factors that characterize the urban-rural divide. In addition, other factors, such as insurance coverage, play a more important role than distance on the stage of diagnosis of breast cancer. Also, the availability of transportation has greatly shorted the distance between any two locations in the world, presenting a distance decay effect. Nevertheless, spatial factors are still critical in addressing health disparities. Future studies should look into spatial factors in the neighborhood level to investigate disparities in the stage of cancer diagnosis.

Examining the Effect of Distance to Mammography Facilities on Late-stage Diagnosis of Breast Cancer

Weichuan Dong
Health Services Research and Spatial Analyst
Department of Population and Quantitative Health Sciences
School of Medicine, Case Western Reserve University

PQHS 500
Design and Analysis of Observational Studies

4/23/2020

Background

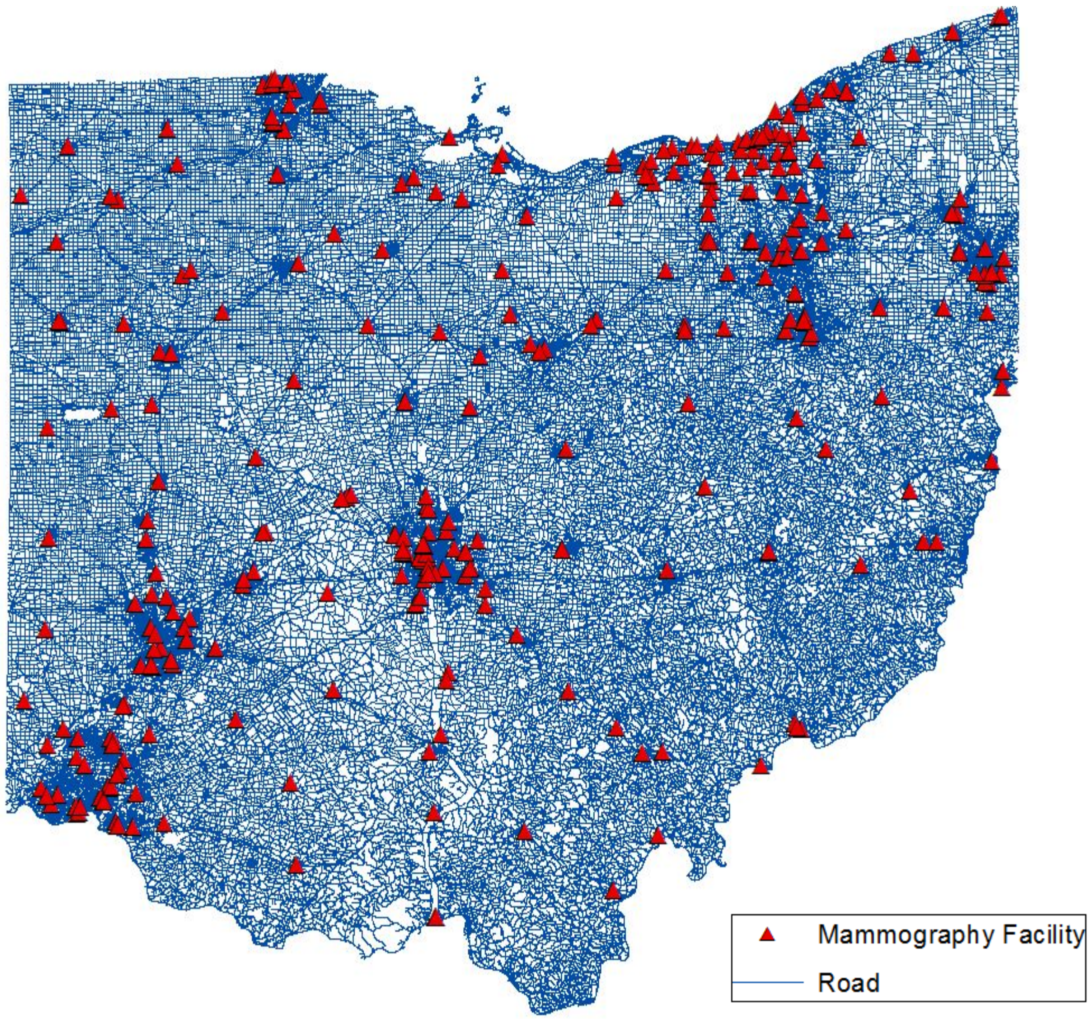
- Female Breast Cancer in 2019
  - In Ohio: 10,240 new cases – death rate 16.7% (Ohio) vs 15.5% (U.S.)
- Early diagnosis – better chances of survival
  - Mammography screening
  - Awareness of risk factors and symptoms

Source: U.S. FDA website

Background

Mammography Facilities in Ohio

- Total number: 335
- Disproportionate availability of facilities across space



Research Question

Objective

To Explore the effect of distance from patient residential locations to the nearest mammography facilities on later stage at diagnosis of breast cancer.

Does longer distance to mammography facility lead to later stage diagnosis of breast cancer?

Data Source and Participants

- Ohio Cancer Incidence Surveillance System (OCISS)
  - 2016 newly diagnosed with local, regional, or distant stage of breast cancer
  - Women with age between 45 and 70
  - Number of participants: 5 465
- Mammography Facility Database (FDA)
- U.S. Census (Contextual level variables)

Exposure and Outcome

Exposure

Road distance calculated from residential location to the nearest facility with ArcGIS

Treatment: longer distance (1043 cases)

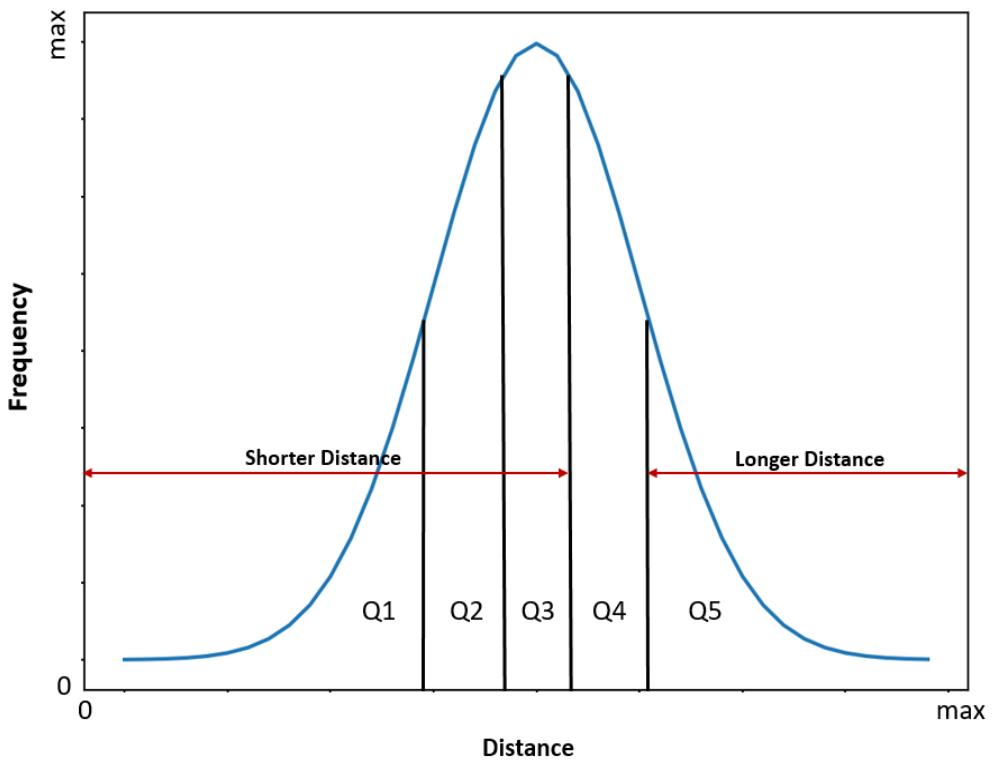
Control: shorter Distance (3128 cases)

Outcome

Late-stage (regional and distant)

Early-stage (local)

Distances classified by quintile



Covariates

- Demographic and socioeconomic
  - age, race, ethnicity, marital status, insurance, occupation
- Contextual:
  - Area Deprivation Index (ADI)- level of neighborhood deprivation at block group level
  - Rural-urban commuting area code (RUCA) – rankings from 1 to 10 measuring population density, urbanization, and daily commuting of the census tract
  - Percent of women greater than 16 years of age with high school diploma
  - Percent of households below poverty level
  - Percent of households with no vehicle for workers

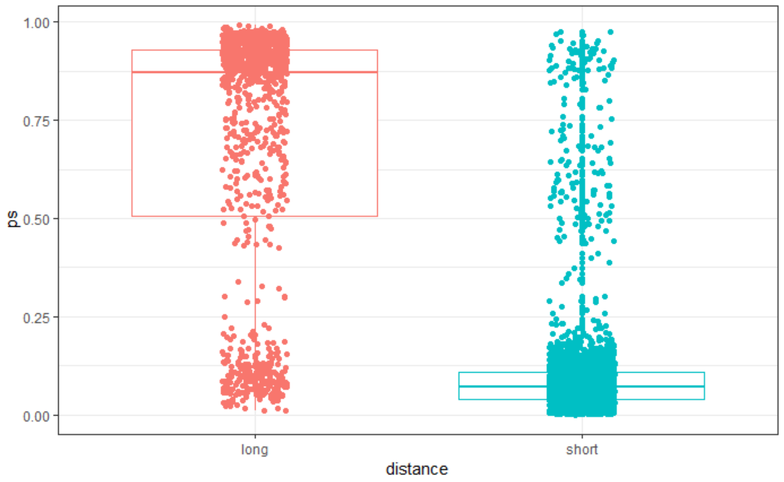
Table 1

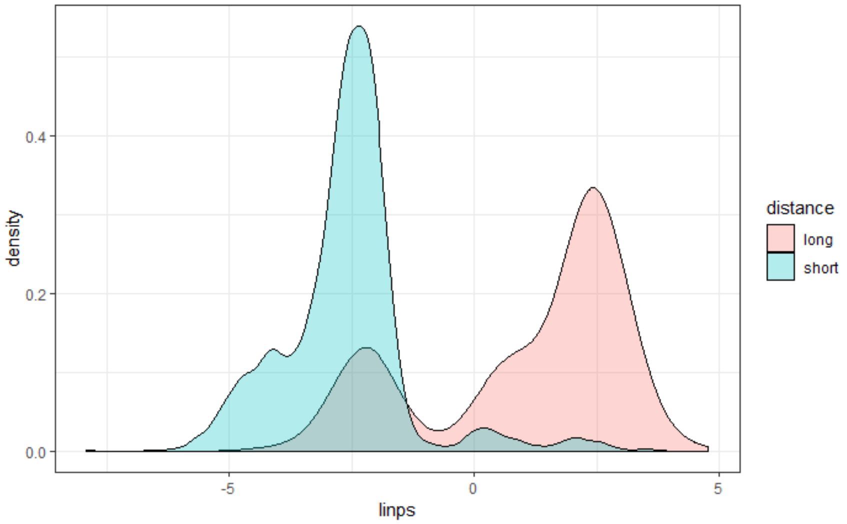
Patient Characteristics	Long	Short	p
n	1043	3128	
Stage = Late (%)	358 (34.3)	1062 (34.0)	0.86
Age at diagnosis (mean (SD))	58.71 (6.92)	58.91 (6.80)	0.4
Race and Ethnicity (%)			<0.01
Non-Hispanic Black	*	489 (15.6)	
Non-Hispanic White	1024 (98.2)	2538 (81.1)	
Other	*	101 (3.2)	
Marital Status = Married/Partnered (%)	777 (74.5)	1825 (58.3)	<0.01
Insurance (%)			<0.01
Medicaid	75 (7.2)	330 (10.5)	
Medicare	309 (29.6)	876 (28.0)	
Other Insurance	63 (6.0)	119 (3.8)	
Private	585 (56.1)	1745 (55.8)	
Uninsured	11 (1.1)	58 (1.9)	
Occupation (%)			<0.01
Education	59 (5.7)	191 (6.1)	
Health related	98 (9.4)	326 (10.4)	
Mangaer, Business, Science, Art	80 (7.7)	307 (9.8)	
Retired	85 (8.1)	184 (5.9)	
Sale, Office, Service, Labor	304 (29.1)	914 (29.2)	
Unemployed, Home, Disabled	147 (14.1)	276 (8.8)	
Unknown	270 (25.9)	930 (29.7)	

Patient Characteristics	long	short	p
n	1043	3128	
Pct women high school diploma (mean (SD))	90.02 (6.19)	90.97 (6.91)	<0.01
Pct women below Poverty (mean (SD))	10.85 (5.92)	14.03 (11.79)	<0.01
Pct household with vehicle (%)			<0.01
1-very high	239 (22.9)	547 (17.5)	
2-high	276 (26.5)	552 (17.6)	
3-medium	195 (18.7)	624 (19.9)	
4-low	200 (19.2)	661 (21.1)	
5-very low	133 (12.8)	744 (23.8)	
Rural Urban Communting Area (%)			<0.01
1-Metro core	202 (19.4)	2656 (84.9)	
2-Metro Commuting	405 (38.8)	51 (1.6)	
3-Micro Core	39 (3.7)	298 (9.5)	
4-Micro Commuting	222 (21.3)	14 (0.4)	
5-Small Town/Rural	175 (16.8)	109 (3.5)	
Area Deprivation Index (mean (SD))	93.59 (11.57)	95.01 (20.72)	0.04

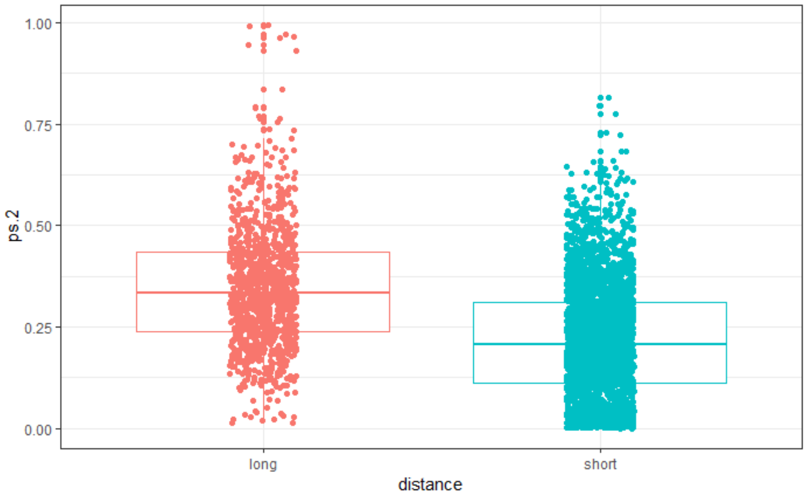
Propensity Score Distribution

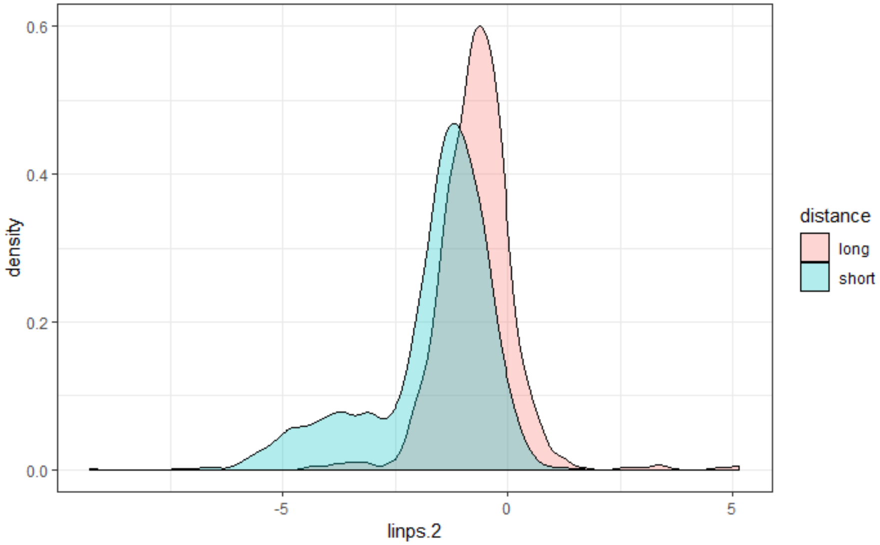
With RUCA as a covariate





Without RUCA as a covariate





1:1 Match Without Replacement

		With RUCA	Without RUCA
Rubin's Rule 1	before match	167.94	75.05
	after match	121.44	6.94
Rubin's Rule 2	before match	2.47	0.38
	after match	2.67	1.42

We decided not to include RUCA as a covariate!

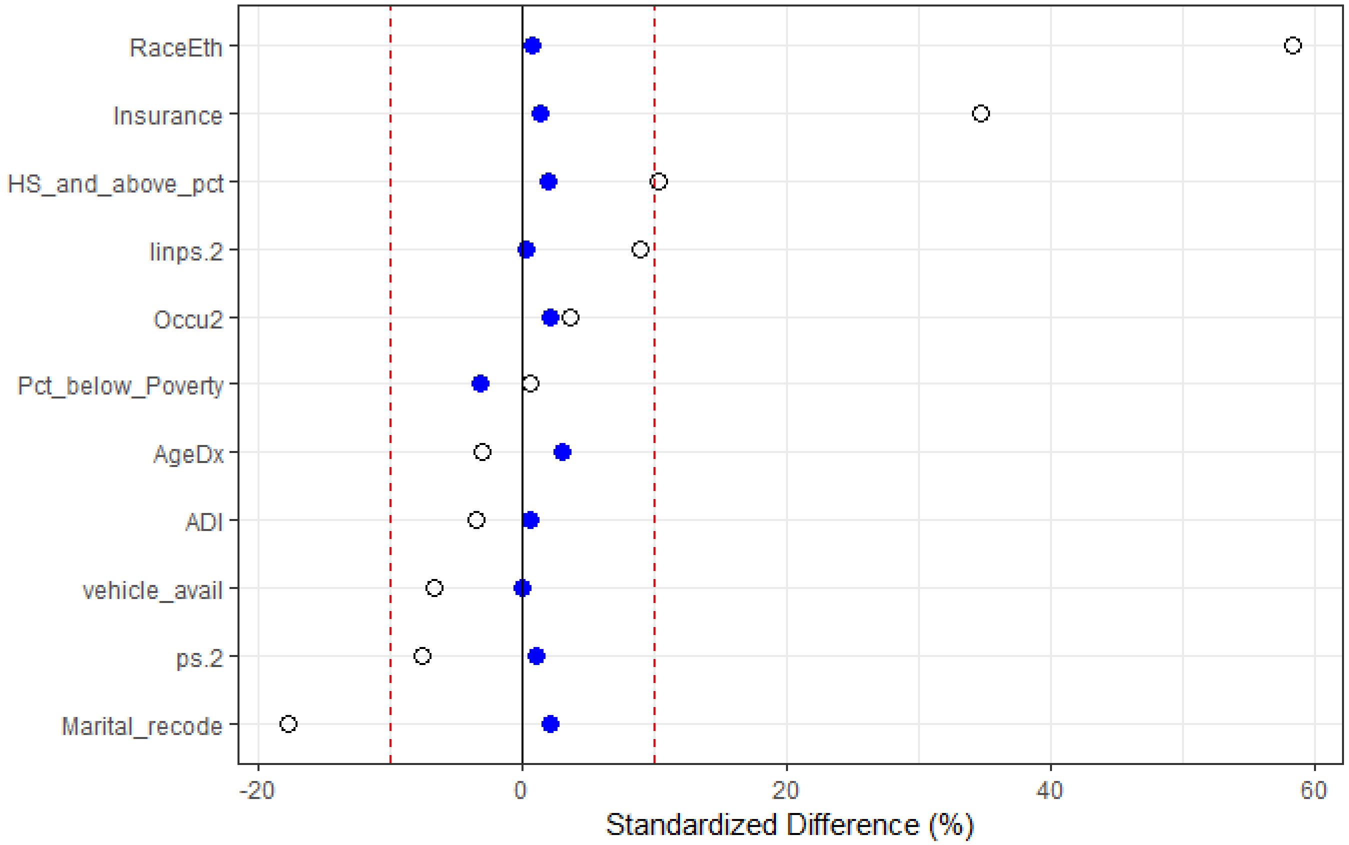
Unadjusted Model

OR: 1.02 (95% 0.88, 1.17)

Matched Model

OR: 1.03 (95% CI: 0.86, 1.24)

Covariate Balance Without RUCA

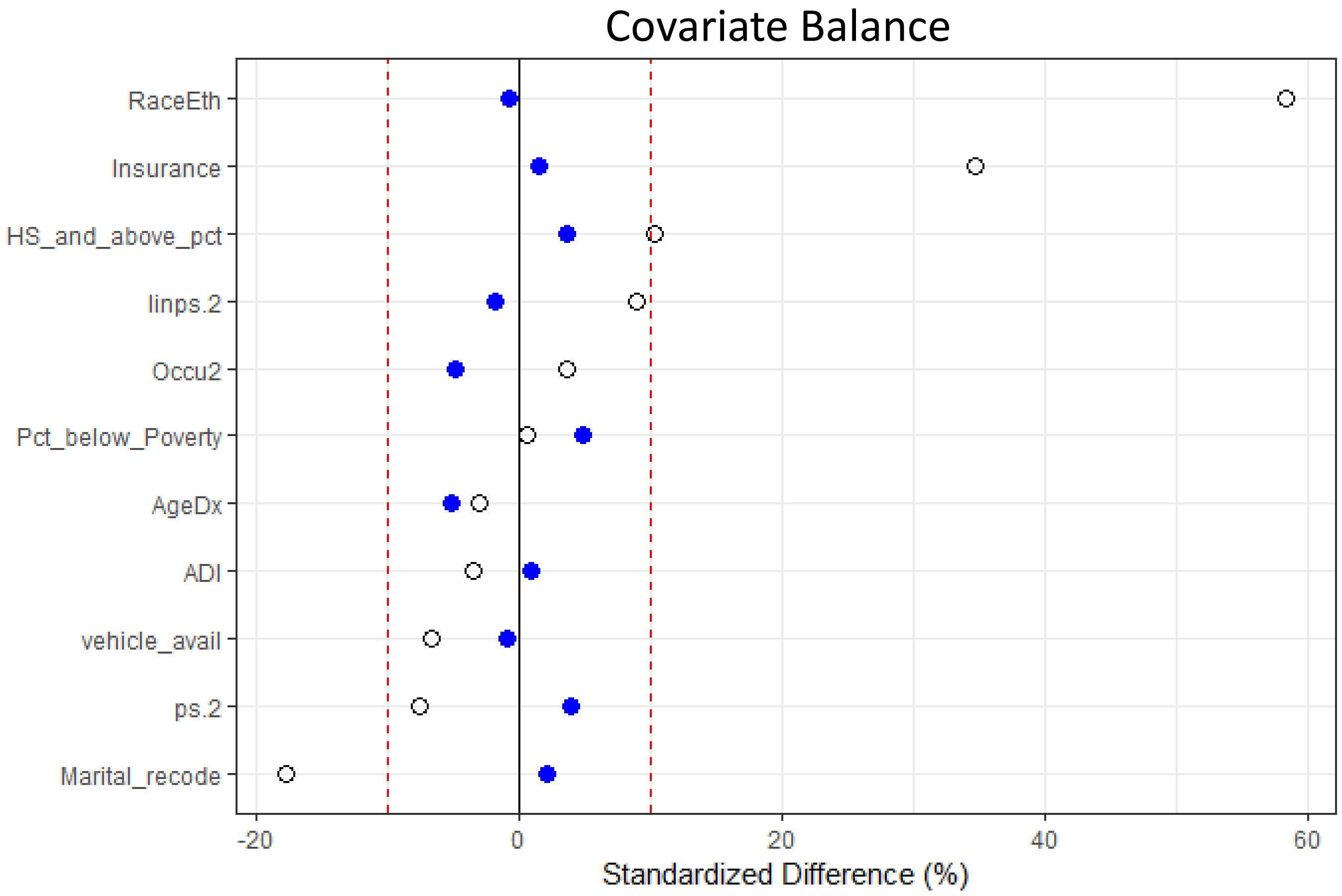


1:1 Match With Replacement

Rubin's Rule 1	before match	167.94
	after match	2.27
Rubin's Rule 2	before match	2.47
	after match	1.22

Matched Outcome

OR: 1.00 (95% CI: 0.84, 1.20)

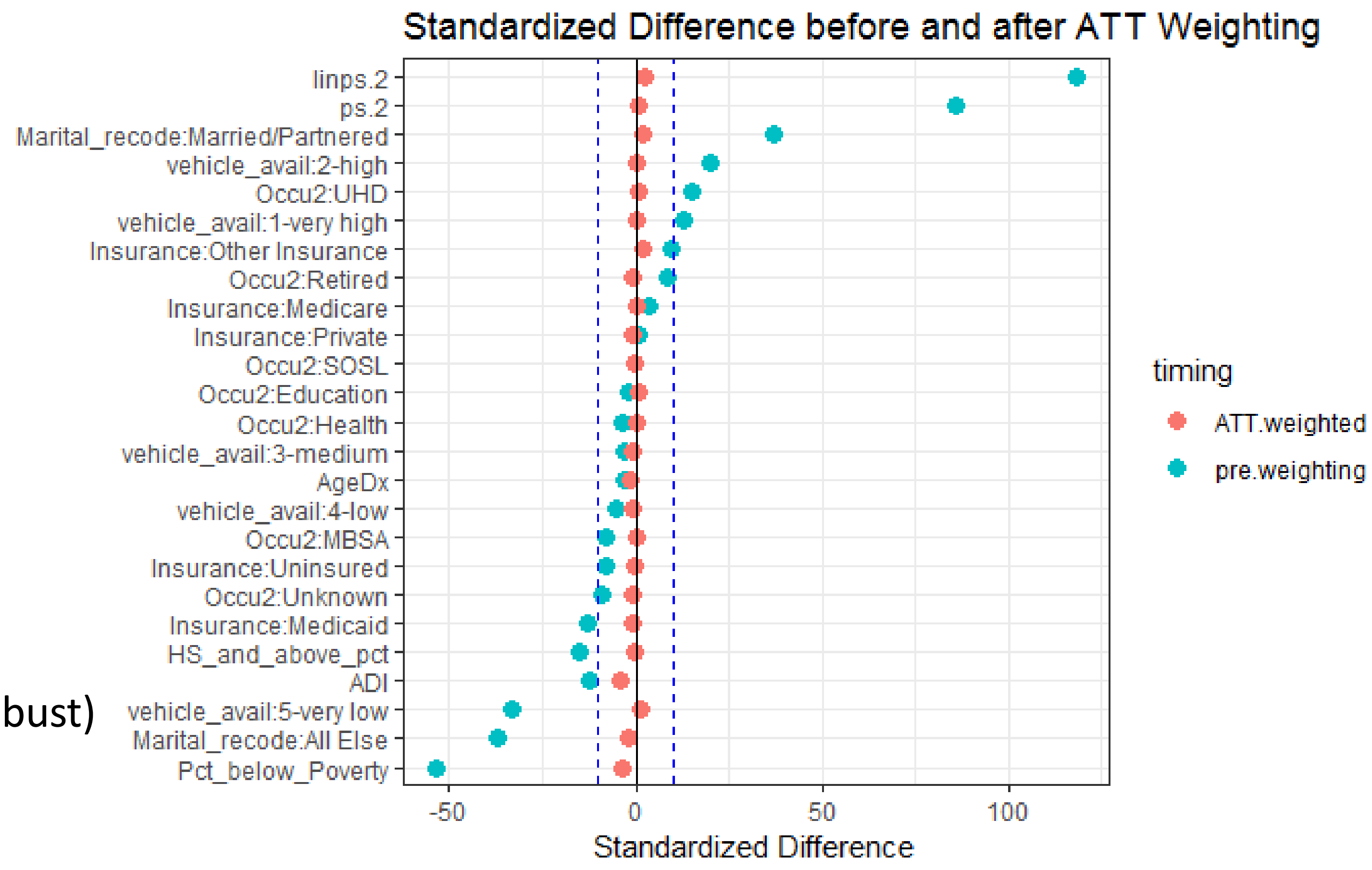


ATT propensity score weighting

Rubin's Rule 1	before match	167.94
	after match	2.3
Rubin's Rule 2	before match	2.47
	after match	1.21

Outcome

- Weighting
  OR: 1.08 (95% CI: 0.91, 1.27)
- Weighting w/ adjustment for linear ps (Double-Robust)
  OR: 1.07 (95% CI: 0.84, 1.37)



Analysis for Subgroups

		Subgroup			
Method	**Measure**	**Medicaid & Uninsured**	**Medicare & Private**	**low vehicle availability**	**Non-Metro Area**
1:1 match with replacement	Rubin's Rule 1	Yes	yes	yes	yes
	Rubin's Rule 2	yes	Yes	no	no
	Love Plot Performance	low	high	medium	high
	Outcome	OR: 0.79 (95% CI: 0.43, 1.45)	OR: 1.12 (95% CI: 0.91, 1.38)	OR: 1.07 (95% CI: 0.77, 1.49)	OR: 1.04 (95% CI 0.7, 1.55)
Weighting	Rubin's Rule 1	yes	-	-	yes
	Rubin's Rule 2	yes	-	-	barly yes
	Love Plot Performance	medium	-	-	low
	Outcome	OR: 1.12 (95% CI: 0.66, 1.90)	-	-	OR: 1.17 (95% CI: 0.79, 1.72)
	Double-Robust Outcome	OR: 1.12 (95% CI: 0.66, 1.91)	-	-	OR: 1.14 (95% CI: 0.80, 1.63)
Generalized boosted modeling for propensity score	Rubin's Rule 1	-	-	-	no
	Rubin's Rule 2	-	-	-	no
	Love Plot Performance	-	-	-	medium
	Outcome	-	-	-	-

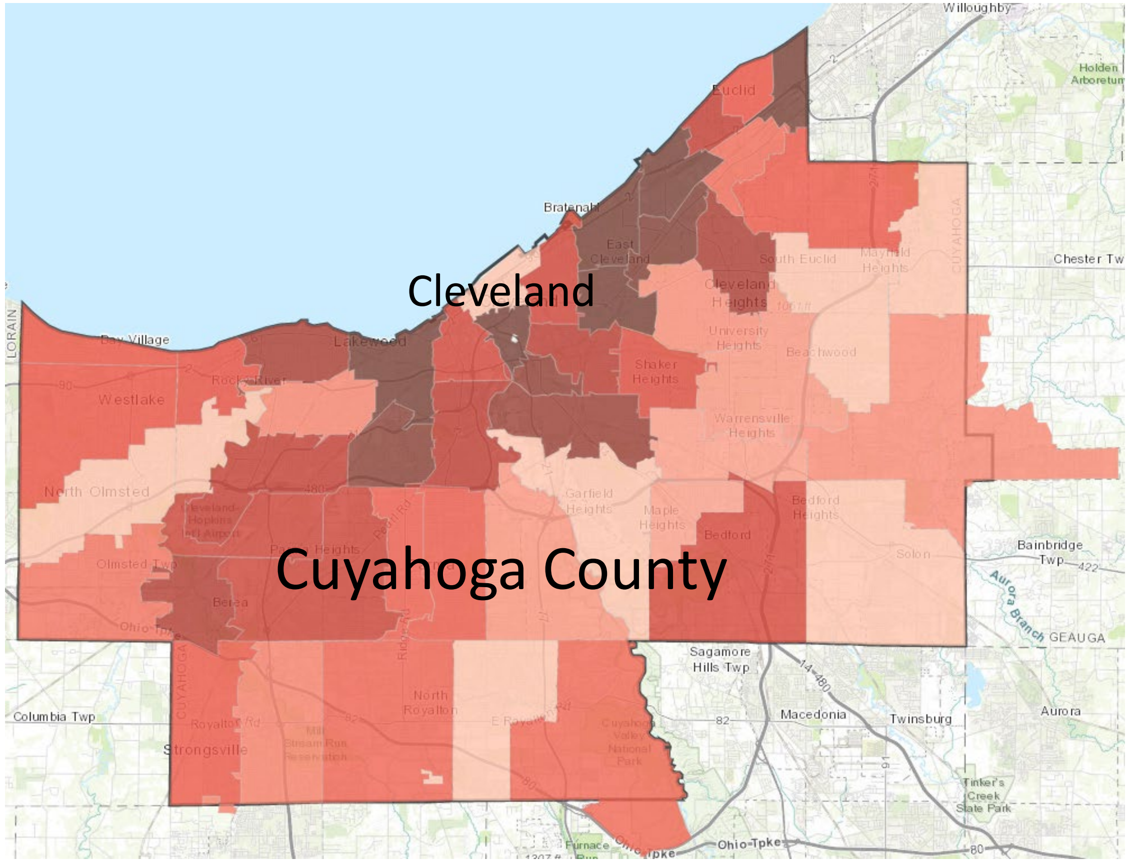
No significant effect of distance on stage in any of the subgroups!

Conclusion

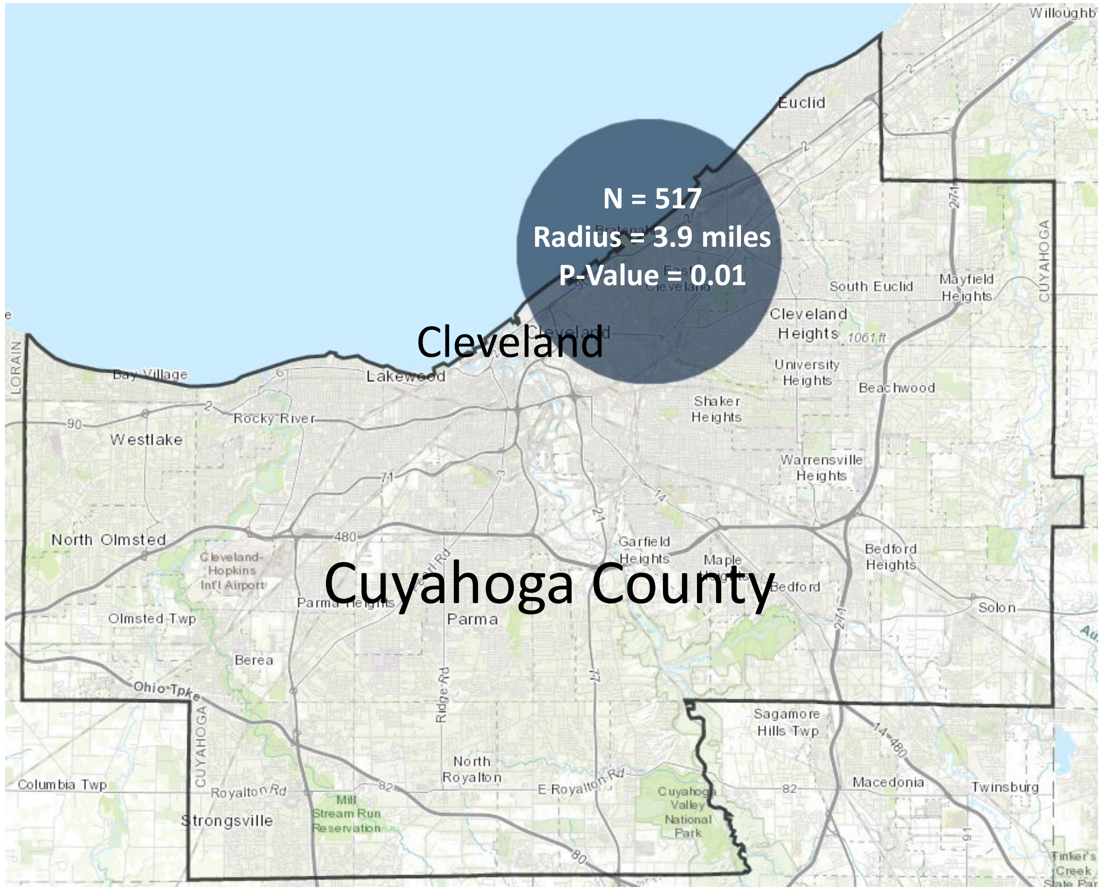
- No statistically significant effect of distance to mammography facility on stage at diagnosis of breast cancer in the overall group and on any of the subgroups
- Various propensity score methods have similar results
- Possible explanation
  - In a rust belt state like Ohio, people living in urban area are more likely to be disadvantaged in many health outcomes
  - Urban-rural disparities are so significant that people living in different areas are hard to match
  - Other factors, such as insurance coverage, play more important role than distance
  - The availability of transportation leads to distance decay
    - Distance does not matter, but which community you live in does matter!

Related Studies

Proportion Late-Stage Breast Cancer by Zip Code



Significant Spatial Cluster of Late-stage Cases



Later stage breast cancer are more prevalent in urban areas many hospitals and mammography facilities located!

Do Patients with Hemorrhagic Blunt Abdominal and Pelvic Trauma Benefit from the Use of Tranexamic Acid?

AMIN SAAD, MD

PQHS 500

Background: Trauma related injuries

- leading cause of death in people younger than 46 years of age.
- substantial economic burden (671 billion in 2013)
- Hemorrhage is the cause of death in 30-40% of civilian and 80% of combat setting, respectively.
- Hypocoagulability is observed in about 20% of the cases and has been associated with 48-100% mortality rates.

1. Rhee P, Joseph B, Pandit V, et al. Increasing trauma deaths in the United States. *Ann Surg*. 2014;260(1):13-21.
2. Florence C, Haegerich T, Simon T, Zhou C, Luo F. Estimated Lifetime Medical and Work-Loss Costs of Emergency Department-Treated Nonfatal Injuries–United States, 2013. *MMWR Morb Mortal Wkly Rep.* 2015;64(38):1078-1082.
3. Eastridge BJ, Holcomb JB, Shackelford S. Outcomes of traumatic hemorrhagic shock and the epidemiology of preventable death from injury. *Transfusion.* 2019;59(S2):1423-1428.
4. Gall LS, Brohi K, Davenport RA. Diagnosis and Treatment of Hyperfibrinolysis in Trauma (A European Perspective). *Semin Thromb Hemost.* 2017;43(2):224-234

Background: Examining the effectiveness of TXA

- CRASH 2: early use of TXA reduced in-hospital mortality from 16.0% to 14.5% (1.5% absolute risk reduction, RR 0.91 (0.85-0.97), NNT 67) and risk of death due to bleeding from 5.7% to 4.9% (0.8% risk reduction, NNT 121)[5].
- MATTERs: improved survival with the early use of TXA in injured patients receiving at least 1 unit of blood (OR 7.3; 95% CI 3.02 to 17.32)[6].

5. collaborators C-t, Shakur H, Roberts I, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet.* 2010;376(9734):23-32.
6. Morrison JJ, Dubose JJ, Rasmussen TE, Midwinter MJ. Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) Study. *Arch Surg.* 2012;147(2):113-119.

Background: contradictory evidence

- Valle et al: TXA was associated with increased mortality in patients who underwent emergency surgical intervention directly from the emergency department (27% vs 17%, $p=0.024$)[7].
- Texas: TXA did not reduce in-hospital mortality (OR 0.74; 95% CI 0.38 to 1.40; $p=0.80$) in patients with documented hyperfibrinolysis[8].
- Queen Mary hospital: TXA was protective for adjusted all-cause mortality (OR=0.16 CI 0.27, CI 0.03 to 0.86, $p=0.03$) only in shock trauma patients making it difficult to recommend TXA use in non-shock patients[9].

7. Valle EJ, Allen CJ, Van Haren RM, et al. Do all trauma patients benefit from tranexamic acid? *J Trauma Acute Care Surg*. 2014;76(6):1373-1378.
8. Harvin JA, Peirce CA, Mims MM, et al. The impact of tranexamic acid on mortality in injured patients with hyperfibrinolysis. *J Trauma Acute Care Surg*. 2015;78(5):905-909; discussion 909-911.
9. Cole E, Davenport R, Willett K, Brohi K. Tranexamic Acid Use in Severely Injured Civilian Patients and the Effects on Outcomes. *Ann Surg*. 2015;261(2):390-394. doi:10.1097/sla.0000000000000717

Background: What are trauma surgeons doing?

- In a 2016 online survey conducted by the Eastern Association for the Surgery of Trauma (EAST), only 38% of U.S. civilian trauma surgeons reported using TXA consistently despite the availability of TXA in almost 90% of trauma centers.
- The surgeons attributed their decreased use of TXA to the uncertainty of clinical benefit (47.7%) and unfamiliarity (31.5%)[10].

Jawa RS, Singer A, McCormack JE, Huang EC, Rutigliano DN, Vosswinkel JA. Tranexamic Acid Use in United States Trauma Centers: A National Survey. *Am Surg.* 2016;82(5):439-447

Project aim

- The aim of the study is to assess whether the administration of tranexamic acid (TXA) is associated with improved outcomes in patients with hemorrhagic blunt abdominal and pelvic trauma.

- Hypothesis: TXA use in patients with hemorrhage blunt abdominal trauma is associated will reduce in-hospital mortality.

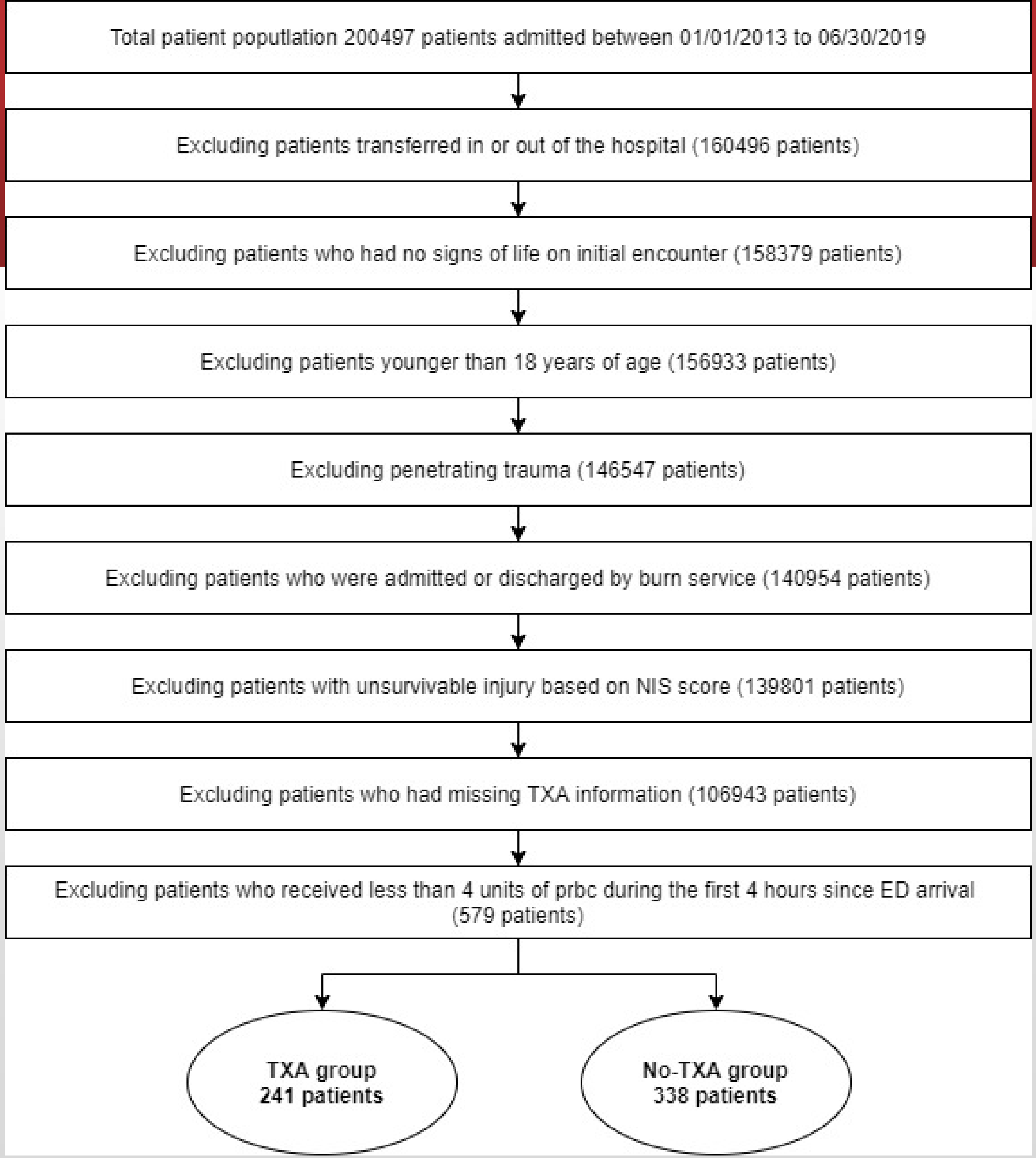
Data source: MTQIP

- Source of the data is the **Michigan Trauma Quality Initiative Program (MTQIP)** database which is the product of a regional collaborative initiative that connects trauma centers within the state of Michigan to focus on specific areas of performance improvement and promote compliance with the process of care for trauma patients a nonpunitive manner.
- MTQIP was chosen since it contains information on TXA use which was incorporated into the database starting with 01/01/2013.
- Access to the MTQIP master date file was obtained after receiving institutional review board (IRB) approval

Outcome, exposure and covariates

- Outcome: In-hospital mortality
- Exposure: TXA administration
- **Covariates:**
  - **Demographics** (age, sex, insurance, ethnicity)
  - **Patient characteristics and morbidities**
    - Smoking, obesity, diabetes, hypertention, COPD, alcohol abuse
  - **Medications**
    - Antiplatelets, anticoagulations, betablockers, statins
  - **Trauma related variables**
    - Trauma activation, Injury score index (NISS)
  - **ER related variables**
    - CPR, intubation, vital signs (BP, pulse), GCS , CPR, intubation, Shock, fluid and blood product resuscitation
  - **Treatments received**
    - Operation, angiographic interventions
  - **In-hospital complications**
    - Return to ICU, return to OR, AKI, ARDS, infectious complications, thrombotic complication, withdrawal of care

Study flow chart



Dealing with Missing Covariate Data

- Dropped variables with more than 15% missing
- Dropped variables with less than 5 observations
- Simple imputation was used to impute missing values for remaining variables using MICE

Table 1 (post-imputation – part 1 of 2)

Table1: Baseline patients demographics and comorbidities	Non-TXA	TXA	p value
Number of patients	338	241	
Age (median [IQR])	47.60 [27.67, 61.94]	48.00 [29.32, 60.00]	0.940
Sex (Males %)	244 (72.2)	177 (73.4)	0.811
Ethnicity (Hispanic %)	8 (2.4)	12 (5.0)	0.143
Insurance (%)			<0.001
Government	62 (18.3)	44 (18.3)	
Private	69 (20.4)	25 (10.4)	
Other	157 (46.4)	149 (61.8)	
None	50 (14.8)	23 (9.5)	
Smoker (%)	57 (16.9)	49 (20.3)	0.34
Diabetes (%)	25 (7.4)	25 (10.4)	0.268
Obesity (%)	26 (7.7)	13 (5.4)	0.358
HTN (%)	66 (19.5)	43 (17.8)	0.687
COPD (%)	14 (4.1)	7 (2.9)	0.576
Alcohol abuse (%)	26 (7.7)	23 (9.5)	0.524
Statin (%)	29 (8.6)	27 (11.2)	0.363
Beta blockers (%)	30 (8.9)	26 (10.8)	0.532
Anti-platelet (%)	0.09 (0.28)	0.10 (0.30)	0.659
Anticoagulants (%)	0.05 (0.22)	0.04 (0.19)	0.459

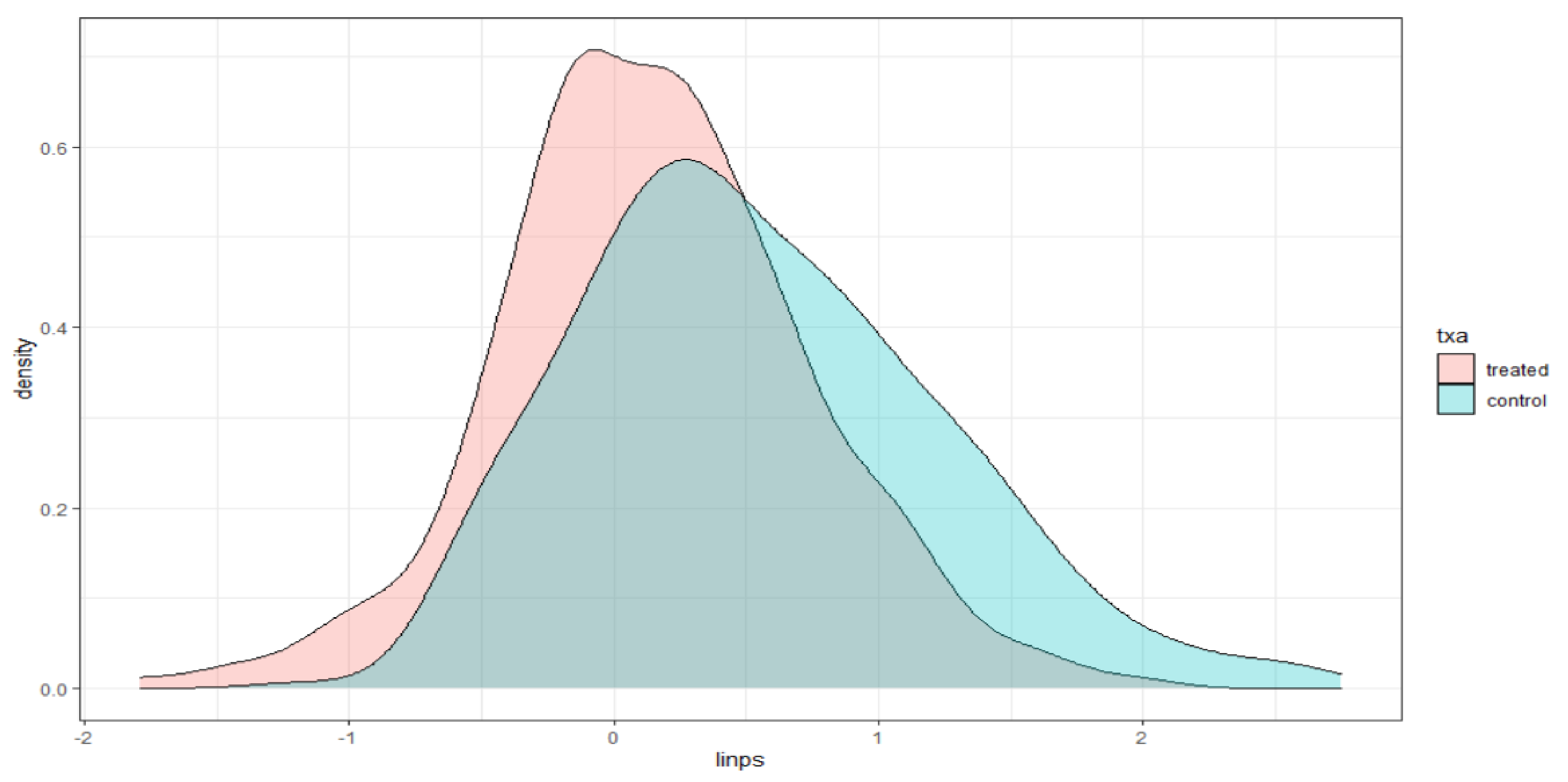
Table 1 (part 2)

	Non-TXA	TXA	p value
Trauma activation type (%)			
Full activation			0.077
Partial activation	273 (80.8)	208 (86.3)	
Trauma Consult	54 (16.0)	31 (12.9)	
NISS (mean (SD))	38.29 (14.49)	42.07 (13.24)	0.001
Prehospital or ED CPR (%)	46 (13.6)	31 (12.9)	0.891
Intubated patient (%)	79 (23.4)	60 (24.9)	0.746
ED pulse (mean (SD))	107.71 (29.78)	110.15 (29.24)	0.328
ED SBP (mean (SD))	103.65 (34.90)	110.29 (38.38)	0.031
Lowest ED SBP (mean (SD))	74.87 (26.69)	73.10 (24.38)	0.417
GCS in ED (median [IQR])	12.00 [3.00, 15.00	11.00 [3.00, 15.00]	0.496 *
Hemodynamic Shock (%)	241 (71.3)	194 (80.5)	0.015
FFP at 24 hours (median [IQR])	6.00 [3.00, 10.00]	8.00 [5.00, 13.00]	<0.001*
Plts at 24 hours (median [IQR])	5.00 [1.00, 10.00]	9.00 [4.00, 16.00]	<0.001*
Cryo at 24 hours (median [IQR])	3.88 (11.03)	9.19 (21.95)	<0.001*
IVF at 24 hours (median [IQR])	6.00 [3.00, 9.00]	6.00 [4.00, 9.00]	0.126*
PRBC at 24 hours (median [IQR])	9.00 [6.00, 14.00]	11.00 [8.00, 18.00]	<0.001*
Angiographic intervention (%)	44 (13.0)	58 (24.1)	0.001
Operation (%)	282 (83.4)	213 (88.4)	0.122
Laparotomy (%)	143 (42.3)	119 (49.4)	0.11
Return to OR (%)	15 (4.4)	18 (7.5)	0.171
ICU days (median [IQR])**	4.00 [1.00, 12.00]	8.00 [2.00, 17.00]	<0.001*
Return to ICU	6 (1.8)	12 (5.0)	0.052
ARDS (%)	16 (4.7)	15 (6.2)	0.55
AKI (%)	13 (3.8)	21 (8.7)	0.023
Infectious complications (%)	73 (21.6)	72 (29.9)	0.03
Thrombotic complications (%)	32 (9.5)	35 (14.5)	0.081
Withdrawal of care	59 (17.5)	49 (20.3)	0.443
Hospital Days (median [IQR])	7.50 [1.00, 20.00]	13.00 [1.00, 23.00]	0.019*
Died In-Hospital (%)	154 (45.6)	94 (39.0)	0.137

Fitting propensity score model

- Variables that were thought to affect the decision of giving TXA was included in the propensity score model
  - Variables included
    - Patient’s demographics
    - Clinical characteristics
    - Vital signs
    - Trauma related variables

Comparison of the Linear PS in the two groups



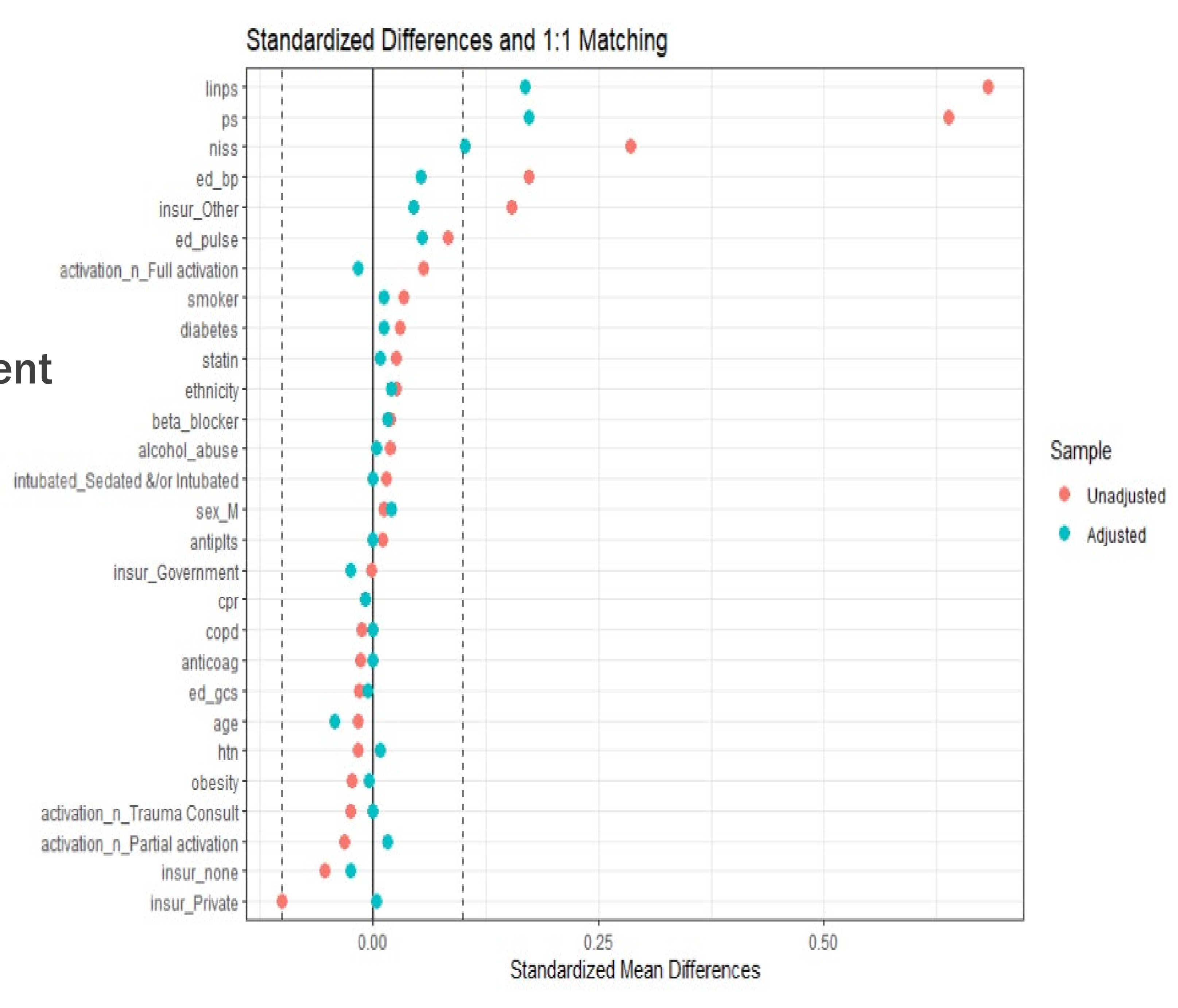
Rubin 1 and 2 before matching

- Rubin 1 = 59.09 we have observed bias and we need to apply a propensity score to our unadjusted analysis
- Rubin 2 = 0.73 the ratio of the variances of the linear propensity score is not in the ideal range between 4/5 and 5/4

1:1 matching

- 241 matched pairs
- Matched without replacement
- Greedy matching

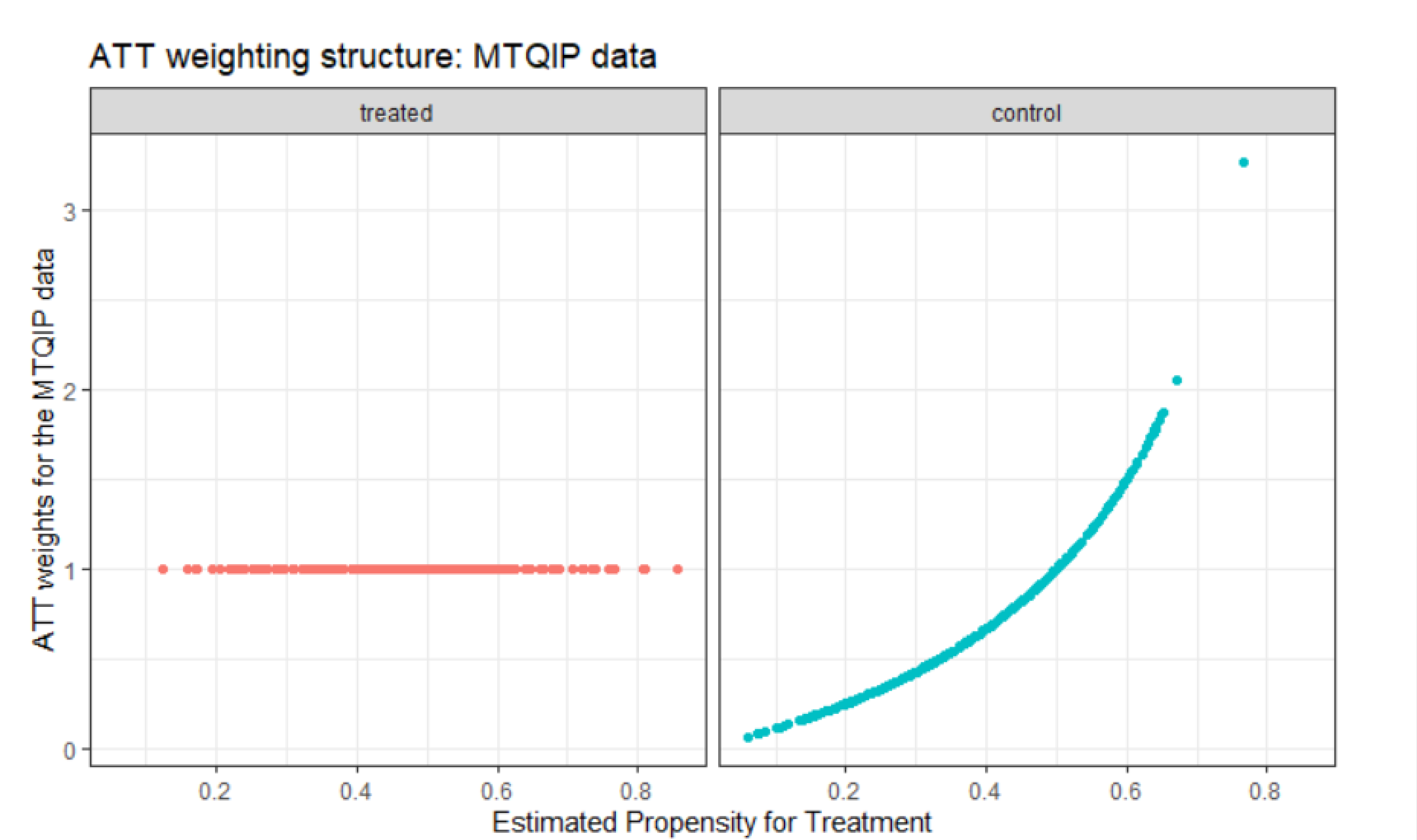
- Rubin 1 = 0.18,
  - improved! (originally 0.59)
- Rubin 2 = 1,37,
  - within 1/2 and 2.
  - (Originally 0.73)

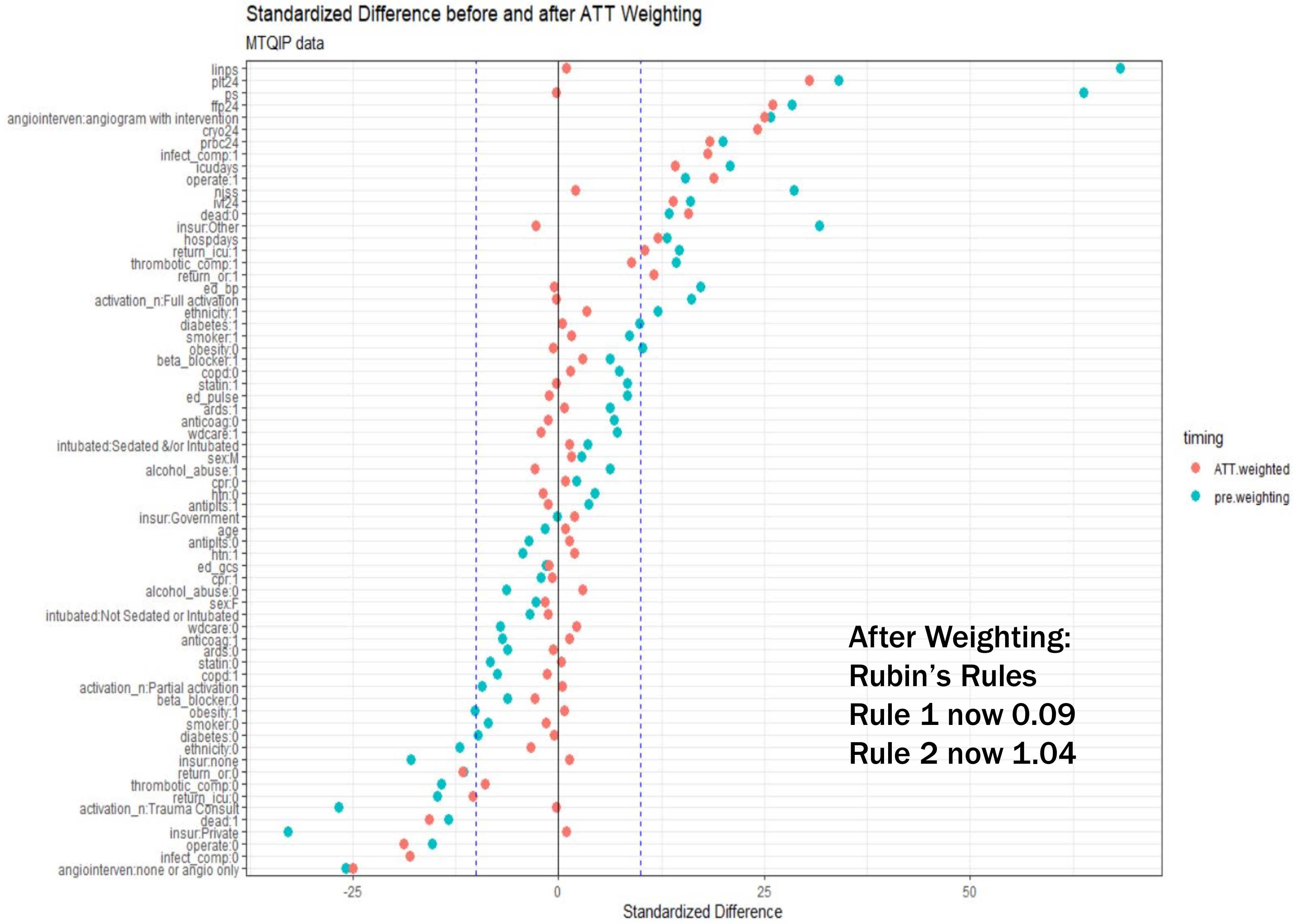


Estimating the causal effect of txa treatment

- Before Matching
  - Unadjusted Odds ratio
  - describes odds of dying in-hospital after being treated with txa (vs. Not treated with txa)
  - 0.77 with 95% CI (0.55, 1.07)
- After Matching
  - Odds Ratio for in-hospital mortality associated with txa is 0.75 with 95% CI (0.49, 1.01)

Analysis 2: weighting by the inverse PS using ATT approach





After Weighting:
Rubin's Rules
Rule 1 now 0.09
Rule 2 now 1.04

Estimating the causal effect of txa treatment

- Before Matching
  - Unadjusted Odds ratio
  - describes odds of dying in-hospital after being treated with txa (vs. Not treated with txa)
  - 0.77 with 95% CI (0.55, 1.07)
- After Matching
  - Odds Ratio for in-hospital mortality associated with txa is 0.75 with 95% CI (0.49, 1.01)
- After Weighting
  - Odds Ratio = 0.73 with 95% CI (0.51, 1.05)

Conclusions

- TXA was shown to have no statistically detectable effect on In-hospital mortality in patients with hemorrhagic blunt abdominal trauma after unadjusted, propensity matched and propensity score weighted analyses.
- The finding is consistent with Harvin et al, who demonstrated that TXA did not reduce in-hospital mortality (OR 0.74; 95% CI 0.38 to 1.40; p=0.80)[8].

Statistical conclusions

1- trying other methodology such subclassifciation by PS, or matching with replacement

2- performing the analysis on a different outcome such as length of hospital stay