Advanced Statistical Methods for Observational Studies

LECTURE 07

regression discontinuity

RD designs

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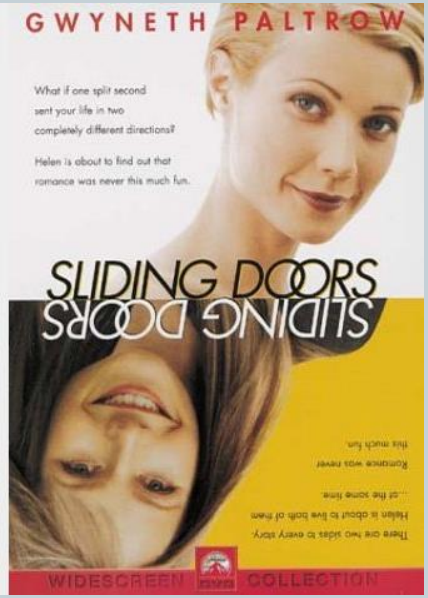

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- Research question: How much benefit does the student receive from being given support for college?
- The naïve comparison is horrid: Those who work to get the NMS are outstanding and those who don't get it are a mixed bag.
- But there are millions of students who take the PSAT every year, maybe we can find a subgroup.

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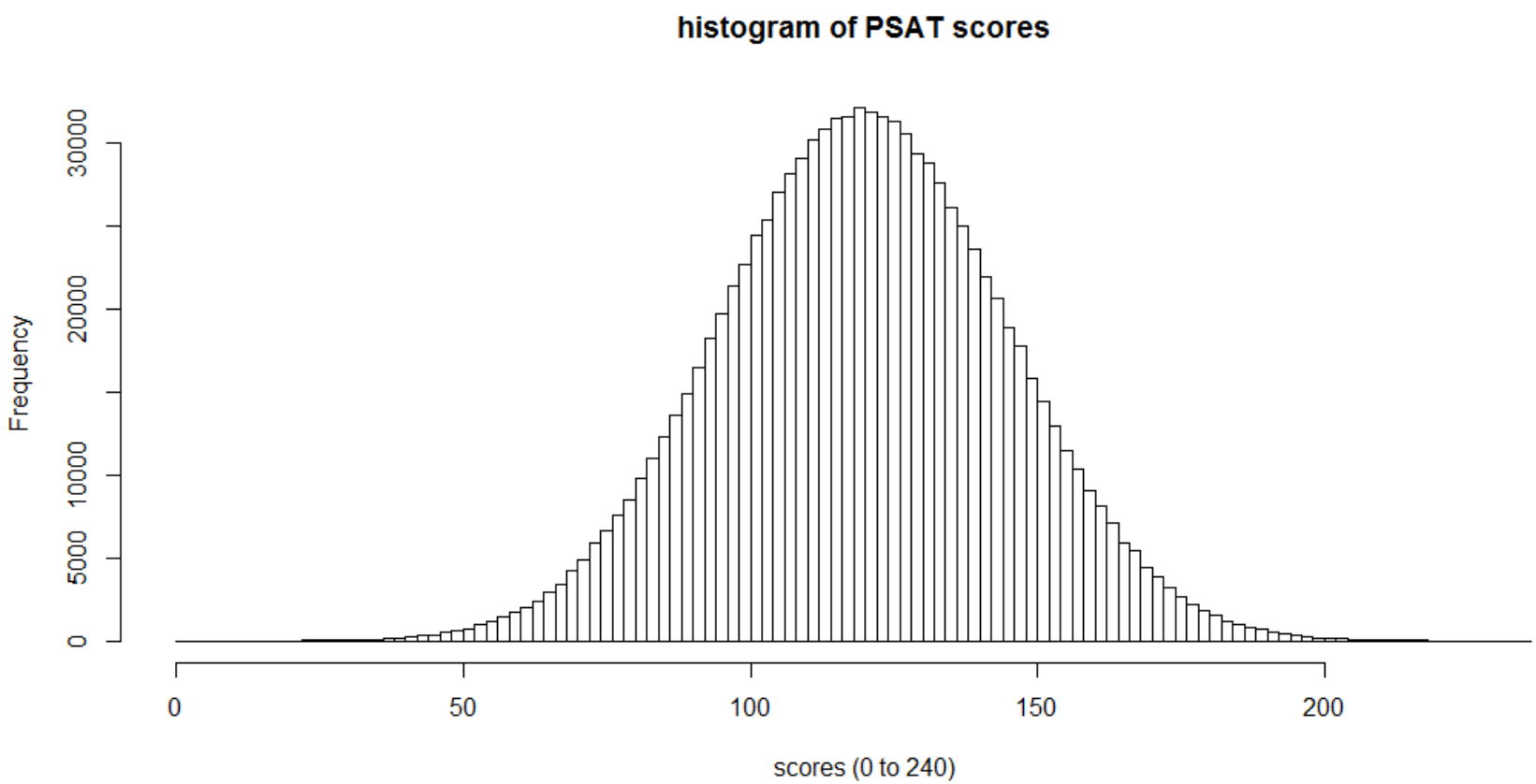

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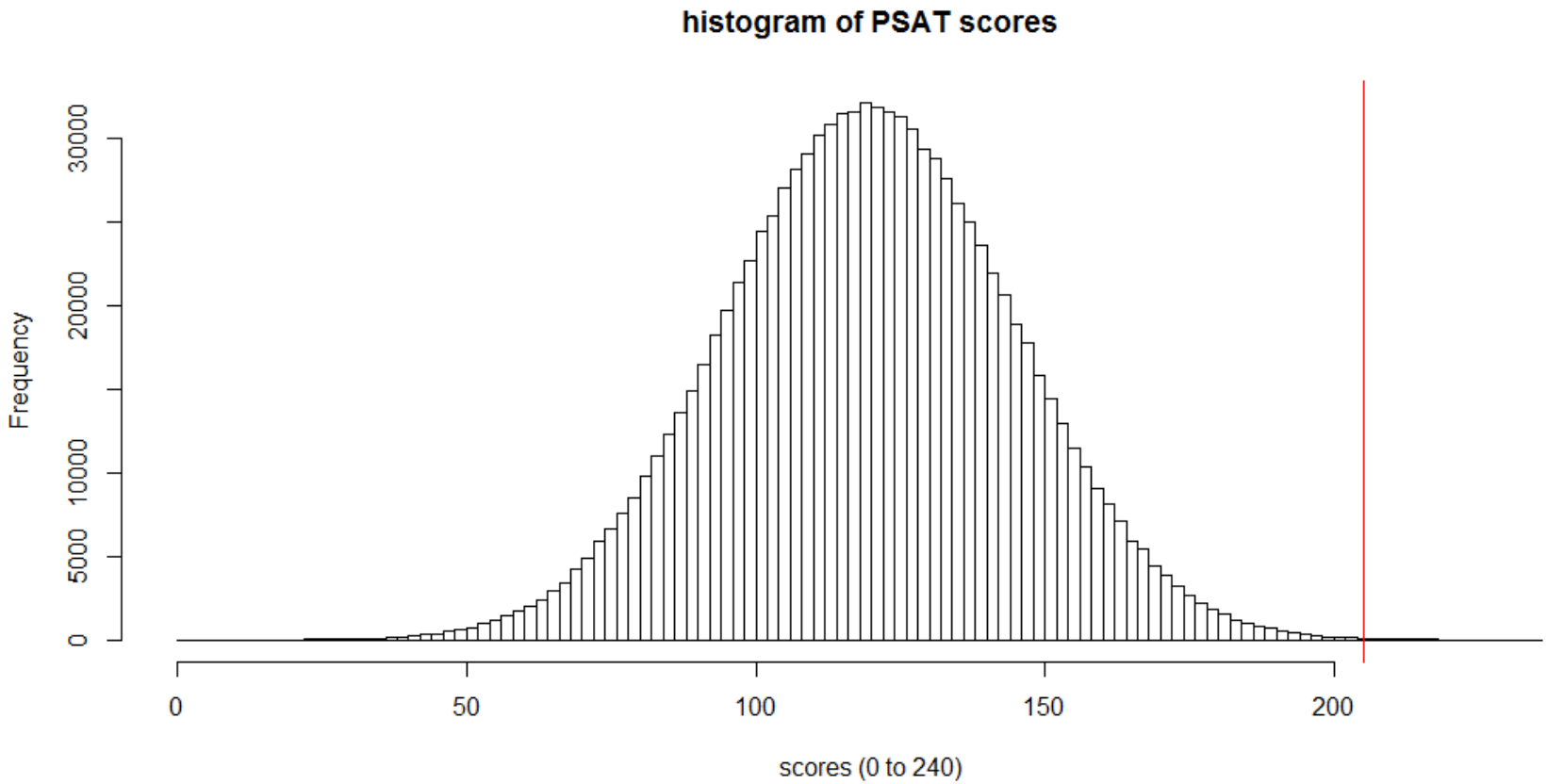

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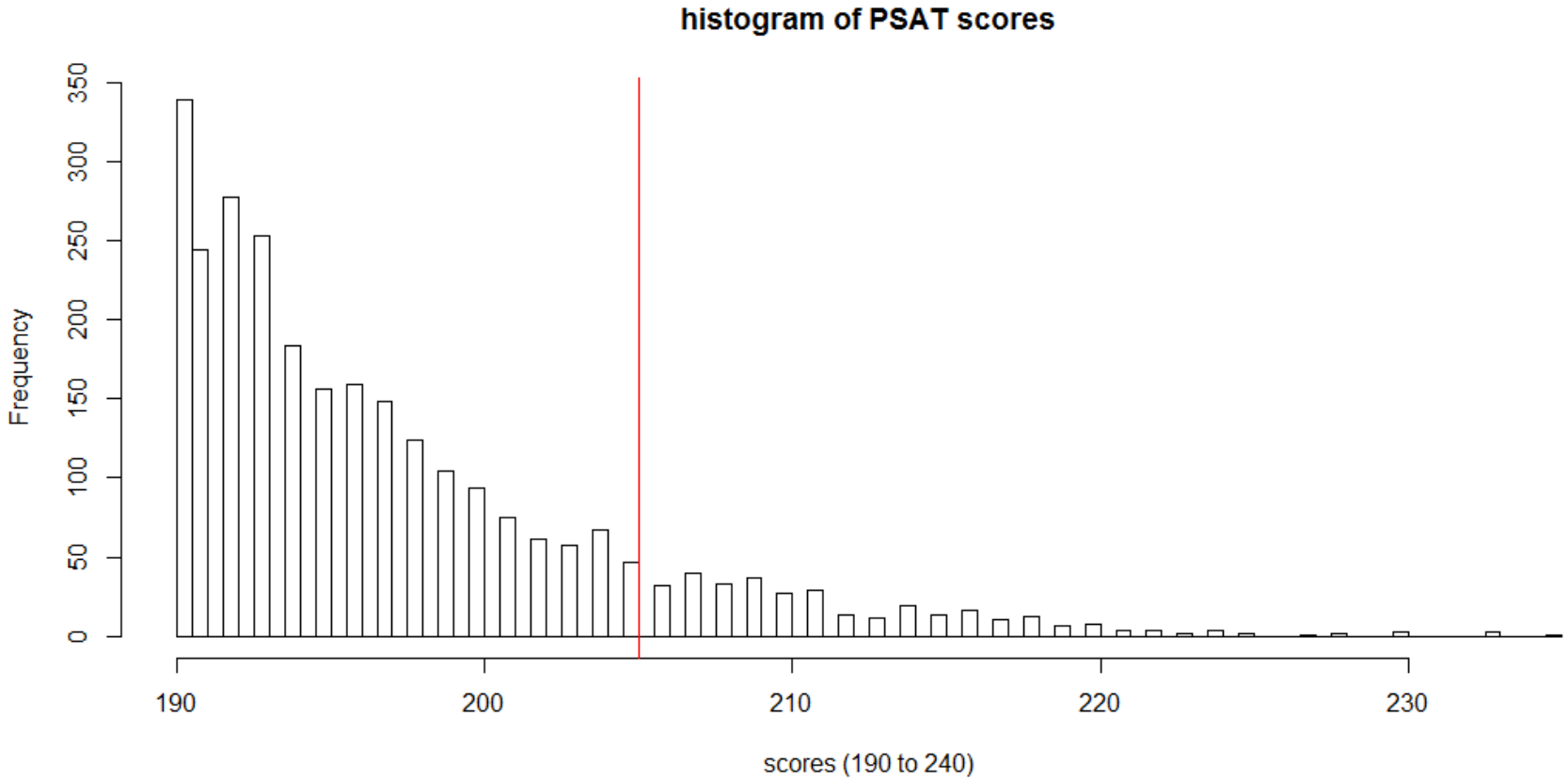

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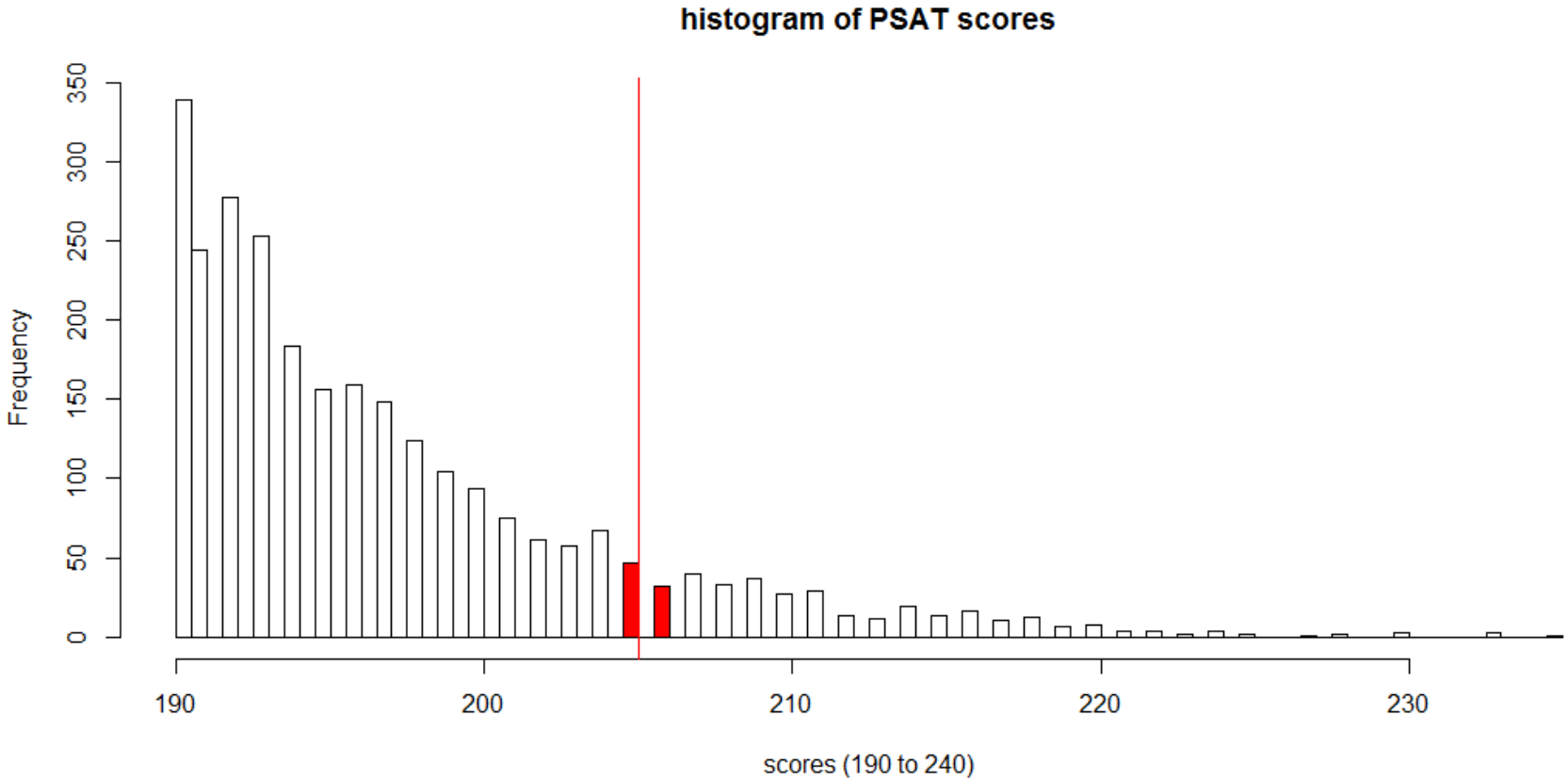

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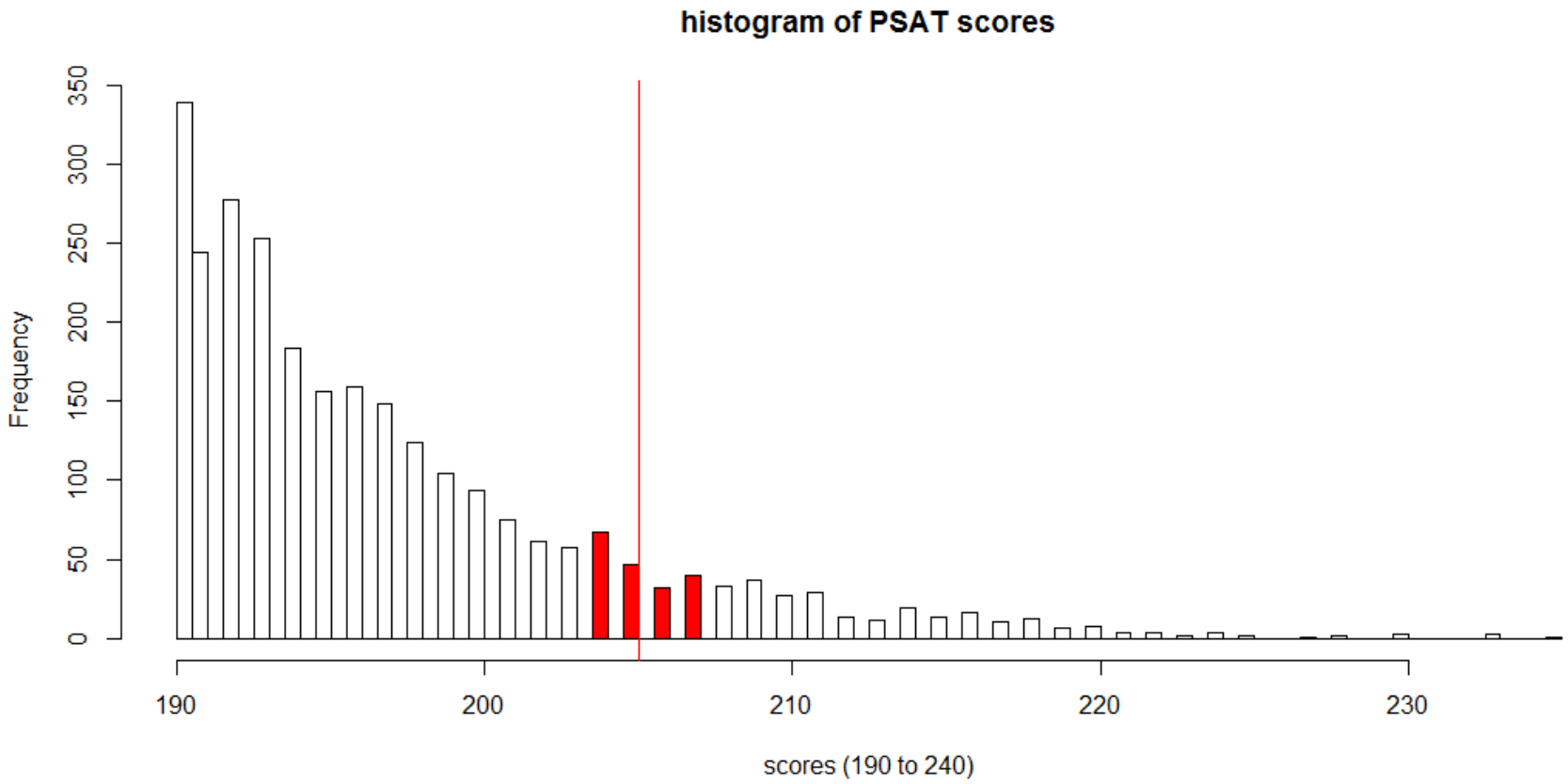

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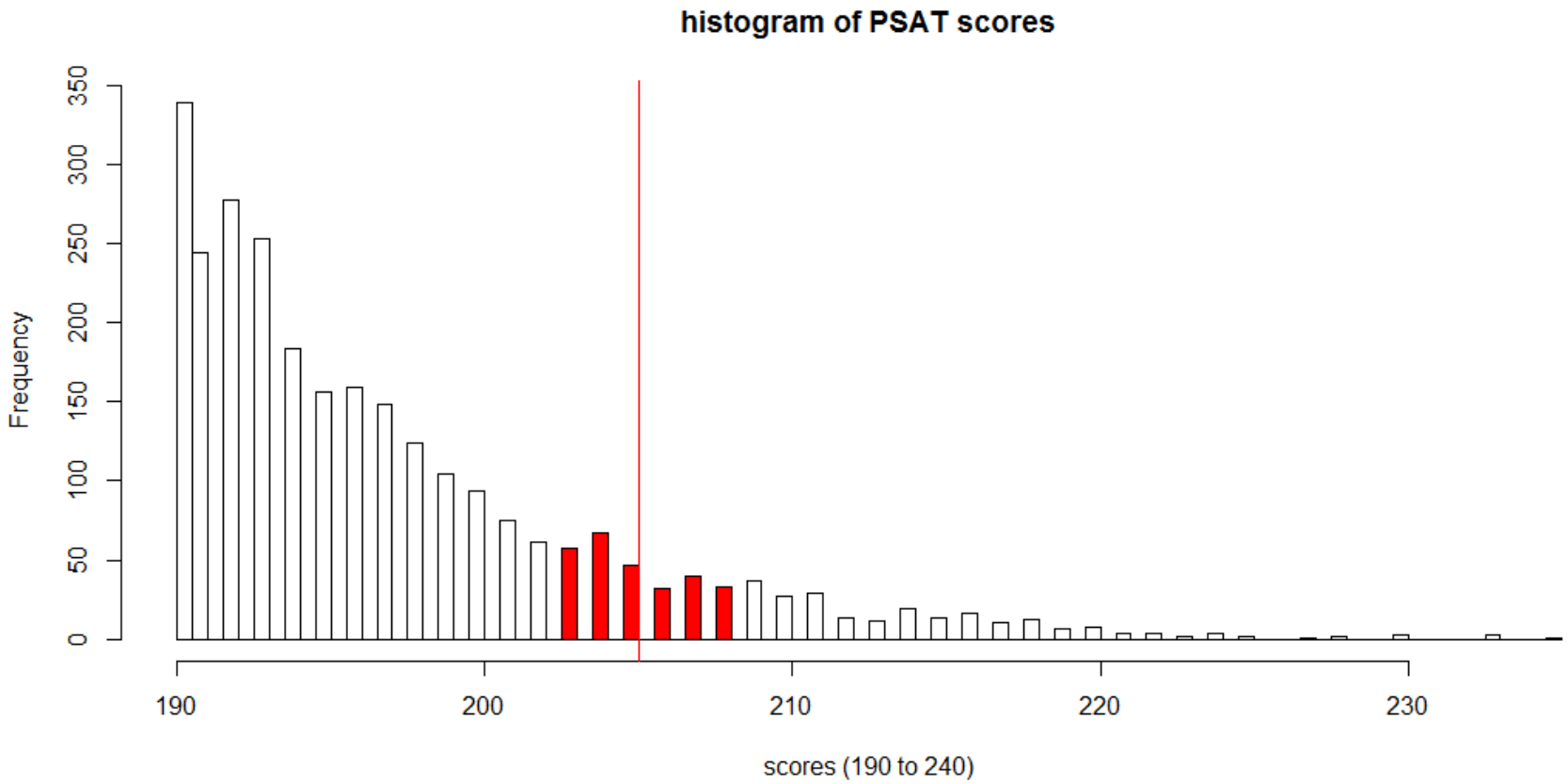

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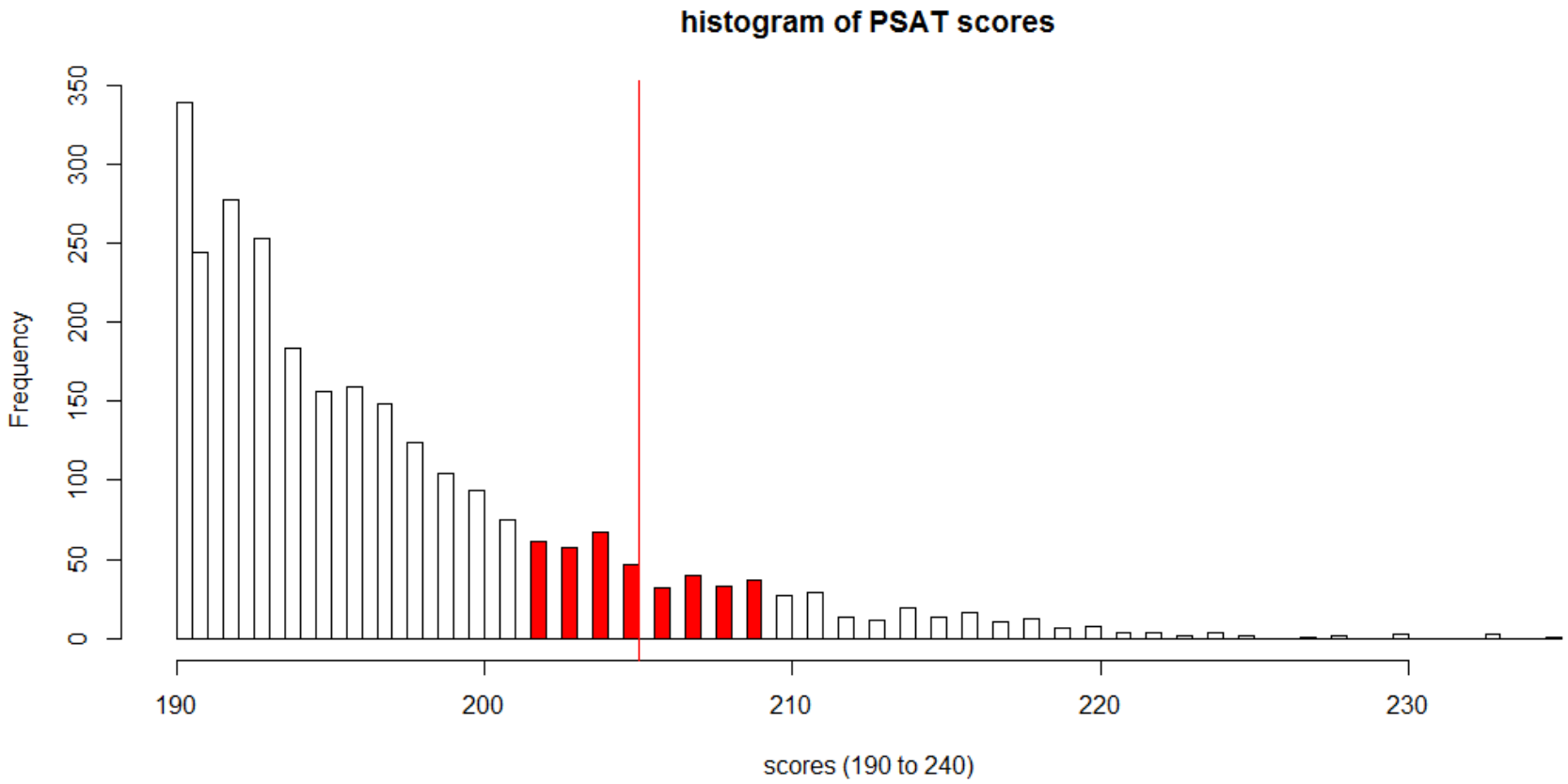

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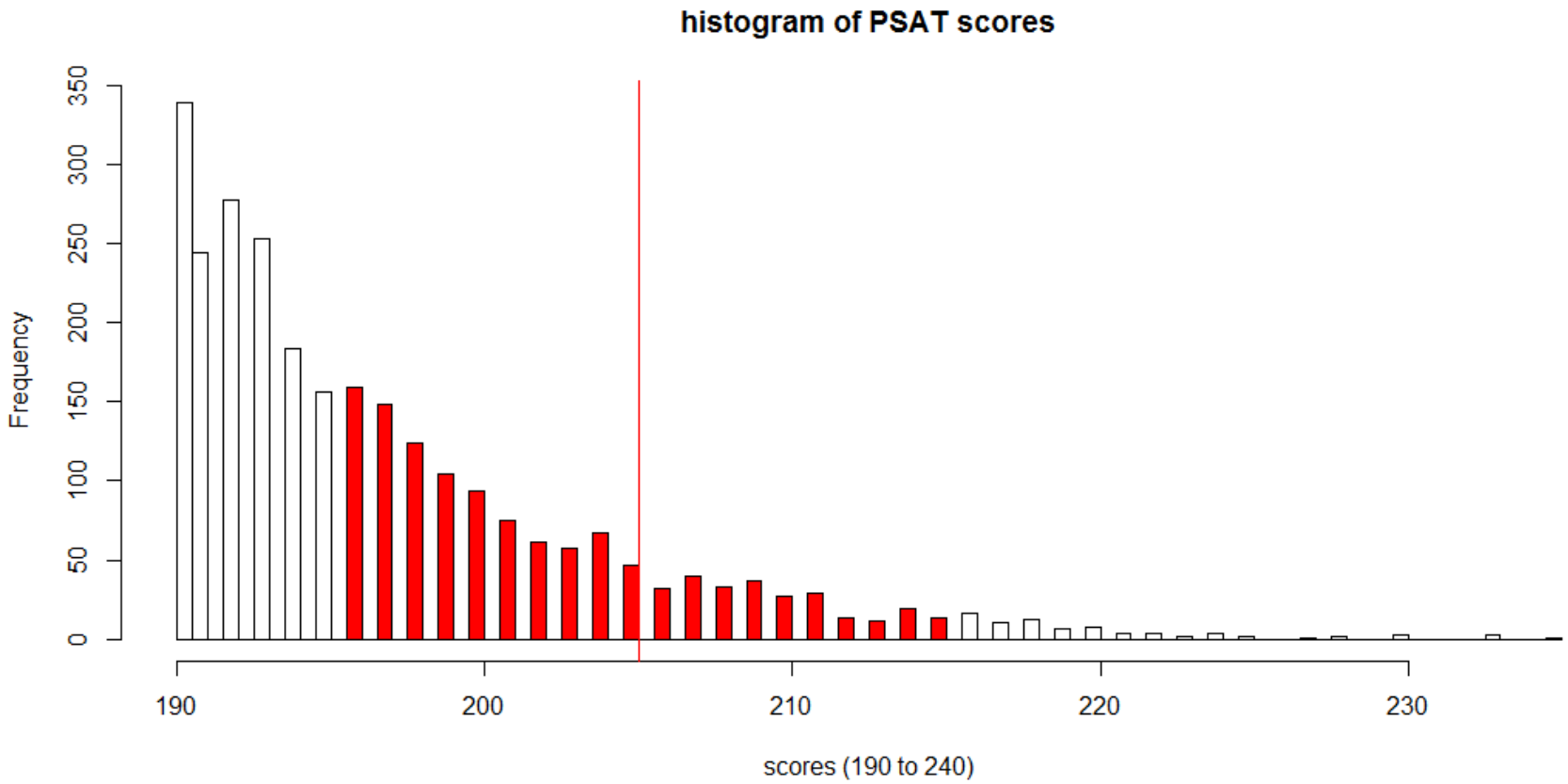

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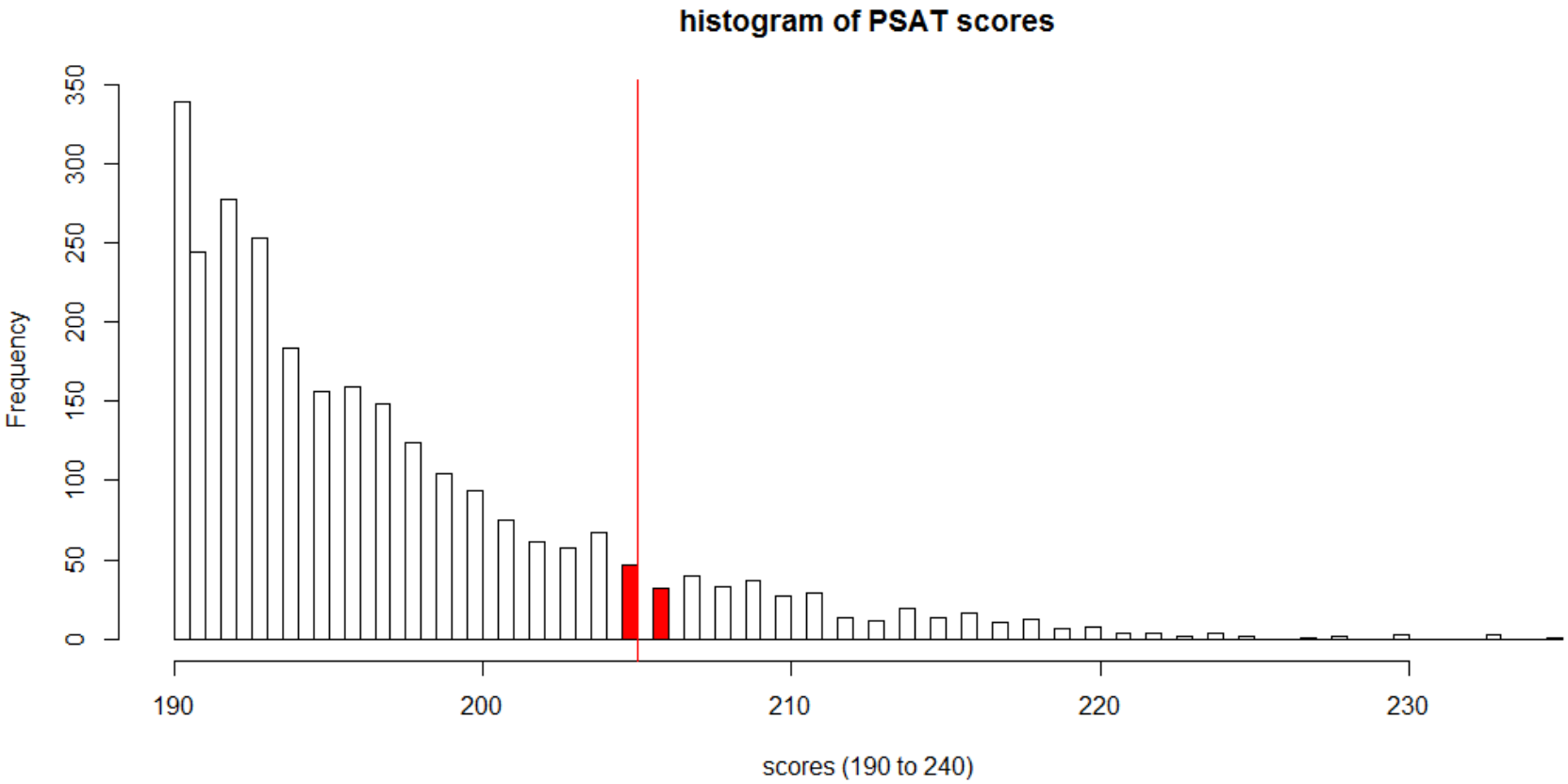

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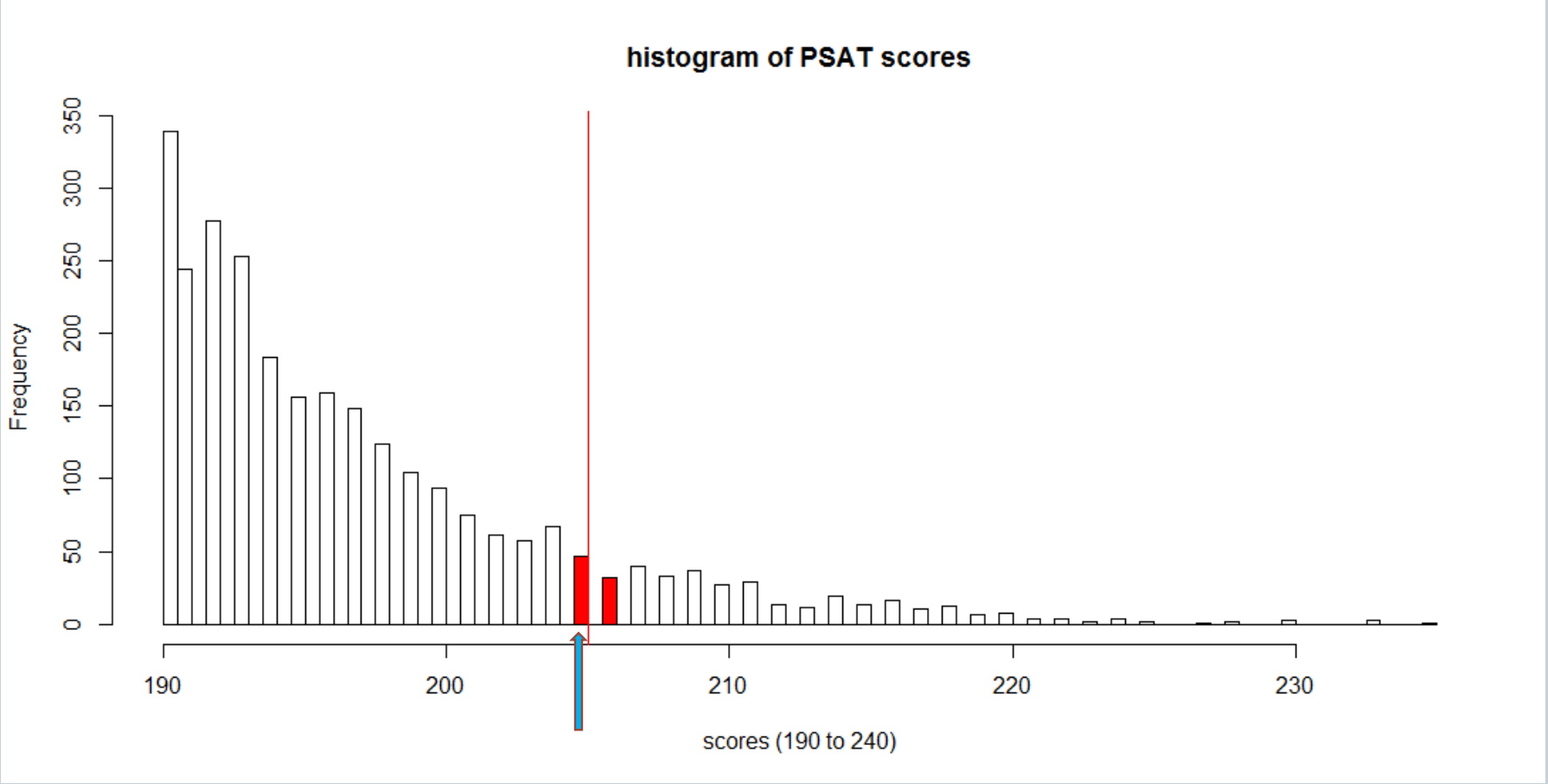

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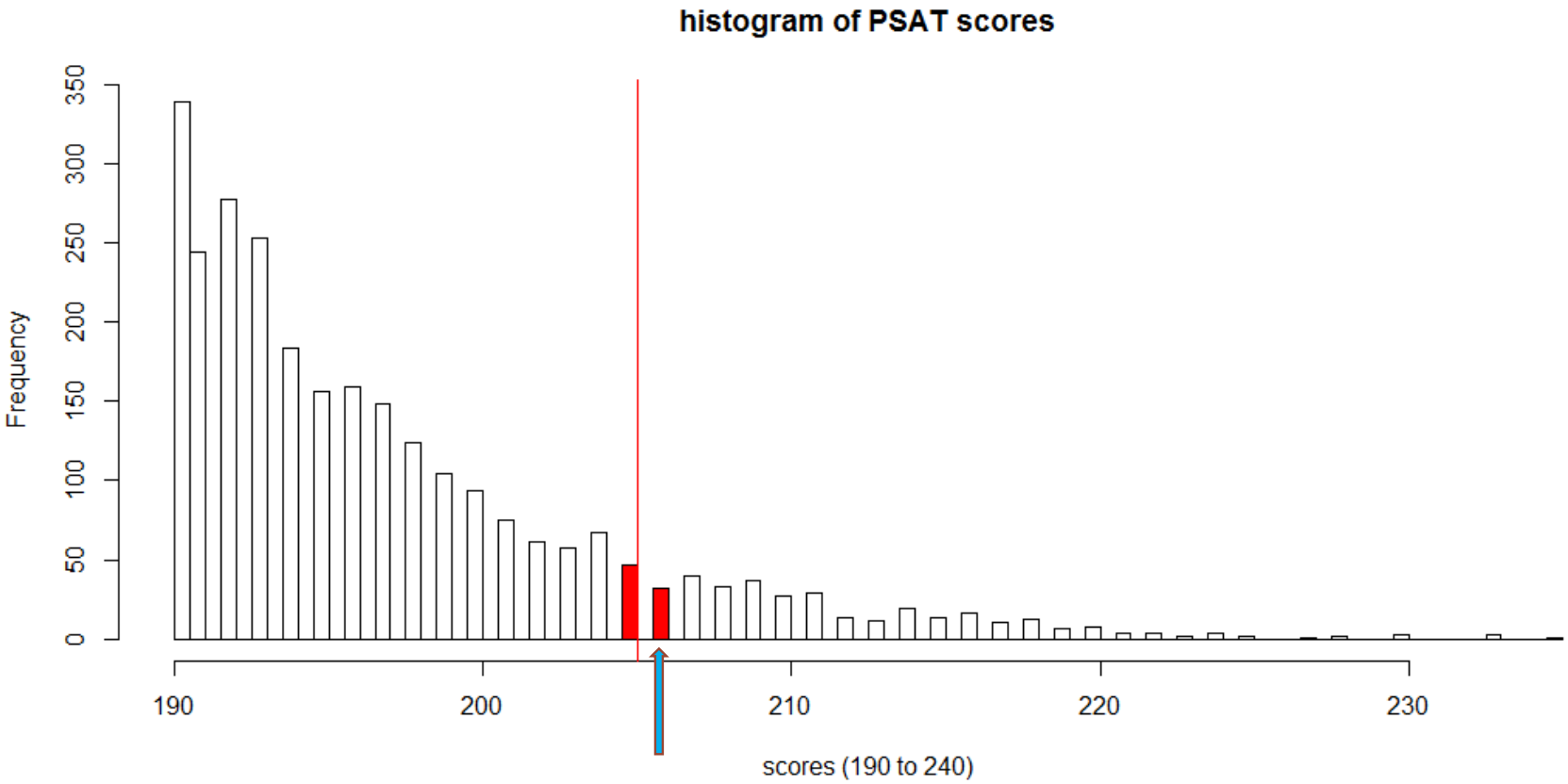

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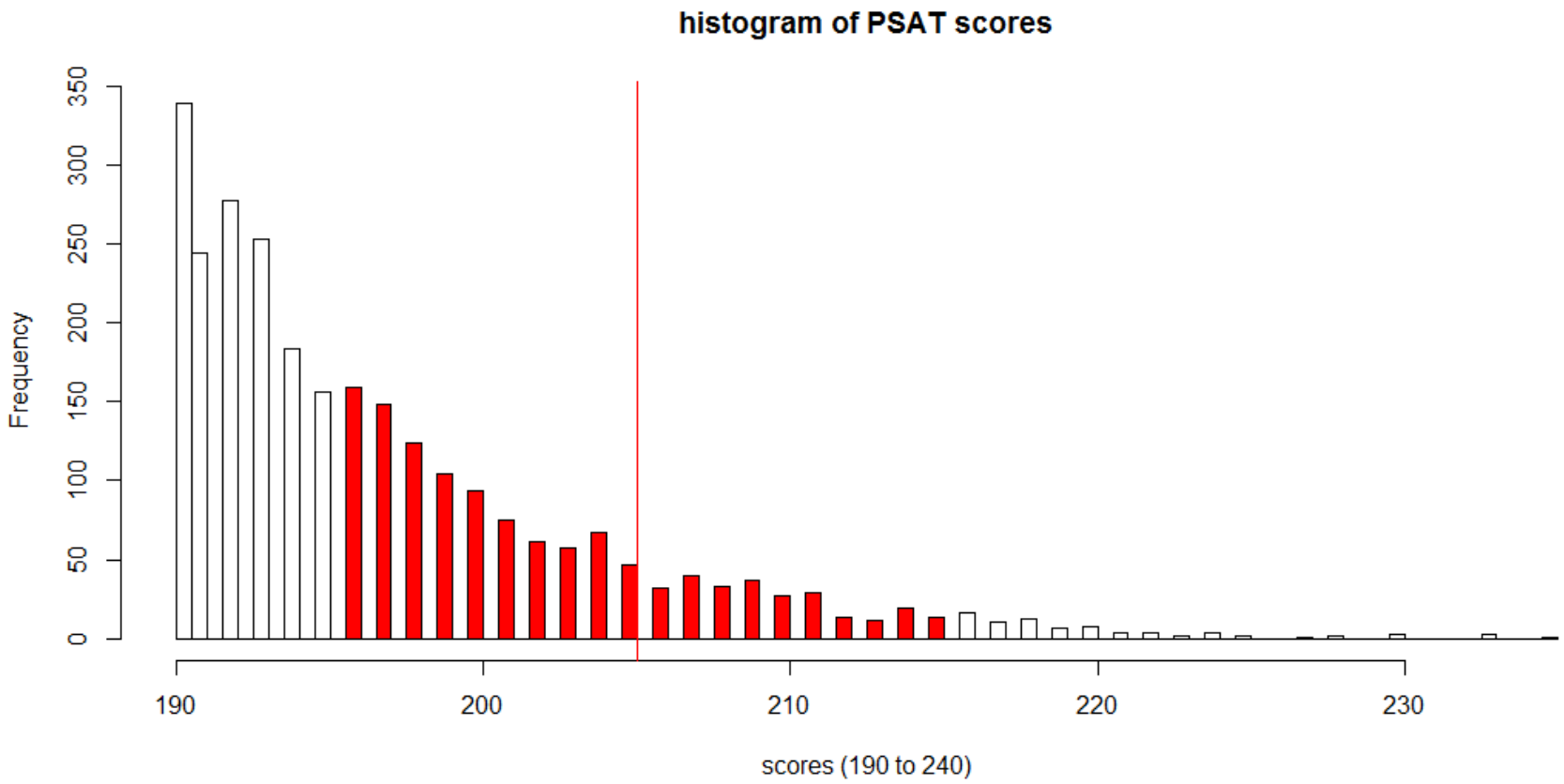

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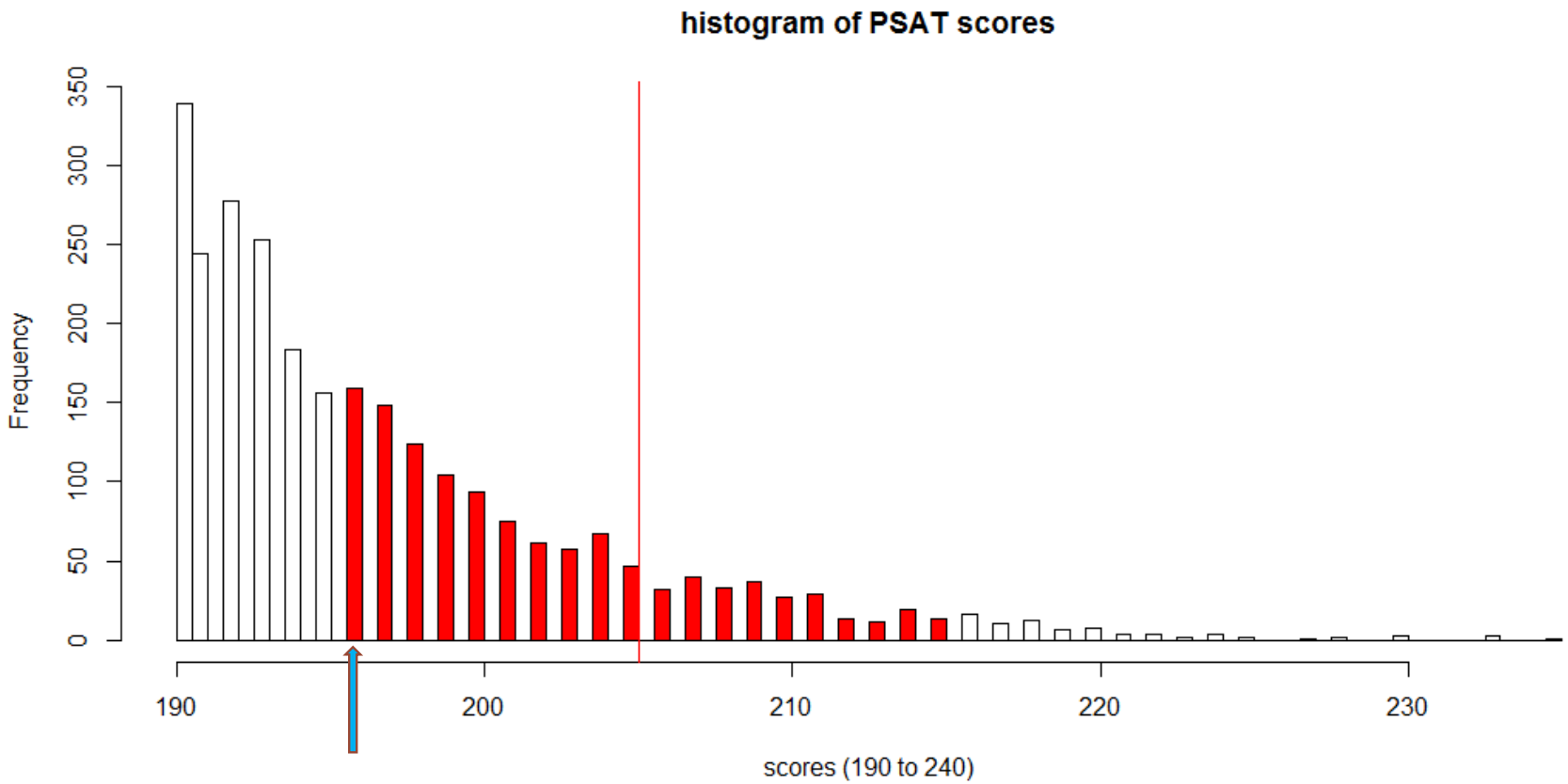

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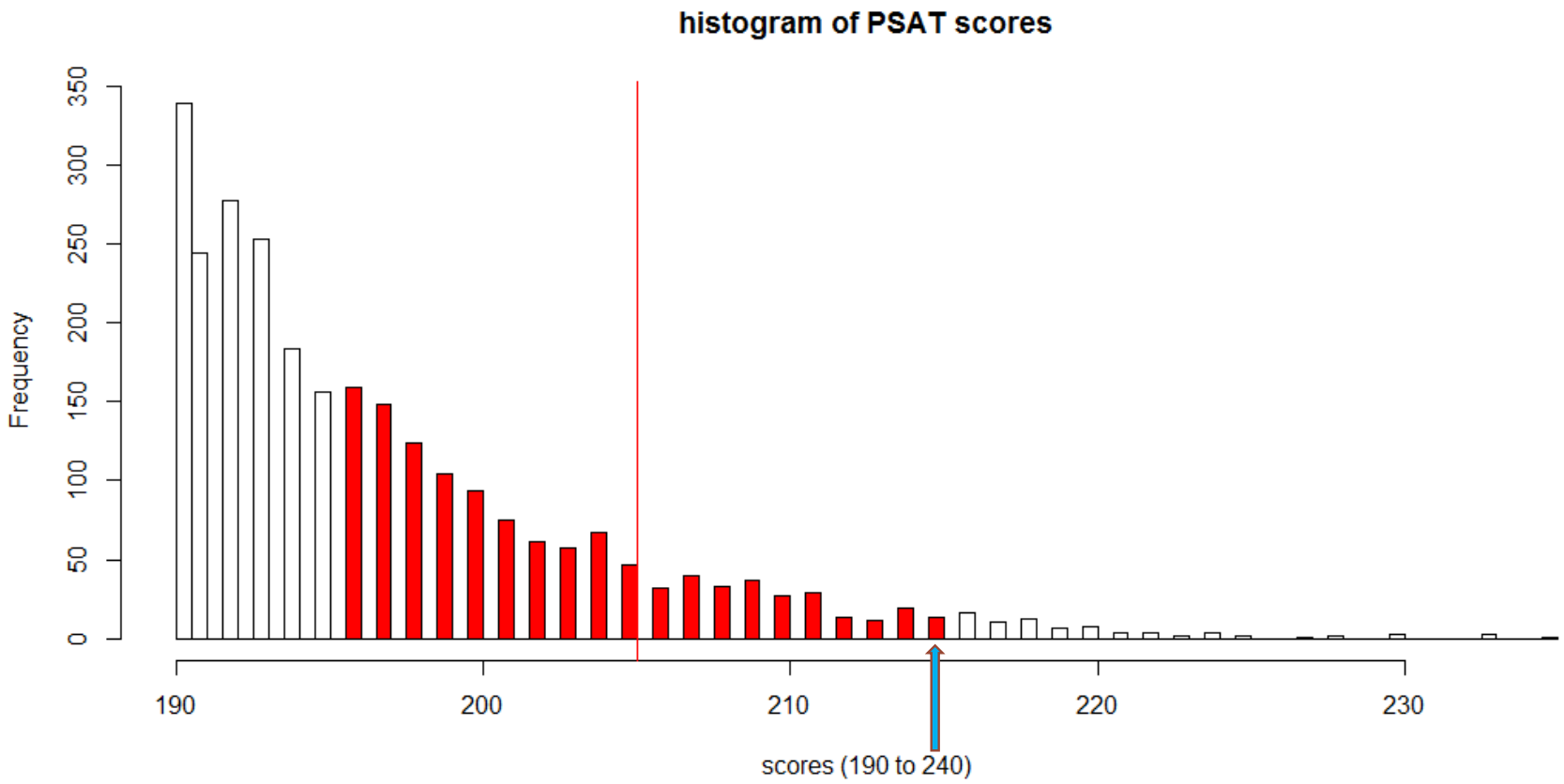

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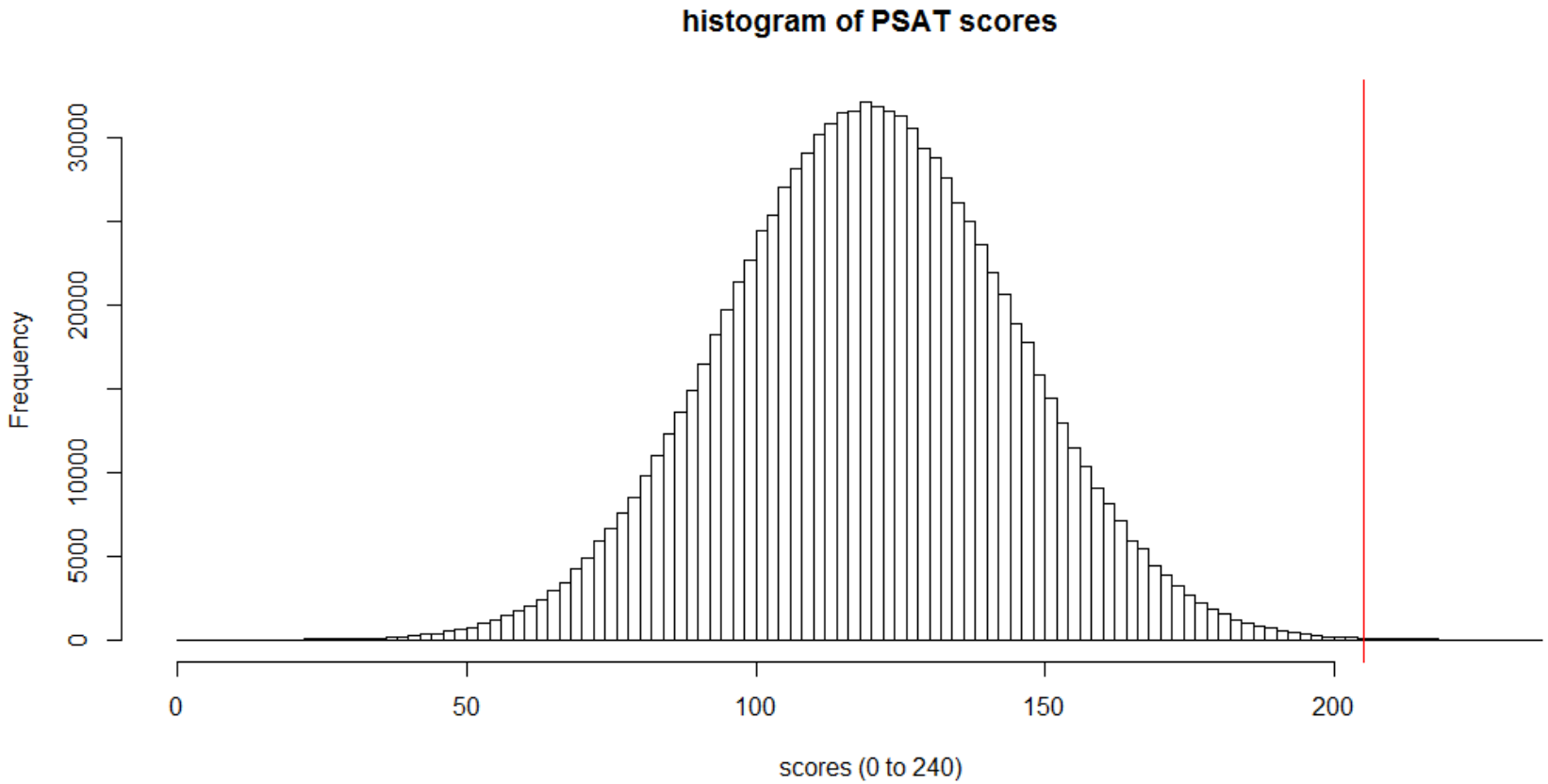

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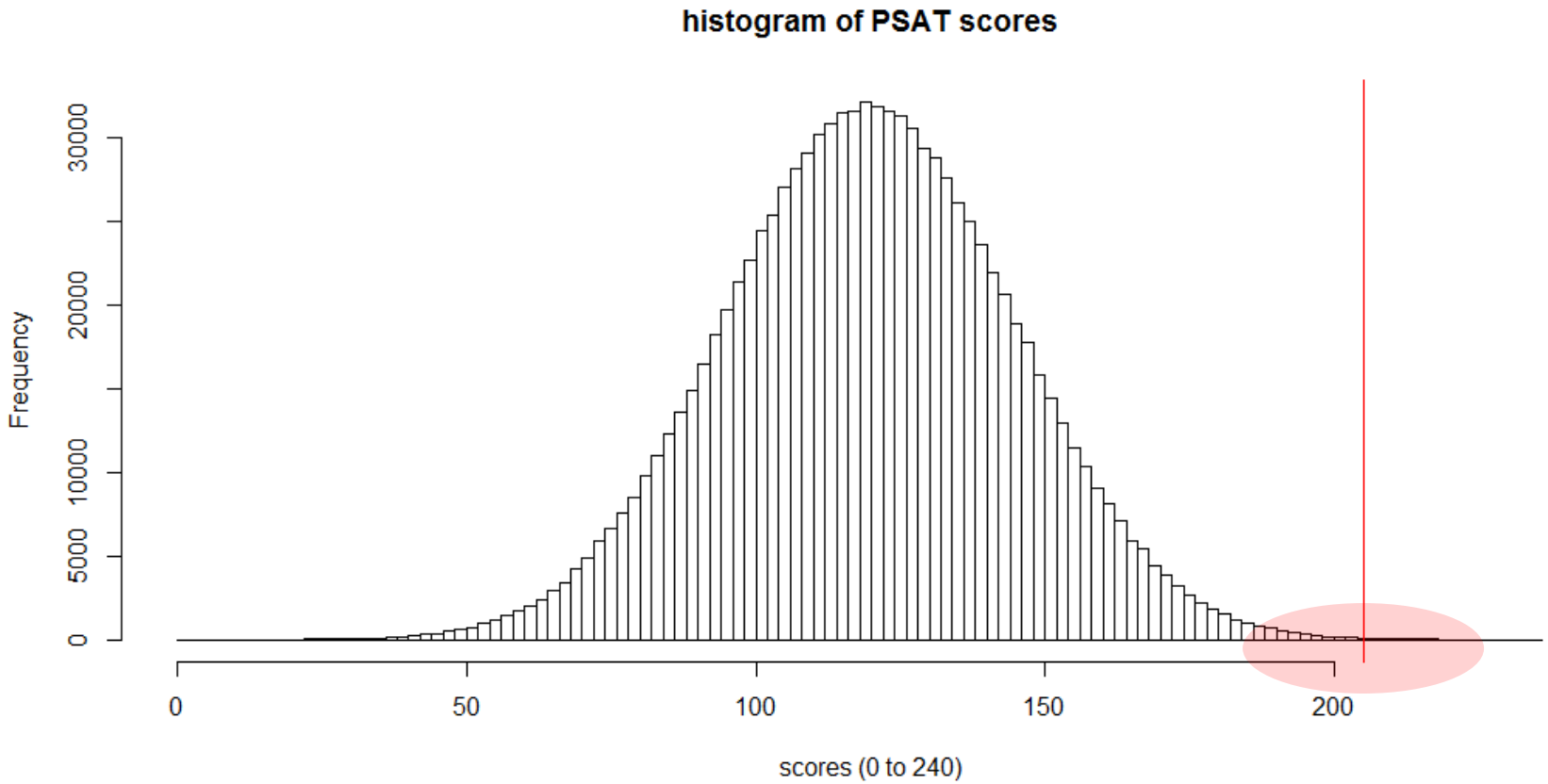

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- The *localness* is really important. Think: the exact cutoff point is a bit arbitrary, but it's being made in a covariate that is really important and meaningful for the context.

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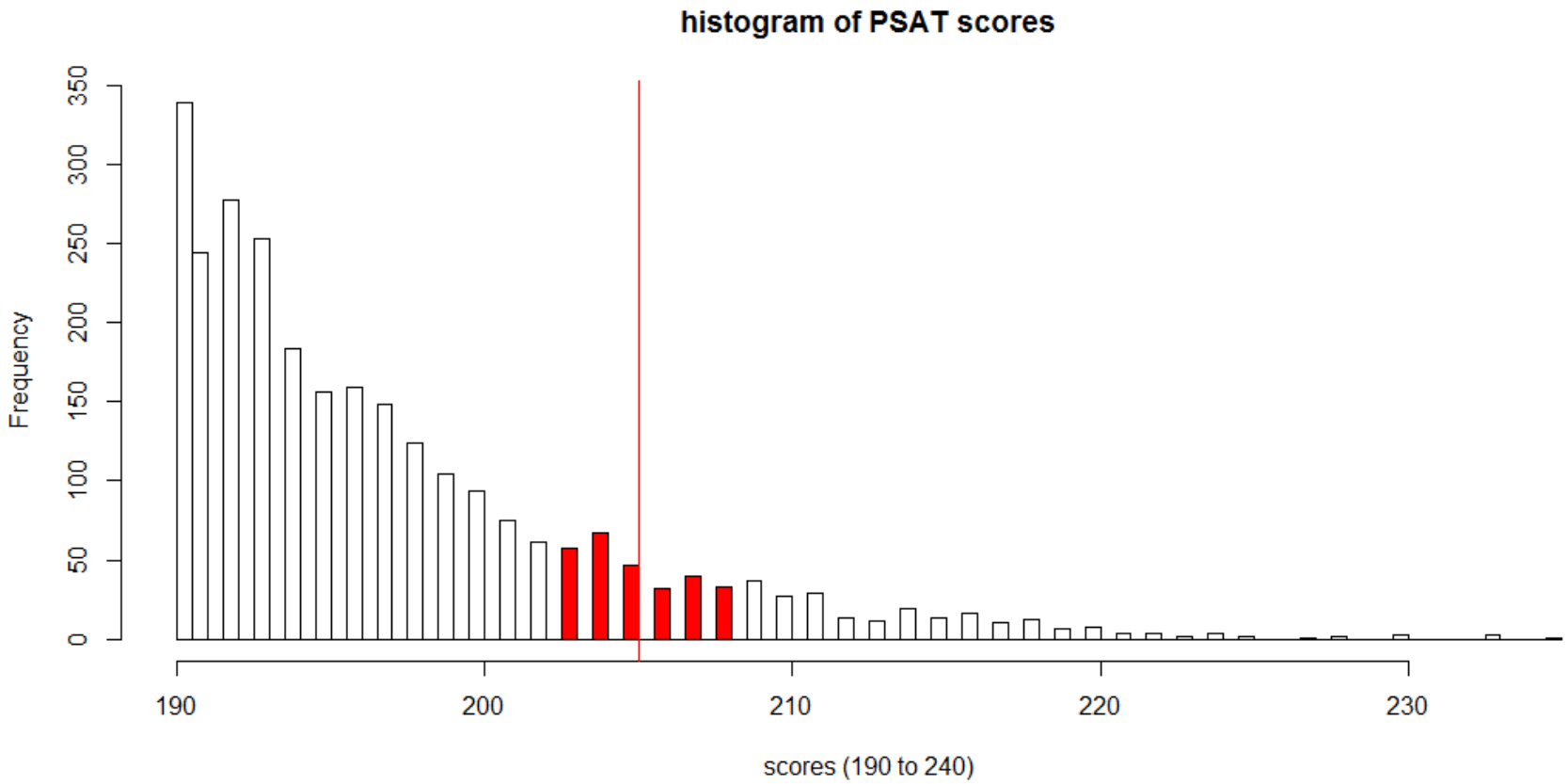

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- Many economists will use some kind of SEM (Cuesta and Imai):

$$income_{i,j} = y_i + \beta * d_j + u_{i,j}$$

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P(scholarship)

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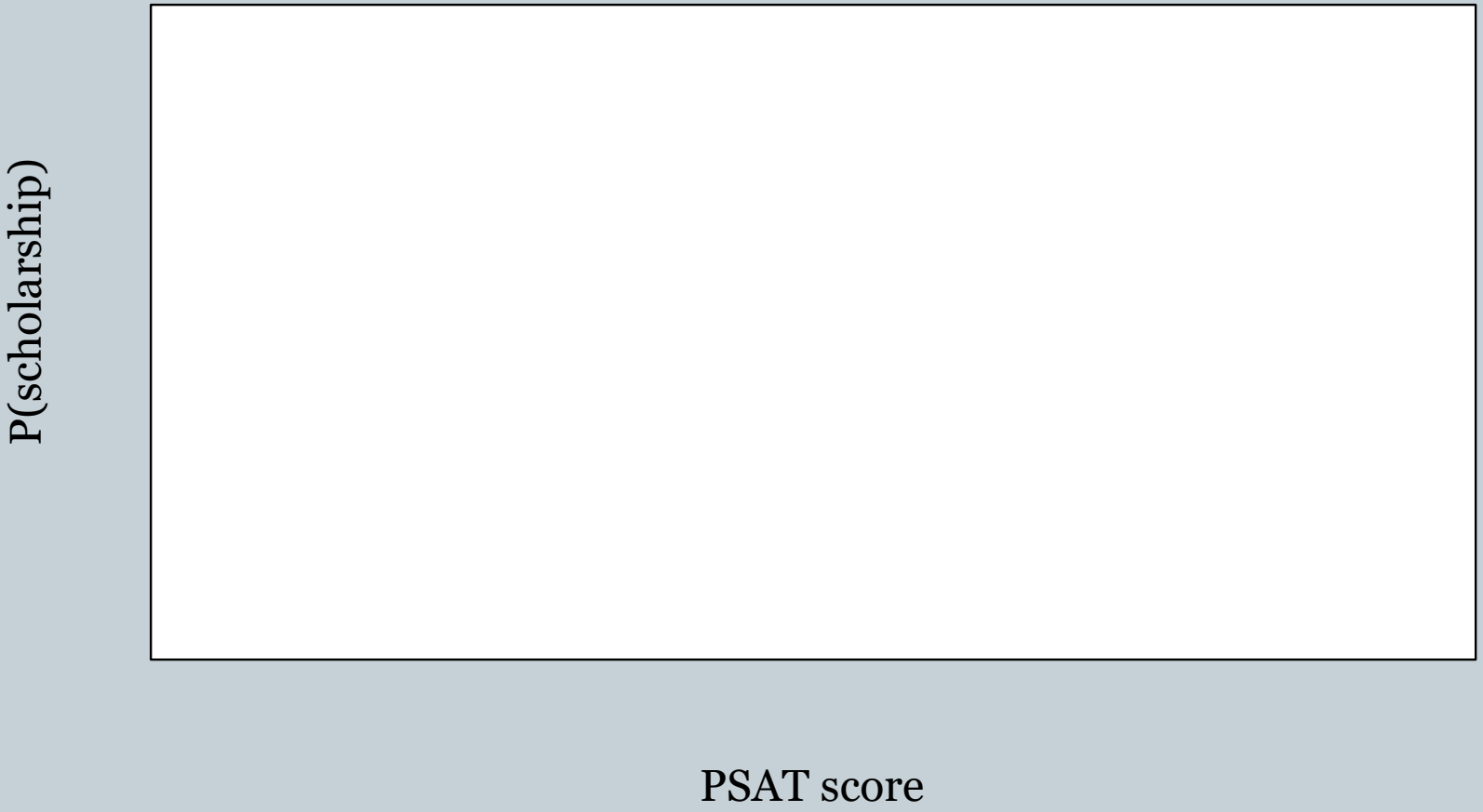

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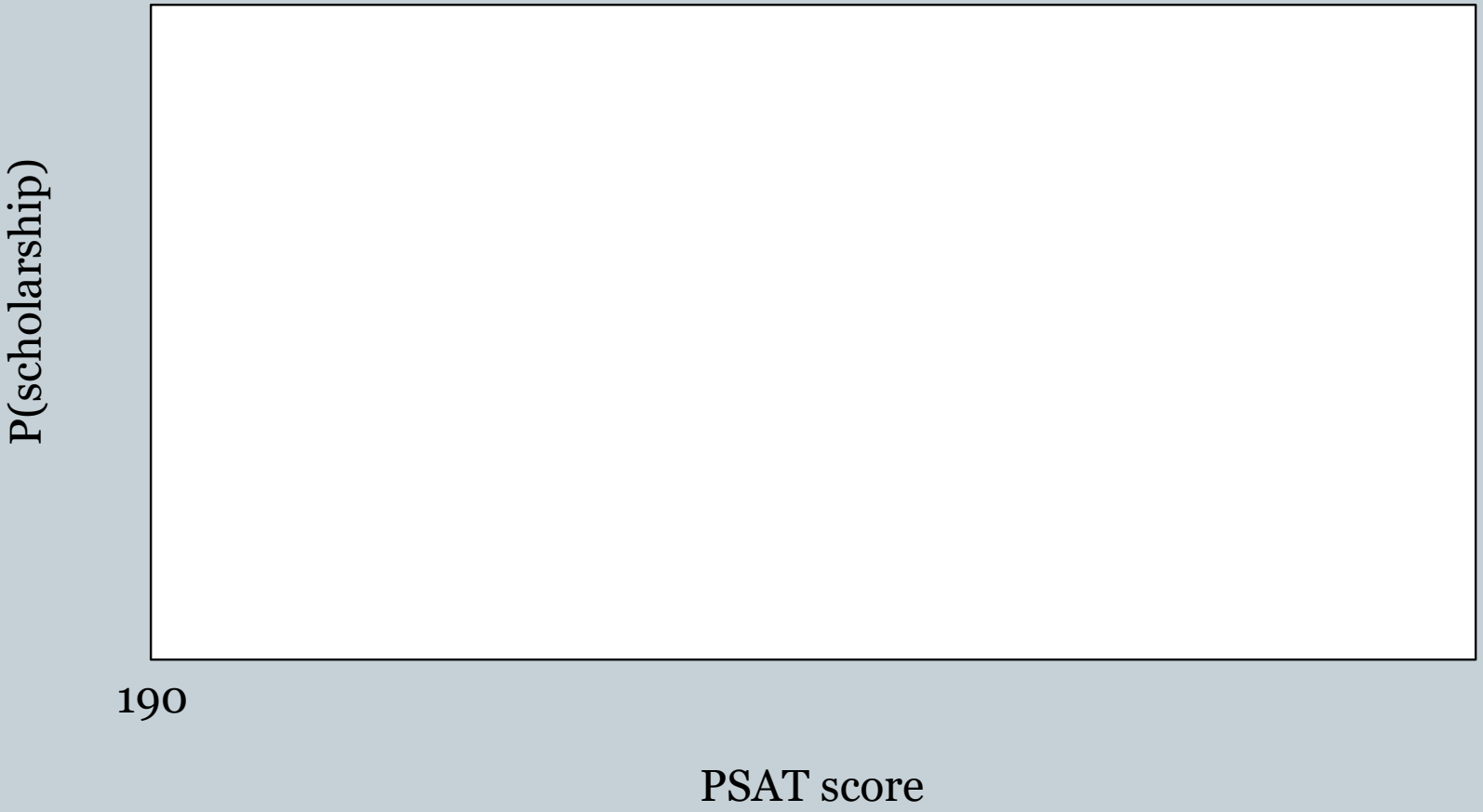

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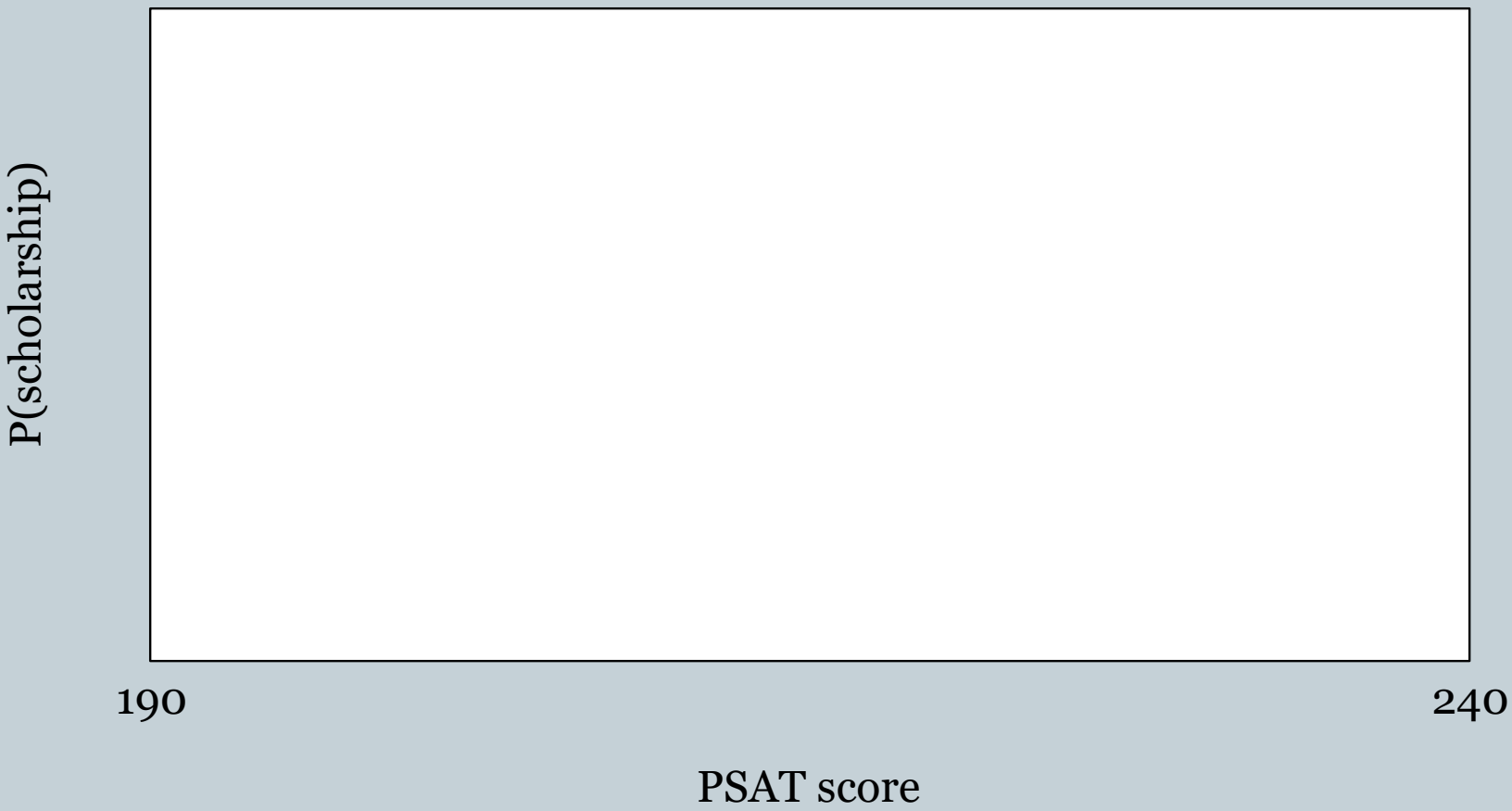

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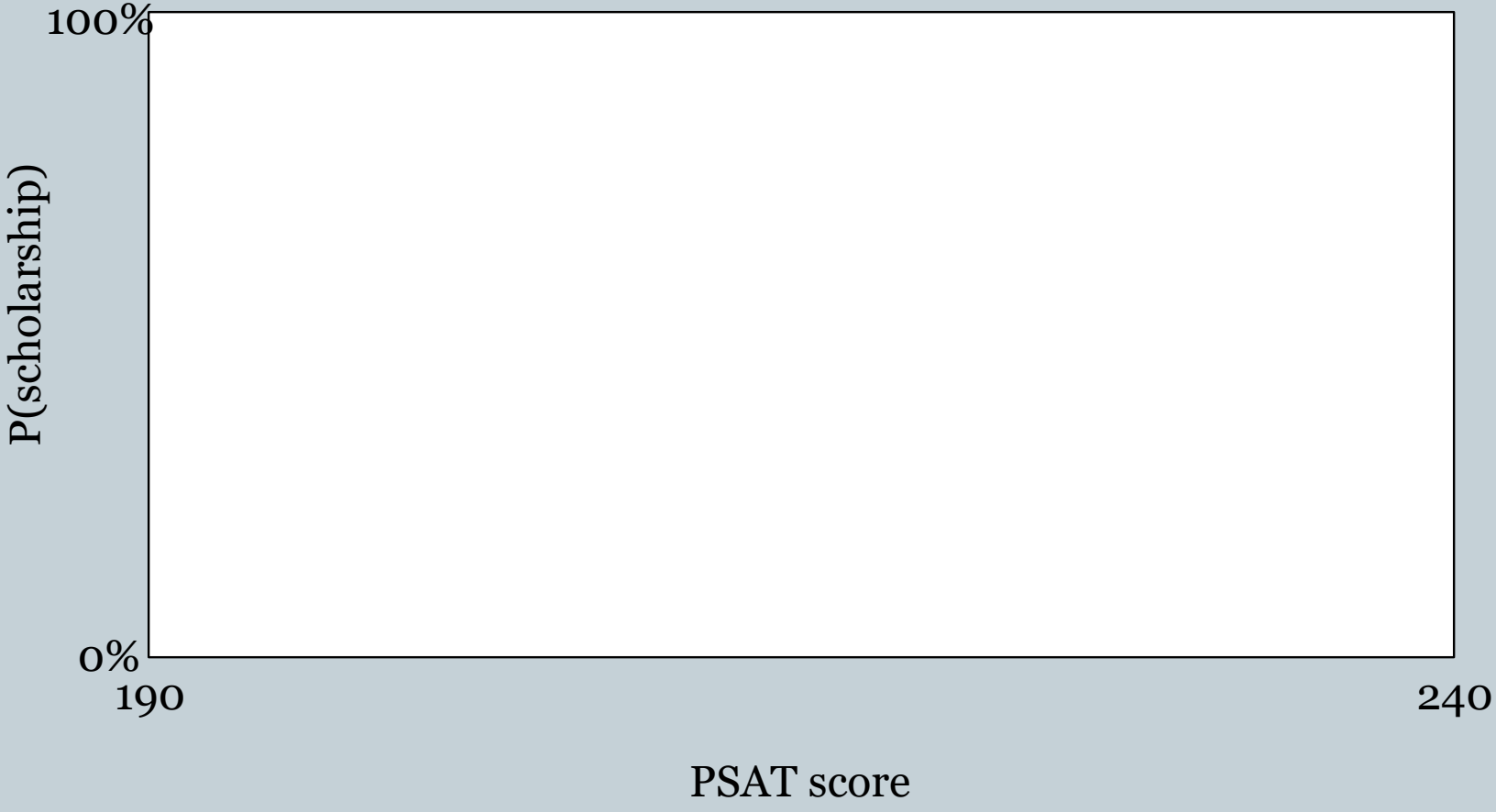

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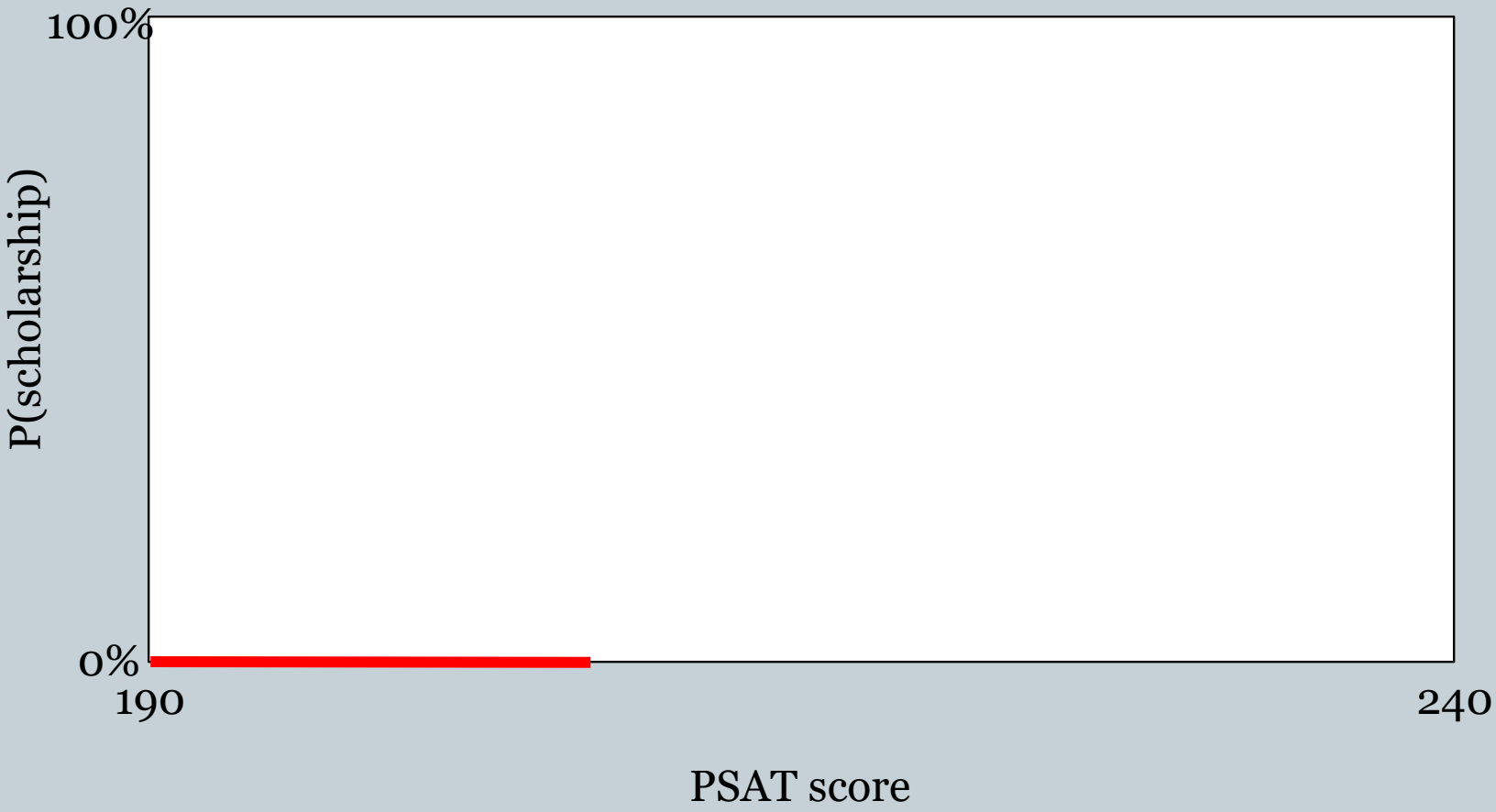

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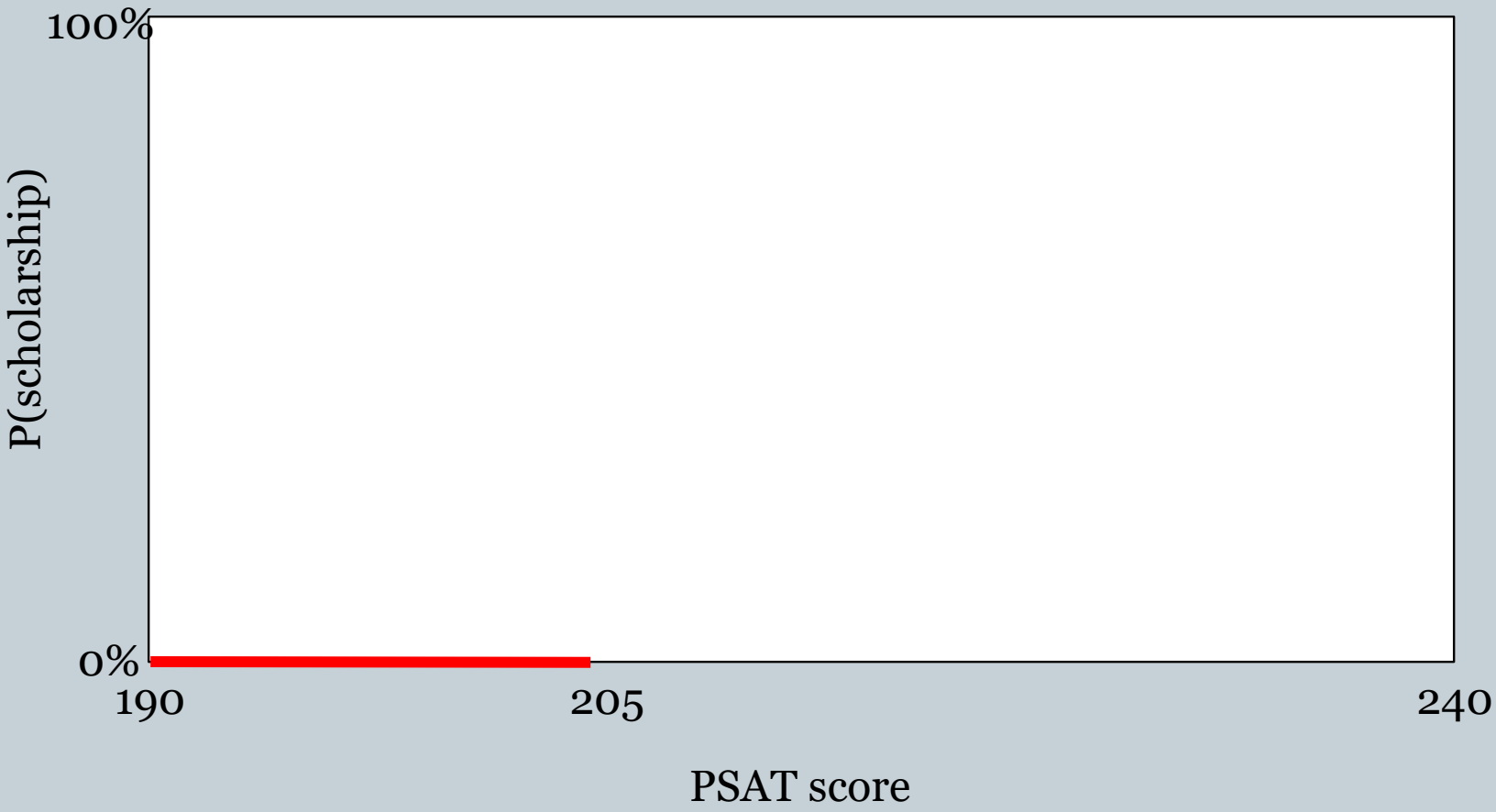

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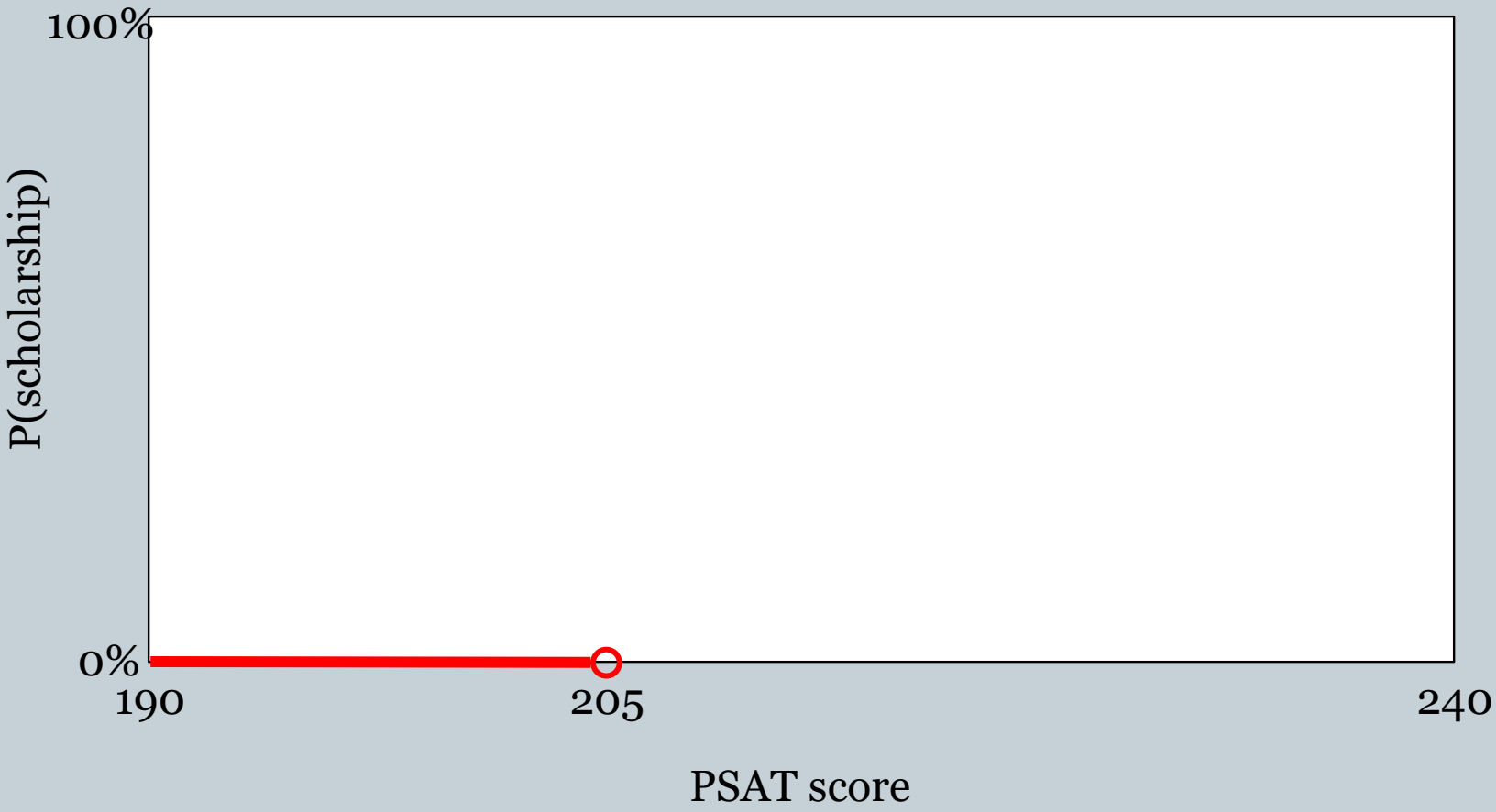

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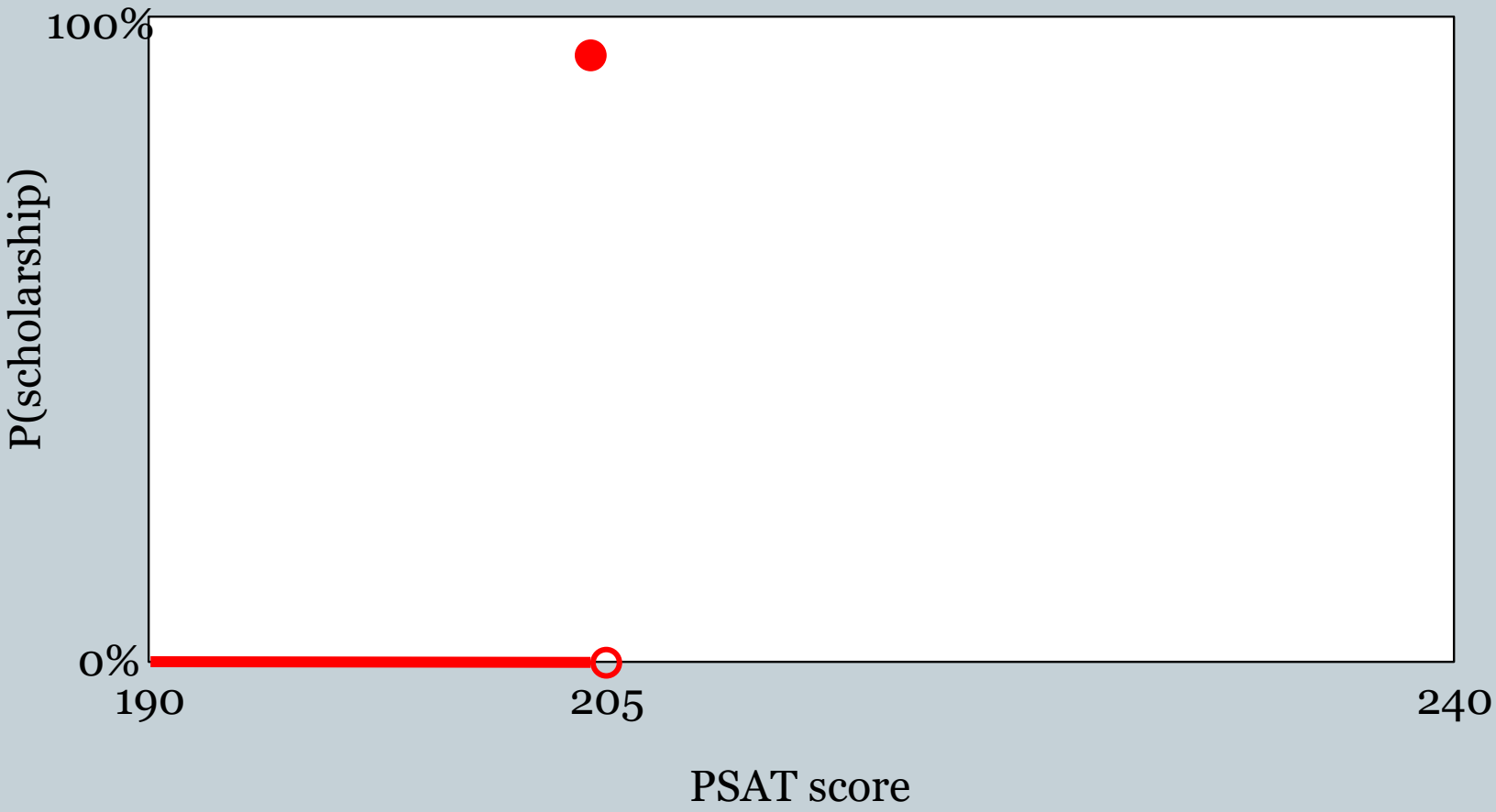

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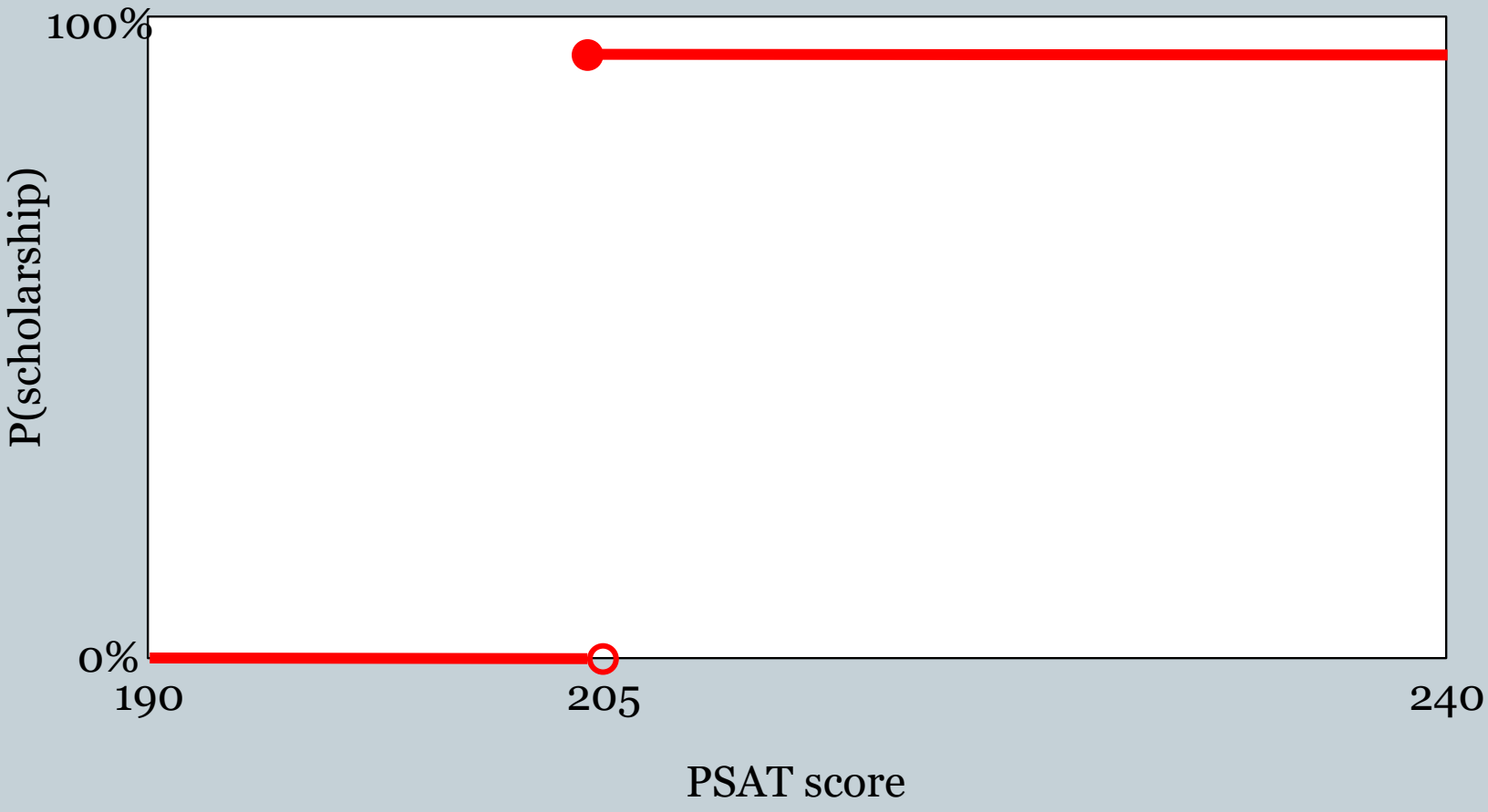
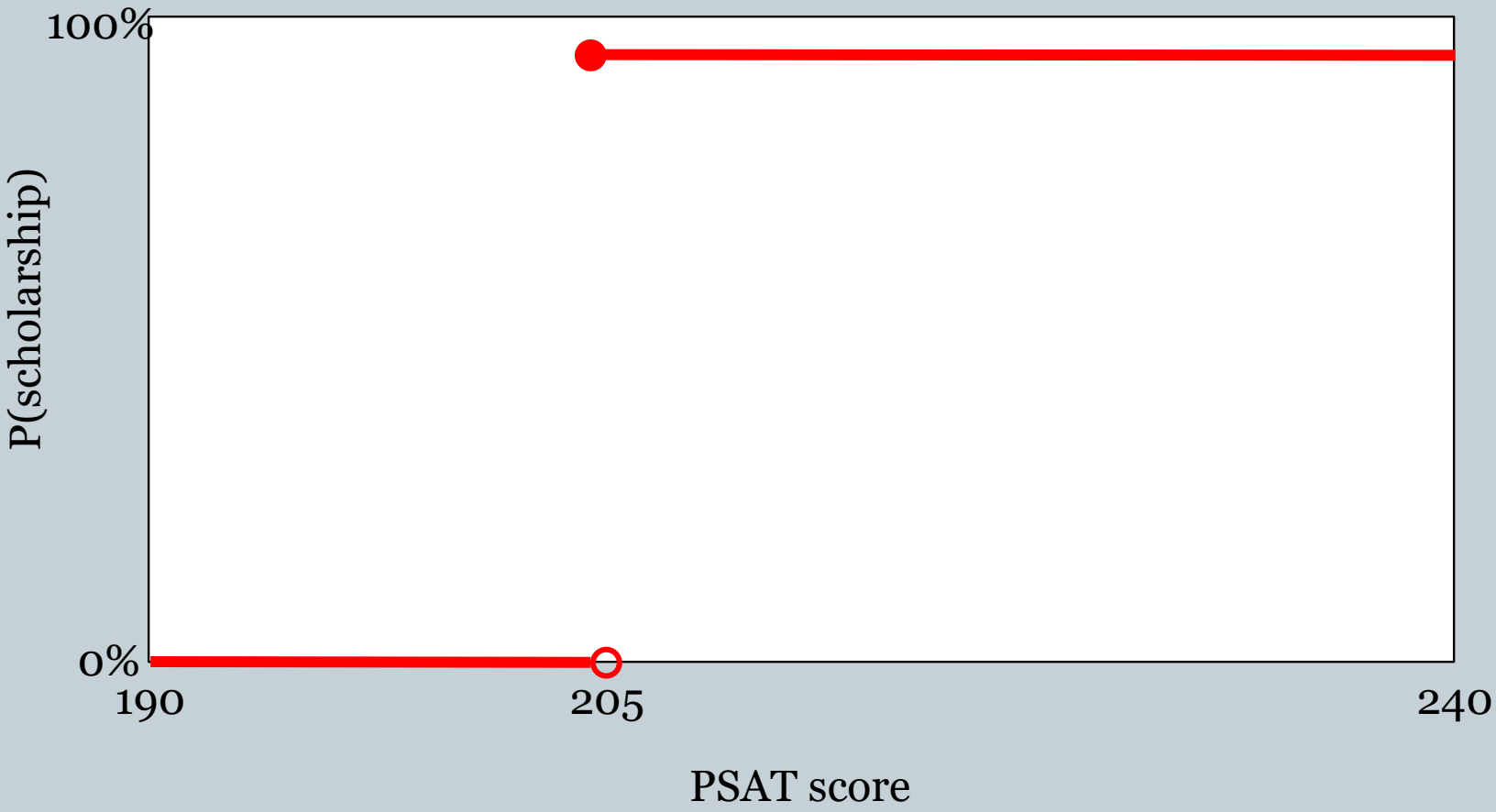


fuzzy RD designs



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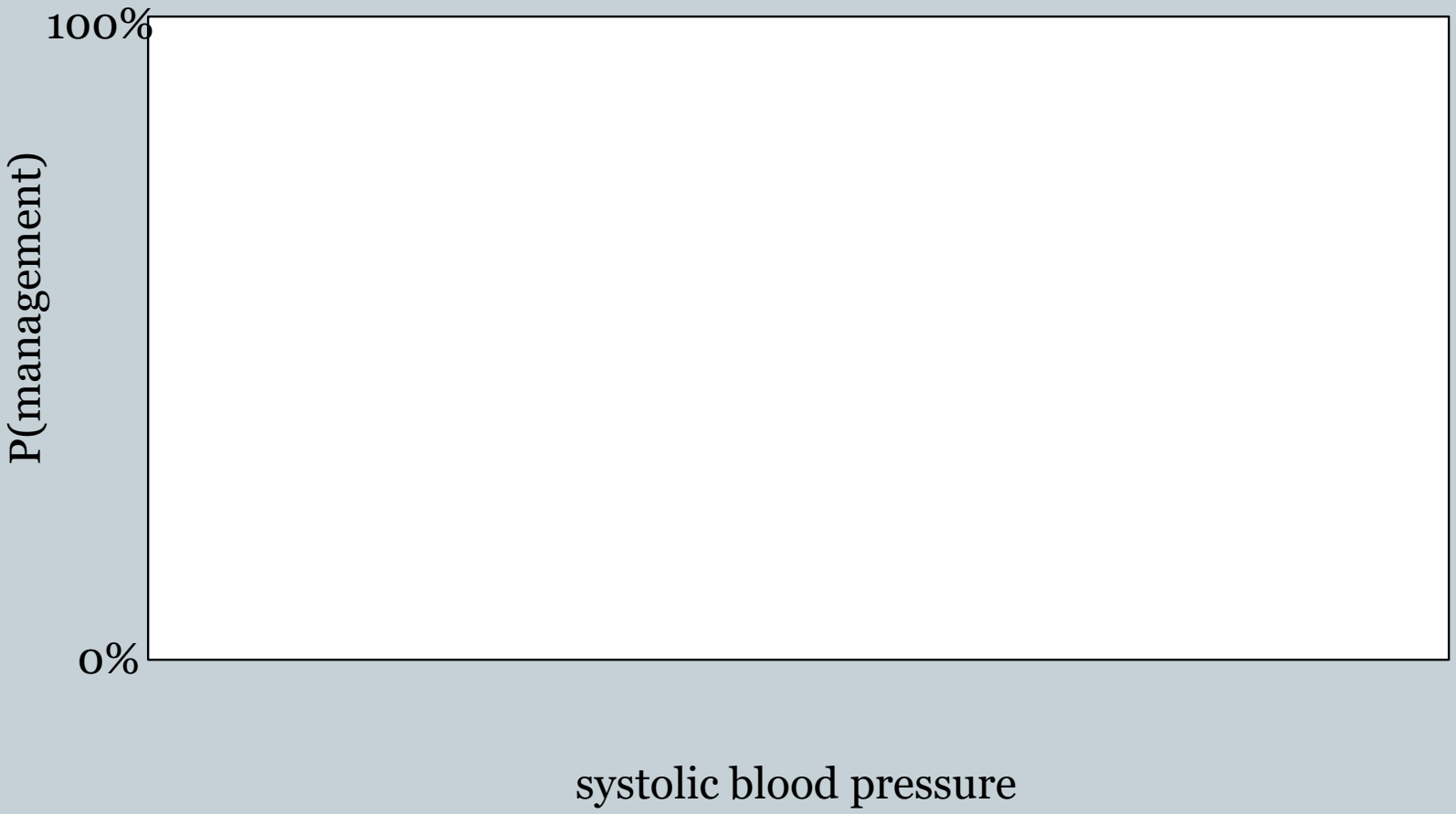

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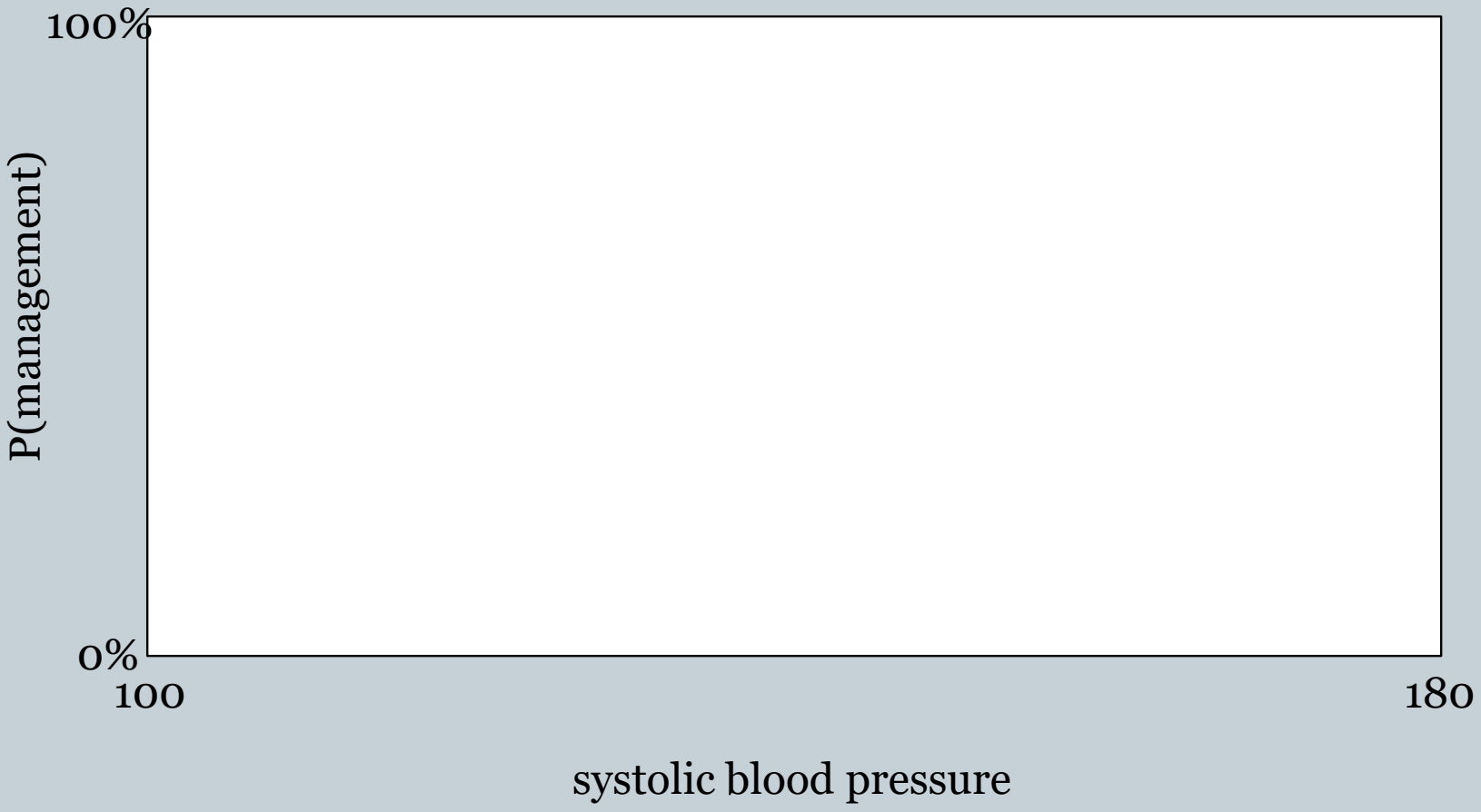

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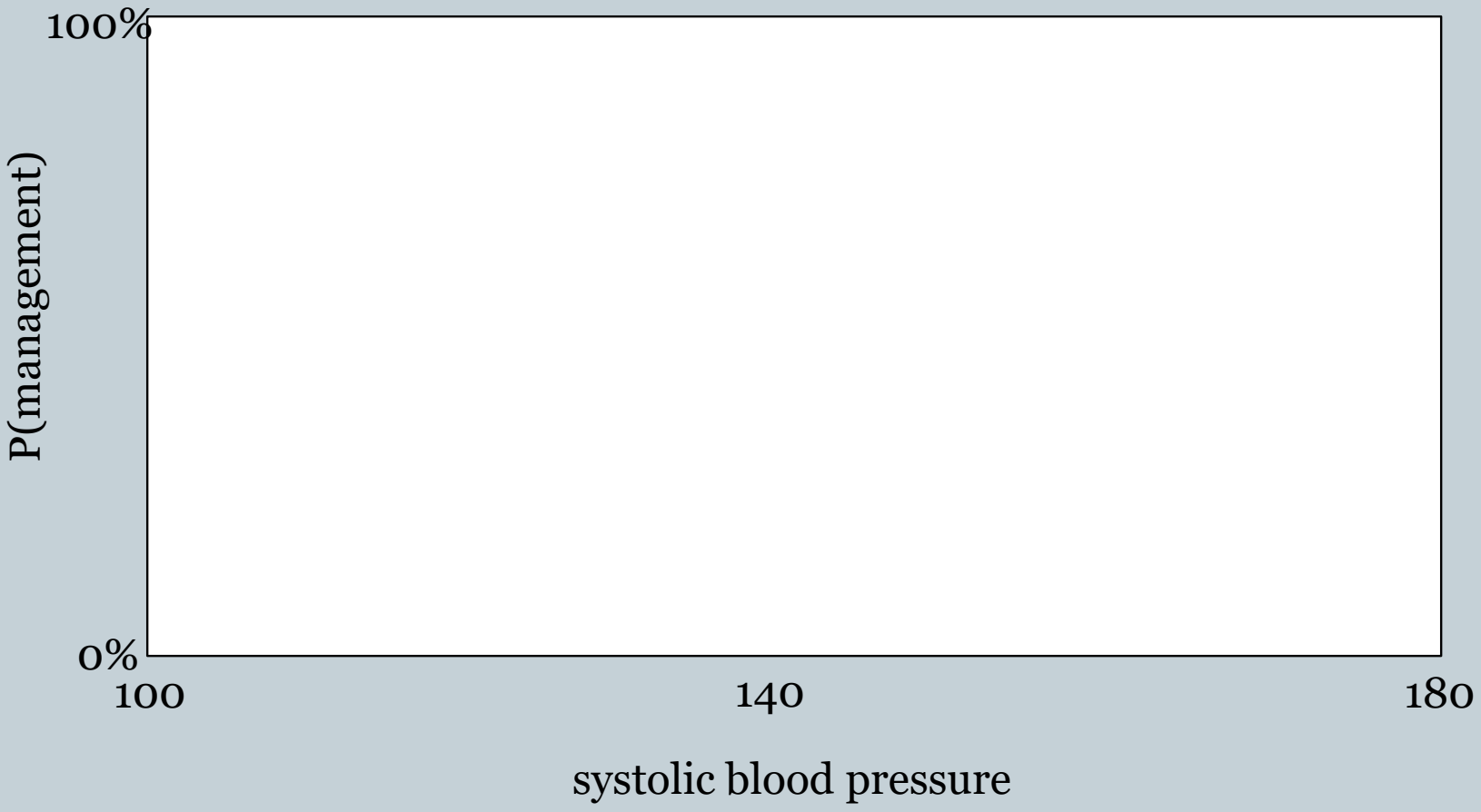

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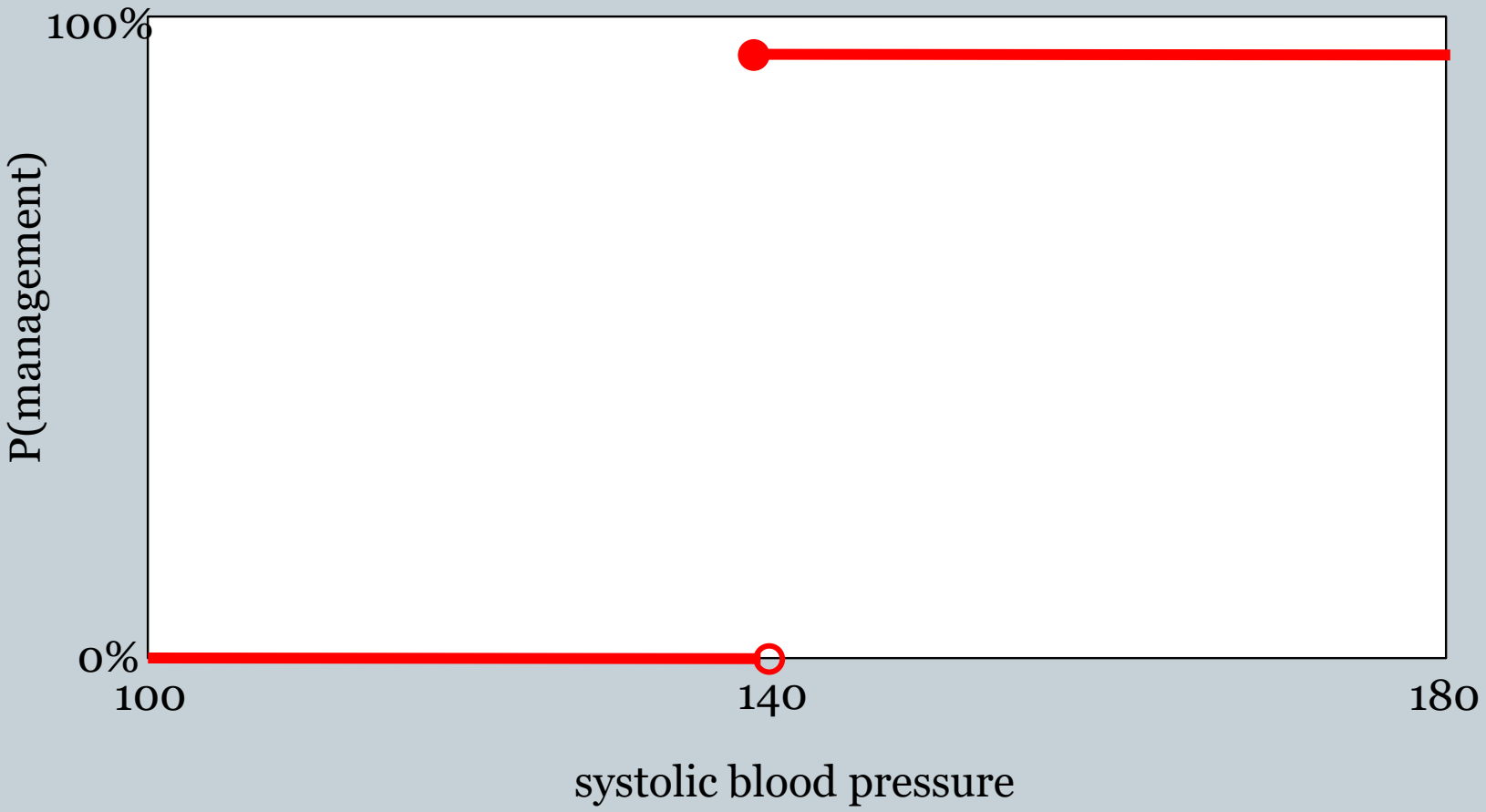

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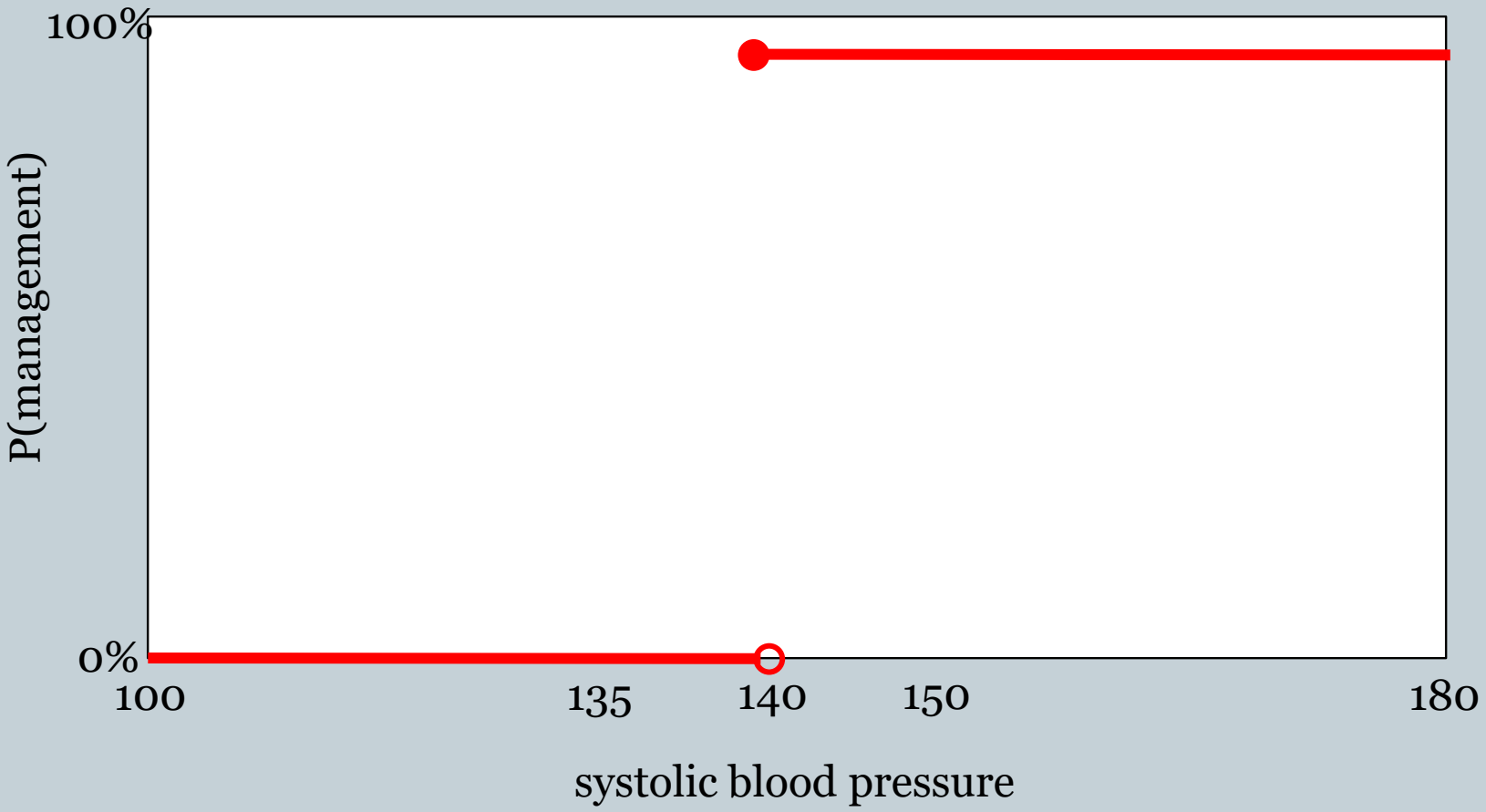

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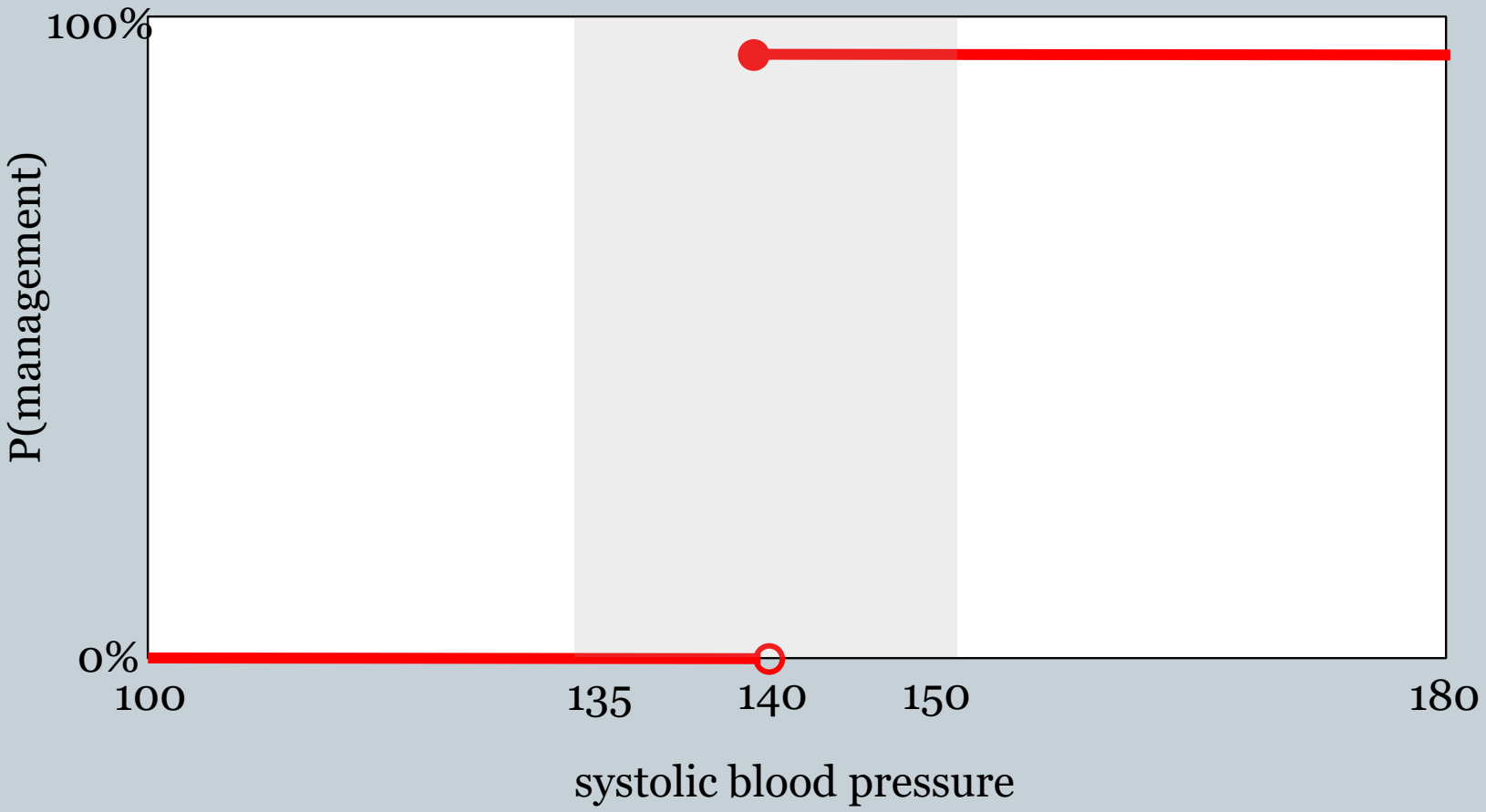

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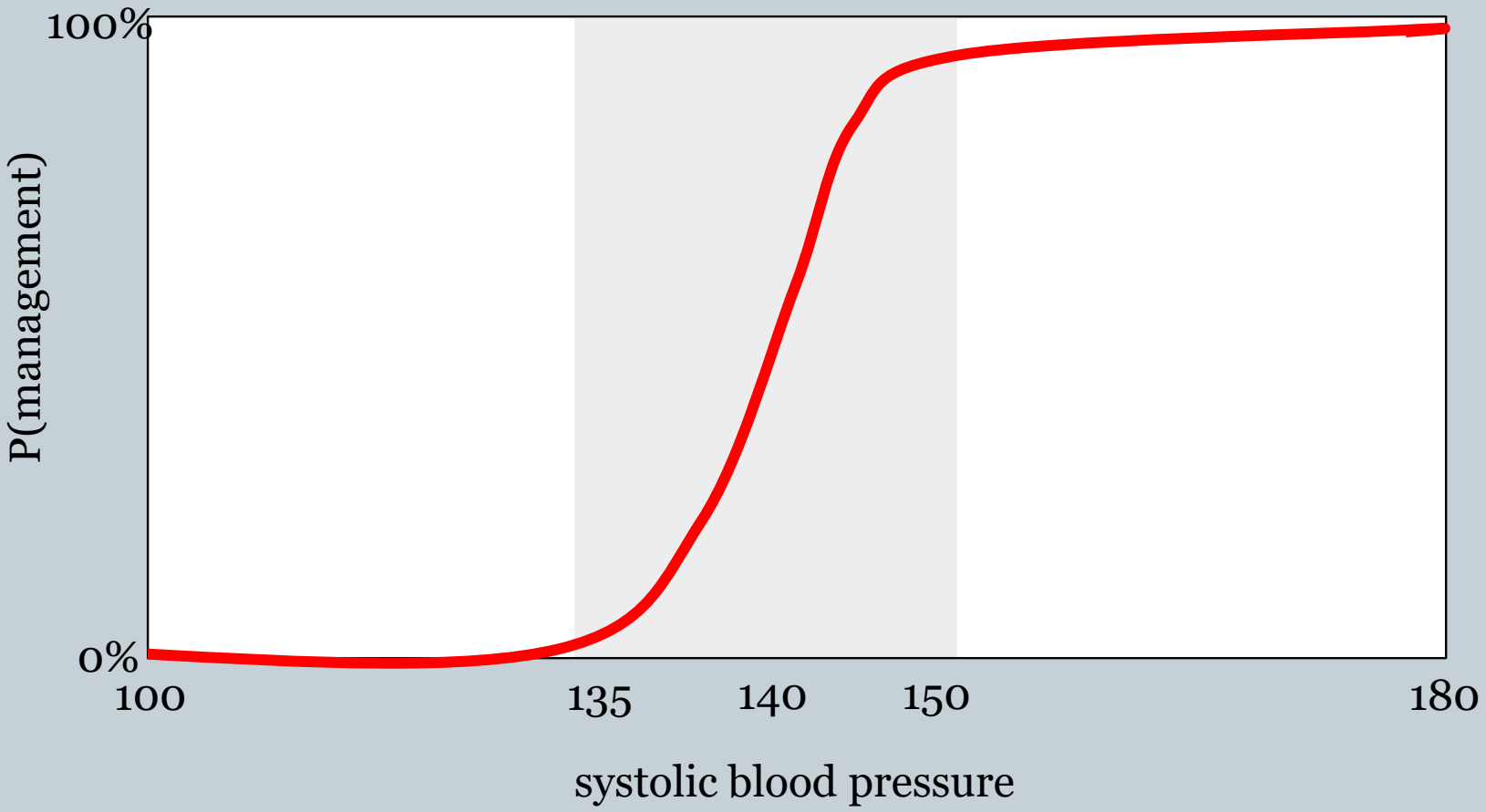
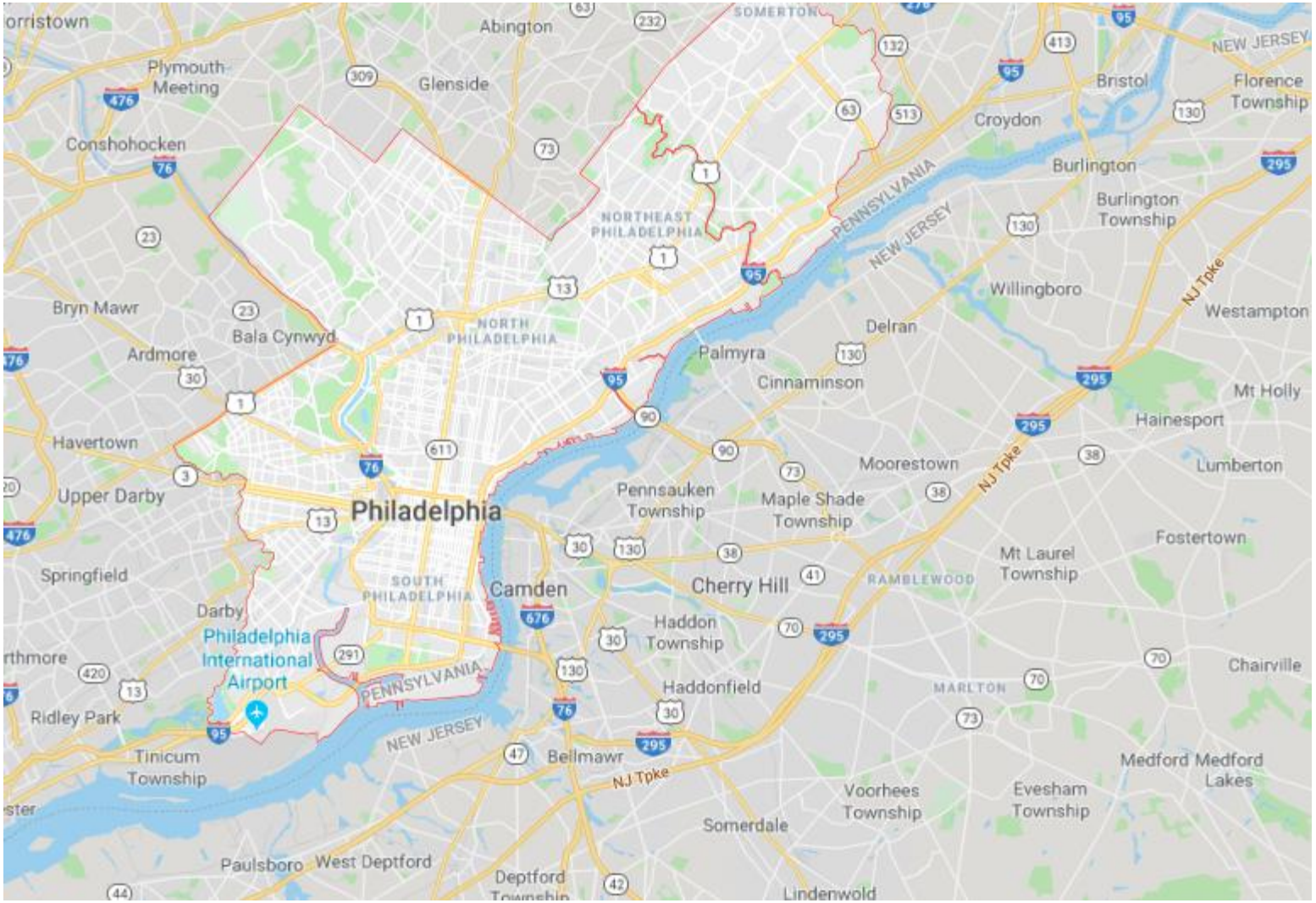
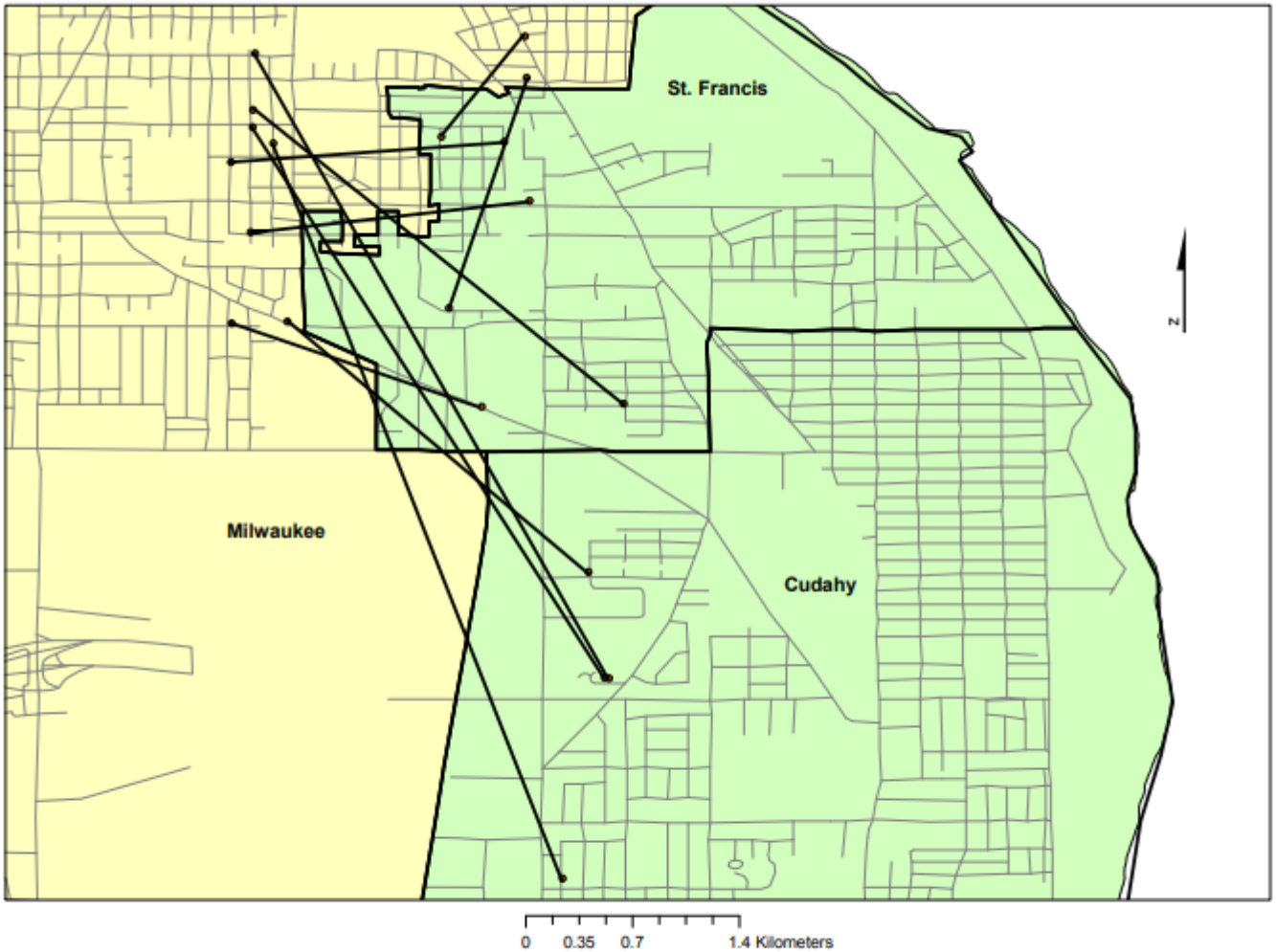


Card and Krueger: minimum wages

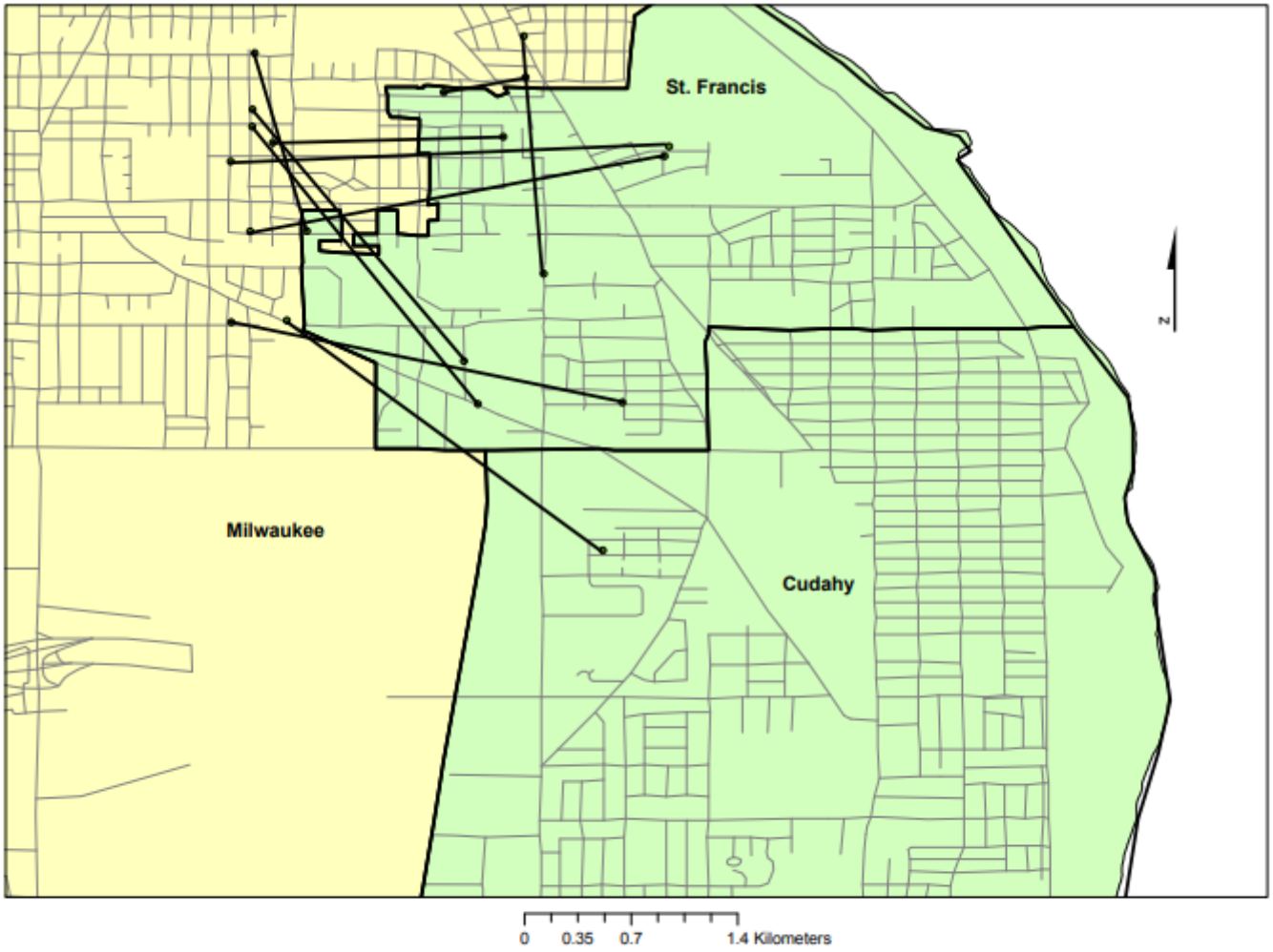


https://www.nber.org/papers/w4509.pdf

Keele et al: getting the vote out

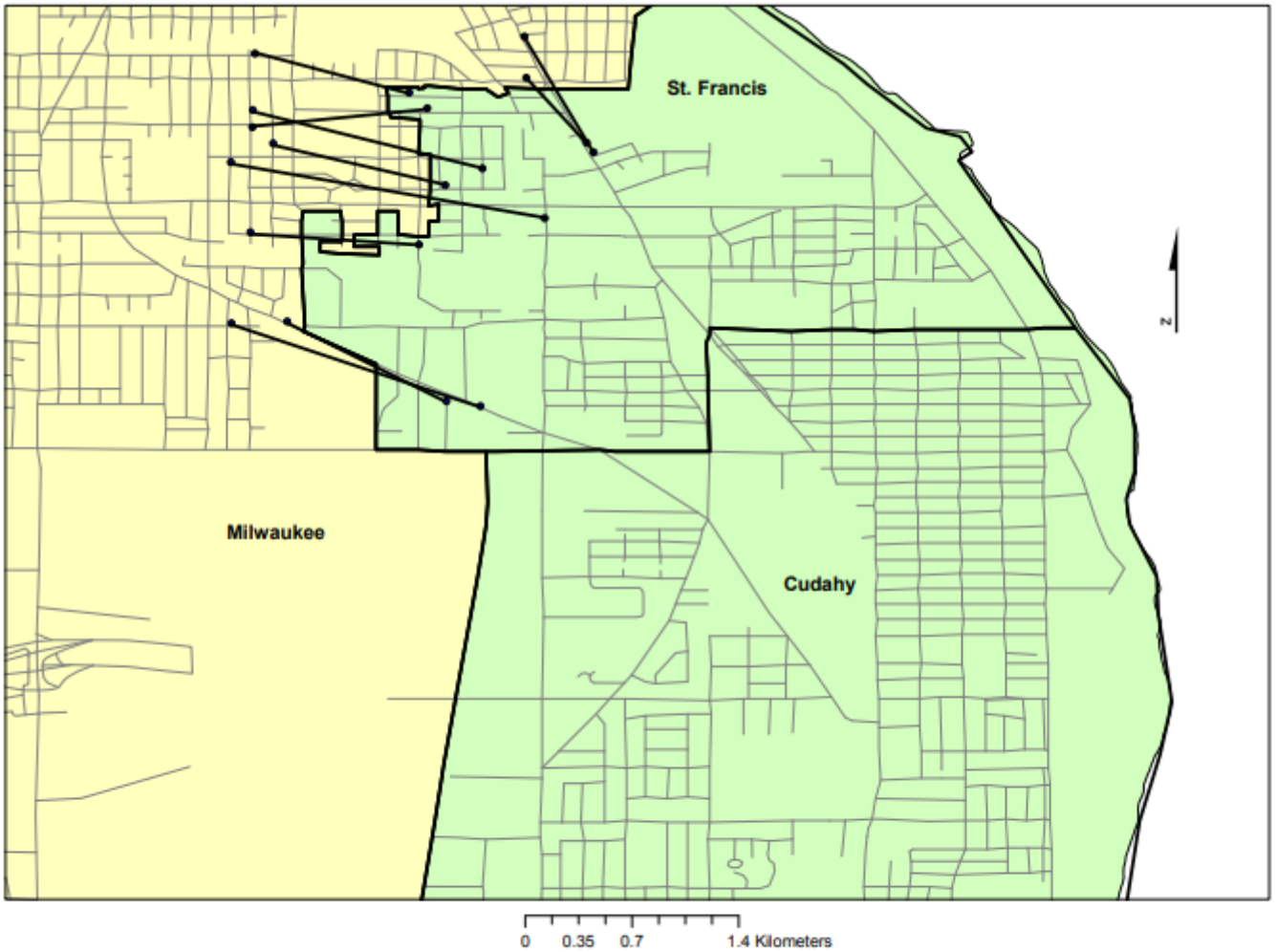


(a) Design 1 - Covariates Only Match



(b) Design 2 - Distance Only Match

https://www0.gsb.columbia.edu/mygsb/faculty/research/pubfiles/6137/GeoMatch.pdf



(c) Design 3 - Covariates and Distance Match

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  - Is the randomness really unconnected with the variables you are concerned may be causing confounding?
- Consider how far from the cutoff point to use.

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- Discuss the randomness
  - Comes from lack of precise control around the cutoff point.
  - Is the randomness really unconnected with the variables you are concerned may be causing confounding?
- Consider how far from the cutoff point to use.
- Do a Table 1 of above and below cutoff.

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- Bottom line: RD tries to set up like an RCT. The randomness, though, is still "off-stage."
- Inference can be done like the pscore set up (sharp RD).

“case-control” studies

case-noncase

case-noncase

- Several different names

case-noncase

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- Developed for looking for causes of rare outcomes

case-noncase

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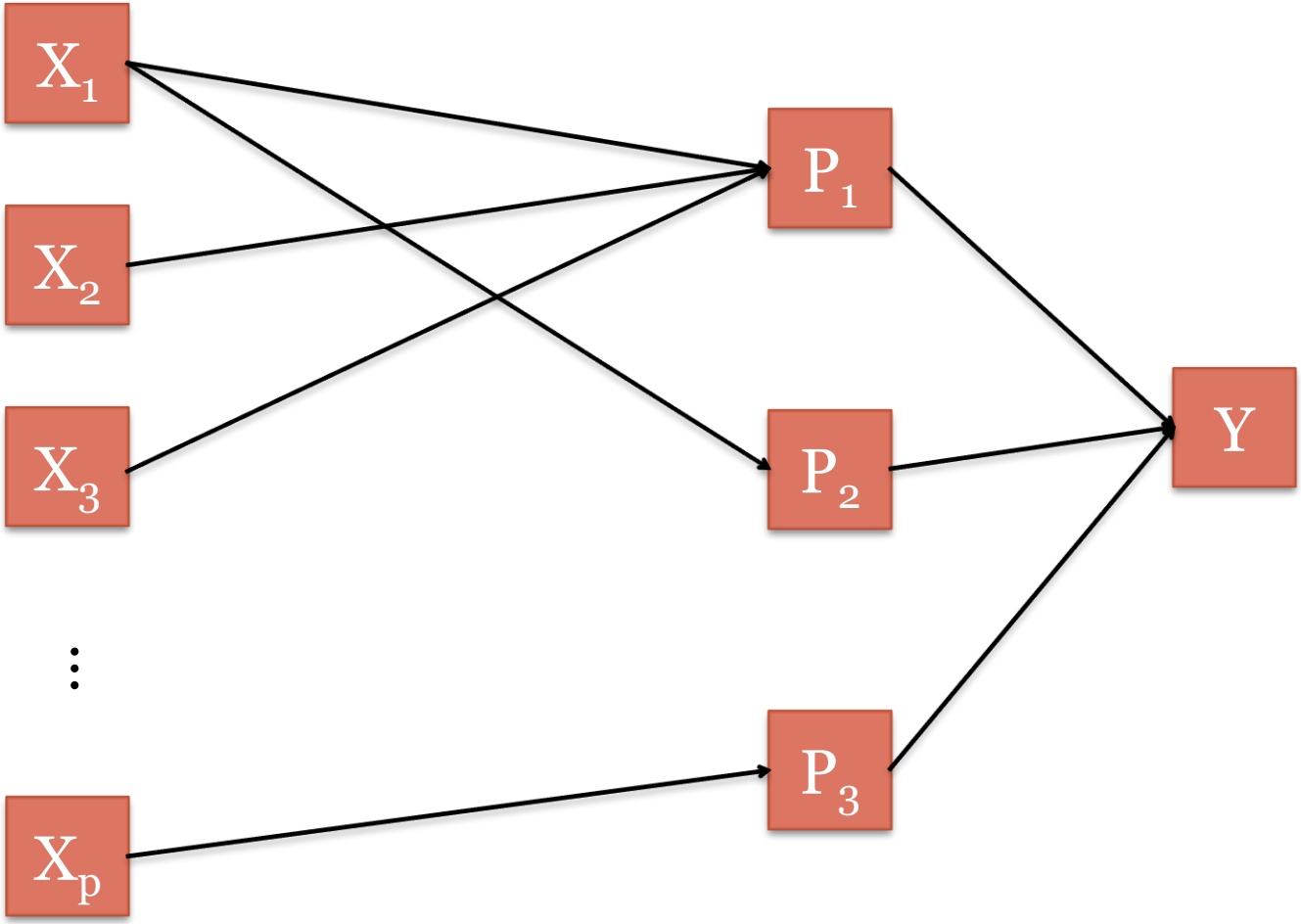
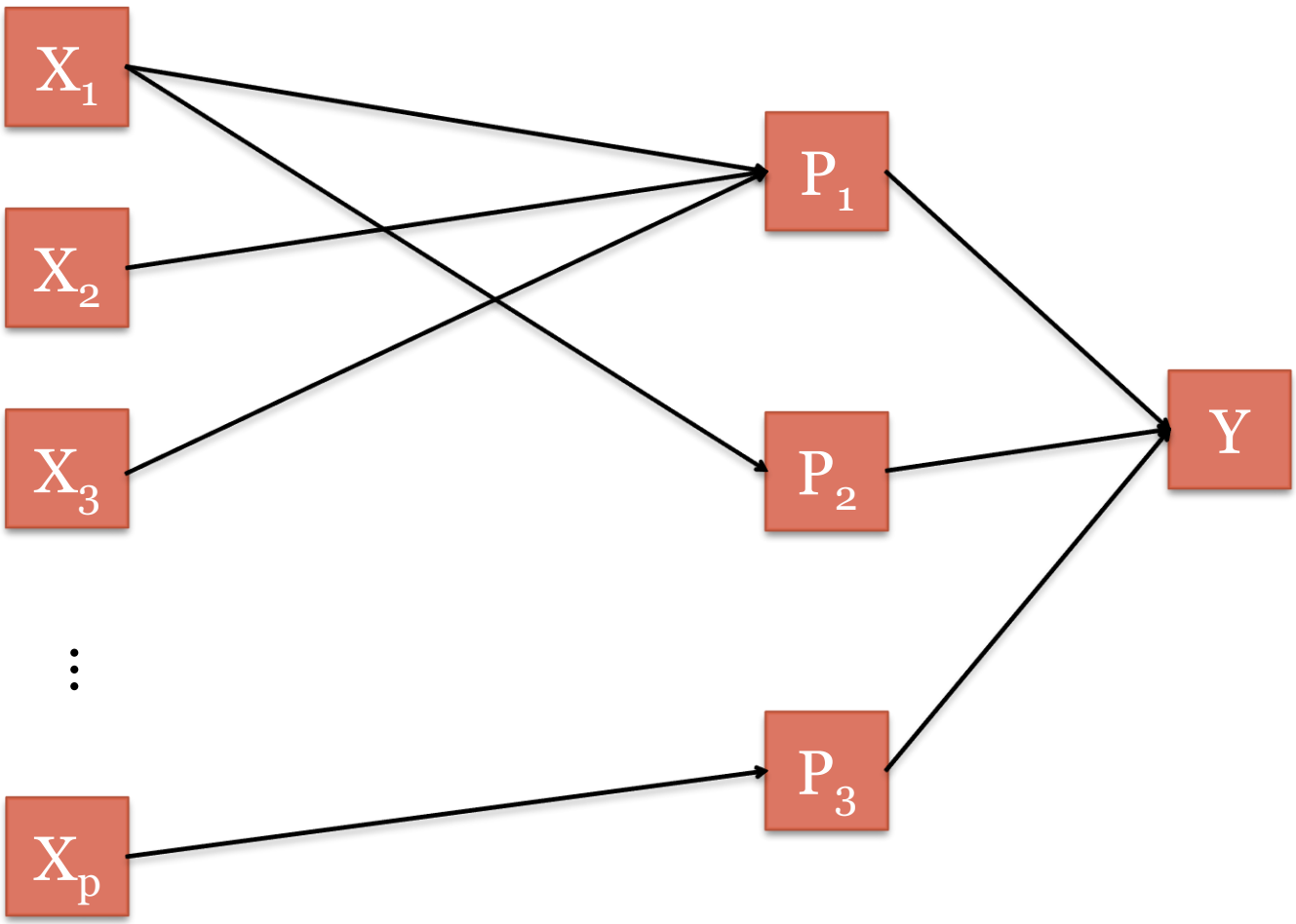
case-noncase

- Several different names
- Developed for looking for causes of rare outcomes
- Staple of epi
- Out-of-favor in modern causal inference
- If you're being intellectually lazy then these studies feel a bit similar to what we've been doing.
- The structure of argument is much weaker than what we've been doing.

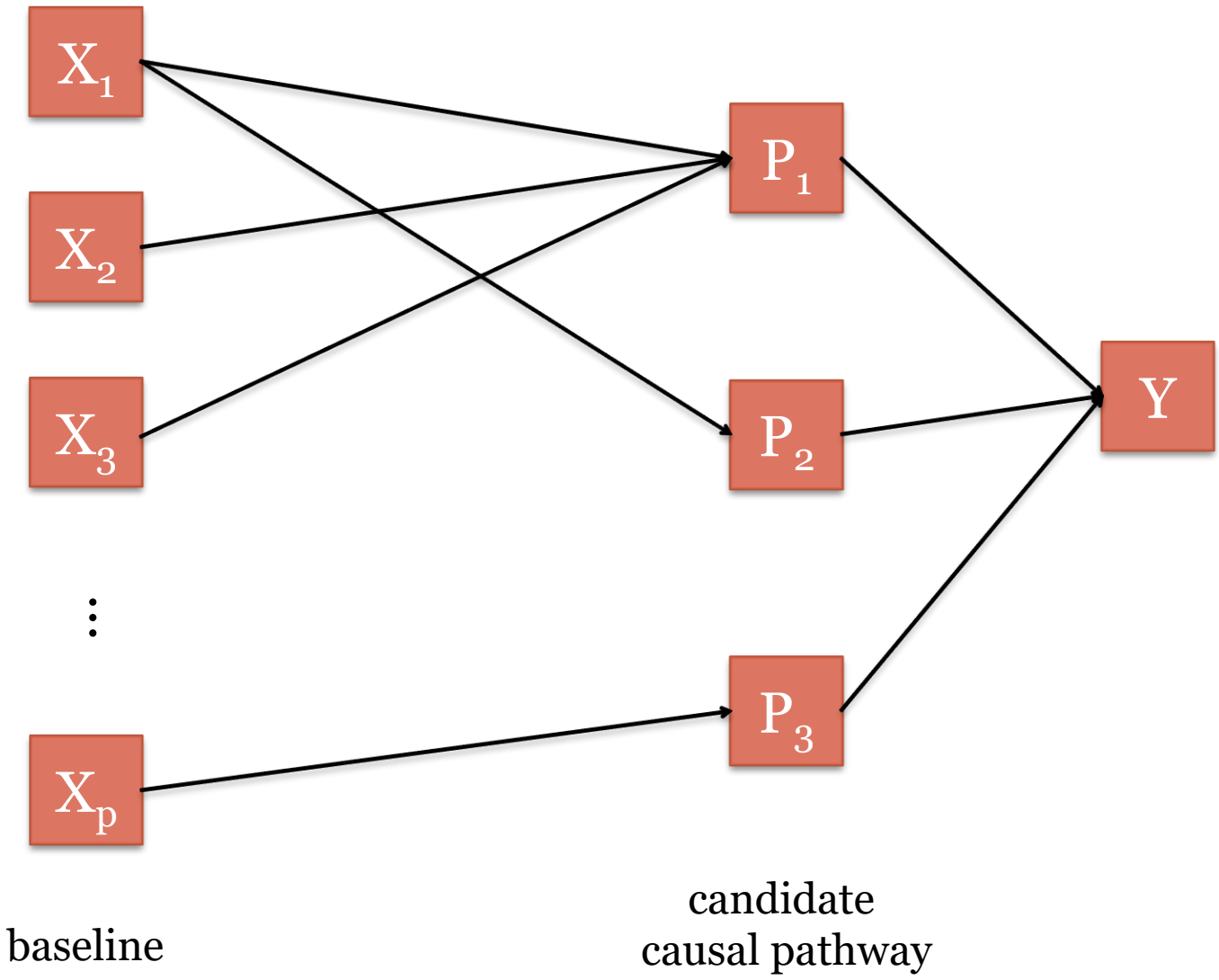
case-noncase

- Diagram of what we've been doing (start with cause and look at an outcome) – swap structure and go backward from outcome to candidate causes.


X_1
X_2
X_3
X_p
P_1
P_2
P_3
Y



baseline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X_2
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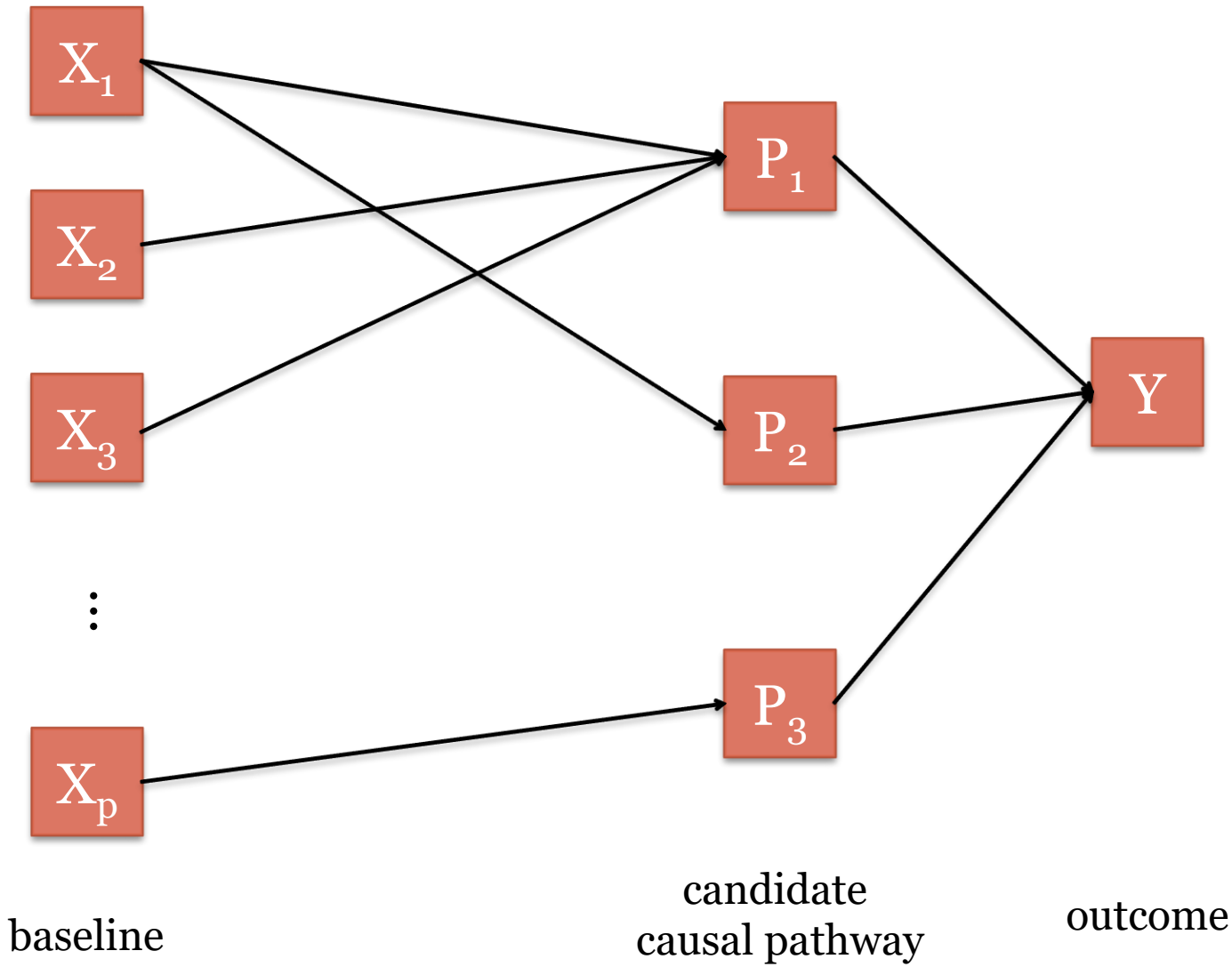
X_p
P_1
P_2
P_3
Y
baseline
candidate
causal pathway


X_1
X_2
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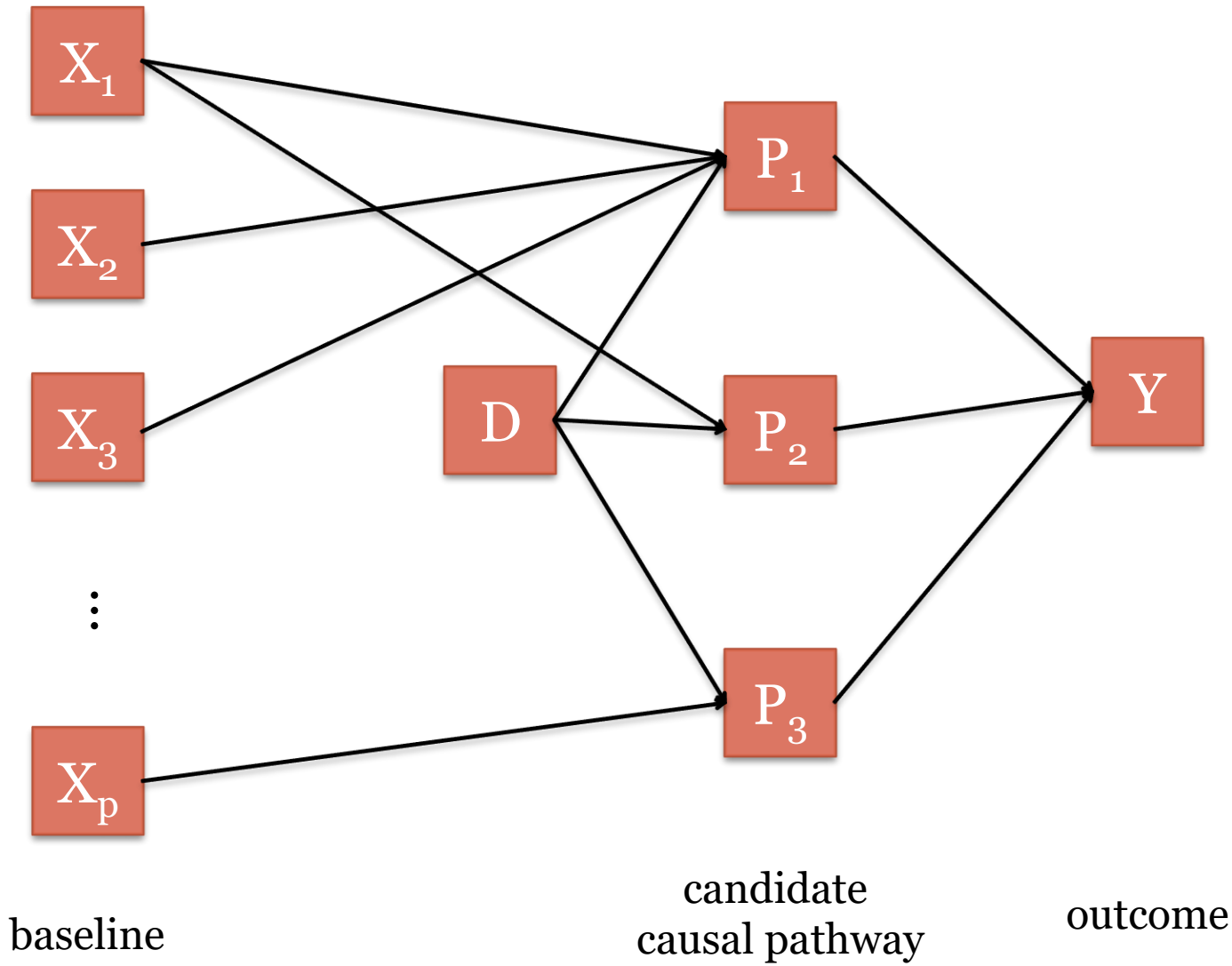
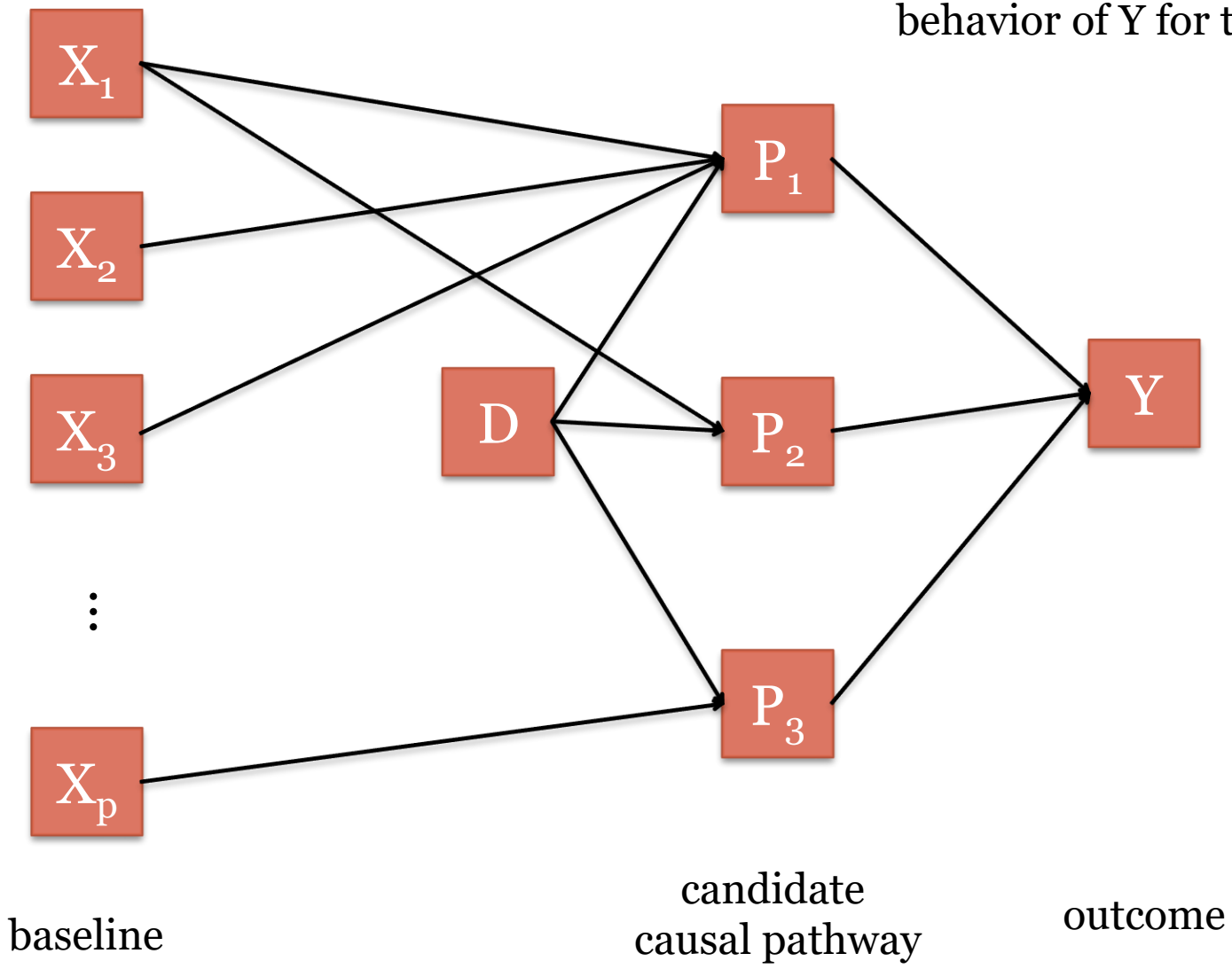
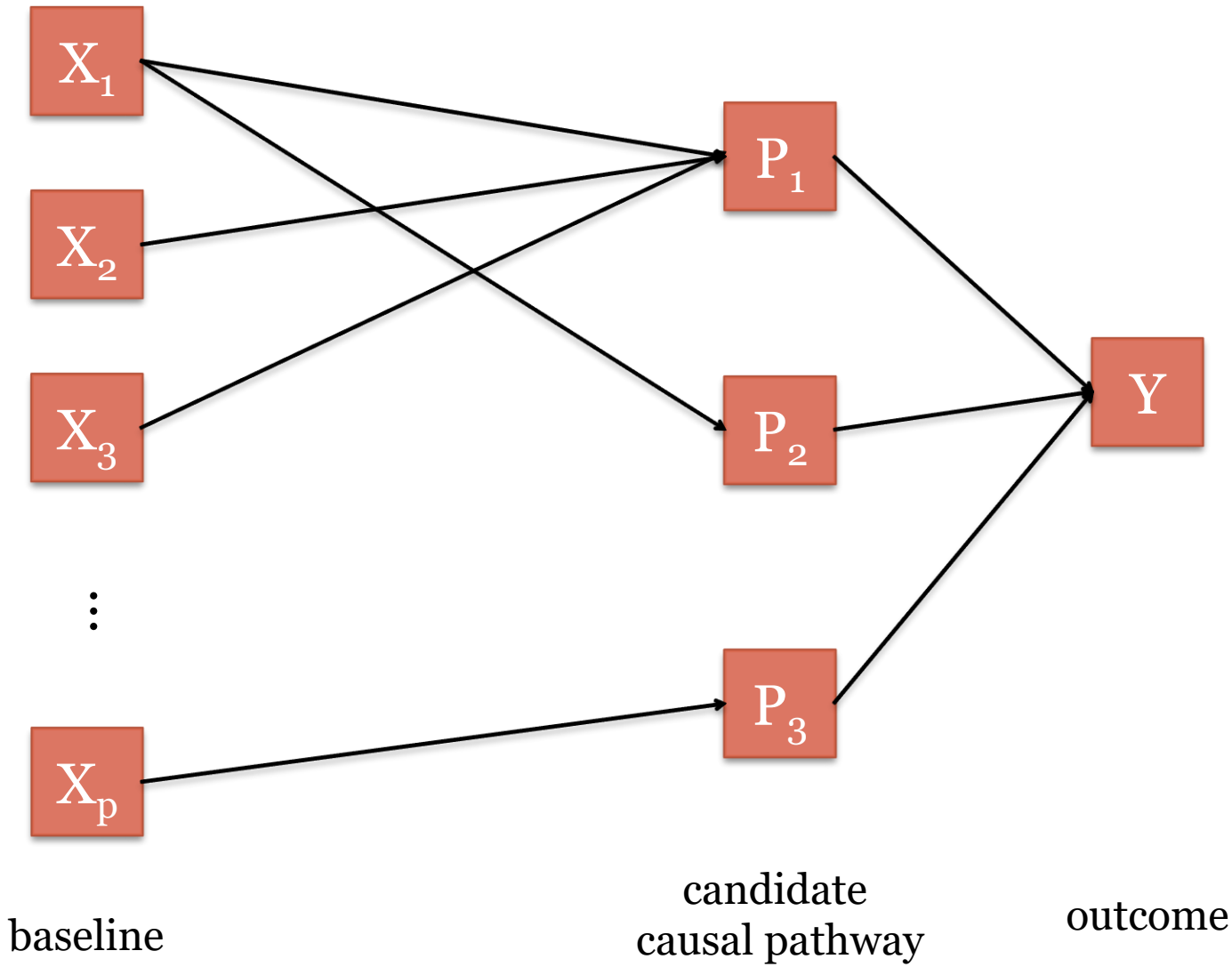
X_p
P_1
P_2
P_3
Y
baseline
candidate
causal pathway
outcome


X_1
X_2
X_3
X_p
D
P_1
P_2
P_3
Y
baseline
candidate
causal pathway
outcome

Contrast $d_i = 1, d_j = 0$. Then compare behavior of Y for the two groups.




X_1
X_2
X_3
X_p
P_1
P_2
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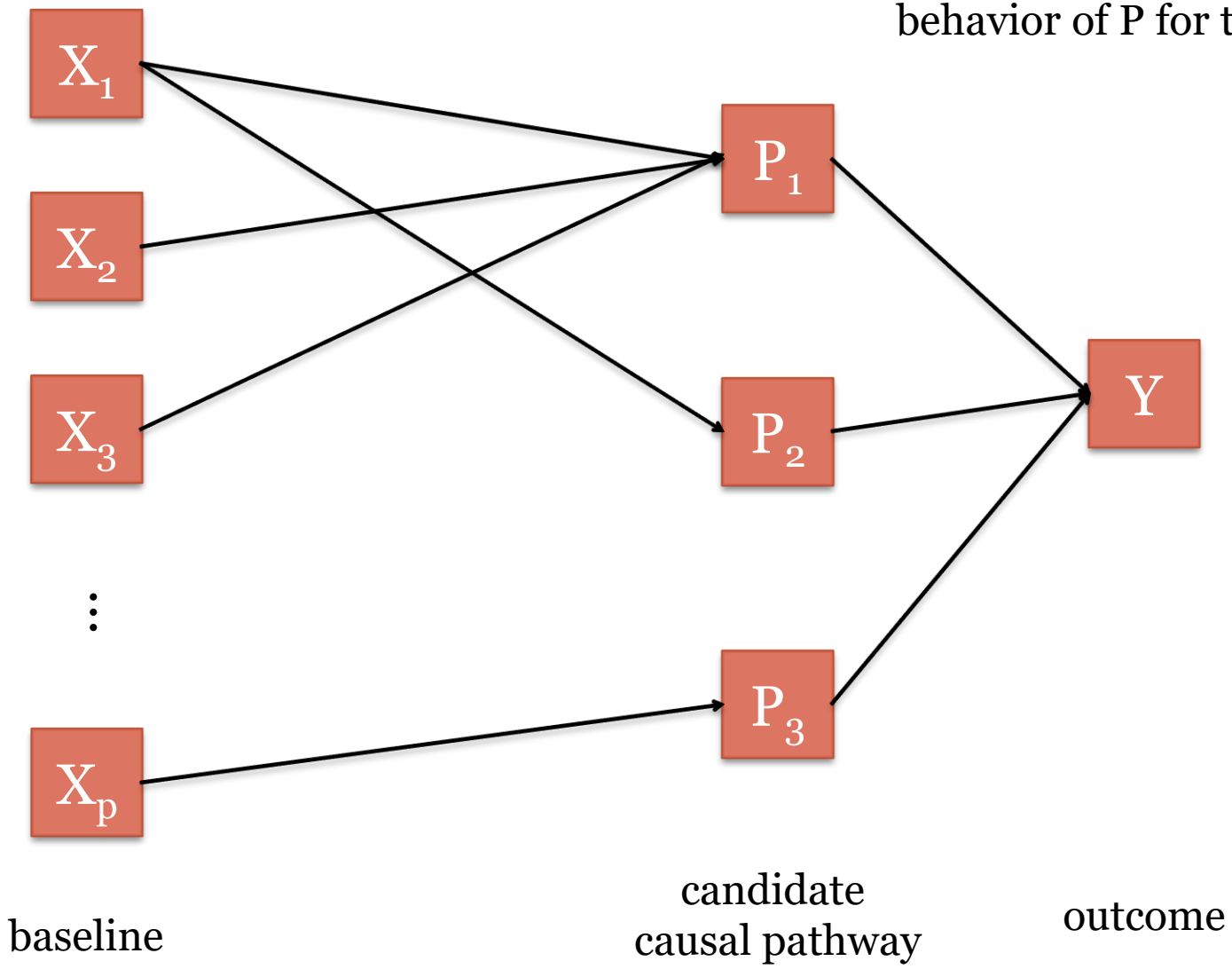
Y
baseline
candidate
causal pathway
outcome

Contrast $y_i = 1, y_j = 0$. Then compare behavior of P for the two groups.



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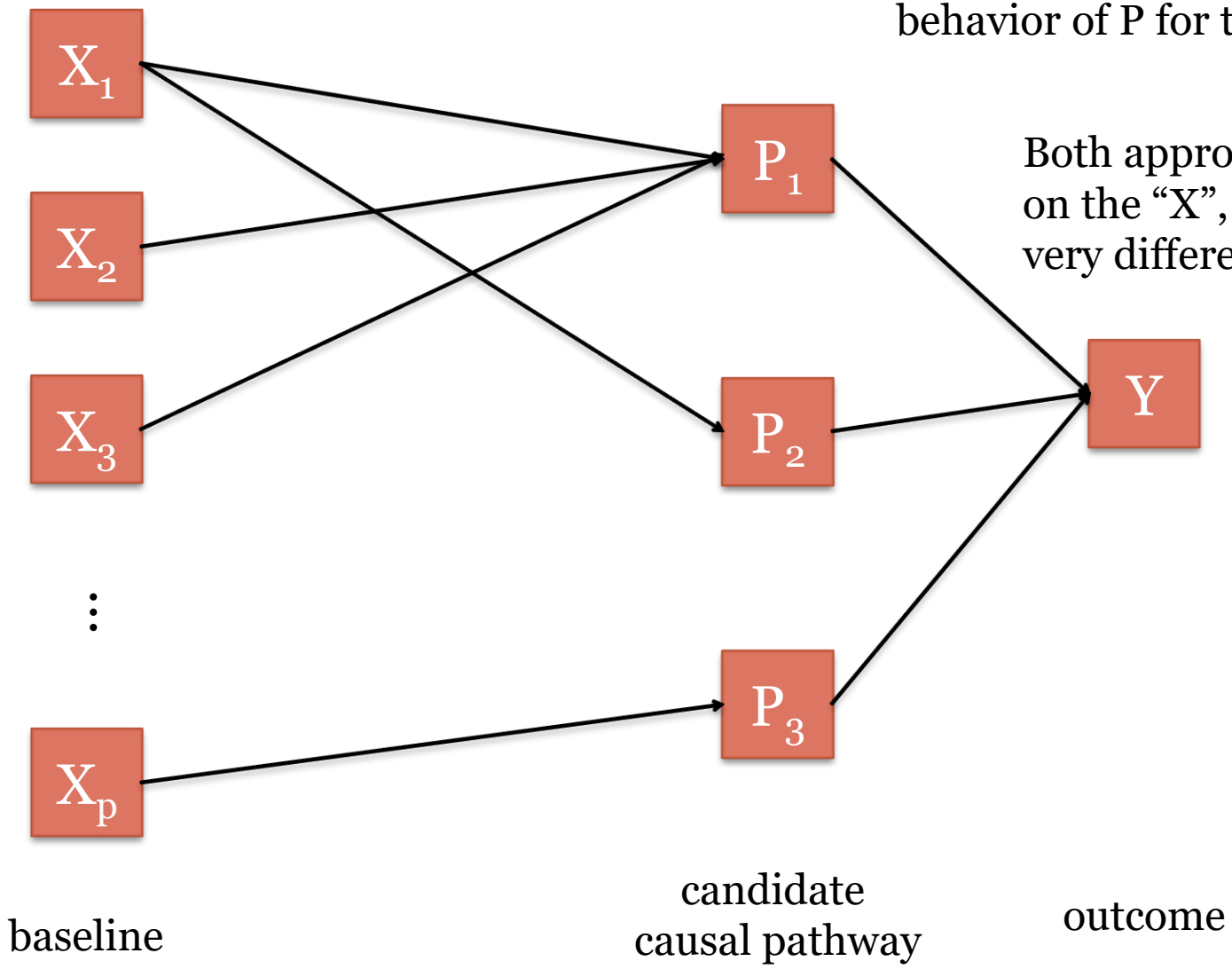
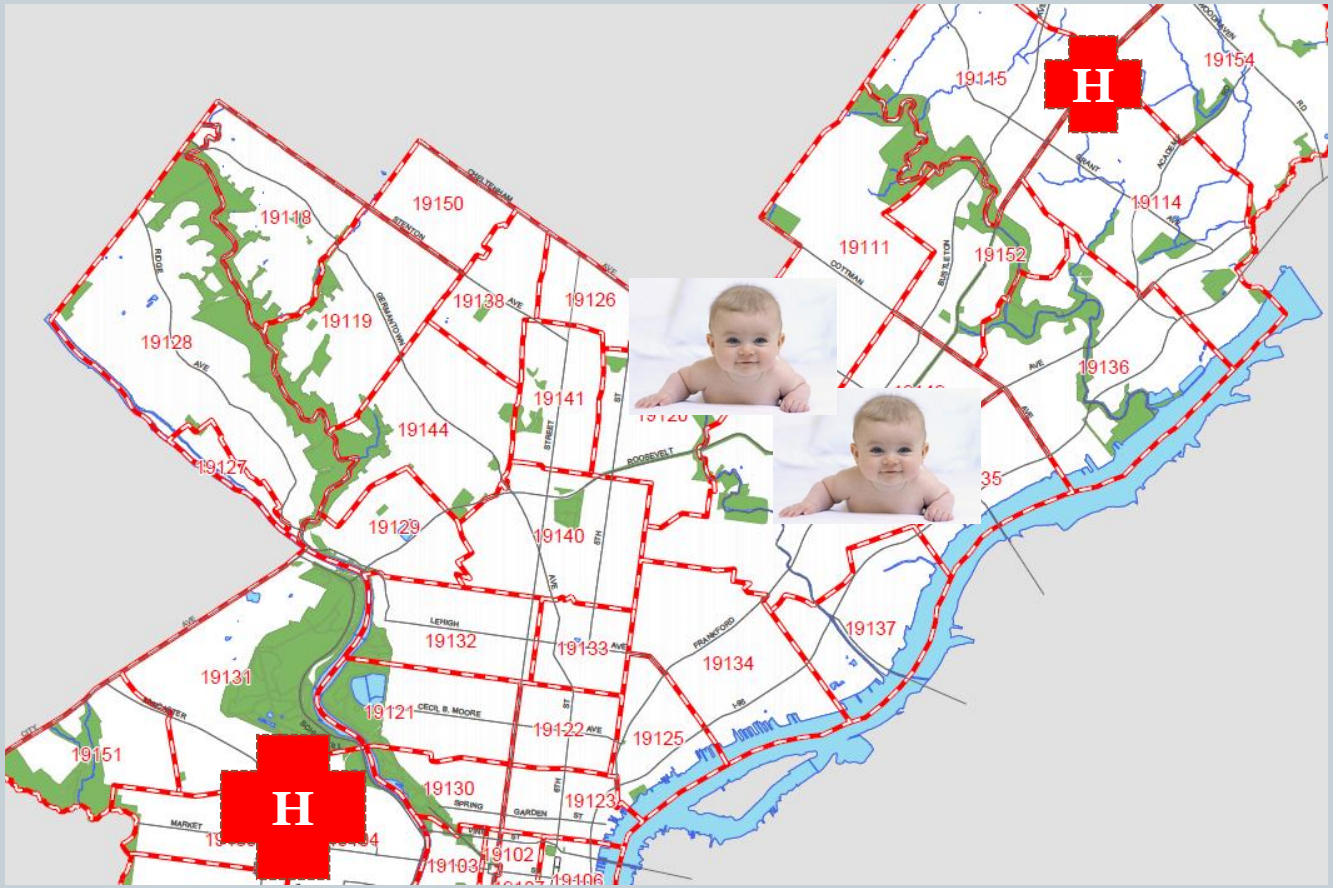
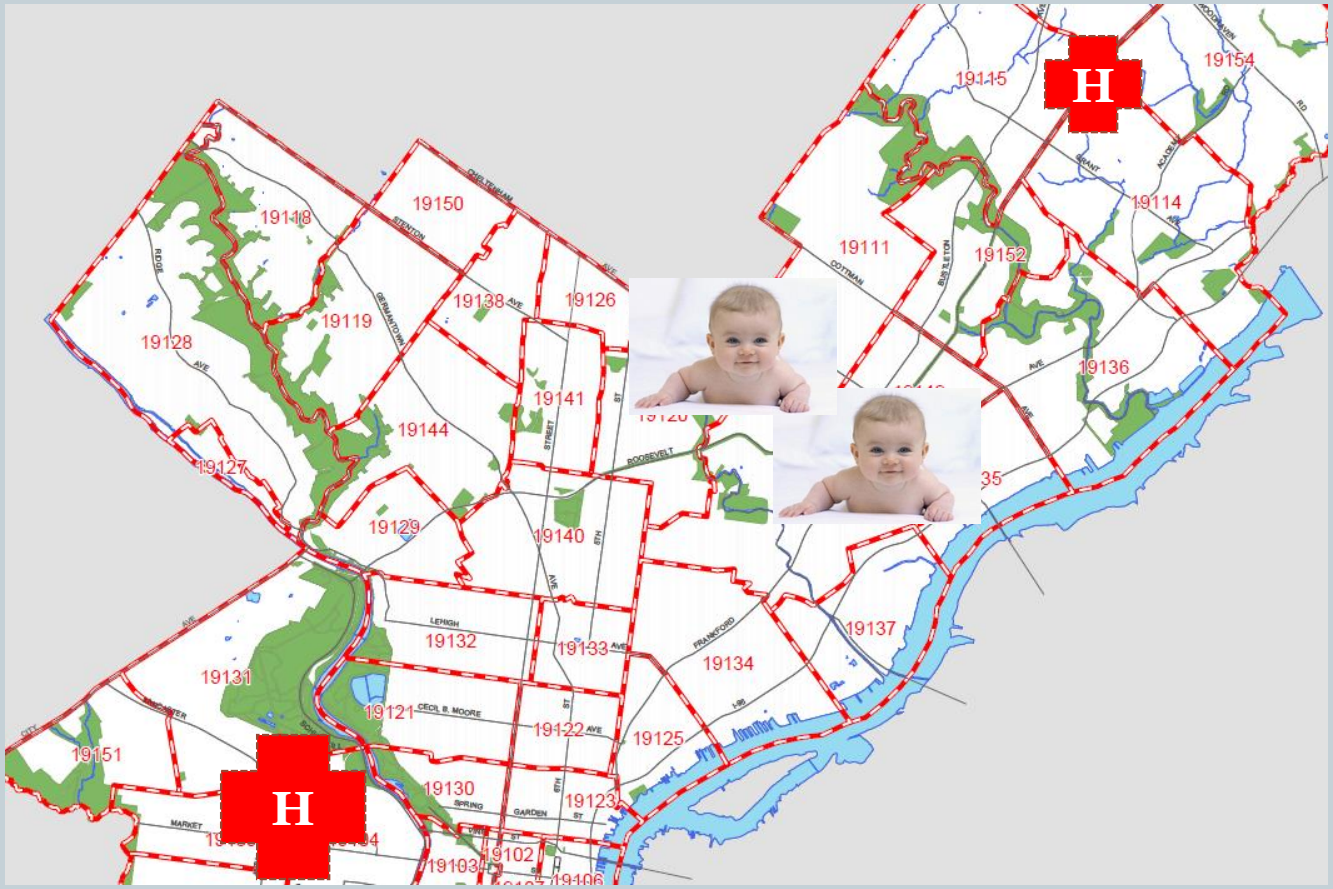


Both approaches condition on the "X", but match between very different types of groups.

pscore matching

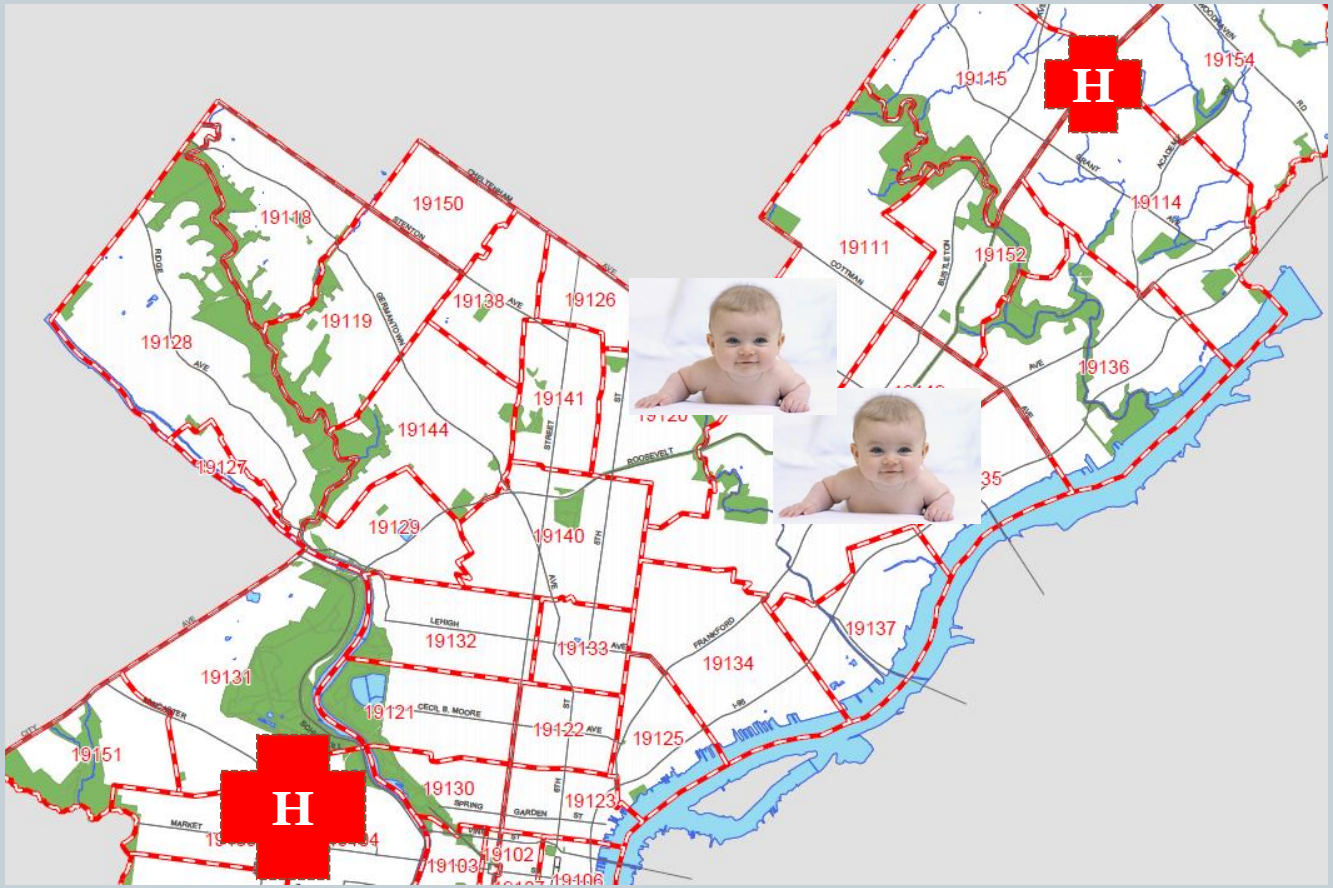


pscore matching



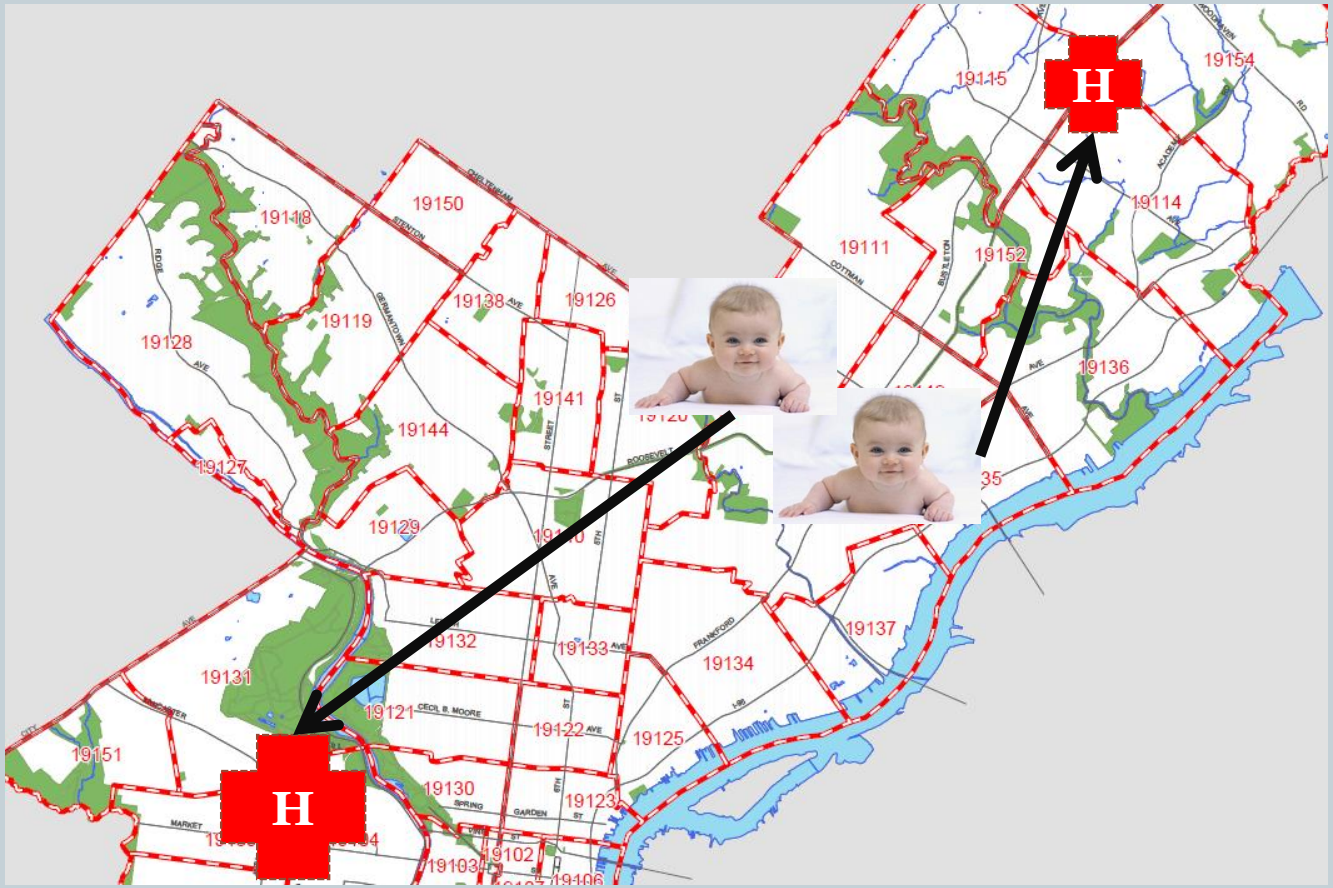
Use pre-intervention covariates to fit a pscore.

pscore matching



Use pre-intervention covariates to fit a pscore. Match on pscore between observations that used t=1 vs t=0.

pscore matching



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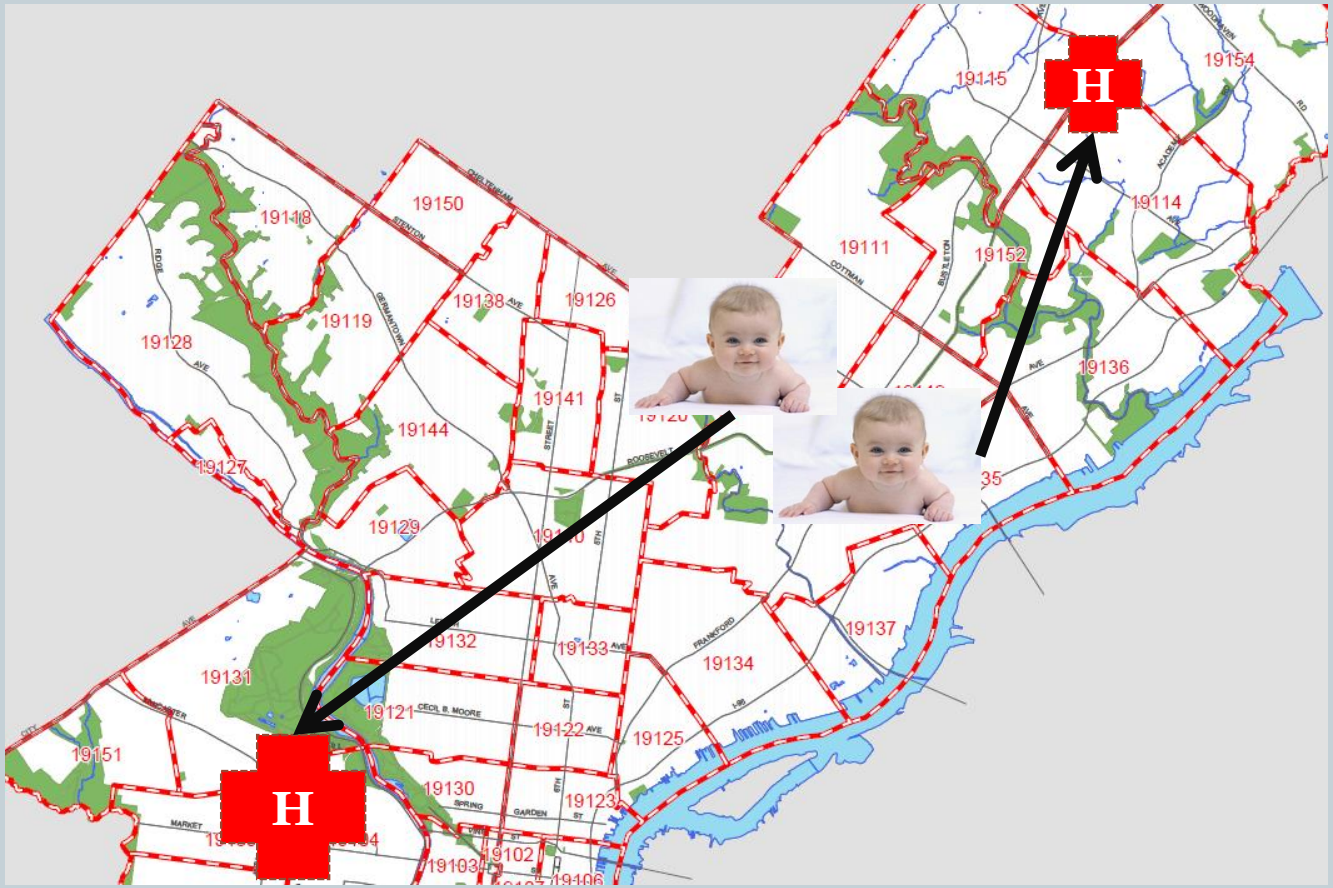
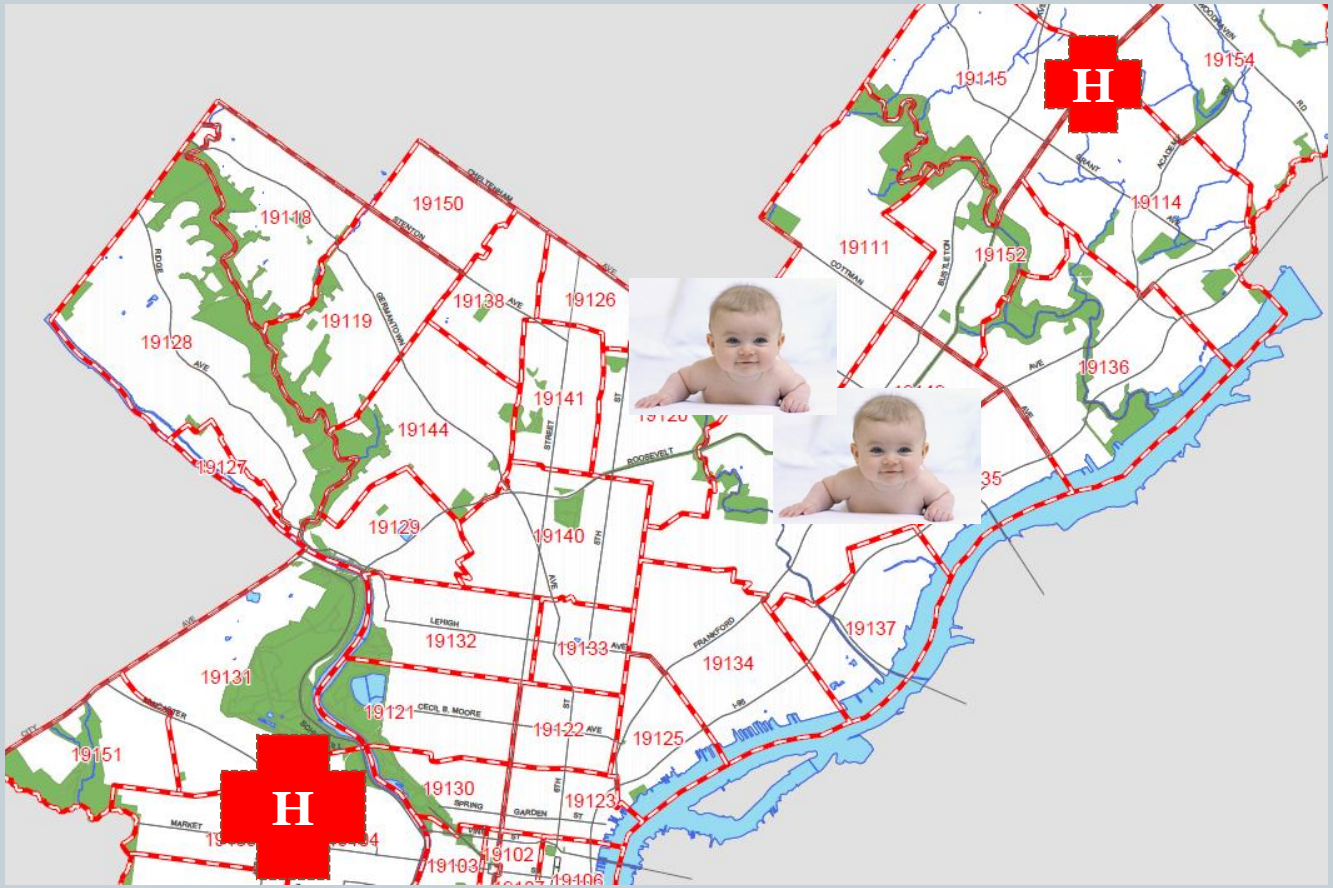


Use pre-intervention covariates to fit a pscore. Match on pscore between observations that used t=1 vs t=0. Examine distributions of outcomes between the two groups.

case-control matching



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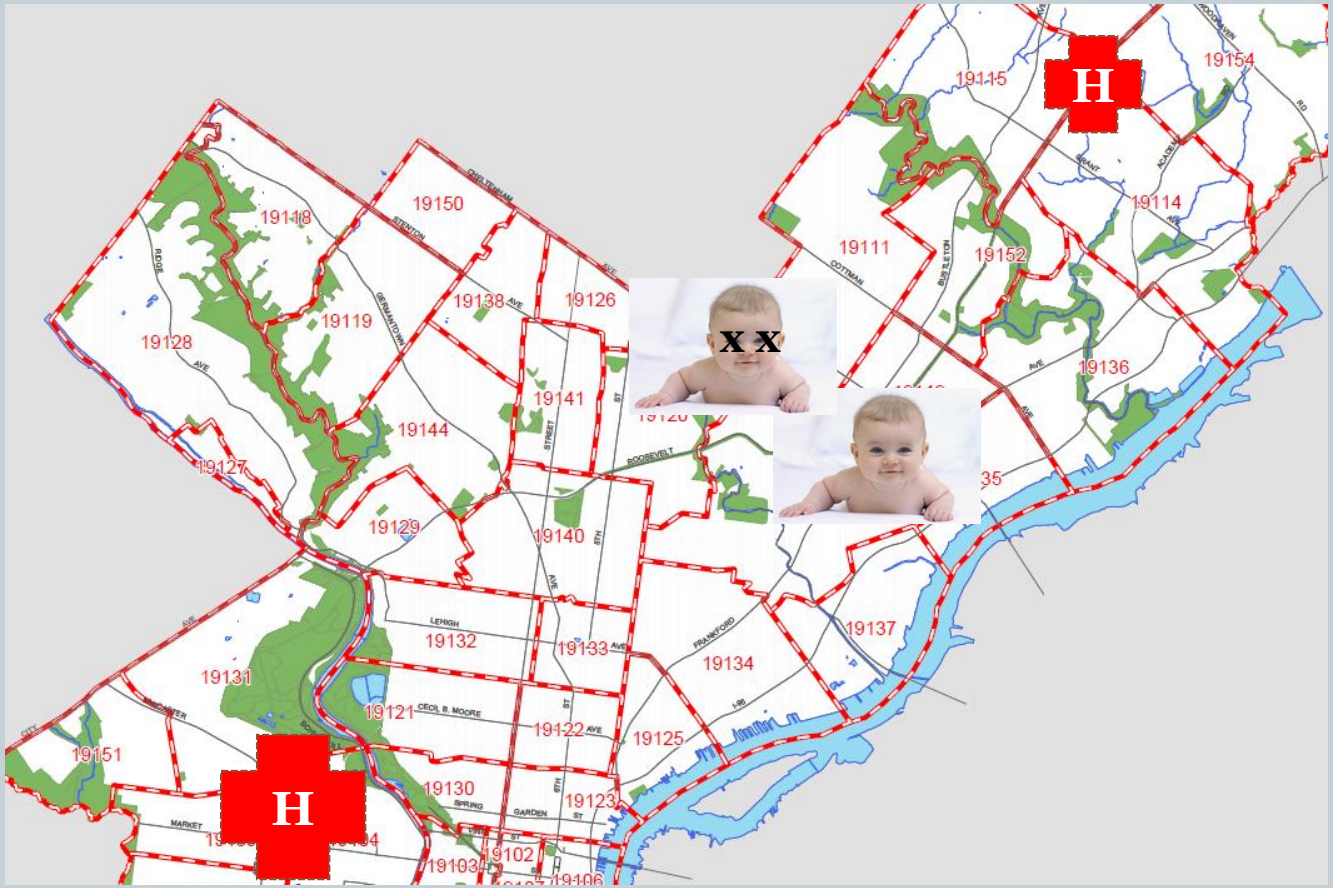
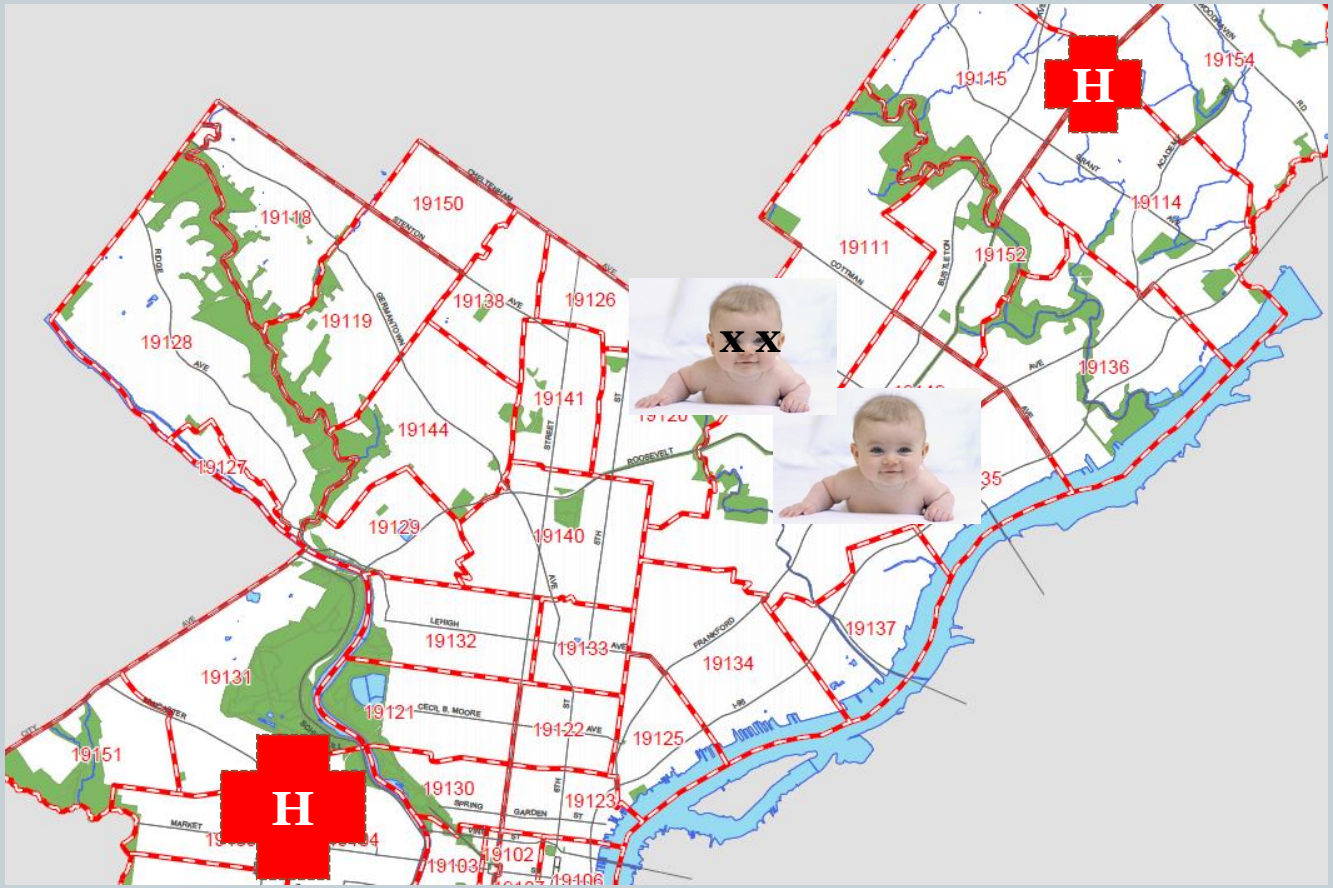
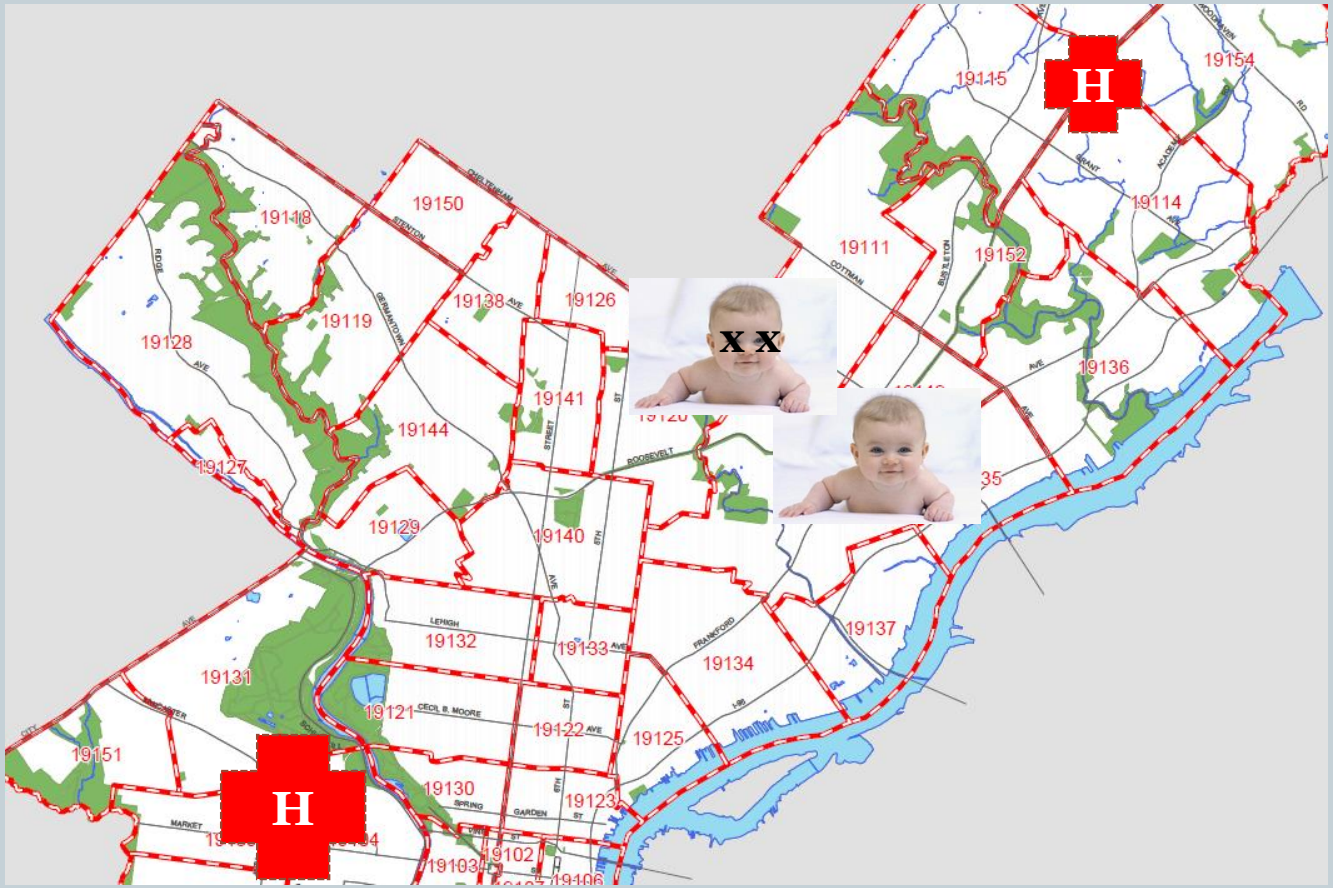


case-control matching



Use pre-intervention covariates to match.

case-control matching



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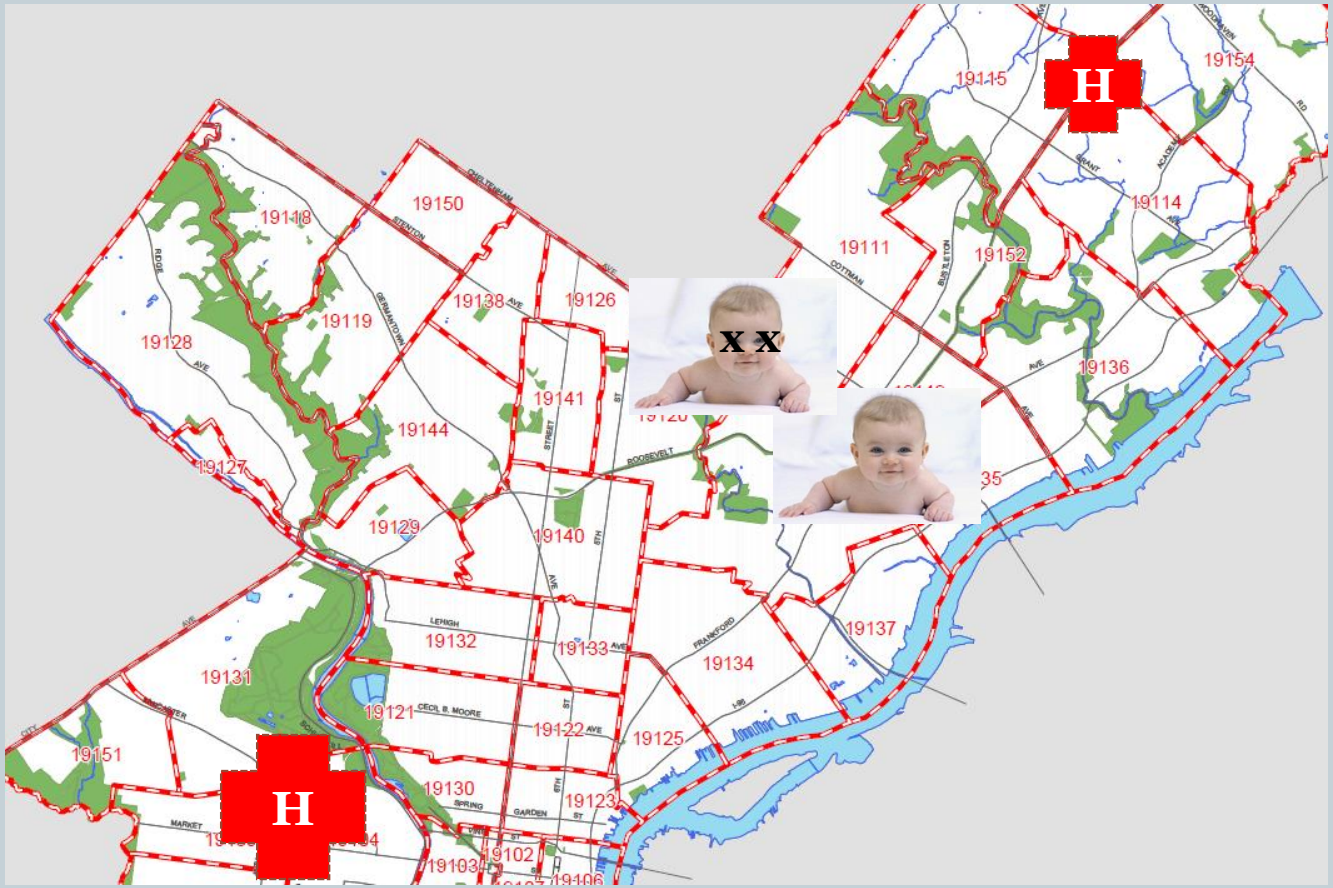

Use pre-intervention covariates to match. Match between observations y=1 vs y=0.
Examine distributions of candidate causes between the two groups.

case-noncase

case-noncase

- Match from Y=1 to Y=0 on all baseline characteristics…

case-noncase

- Match from Y=1 to Y=0 on all baseline characteristics, POSSIBLY some intermediate variables…

case-noncase

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  - For the matching we've discussed in this class we've got all we need: (d, y).

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  - For the matching we've discussed in this class we've got all we need: (d, y). It's not clear that we have all the d that cause variation in y.

case-noncase

You know the difference in logical reasoning here.

case-noncase

You know the difference in logical reasoning here.

Canonical archetypes:

case-noncase

You know the difference in logical reasoning here.

Canonical archetypes:

scientist

case-noncase

You know the difference in logical reasoning here.

Canonical archetypes:

scientist

detective

isolation

isolation by design

- Natural experiments:

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isolation by design

- Natural experiments:
  - Natural experiments are a type of observational study, that is, a study of the effects caused by treatments when random assignment is infeasible or unethical.

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isolation by design

- Natural experiments:
  - Natural experiments are a type of observational study, that is, a study of the effects caused by treatments when random assignment is infeasible or unethical.
  - What distinguishes a natural experiment from other observational studies is the emphasis placed upon finding unusual circumstances in which treatment assignment, though not randomized, seems to resemble randomized assignment in that it is haphazard, not the result of deliberation or considered judgement, not confounded by the typical attributes that determine treatment assignment in a particular empirical field.

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regionalizing care for acute type A aortic dissections

https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.038867

Andrew B. Goldstone, MD,PhD, Peter Chiu, MD, Michael Baiocchi, PhD, Bharathi Lingala, PhD, Michael P. Fischbein, MD, PhD, Joseph Woo, MD

acute aortic dissection

acute aortic dissection

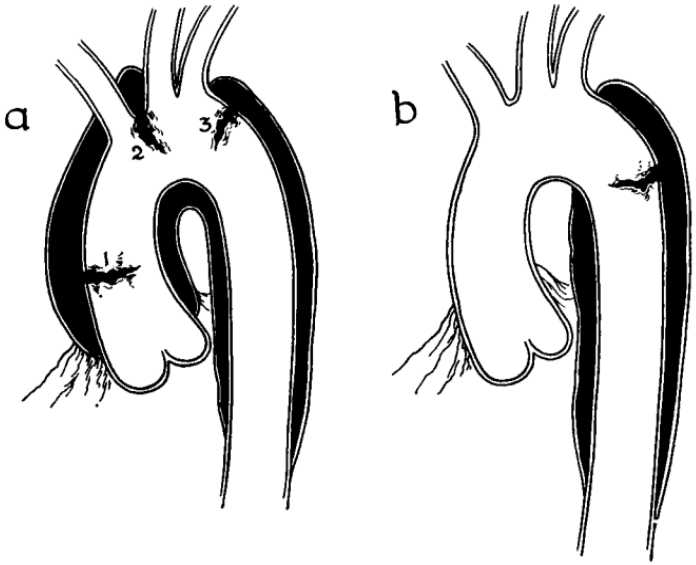
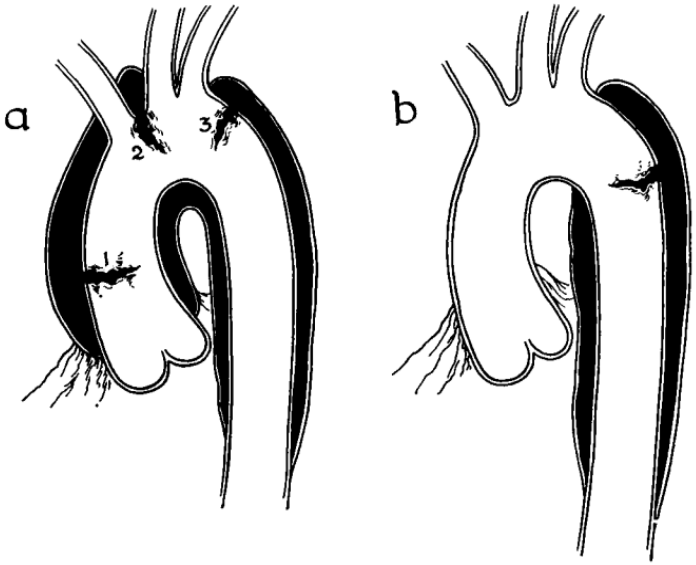


FIG. 3. Classification of aortic dissections. In type A the ascending aorta is dissected (a). *The intimal tear has always been at position* 1, *but it can occur at positions* 2 *or* 3 *(see text). In type B dissection the dissection is limited to the descending aorta* (b), *and the intimal tear is usually within 2 to 5 cm. of the left subclavian artery.*

Daily et al., *Ann Thorac Surg,* 1970

acute aortic dissection



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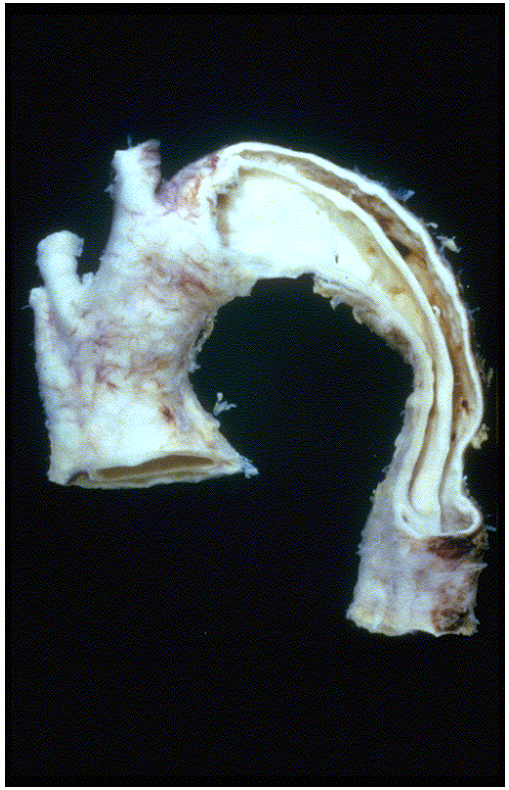
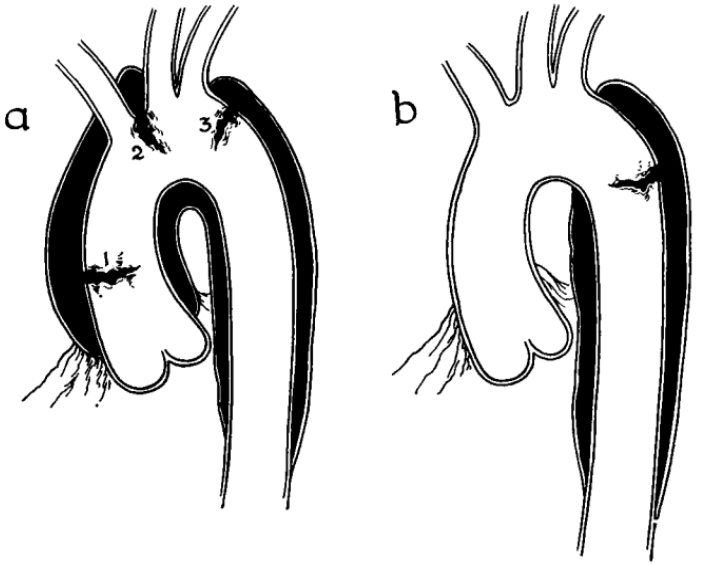


Daily et al., *Ann Thorac Surg,* 1970

acute aortic dissection



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aortic dissection

aortic dissection

It’s a particularly scary situation:

aortic dissection

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- Incidence is 4-7 per 100,000

aortic dissection

It's a particularly scary situation:

- Incidence is 4-7 per 100,000

- Mortality for untreated acute type A
  - First 24hrs =
  - First 48hrs =

aortic dissection

It's a particularly scary situation:

- Incidence is 4-7 per 100,000

- Mortality for untreated acute type A
  - First 24hrs = 25%
  - First 48hrs =

aortic dissection

It's a particularly scary situation:

- Incidence is 4-7 per 100,000

- Mortality for untreated acute type A
  - First 24hrs = 25%
  - First 48hrs = 40%

aortic dissection

It's a particularly scary situation:

- Incidence is 4-7 per 100,000
- Mortality for untreated acute type A
  - First 24hrs = 25%
  - First 48hrs = 40%
- Upon diagnosis patients are rushed to operating room.

aortic dissection

It's a particularly scary situation:

- Incidence is 4-7 per 100,000
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  - First 24hrs = 25%
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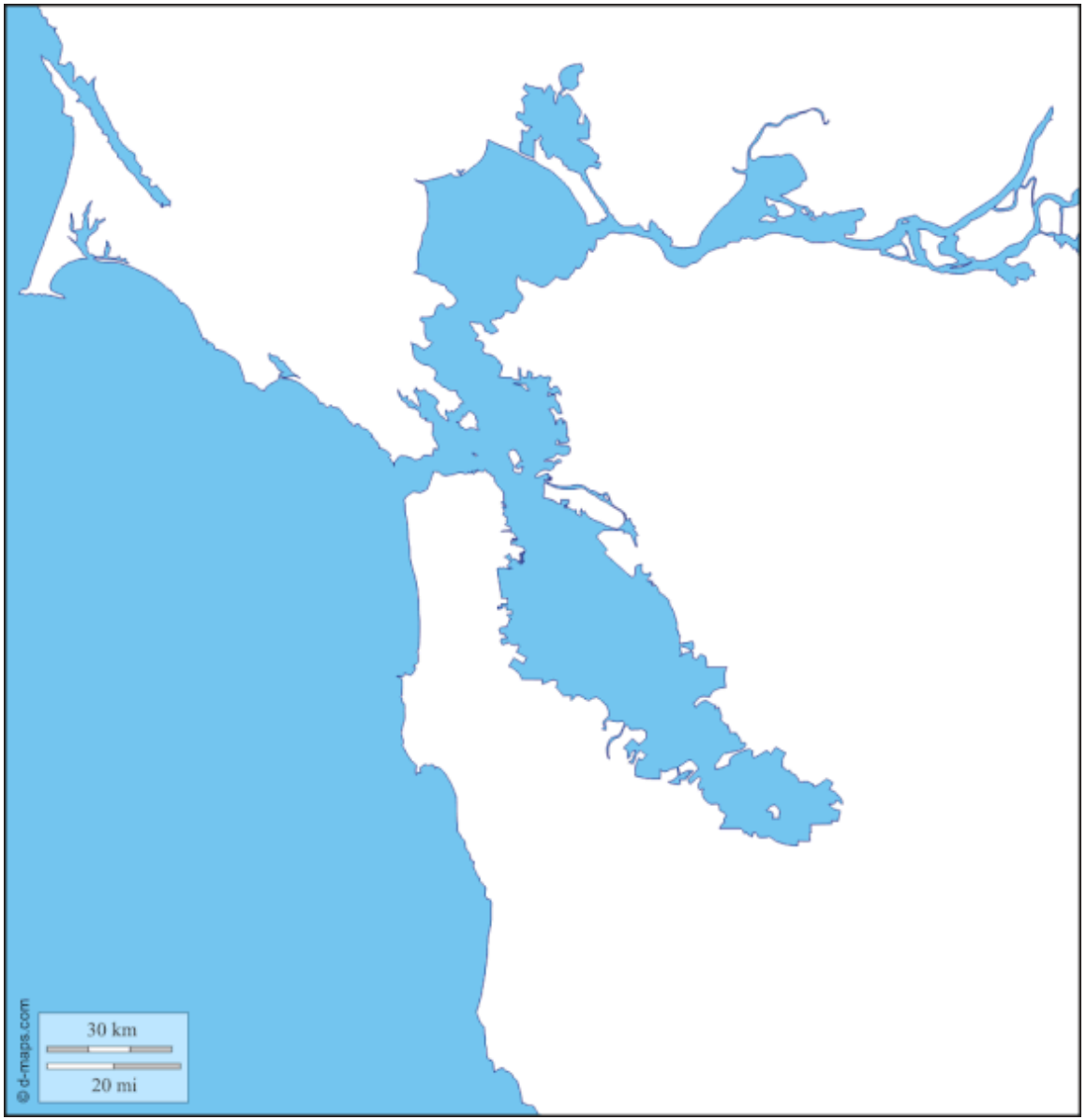
- Upon diagnosis patients are rushed to operating room.
- Operative mortality in the range of 19-28%

aortic dissection

It's a particularly scary situation:

- Incidence is 4-7 per 100,000
- Mortality for untreated acute type A
  - First 24hrs = 25%
  - First 48hrs = 40%
- Upon diagnosis patients are rushed to operating room.
- Operative mortality in the range of 19-28%
- Interfacility transfer = ?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30 km
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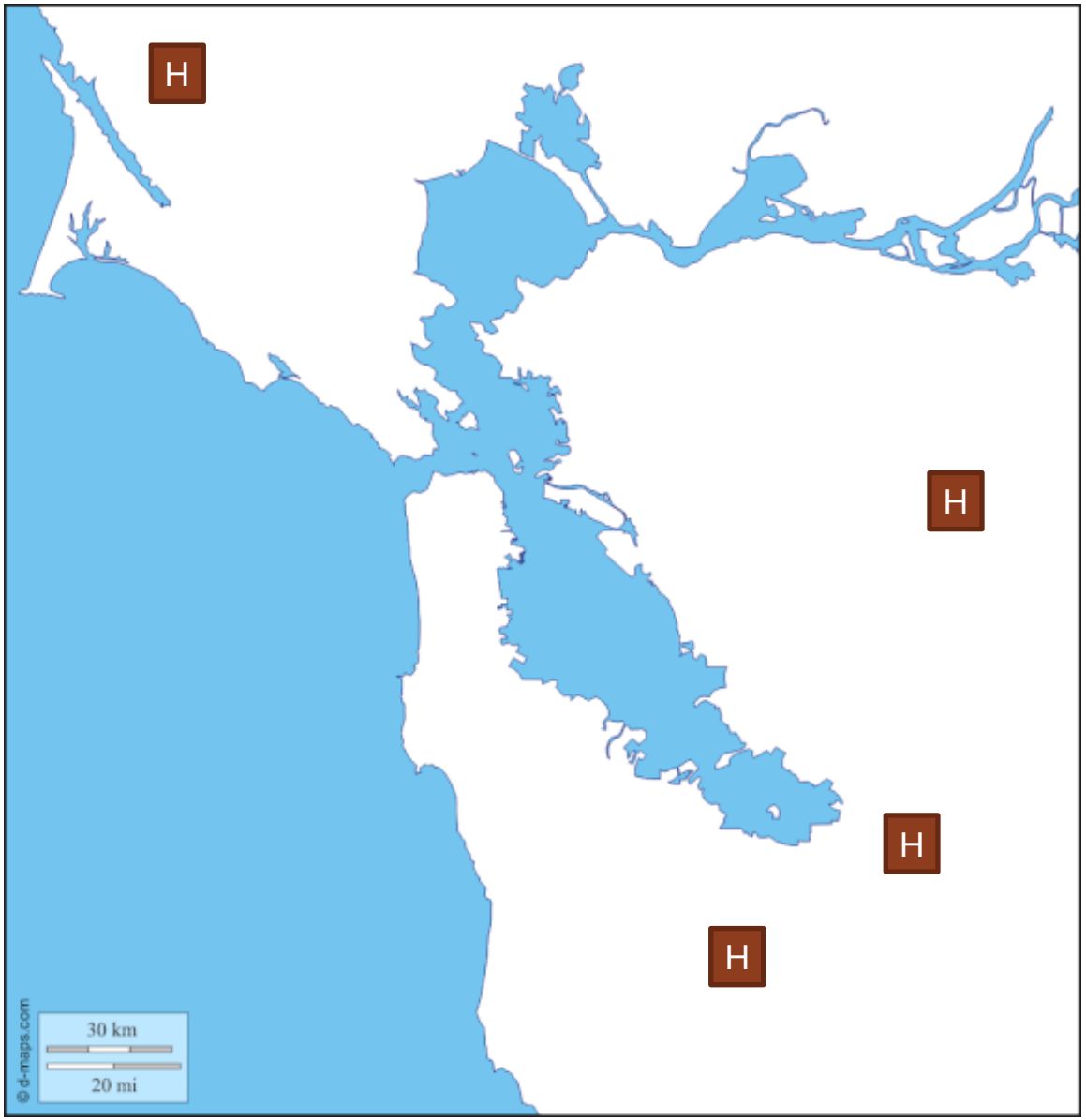
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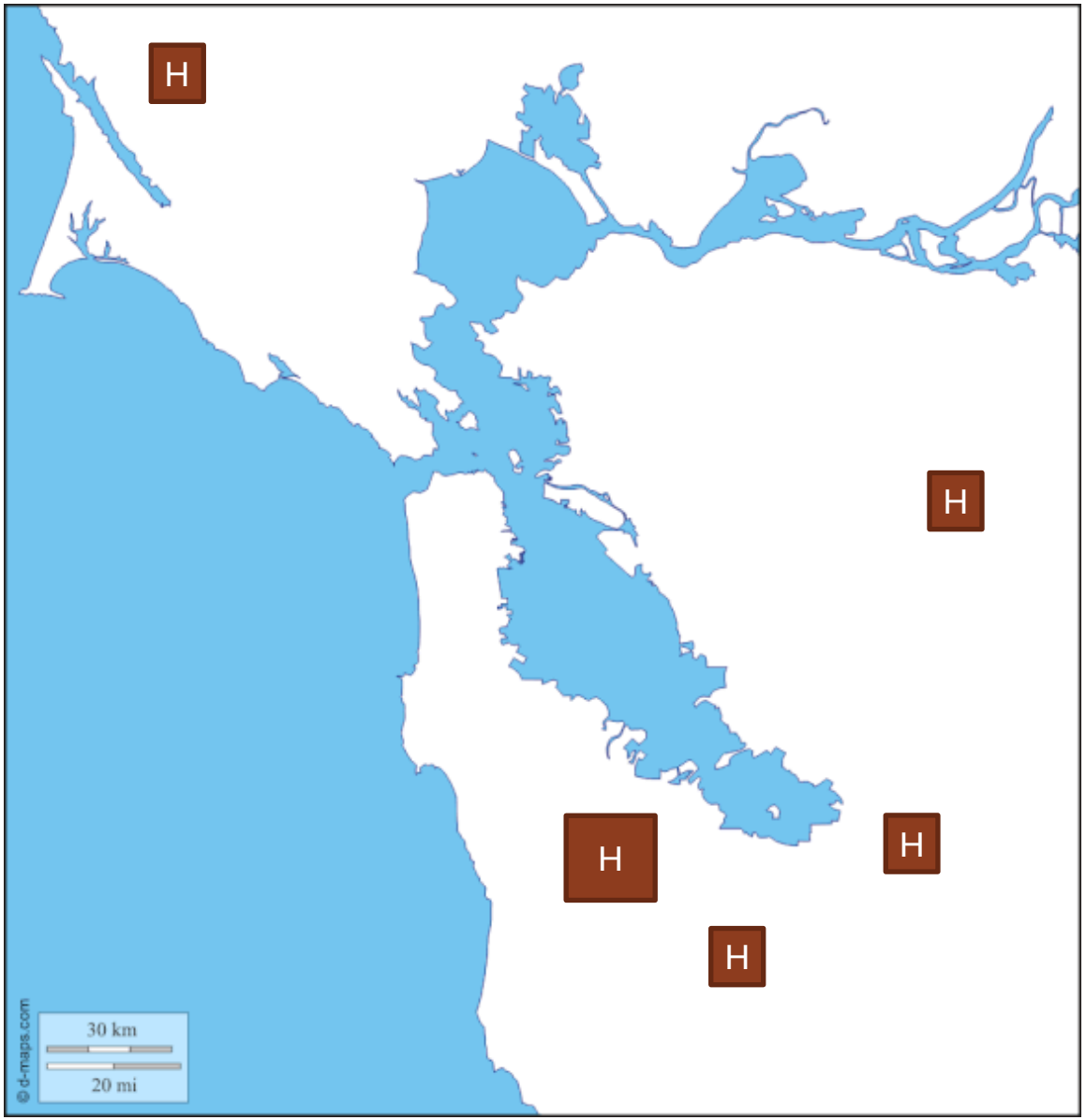
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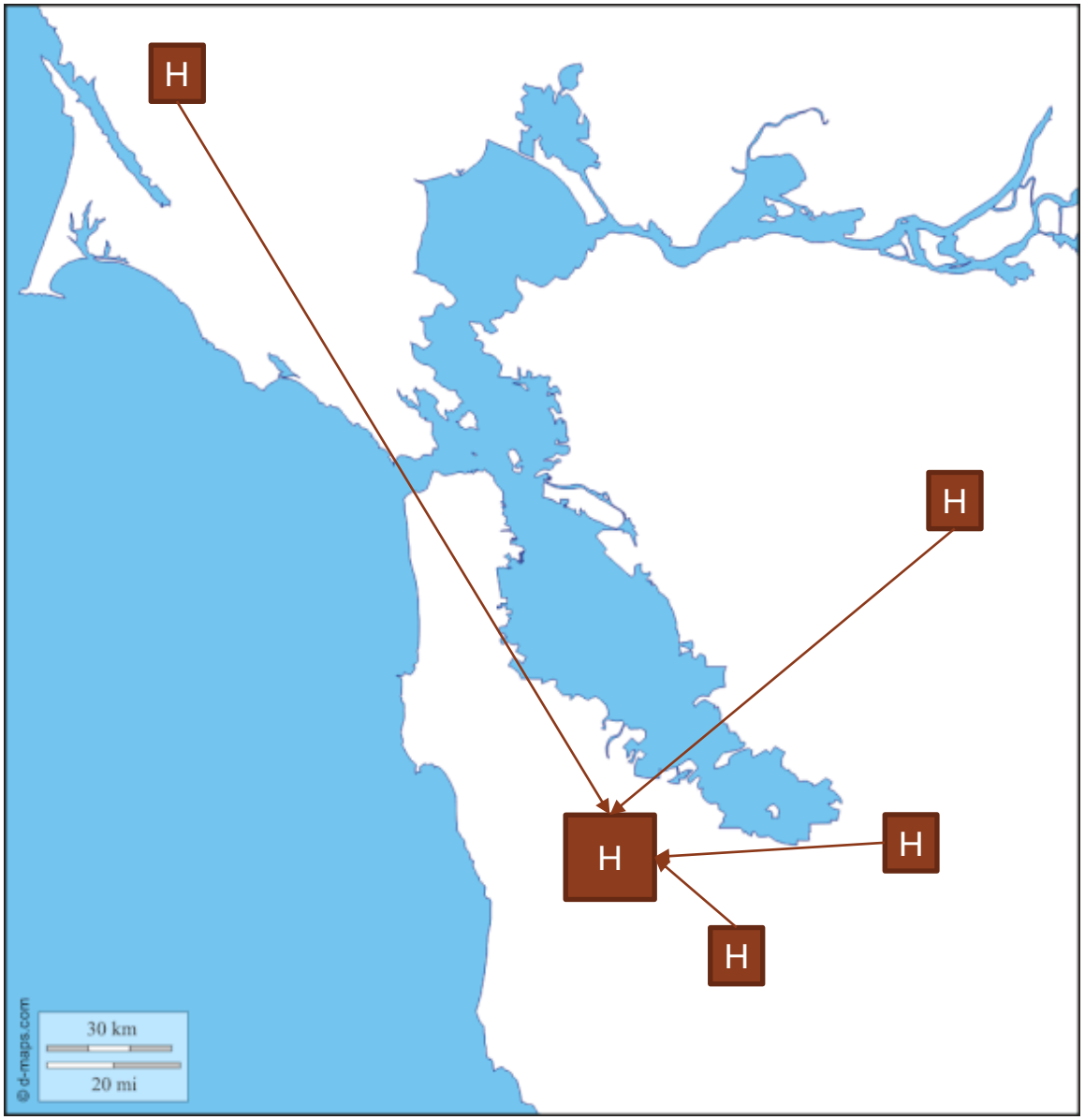
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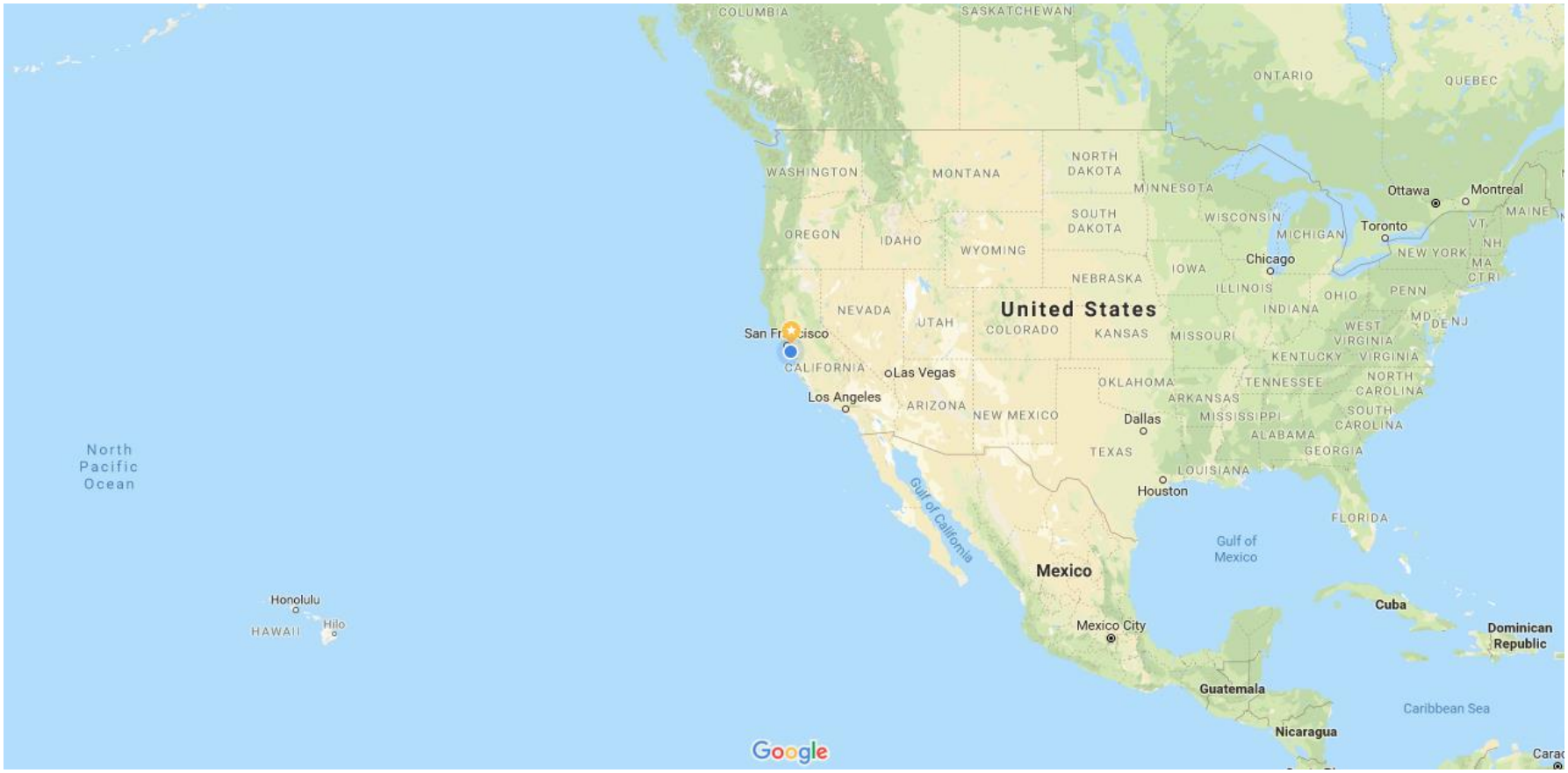
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TEXAS
GEORGIA
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Houston
Gulf of California
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Dominican Republic
Guatemala
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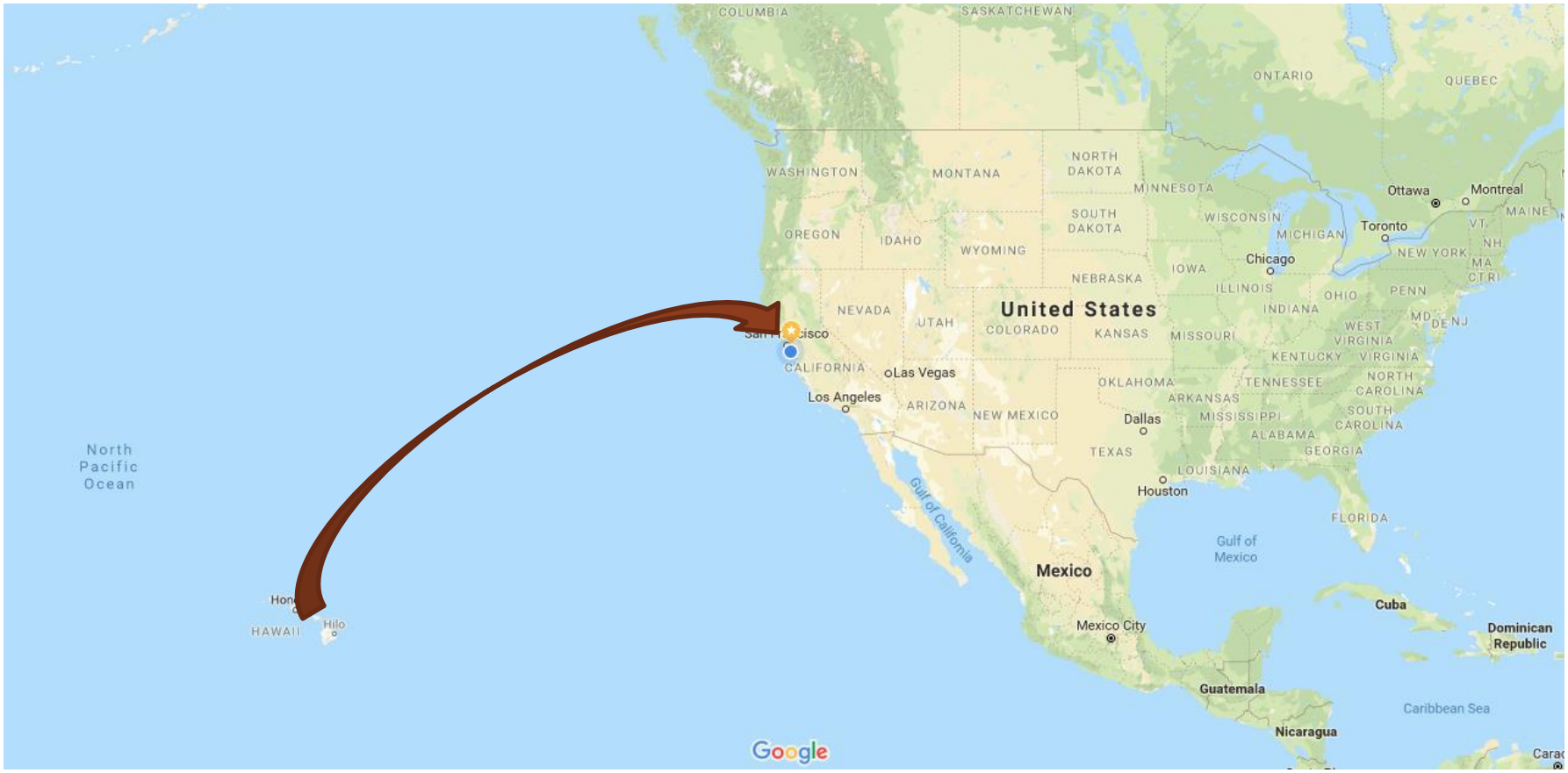
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Cuba
Dominican Republic
Guatemala
Nicaragua
Caribbean Sea
Gulf of Mexico
Gulf of California
North Pacific Ocean
HAWAII
Hilo
Google

policy question

policy question

We know that there are benefits to regionalizing complex care.

policy question

We know that there are benefits to regionalizing complex care. Probably due to a mixture of intraoperative and postoperative care.

policy question

We know that there are benefits to regionalizing complex care. Probably due to a mixture of intraoperative and postoperative care.

But there might an exception here because of the time-sensitivity and fragility of these cases.

policy question

We know that there are benefits to regionalizing complex care. Probably due to a mixture of intraoperative and postoperative care.

But there might an exception here because of the time-sensitivity and fragility of these cases.

Q: What would happen if we regionalized care to high-volume centers?

answering this question

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Logistically: (i) can’t identify patients until they’re at the facility, (ii) likely unable to get consent because these patients are so compromised.

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Perhaps we could move up to a higher level of randomization:

answering this question

Q: What would happen if we regionalized care to high-volume centers?

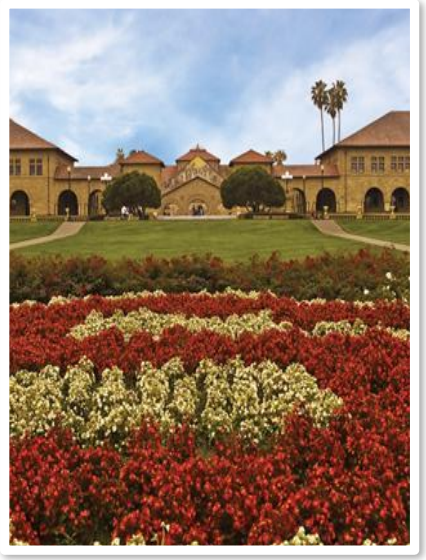
Ideally: individually randomize patients to receive care at high-volume vs low-volume.

Logistically: (i) can't identify patients until they're at the facility, (ii) likely unable to get consent because these patients are so compromised.

Perhaps we could move up to a higher level of randomization: could work with some hospitals to have them implement regionalization, others not.

study design

isolating a natural experiment



control for what you know

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We pulled Medicare claims records from 1999-2014.

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Found about 12,500 type A patients.

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Have 30ish baseline covariates on each patient.

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We pulled Medicare claims records from 1999-2014.

Found about 12,500 type A patients.

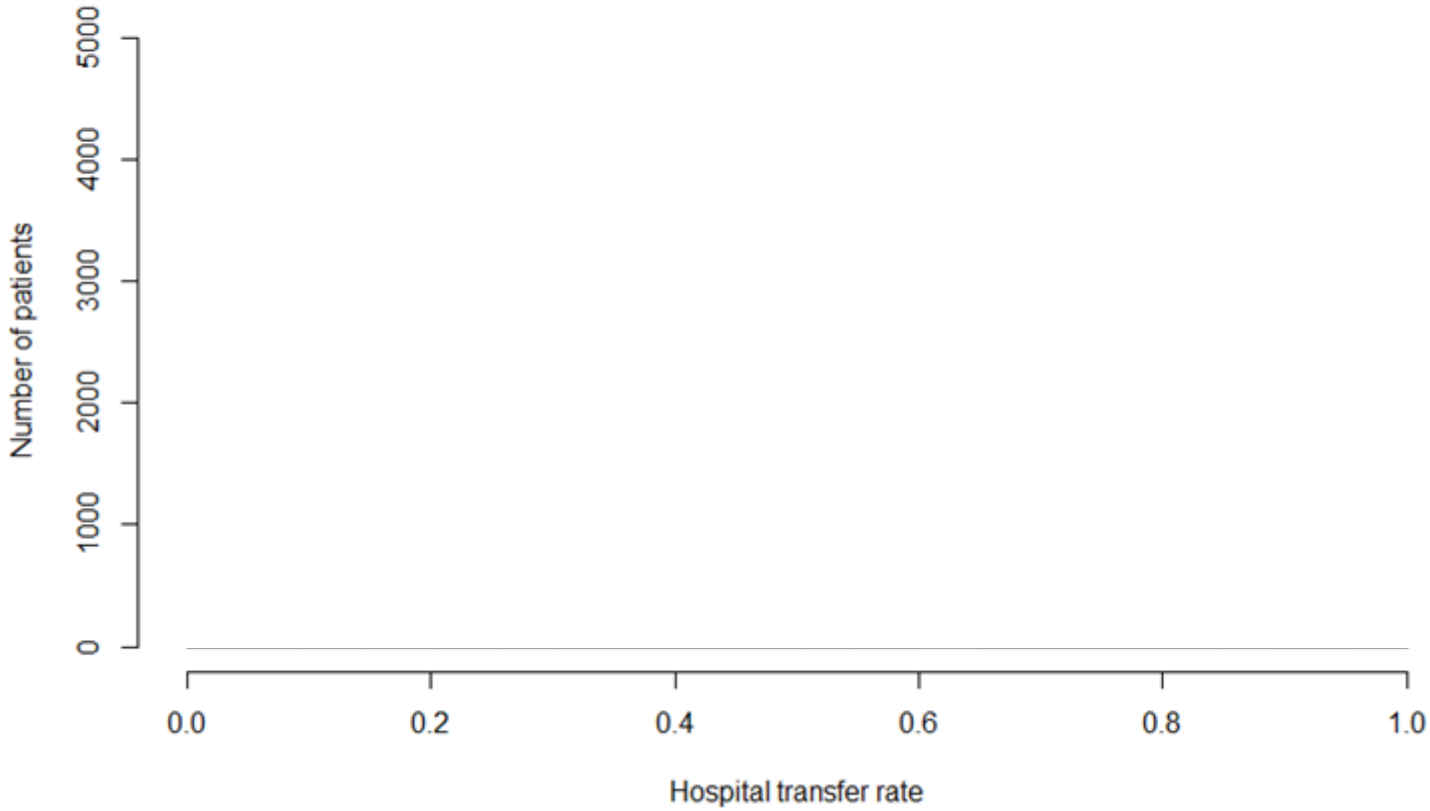
Have 30ish baseline covariates on each patient.

Table 1. Baseline and Operative Characteristics of the Study Population and the Population for the Analysis of Regional

Characteristic	Overall Study Population (N=16,886)	Before Matching: Not Rerouted (N=7910)	Before Matching: Rerouted (N=4520)	SMD
Age - yr	72.44 (9.50)	72.29 (9.46)	72.46 (9.41)	0.017
Age <65 yrs - n (%)	1935 (11.5)	946 (12.0)	510 (11.3)	0.021
Year of surgery - yr	2006.78 (4.57)	2006.71 (4.57)	2006.86 (4.59)	0.033
Male sex - n (%)	9397 (55.6)	4412 (55.8)	2513 (55.6)	0.004
Race - n (%)				
White	14335 (84.9)	6717 (84.9)	3830 (84.7)	0.005
Black	1787 (10.6)	748 (9.5)	534 (11.8)	0.077
Asian	268 (1.6)	177 (2.2)	48 (1.1)	0.092
Hispanic	191 (1.1)	98 (1.2)	34 (0.8)	0.049
Other	305 (1.8)	170 (2.1)	74 (1.6)	0.038
Prior myocardial infarction - n (%)	574 (3.4)	279 (3.5)	151 (3.3)	0.01
Alzheimer's dementia - n (%)	806 (4.8)	369 (4.7)	230 (5.1)	0.02
Atrial fibrillation - n (%)	2735 (16.2)	1204 (15.2)	675 (14.9)	0.008
Chronic kidney disease - n (%)	2555 (15.1)	1166 (14.7)	704 (15.6)	0.023
COPD - n (%)	3848 (22.8)	1752 (22.1)	1114 (24.6)	0.059
Congestive heart failure - n (%)	4230 (25.1)	1863 (23.6)	1118 (24.7)	0.028
Diabetes mellitus - n (%)	3049 (18.1)	1364 (17.2)	841 (18.6)	0.036
Hip fracture - n (%)	250 (1.5)	107 (1.4)	82 (1.8)	0.037
Ischemic heart disease - n (%)	7842 (46.4)	3503 (44.3)	2049 (45.3)	0.021
Arthritis - n (%)	2222 (13.2)	1020 (12.9)	571 (12.6)	0.008
Stroke - n (%)	1825 (10.8)	832 (10.5)	502 (11.1)	0.019
Cancer - n (%)	2039 (12.1)	929 (11.7)	557 (12.3)	0.018
Anemia - n (%)	6524 (38.6)	2908 (36.8)	1758 (38.9)	0.044
Hyperlipidemia - n (%)	9249 (54.8)	4247 (53.7)	2490 (55.1)	0.028
Hypertension - n (%)	12225 (72.4)	5618 (71.0)	3326 (73.6)	0.057
Hypothyroidism - n (%)	2329 (13.8)	1099 (13.9)	602 (13.3)	0.017
Region				
New England - n (%)	947 (5.6)	273 (3.5)	364 (8.1)	0.199
Mideast - n (%)	3035 (18.0)	839 (10.6)	1121 (24.8)	0.378
Great Lakes - n (%)	3061 (18.1)	1302 (16.5)	910 (20.1)	0.095
Plains - n (%)	1267 (7.5)	689 (8.7)	263 (5.8)	0.112
Southeast - n (%)	4669 (27.7)	2223 (28.1)	1215 (26.9)	0.027
Southwest - n (%)	1504 (8.9)	875 (11.1)	300 (6.6)	0.156
Rocky Mountain - n (%)	460 (2.7)	365 (4.6)	41 (0.9)	0.228
Prior Procedures				
Aortic valve surgery - n (%)	375 (2.2)	163 (2.1)	108 (2.4)	0.022
Thoracic aortic replacement - n (%)	36 (0.2)	10 (0.1)	16 (0.4)	0.046
Thoracoabdominal aortic replacement - n (%)	19 (0.1)	4 (0.1)	9 (0.2)	0.042
TEVAR - n (%)	22 (0.1)	9 (0.1)	7 (0.2)	0.011
EVAR - n (%)	53 (0.3)	25 (0.3)	11 (0.2)	0.014
Abdominal aortic replacement - n (%)	199 (1.2)	84 (1.1)	62 (1.4)	0.028
Mitral valve surgery - n (%)	155 (0.9)	68 (0.9)	41 (0.9)	0.005
Tricuspid valve surgery - n (%)	15 (0.1)	5 (0.1)	6 (0.1)	0.022
CABG - n (%)	988 (5.9)	440 (5.6)	278 (6.2)	0.025
VAD/ECMO - n (%)	14 (0.1)	4 (0.1)	7 (0.2)	0.033
Other cardiac surgery - n (%)	82 (0.5)	33 (0.4)	28 (0.6)	0.028
Index Surgical Procedures				
Aortic valve surgery - n (%)	2428 (14.4)	1056 (13.4)	587 (13.0)	0.011
Aortic root replacement - n (%)	4816 (28.5)	2280 (28.8)	1193 (26.4)	0.054
Ascending aortic replacement - n (%)	12228 (72.4)	5700 (72.1)	3362 (74.4)	0.052
Aortic arch replacement - n (%)	3044 (18.0)	799 (10.1)	1214 (26.9)	0.442
Descending thoracic aortic replacement - n (%)	195 (1.2)	73 (0.9)	62 (1.4)	0.042
Thoracoabdominal aortic replacement - n (%)	25 (0.1)	13 (0.2)	5 (0.1)	0.015
TEVAR - n (%)	154 (0.9)	37 (0.5)	62 (1.4)	0.095
EVAR - n (%)	19 (0.1)	8 (0.1)	6 (0.1)	0.009
Abdominal aortic replacement - n (%)	39 (0.2)	23 (0.3)	7 (0.2)	0.029
CABG - n (%)	4181 (24.8)	2029 (25.7)	866 (19.2)	0.156
Other valve surgery - n (%)	8 (0.0)	5 (0.1)	0 (0.0)	0.036
Other cardiac surgery - n (%)	340 (2.0)	133 (1.7)	79 (1.7)	0.005
Transferred - n (%)	6836 (40.5)	2316 (29.3)	4520 (100.0)	2.198
Surgery at high-volume center - n (%)	8976 (53.2)	0 (0.0)	4520 (100.0)	-
Rerouted - n (%)	4520 (36.4)	0 (0.0)	4520 (100.0)	-

*Plus-minus values are means +/- standard deviation. Variables excluded from table though well-balanced (SMD <0.1): osteoporosis, asthma, hypercorpothyroidism, and depression. CABG, coronary artery bypass graft; COPD, chronic obs

B Distribution of patients presenting to hospitals with varying transfer rates for acute type A aortic dissection



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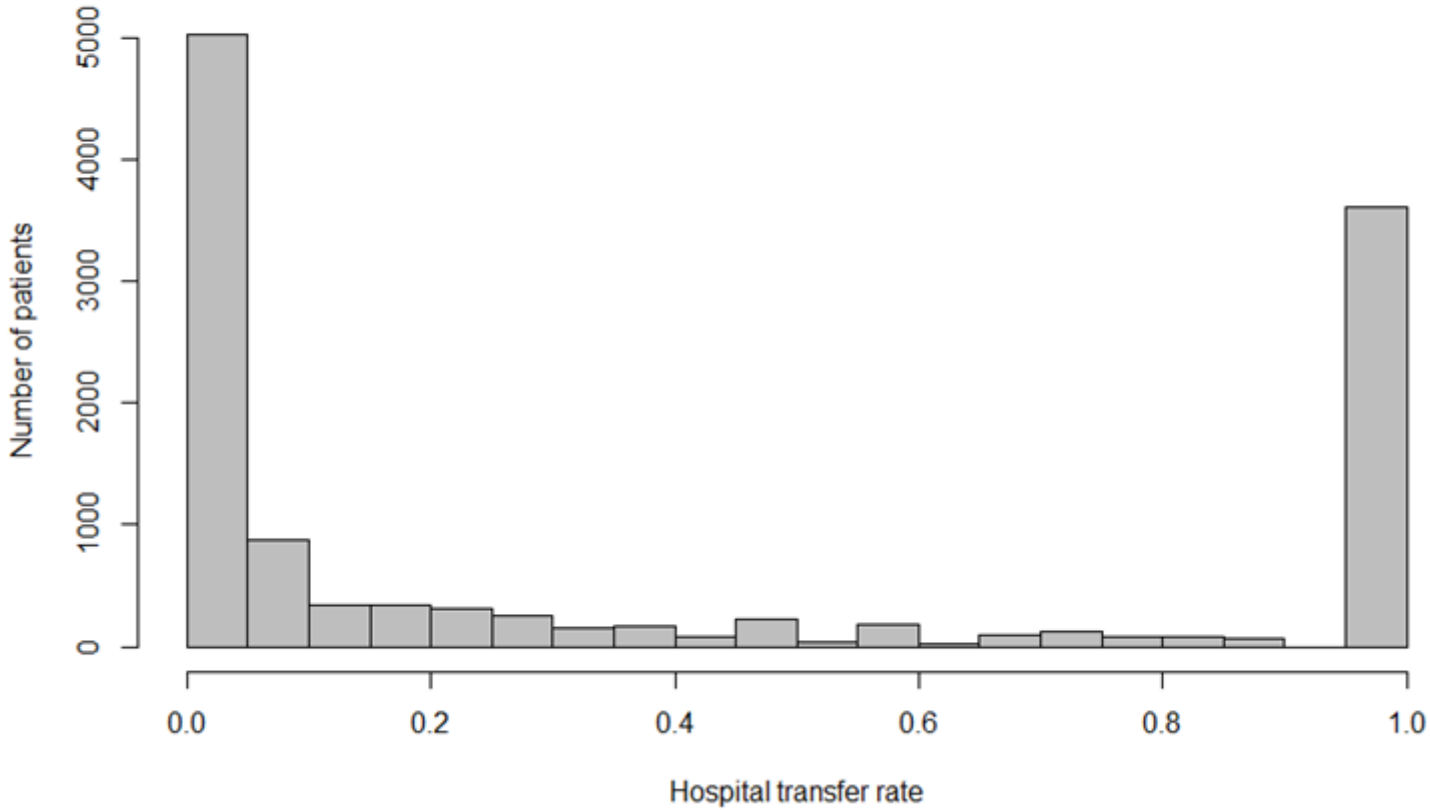
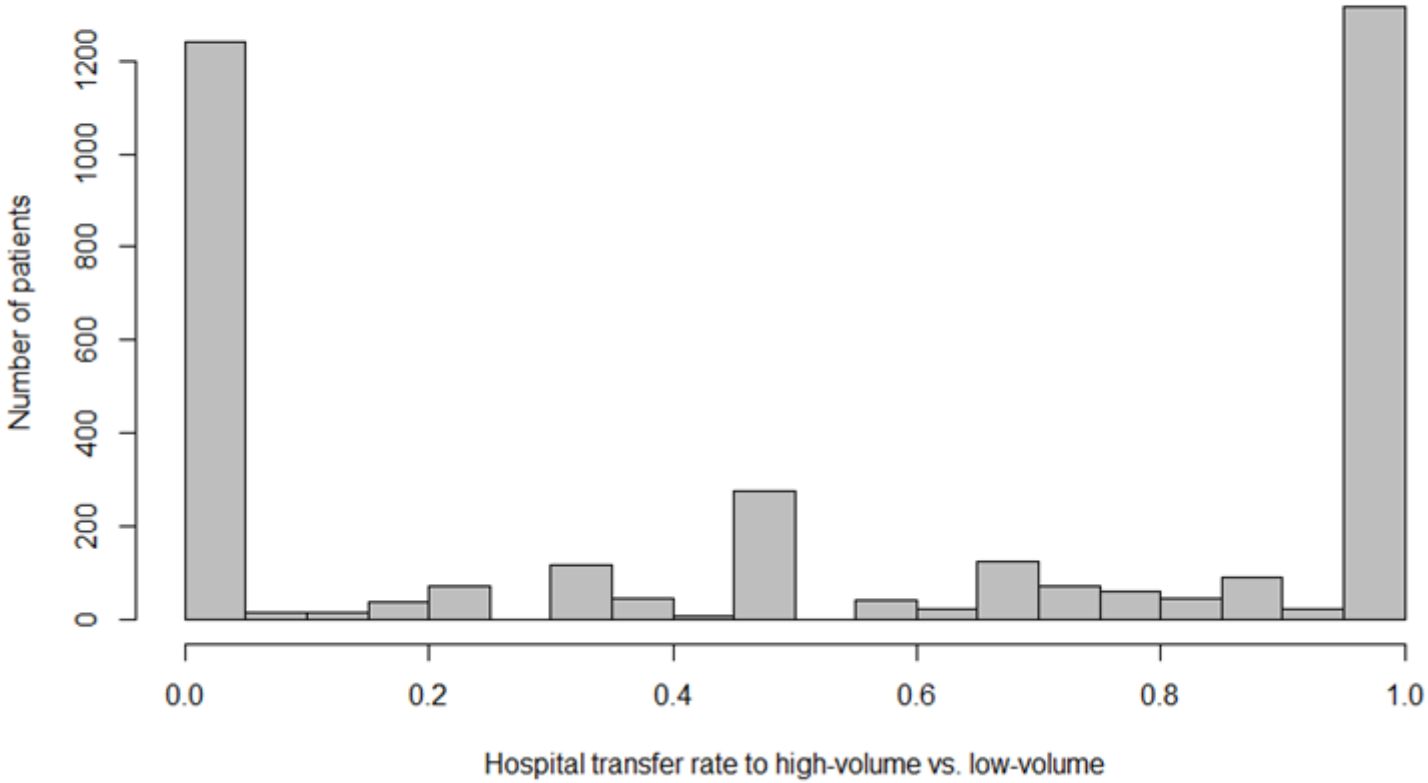


D Distribution of patients presenting to hospitals with varying transfer rates to high-volume centers among hospitals that always transferred patients with acute type A aortic dissection

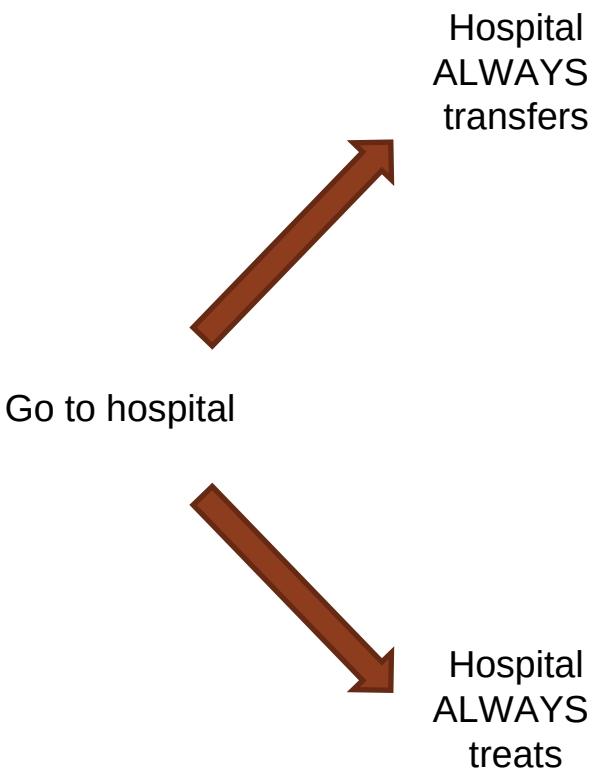


Go to hospital

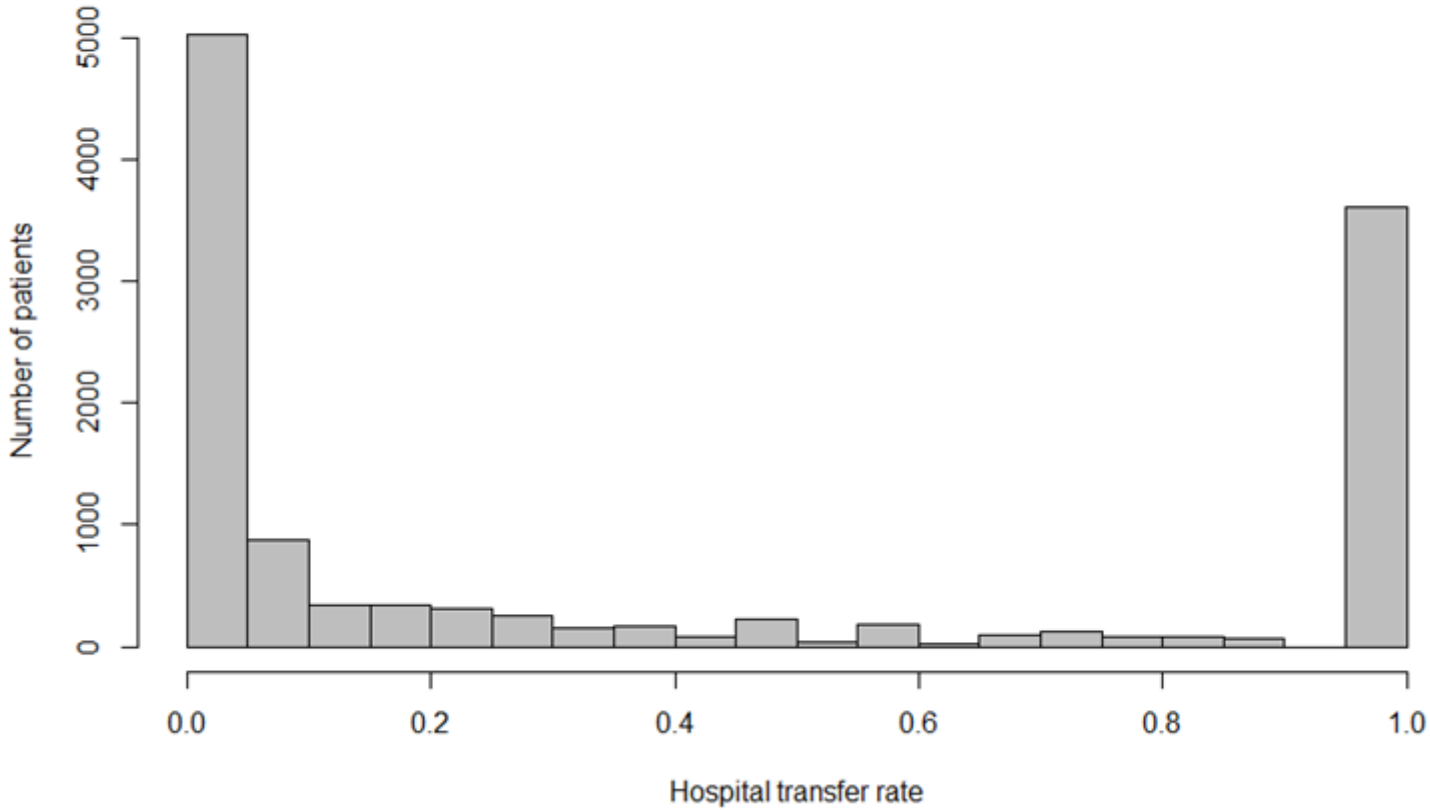
Go to hospital

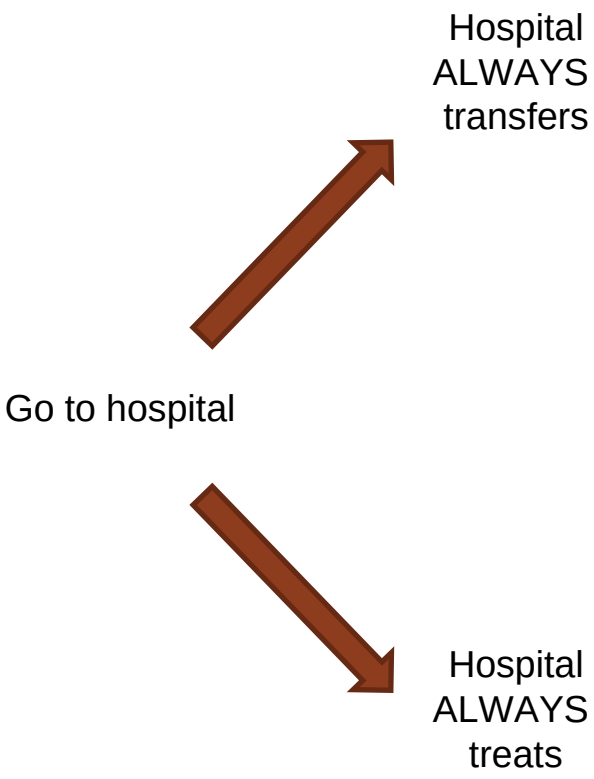
Hospital
ALWAYS
transfers

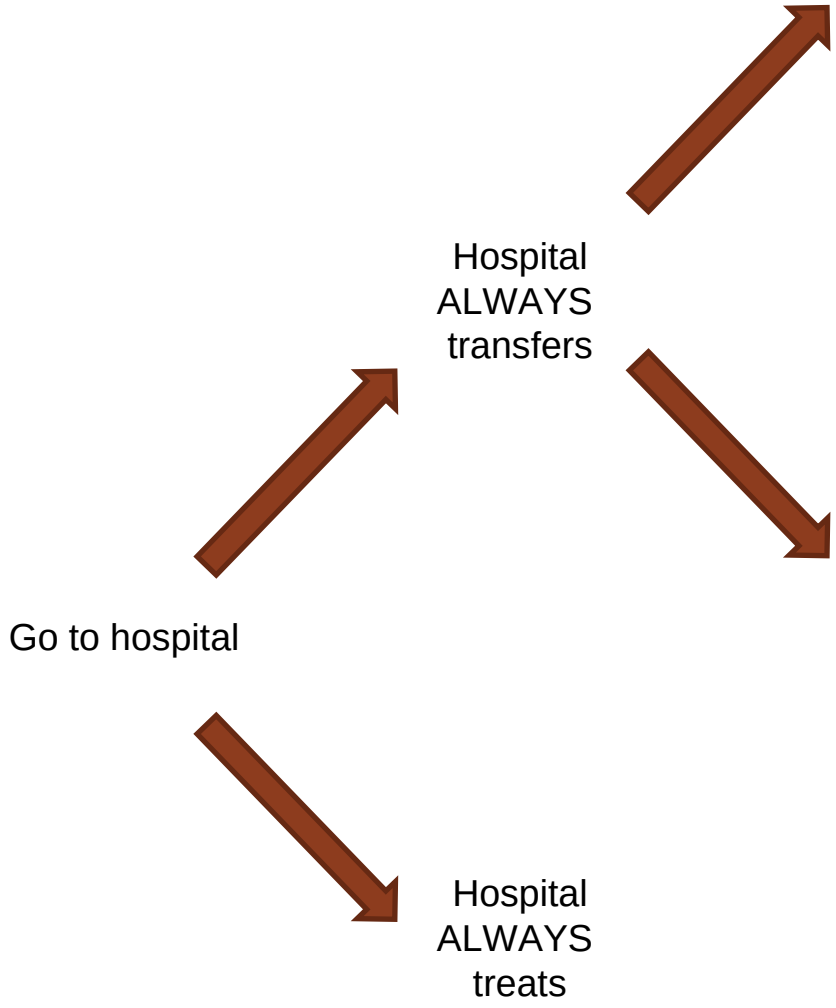
Go to hospital


Hospital ALWAYS transfers
Go to hospital
Hospital ALWAYS treats

B Distribution of patients presenting to hospitals with varying transfer rates for acute type A aortic dissection




Hospital ALWAYS transfers
Go to hospital
Hospital ALWAYS treats


Hospital
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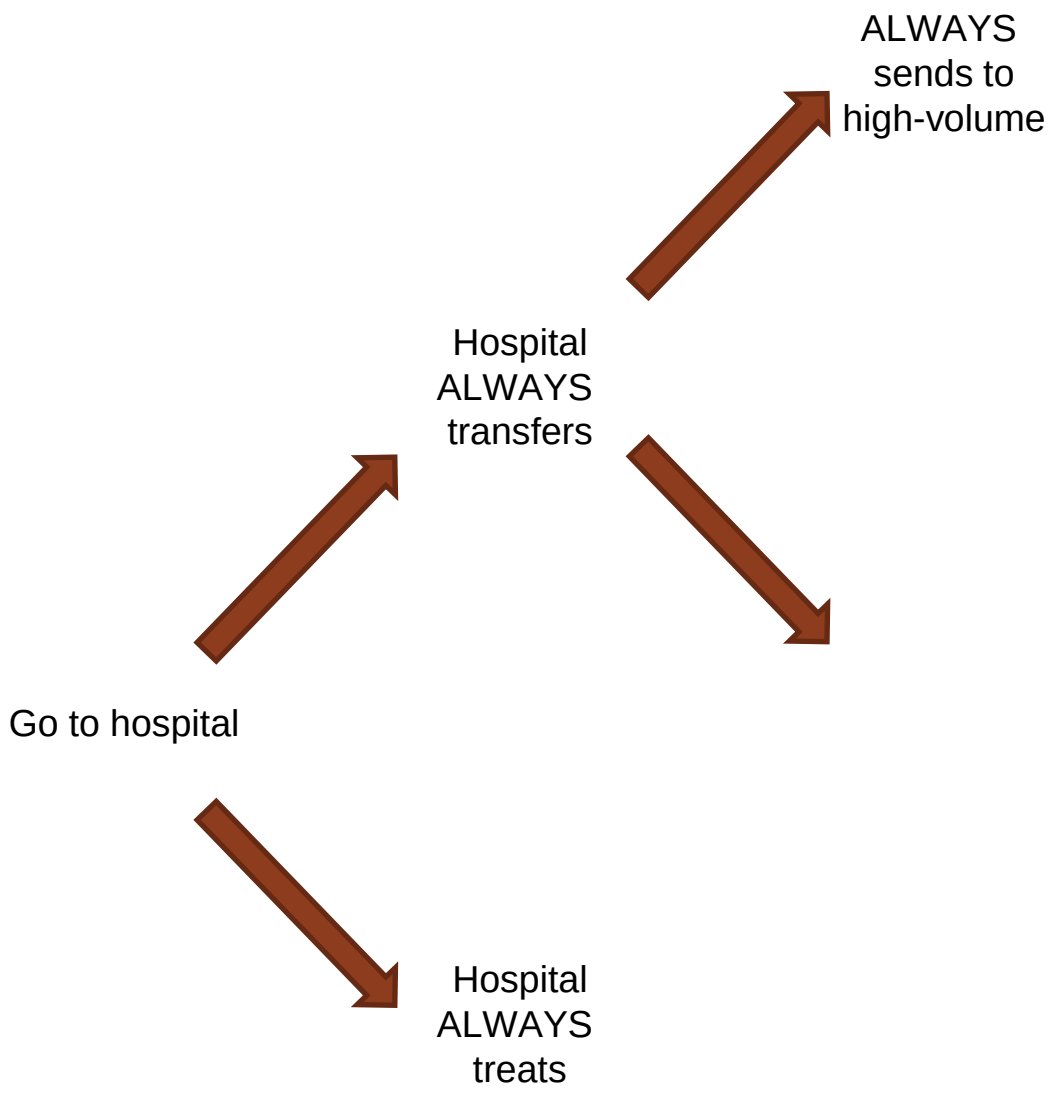
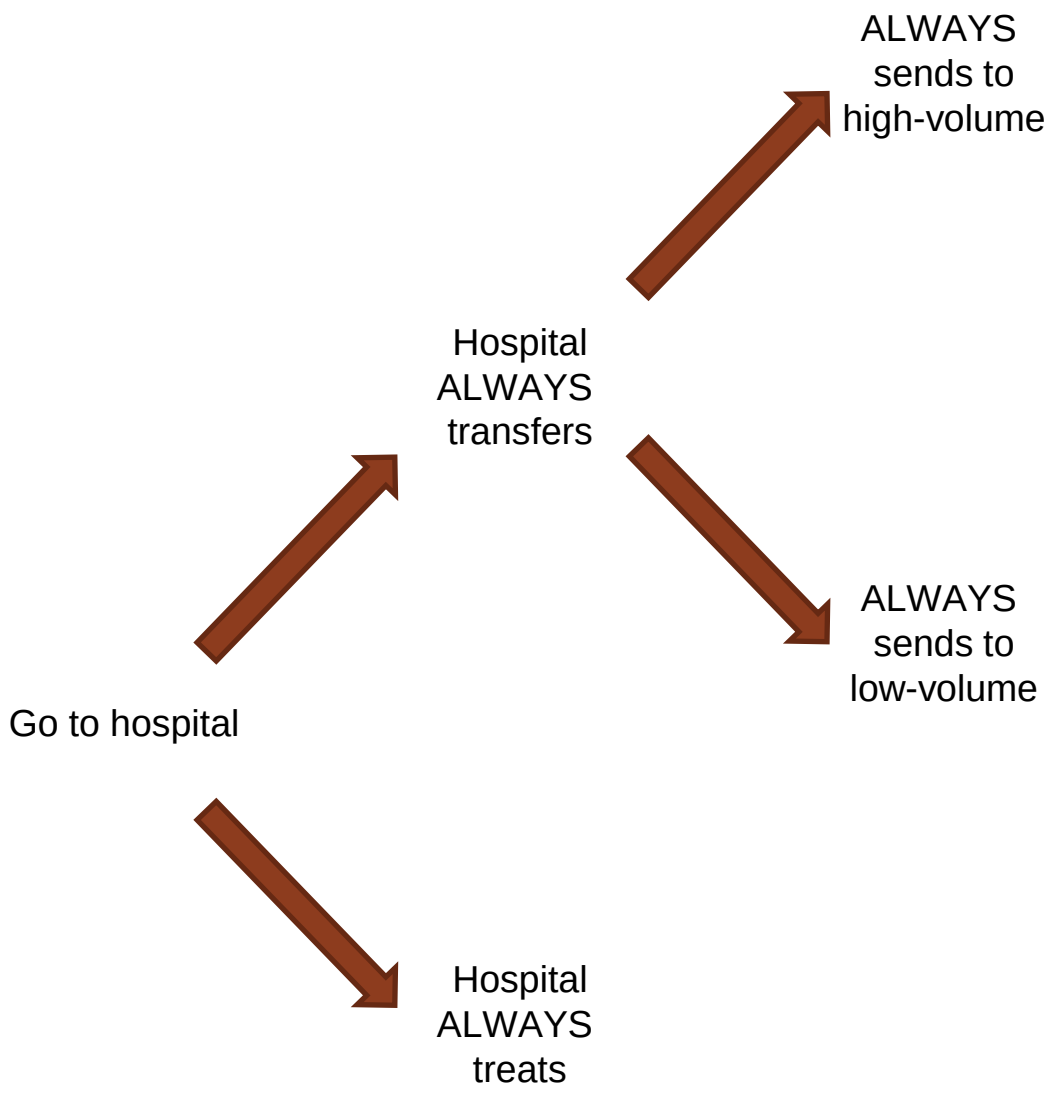
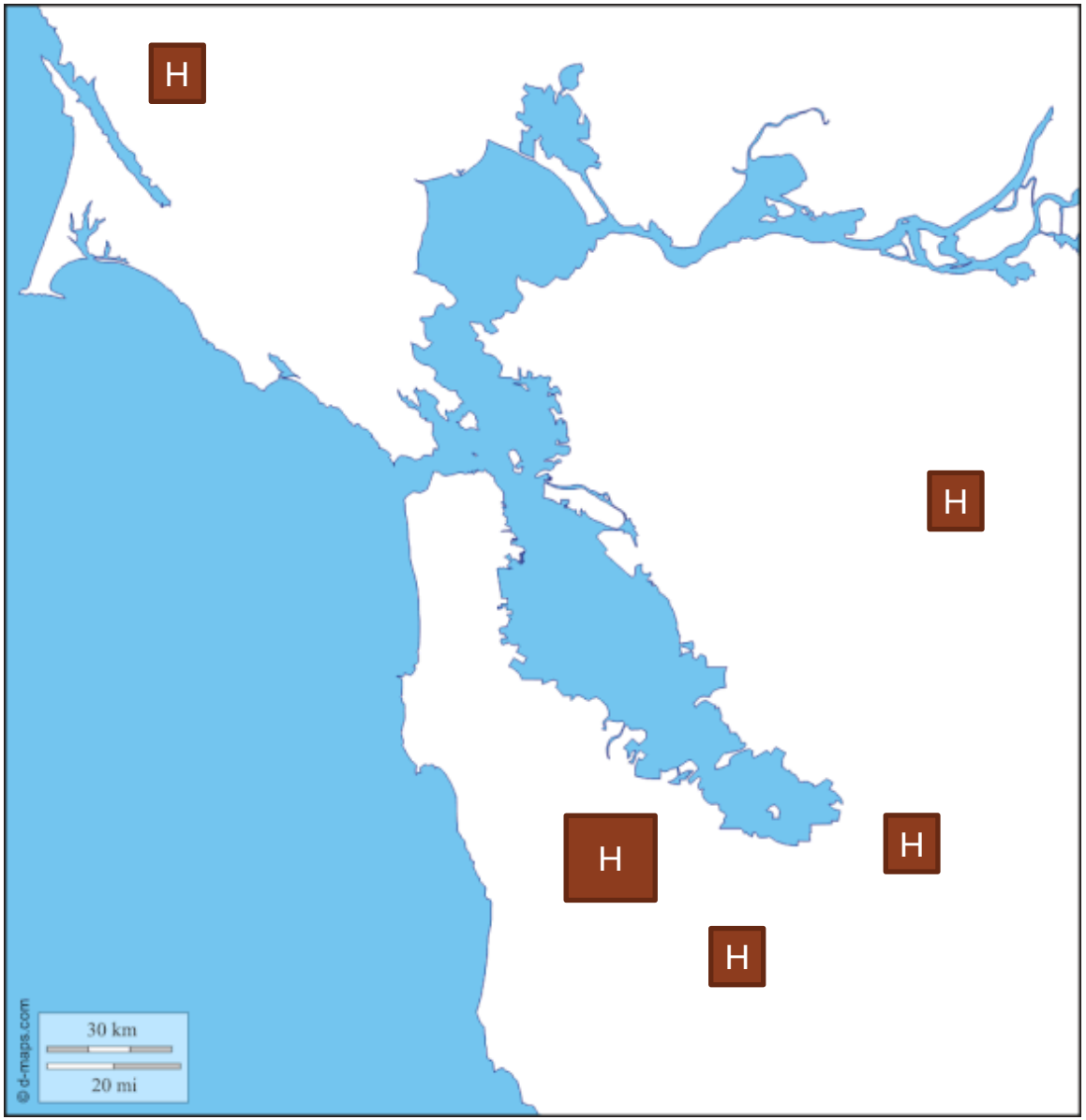
transfers
Go to hospital
Hospital
ALWAYS
treats


ALWAYS sends to high-volume
Hospital ALWAYS transfers
Go to hospital
Hospital ALWAYS treats


ALWAYS sends to high-volume
Hospital ALWAYS transfers
ALWAYS sends to low-volume
Go to hospital
Hospital ALWAYS treats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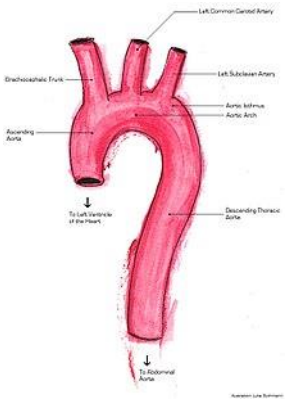
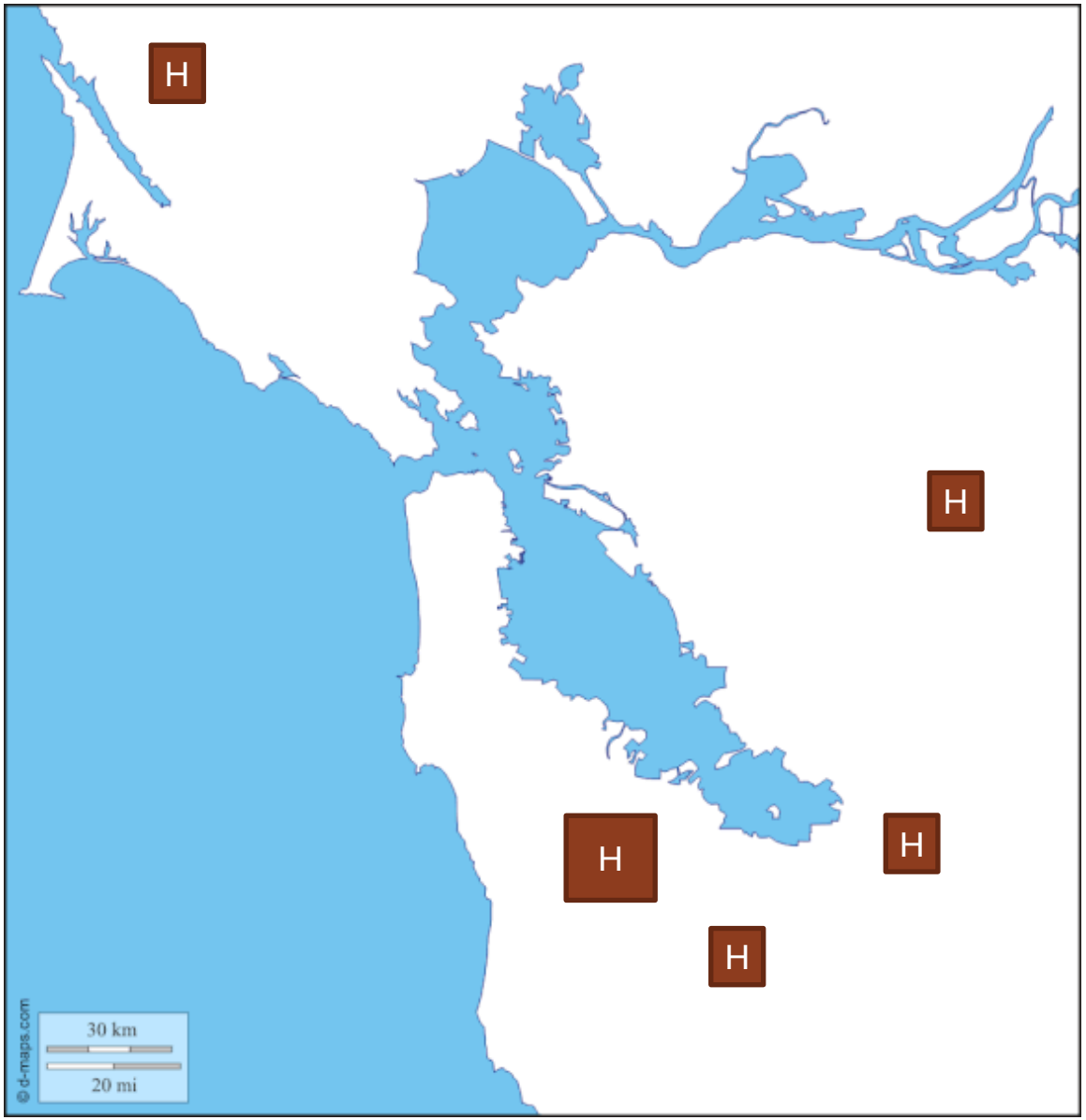

Left Common Carotid Artery
Brachiocephalic Trunk
Left Subclavian Artery
Aortic Isthmus
Aortic Arch
Ascending Aorta
To Left Ventricle of the Heart
Descending Thoracic Aorta
To Abdominal Aorta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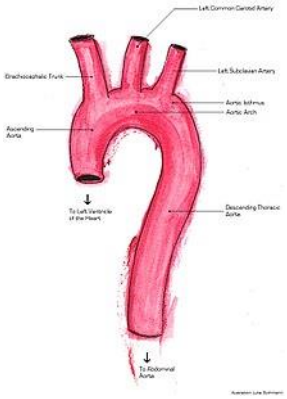
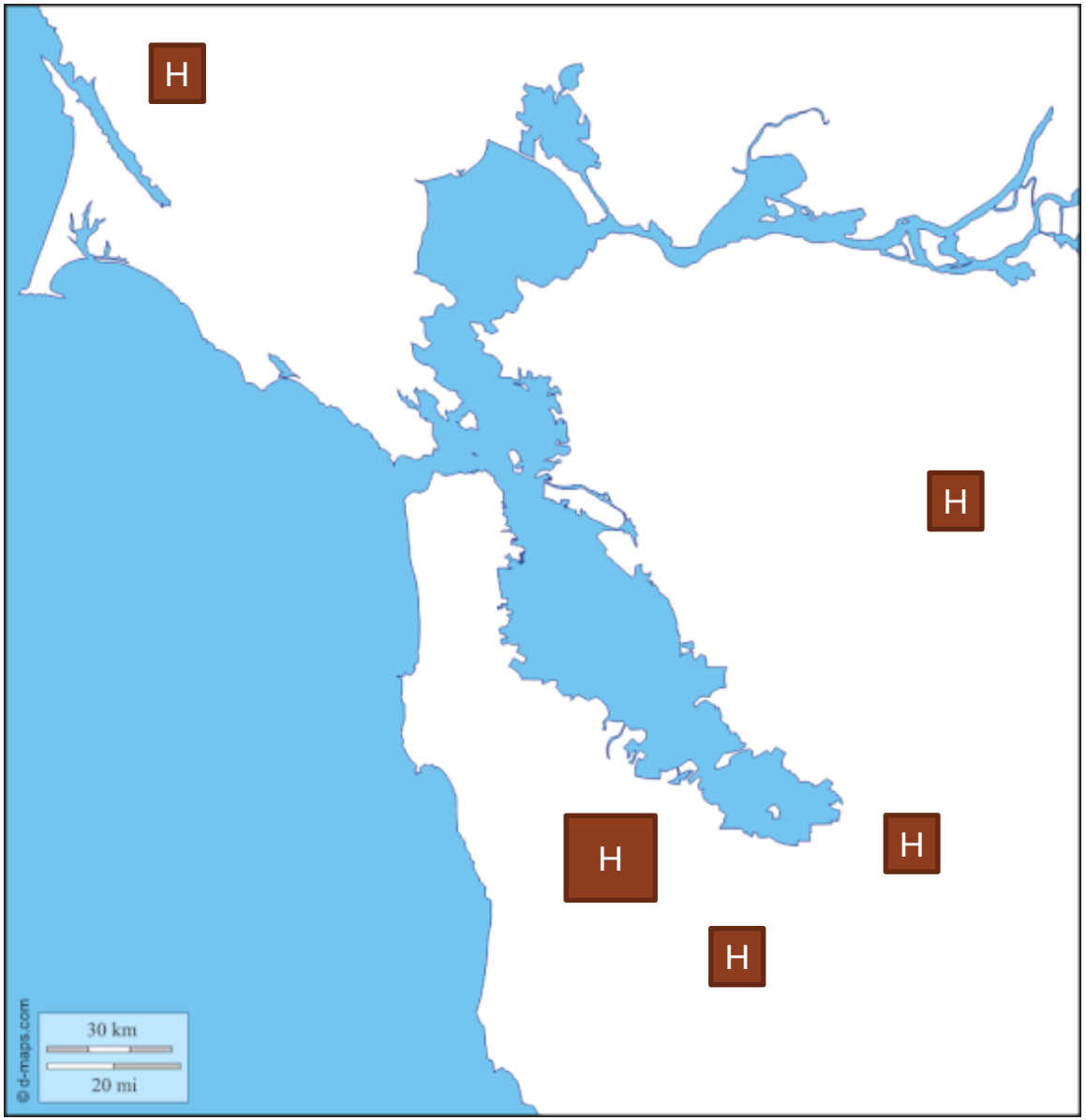

Left Common Carotid Artery
Brachiocephalic Trunk
Left Subclavian Artery
Aortic Isthmus
Aortic Arch
Ascending Aorta
To Left Ventricle of the Heart
Descending Thoracic Aorta
To Abdominal Aorta

< 10/year = low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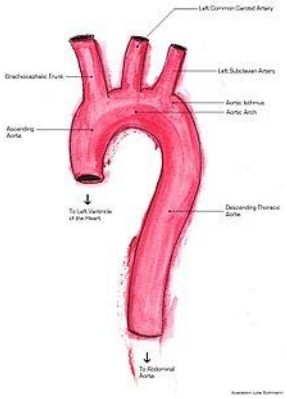
> 10/year = high



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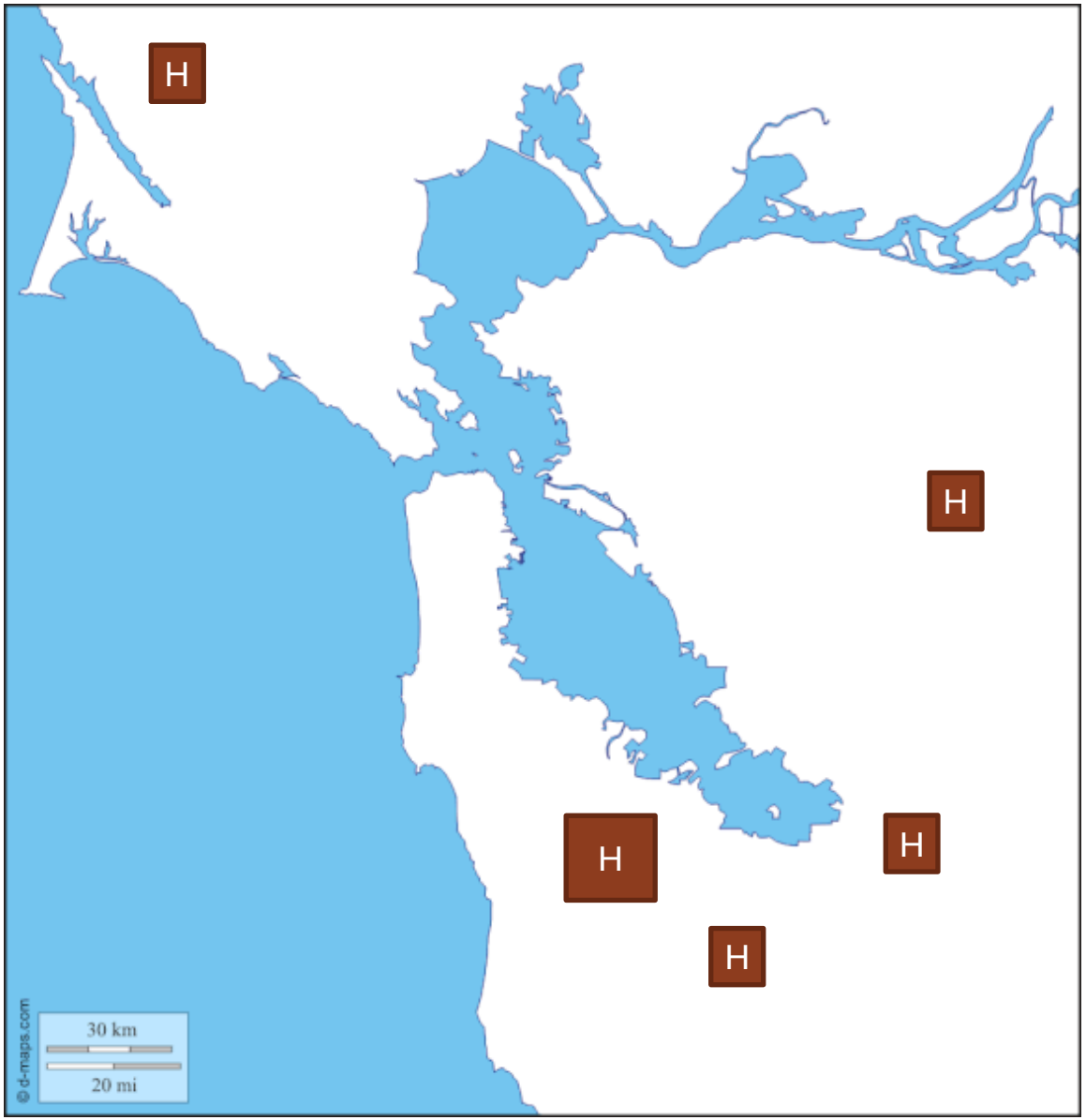
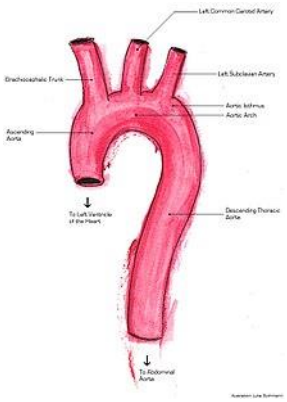


> 10/year = high



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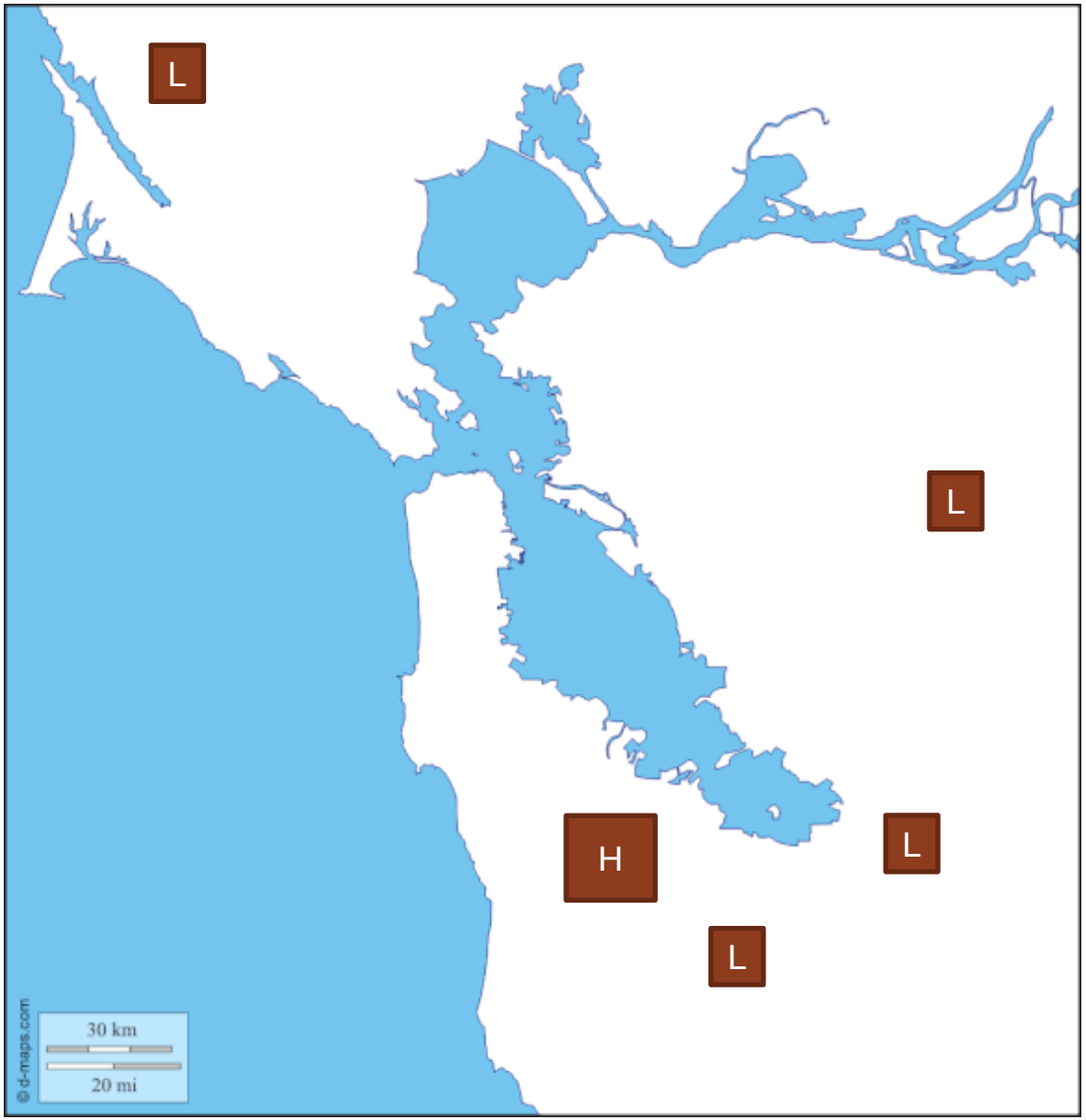

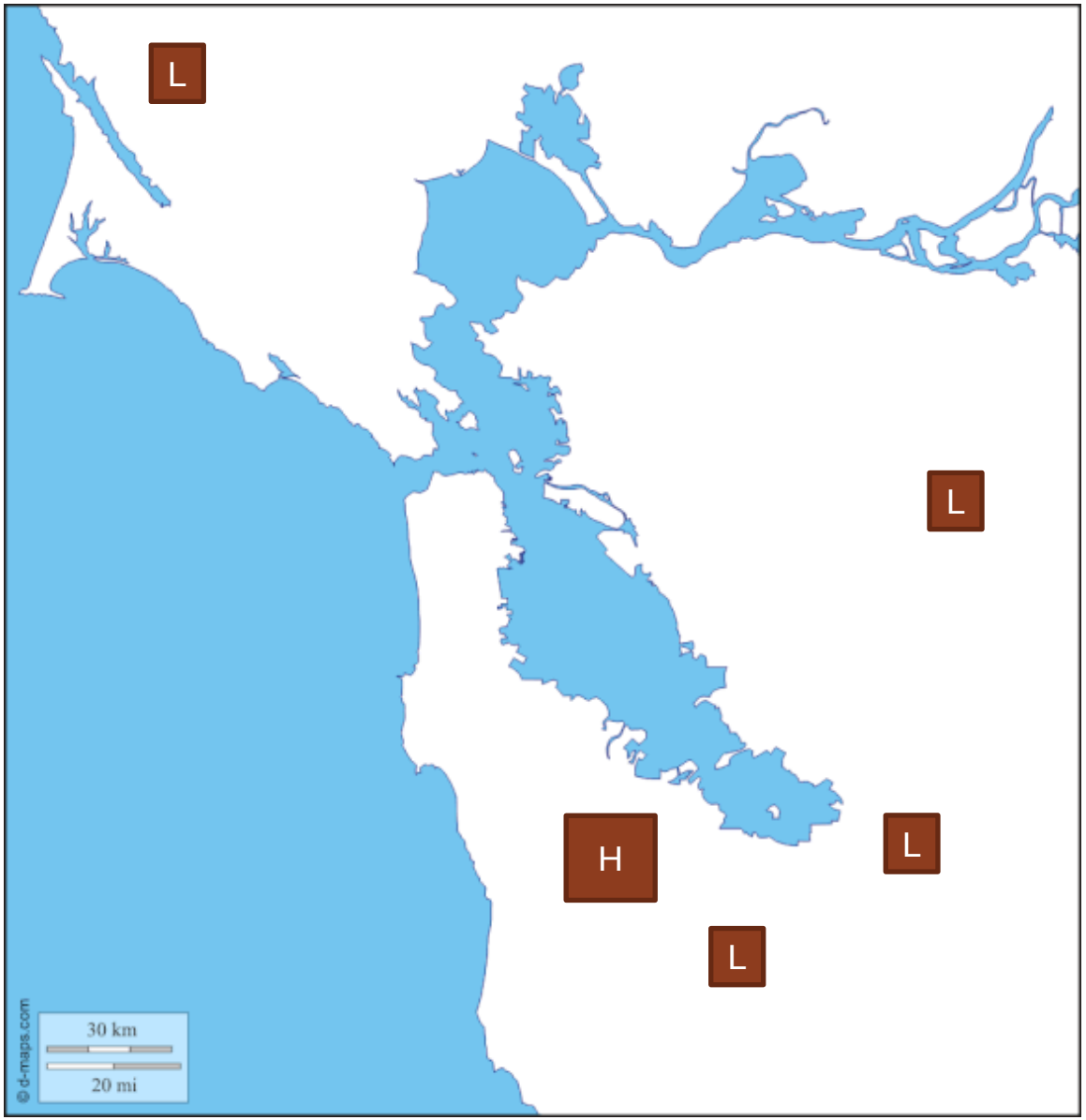
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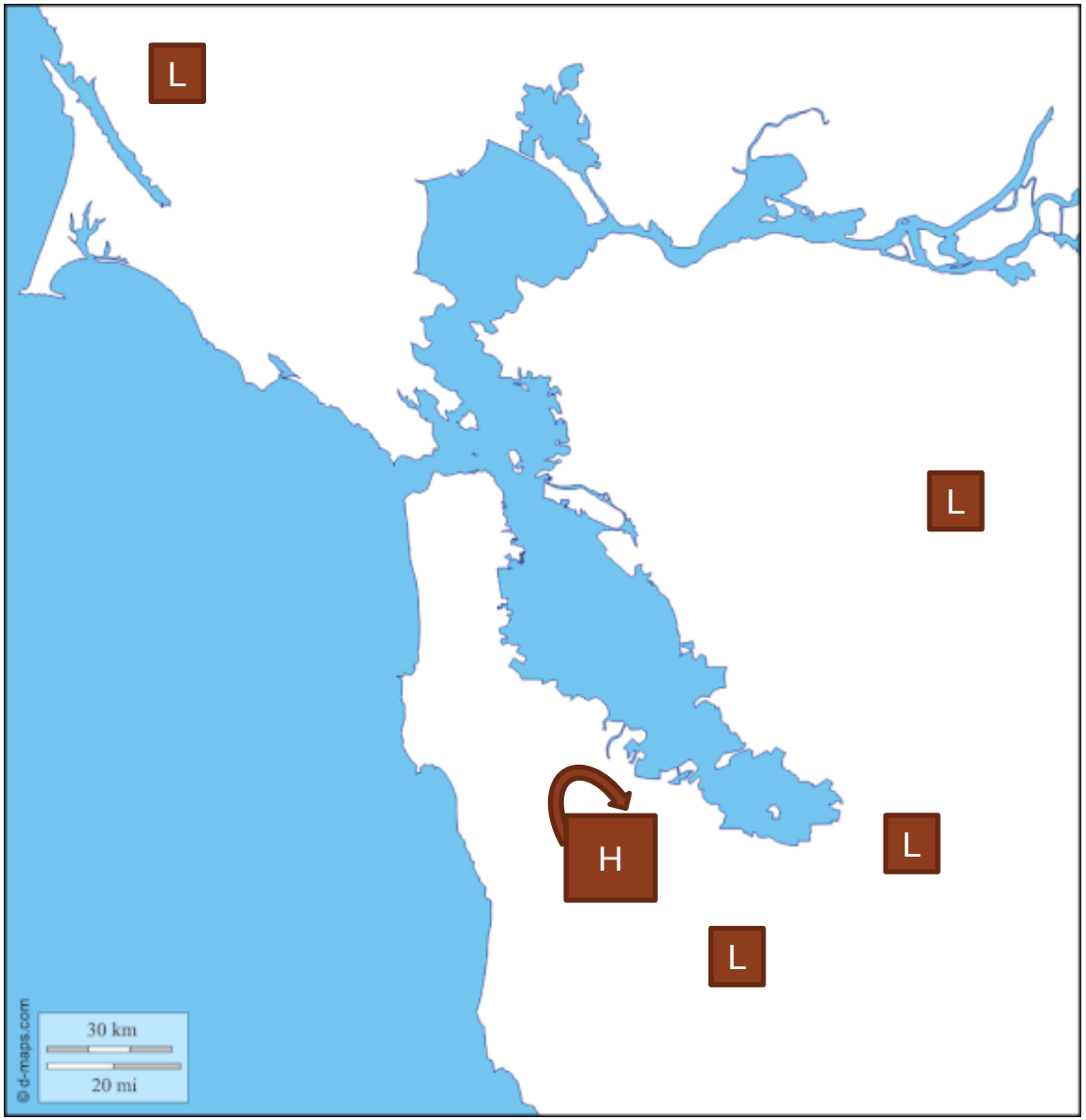
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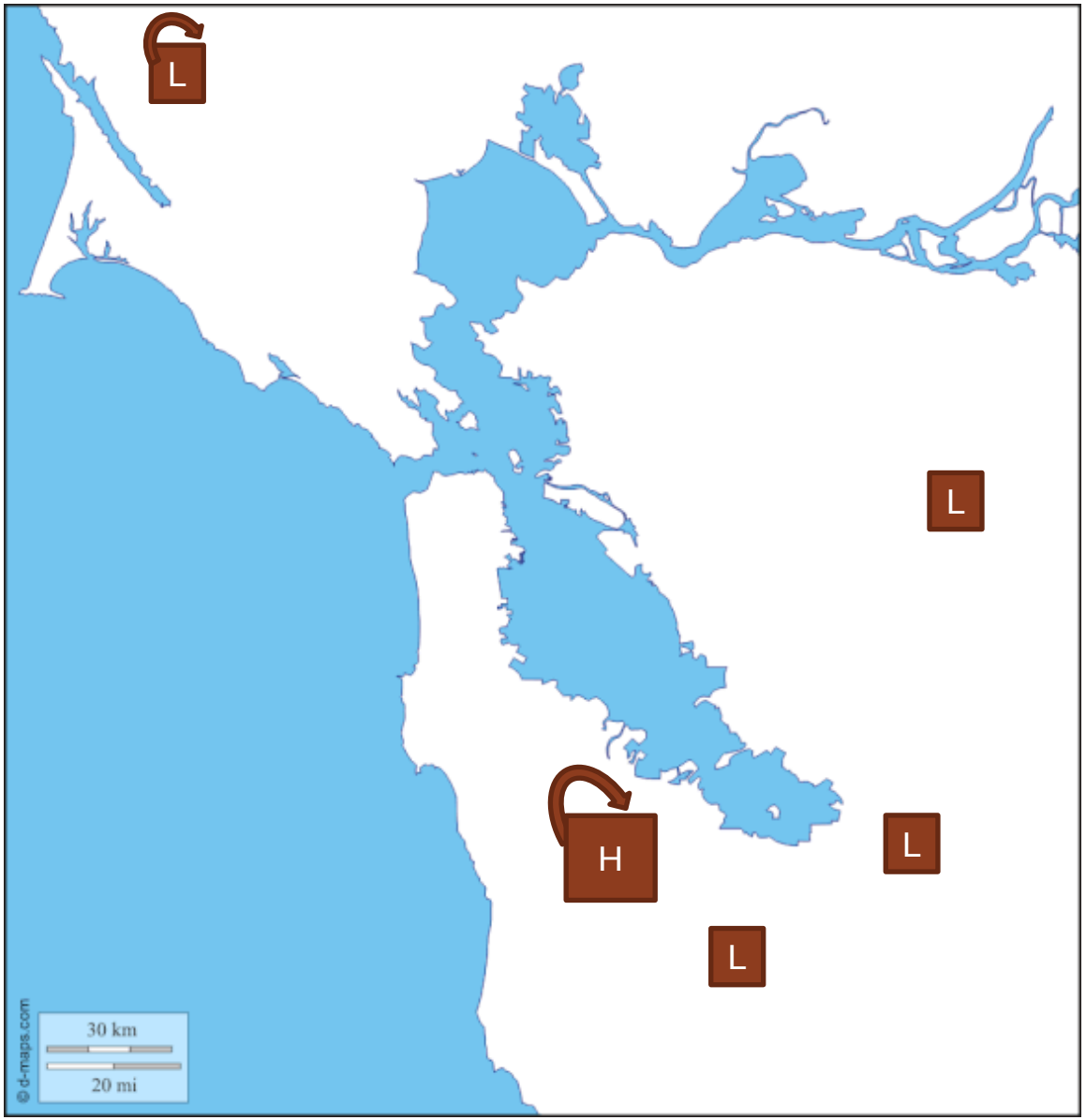
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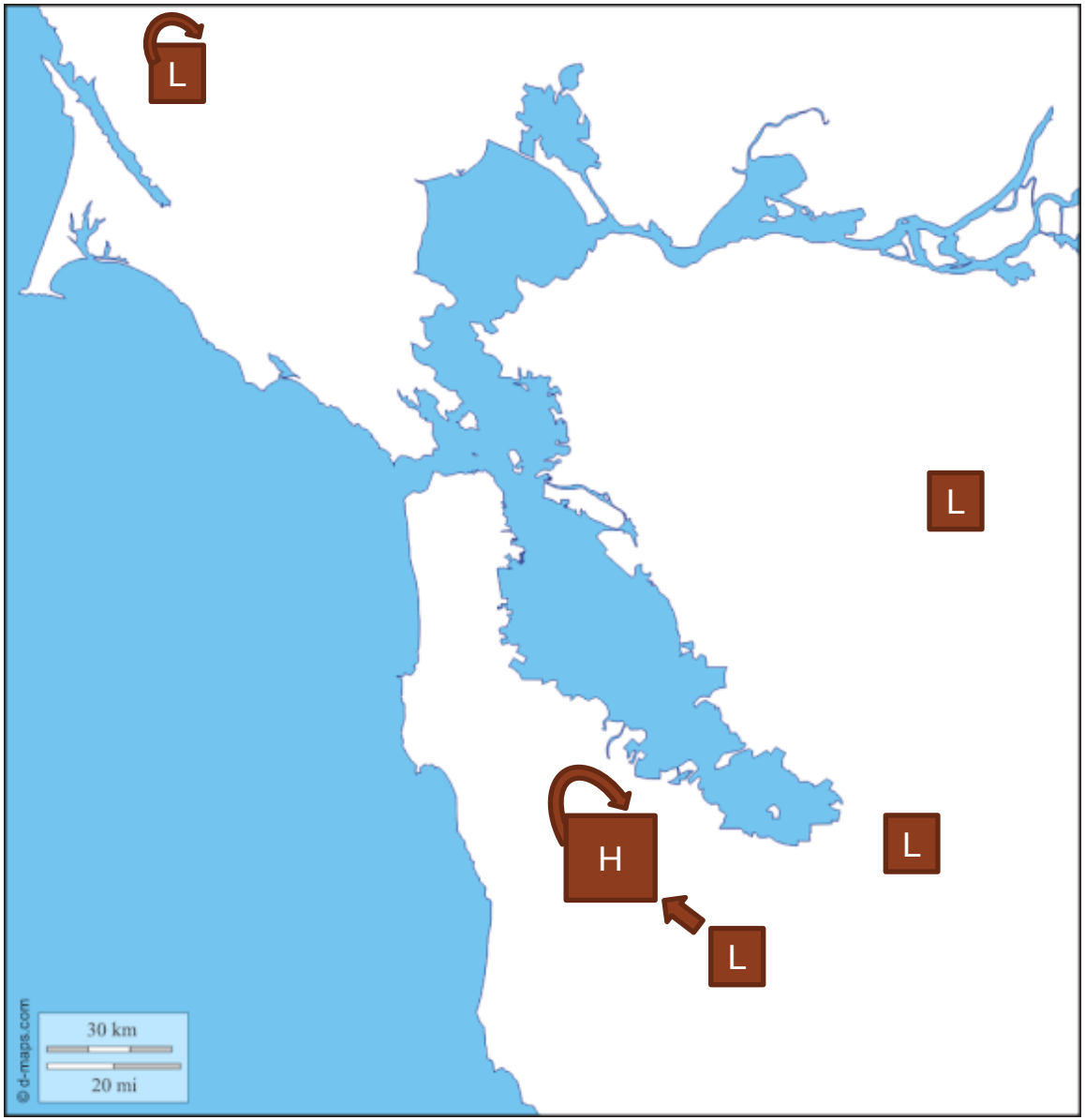
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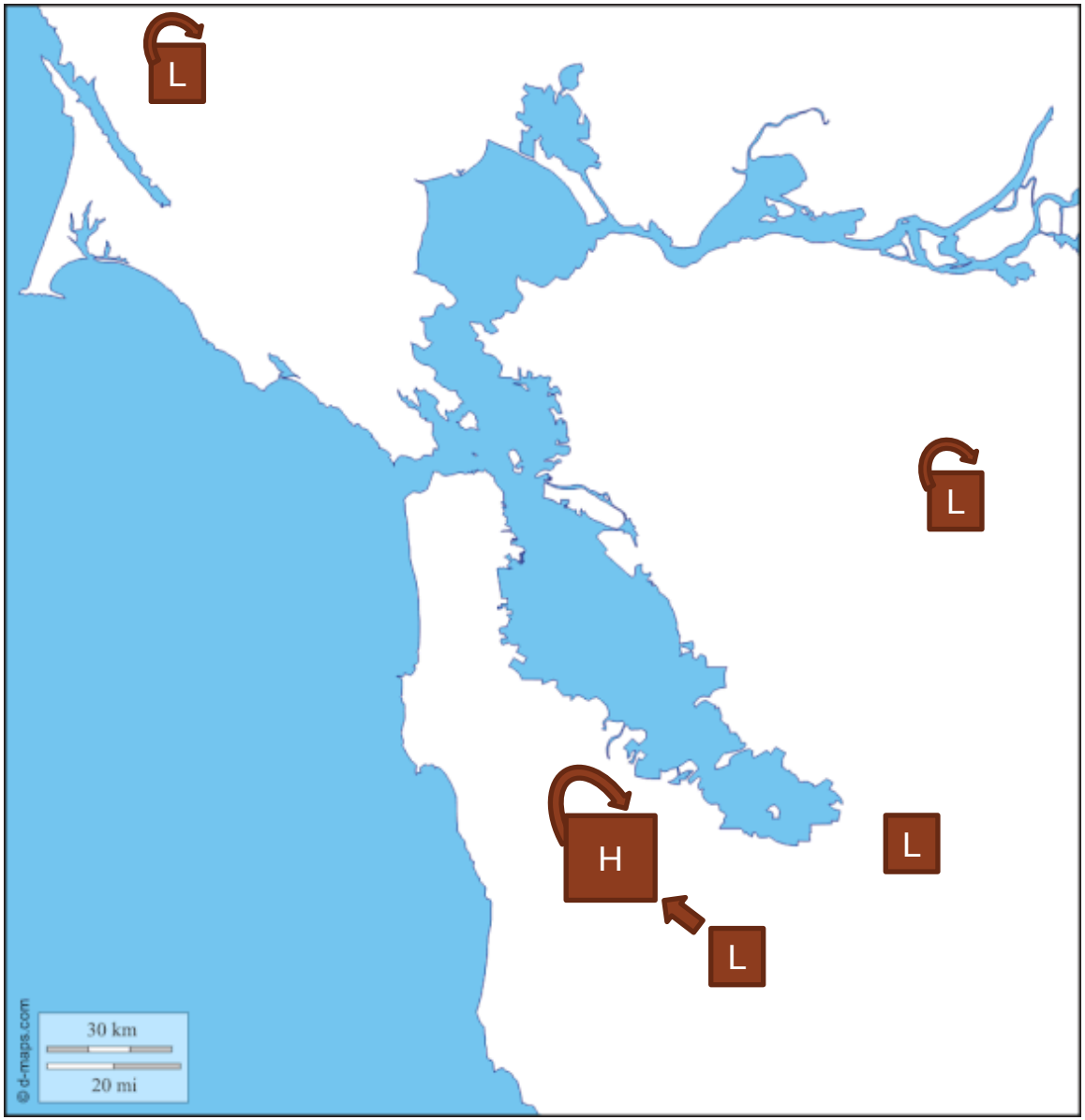
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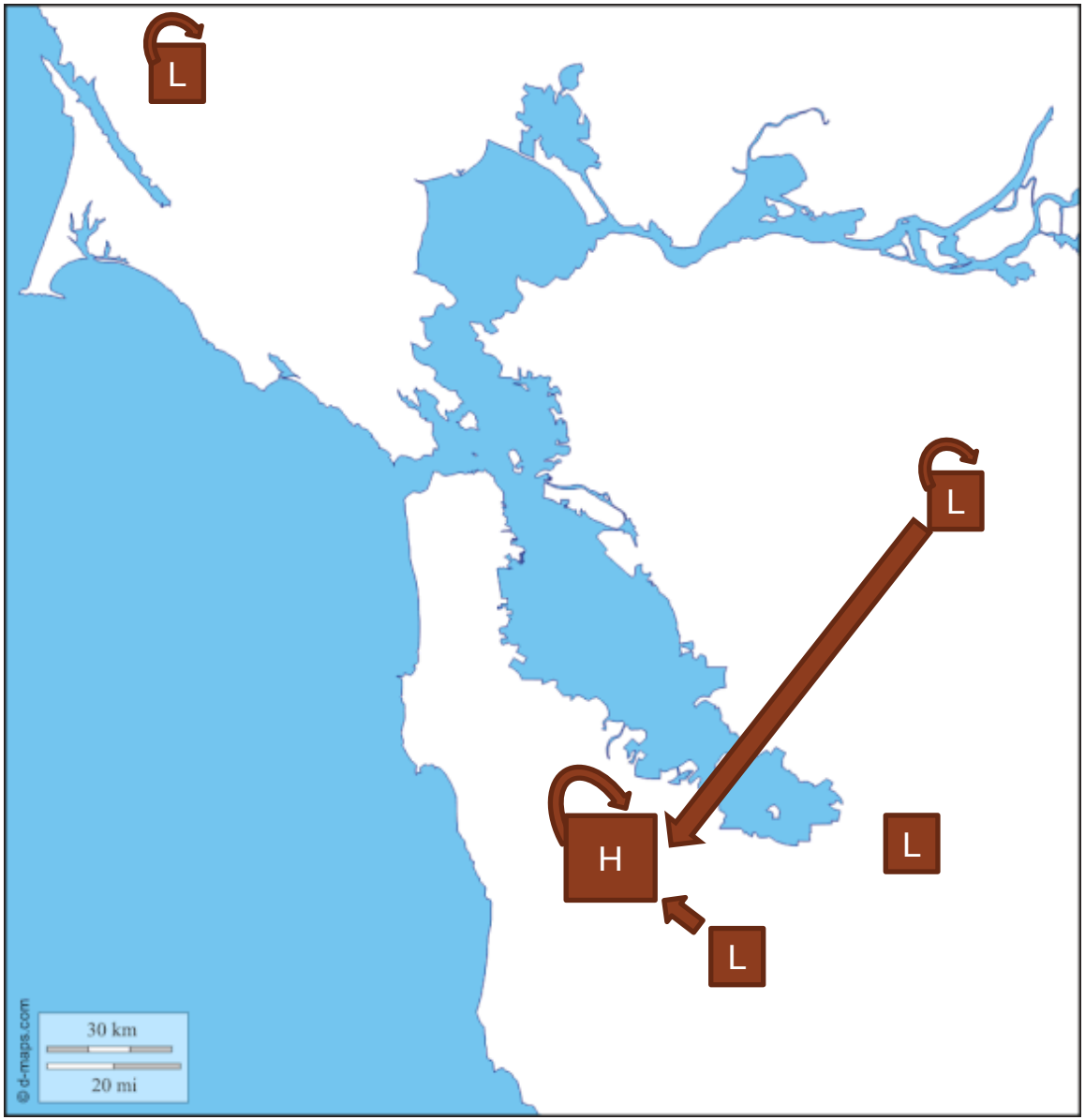
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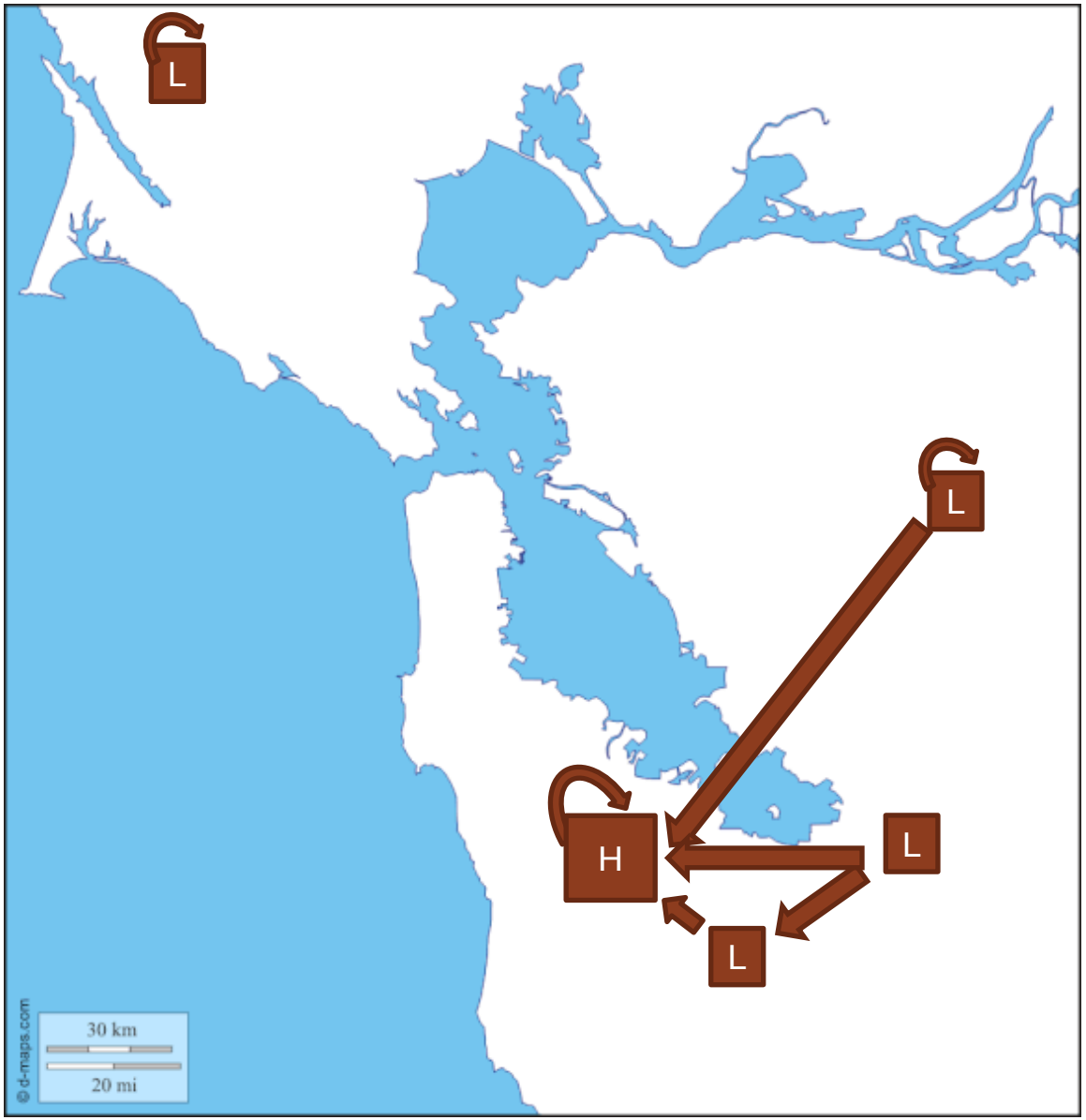
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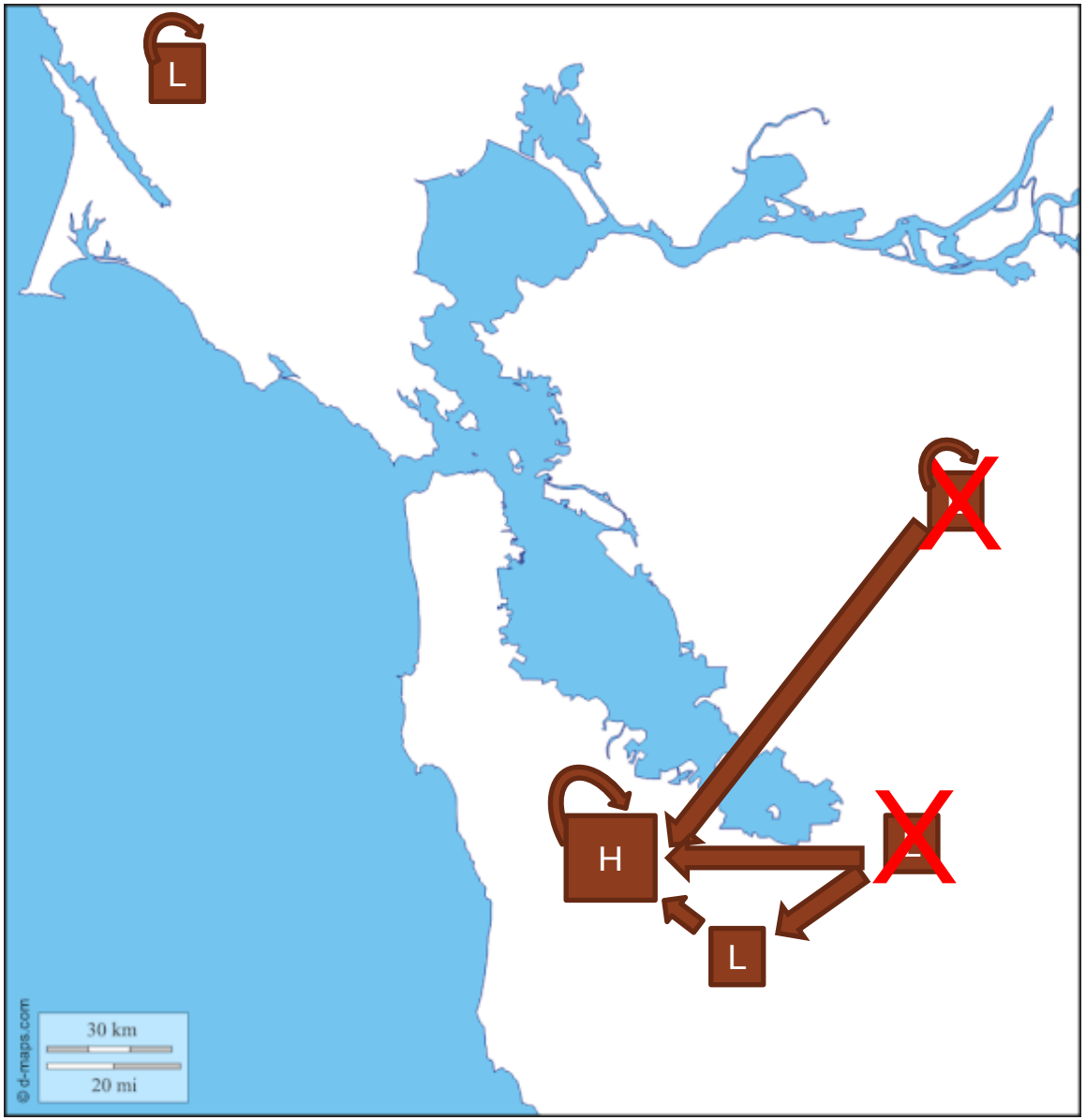
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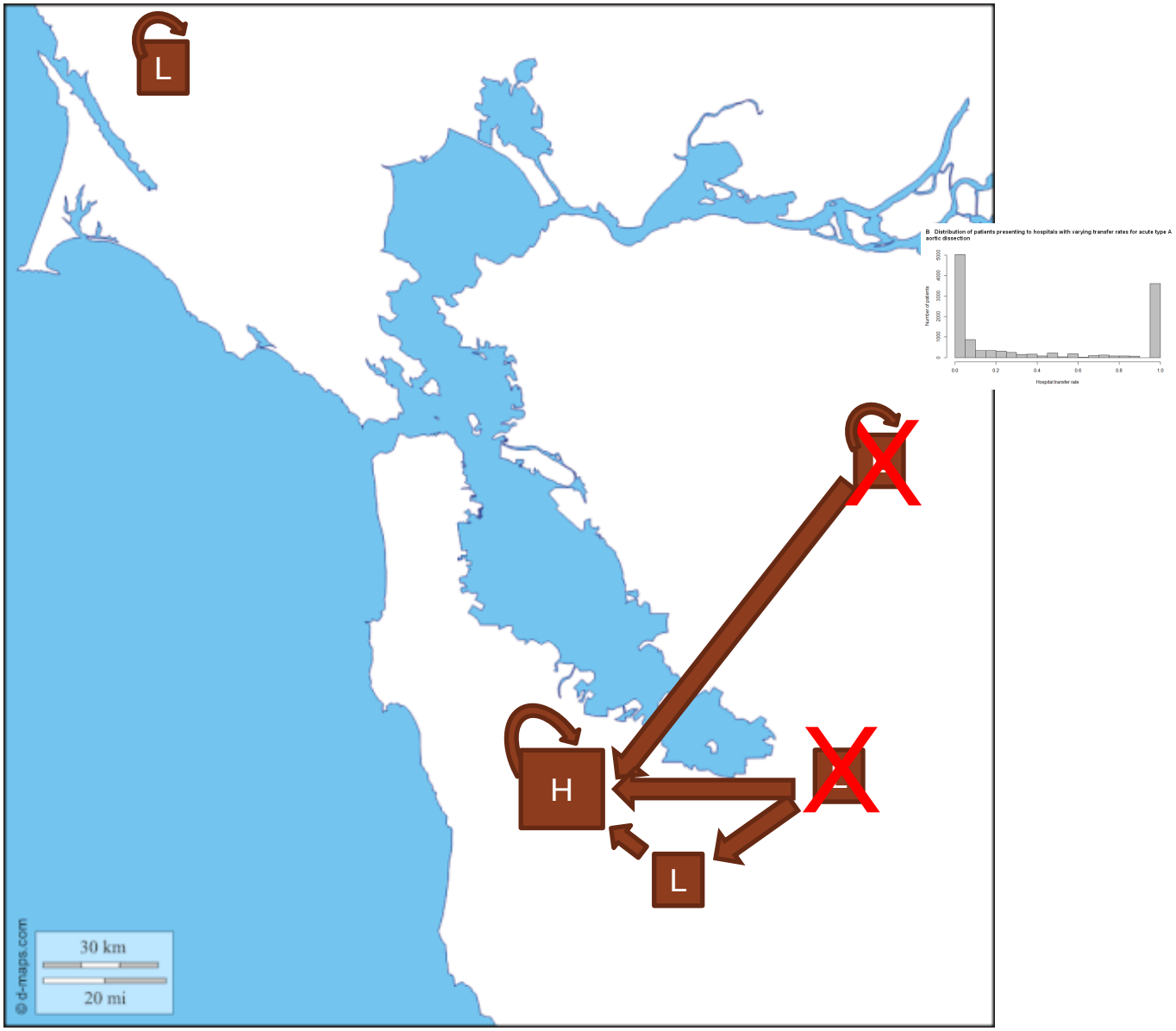
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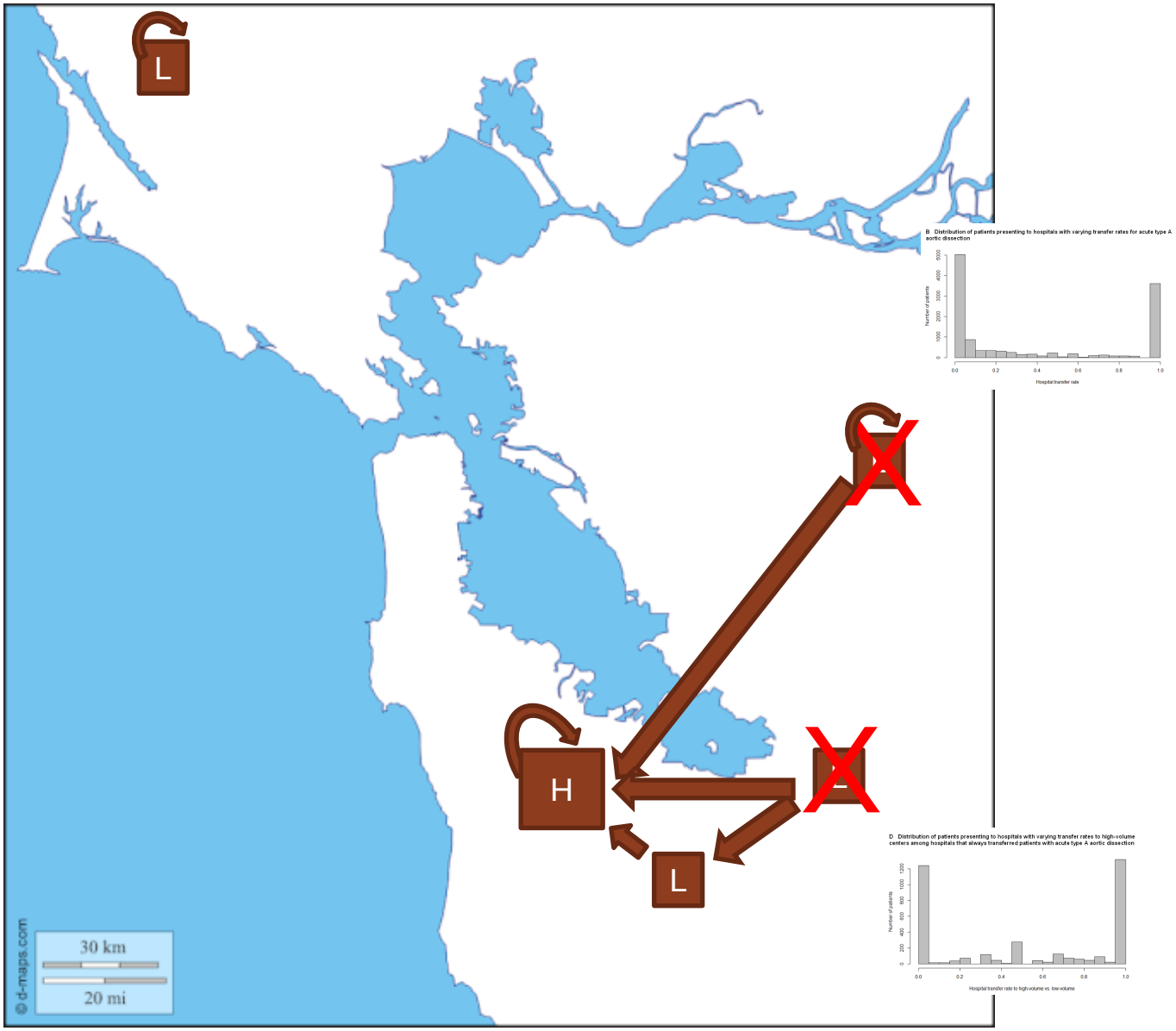
B Distribution of patients presenting to hospitals with varying transfer rates for acute type A aortic dissection
Number of patients
Hospital transfer rate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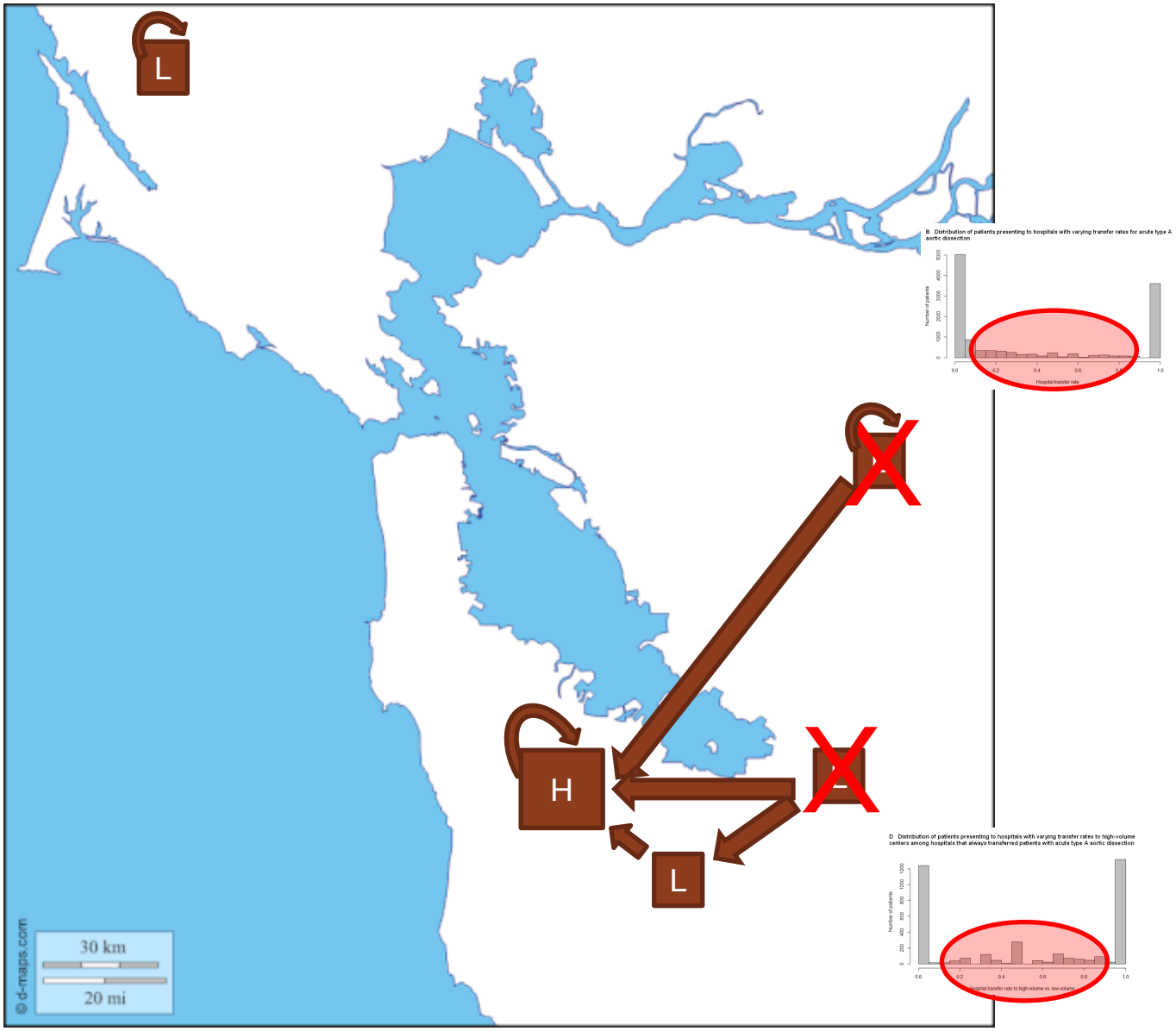
B Distribution of patients presenting to hospitals with varying transfer rates for acute type A aortic dissection
Number of patients
Hospital transfer rate
D Distribution of patients presenting to hospitals with varying transfer rates to high-volume centers among hospitals that always transferred patients with acute type A aortic dissection
Number of patients
Hospital transfer rate to high-volume vs. low-volume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© d-maps.com
B Distribution of patients presenting to hospitals with varying transfer rates for acute type A aortic dissection
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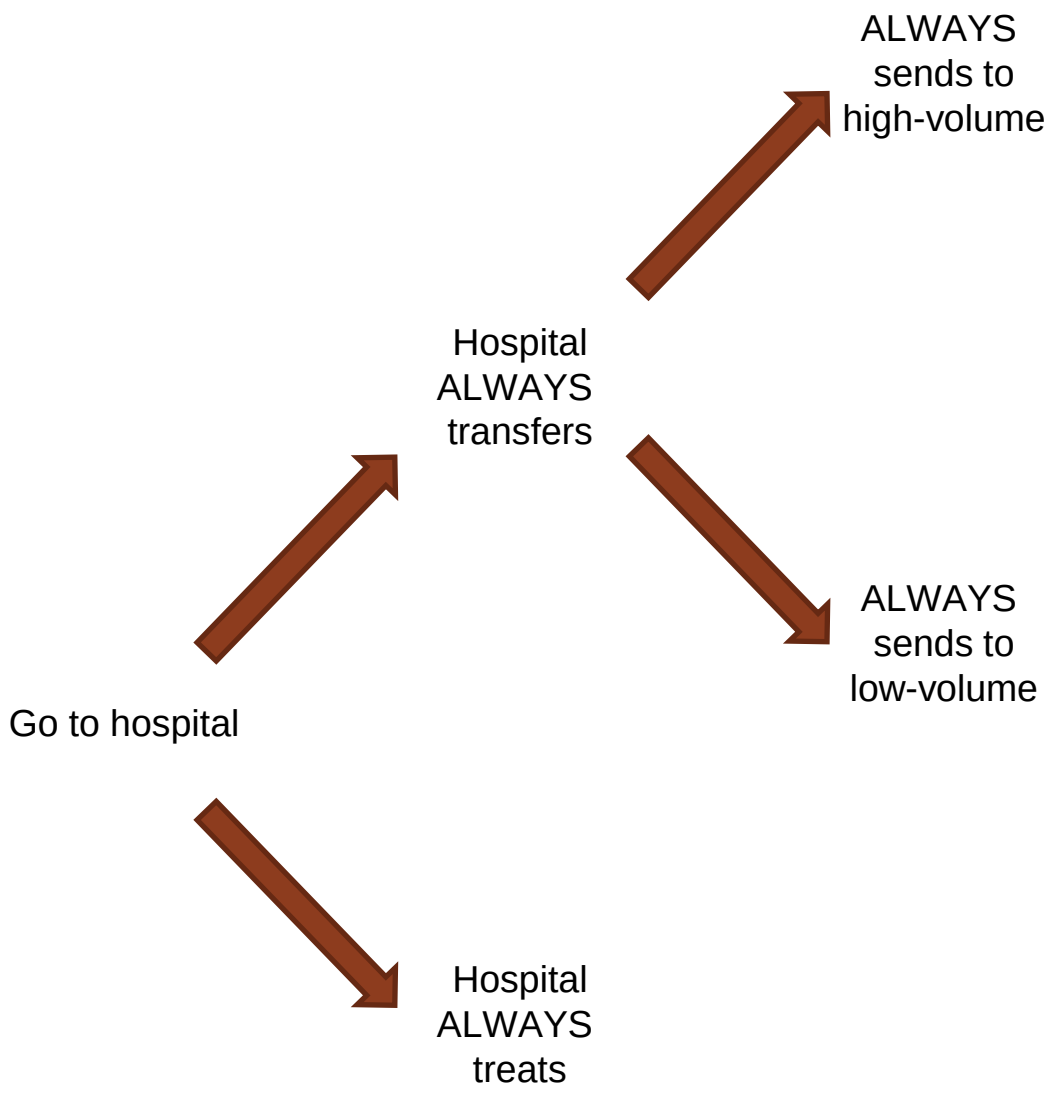
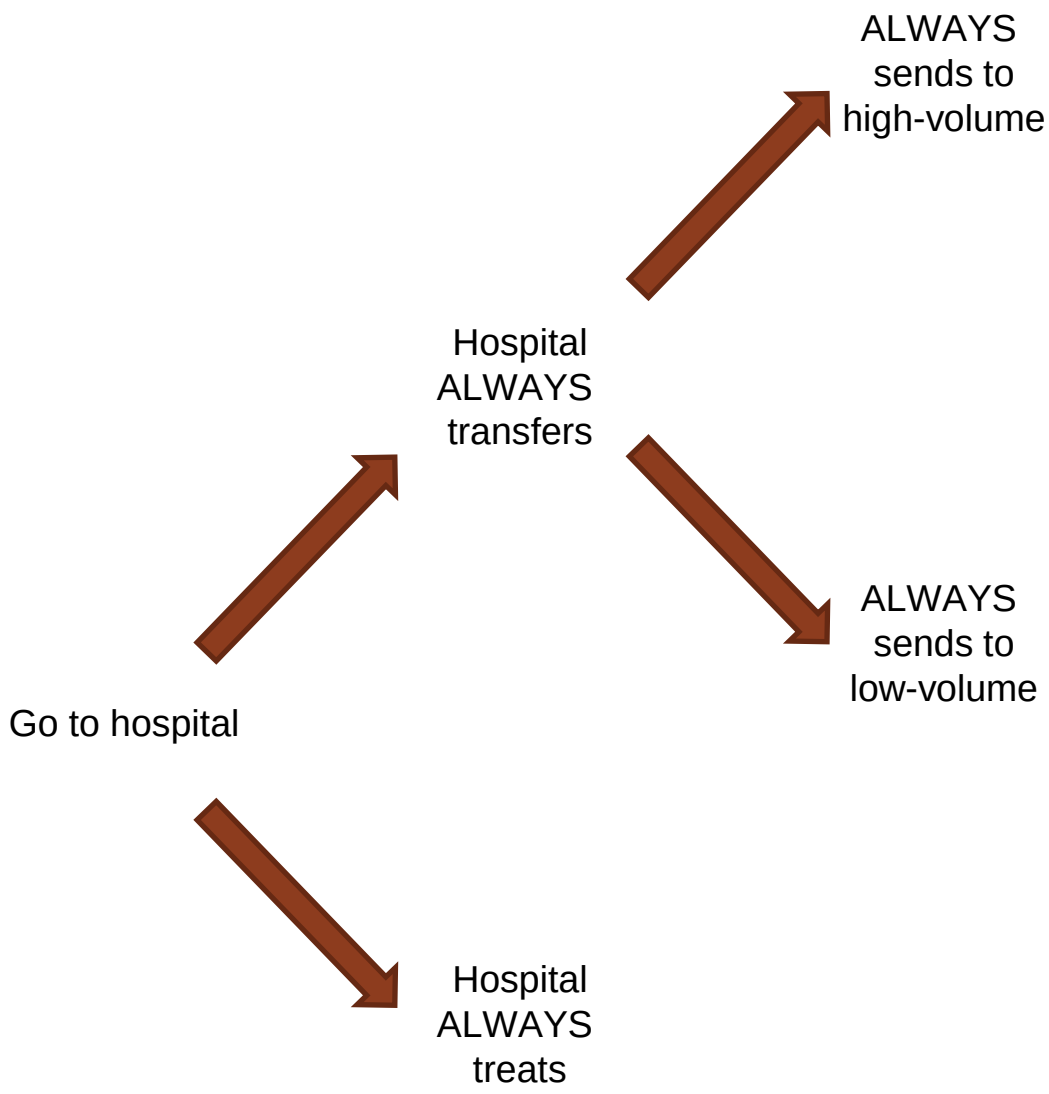
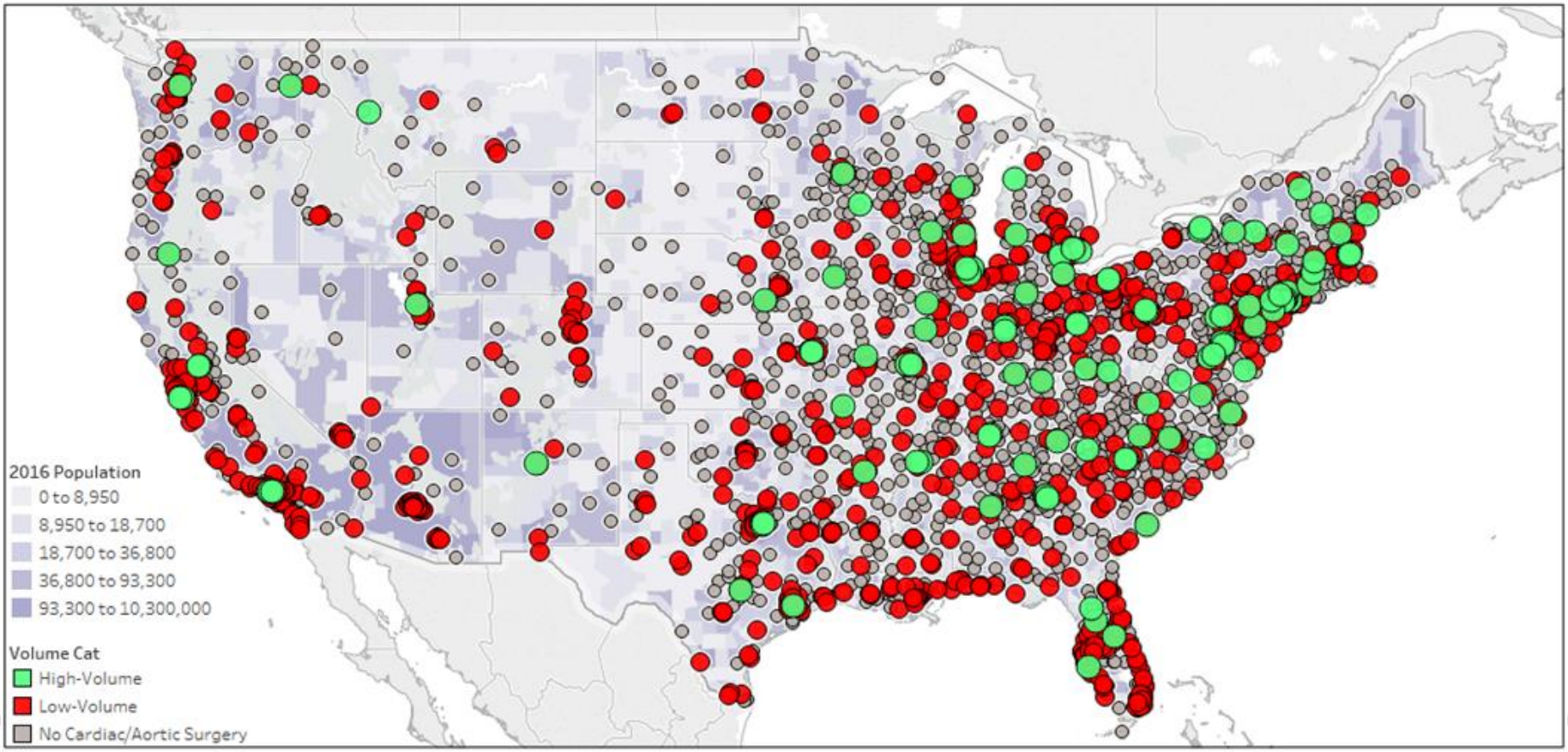
Number of patients
Hospital transfer rate to high-volume vs. low-volume


ALWAYS sends to high-volume
Hospital ALWAYS transfers
ALWAYS sends to low-volume
Go to hospital
Hospital ALWAYS treats



	high	low
transfer		
stay		

A Distribution of United States Hospitals Categorized by Proximal Aortic Surgery Volume, 1999-2010



is our sorting process “orthogonal”?

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is our sorting process “orthogonal”?

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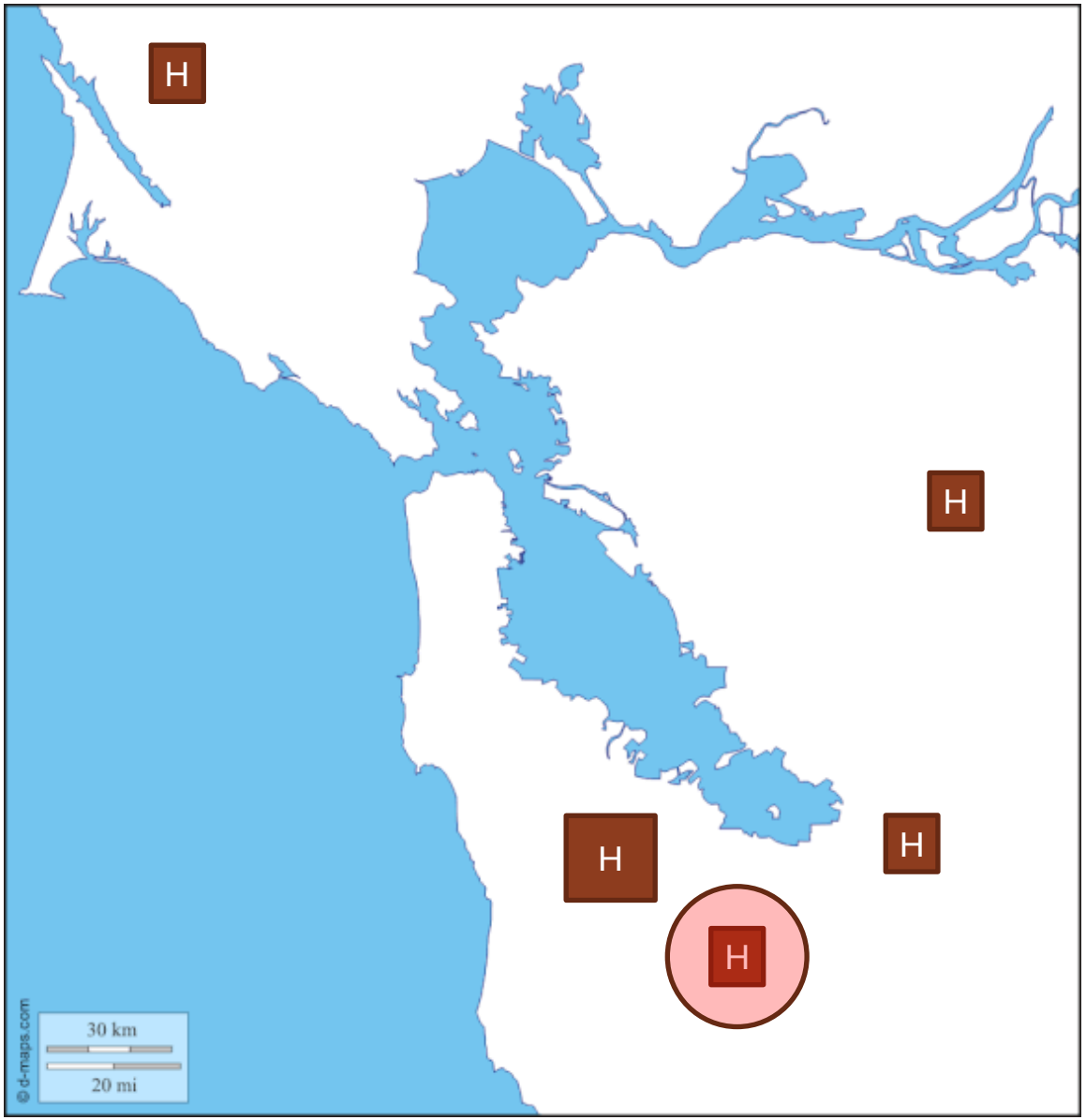
We can punt (a little bit) on the above two questions because we can merely observe that this is, in fact, the case.

How did patients end up at the original hospital?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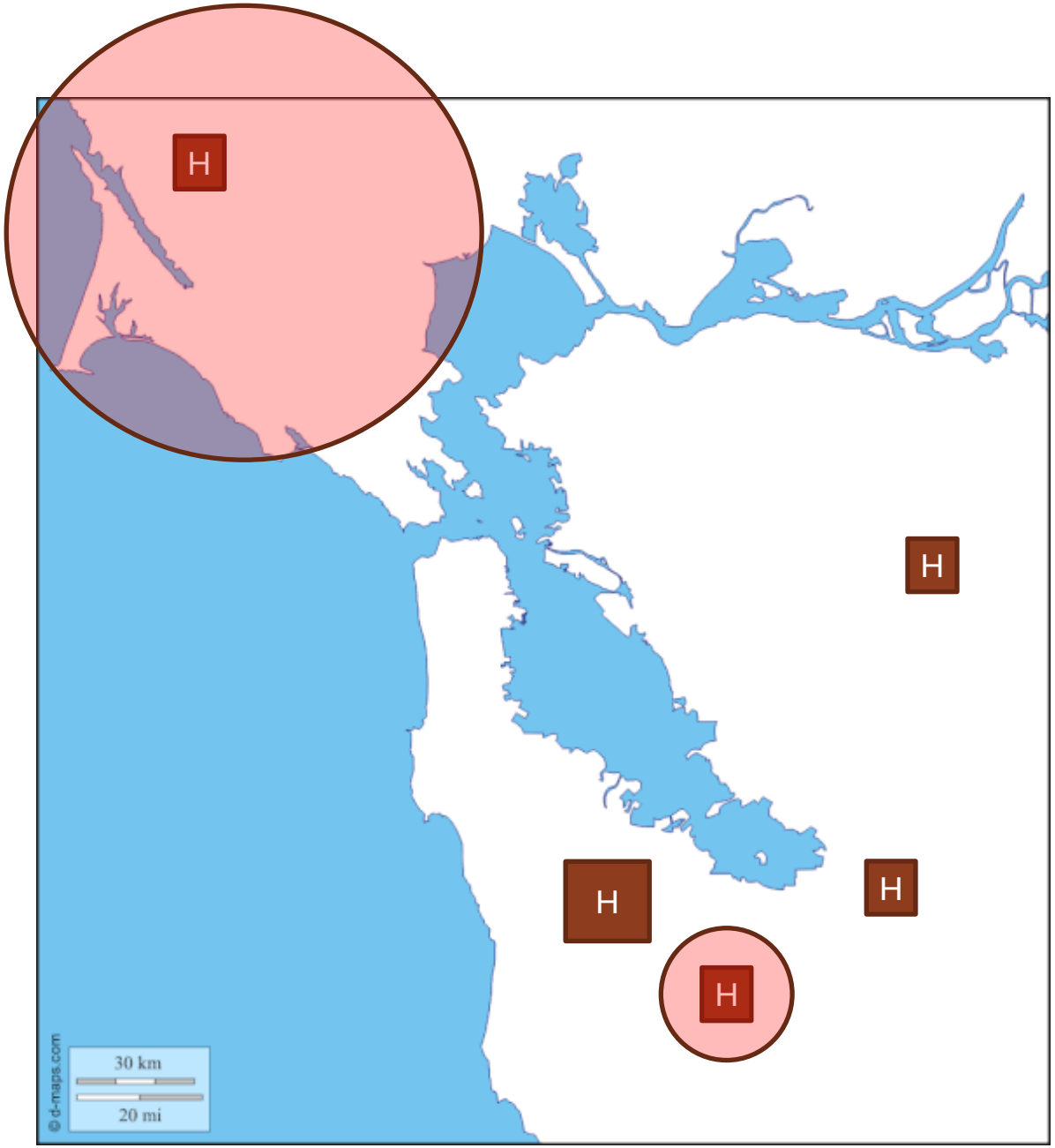
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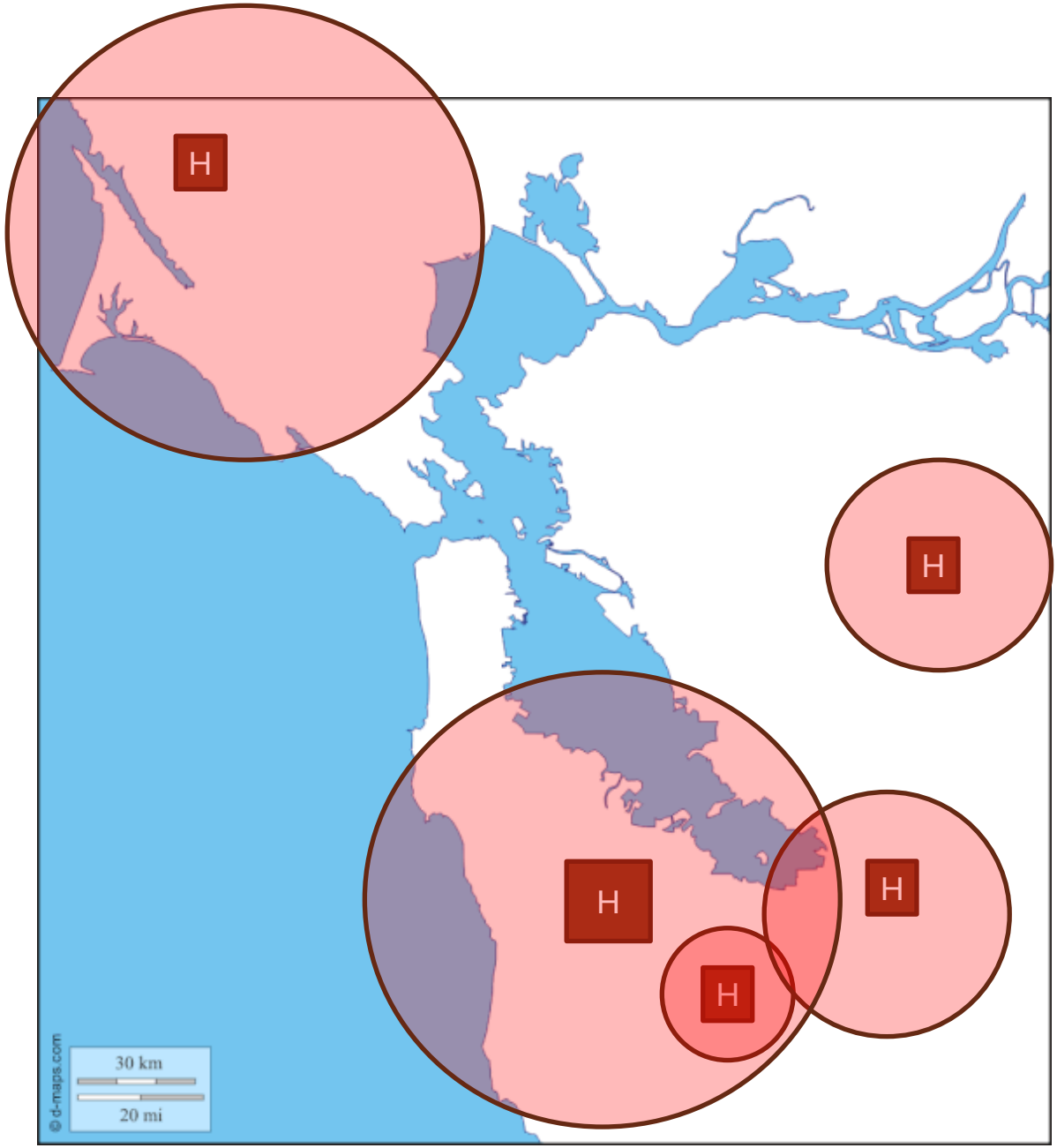
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let’s go find out.

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An undergrad in STATS 60 approached me after class and expressed interest in statistics

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50% patient/family decision

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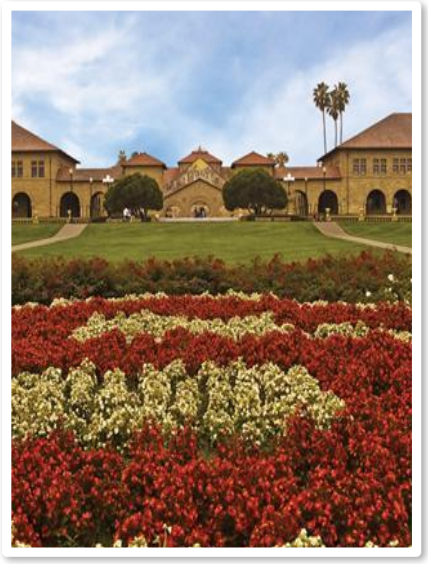
NEMSIS data base: (nearly) all EMS transport records in the USA.
50% patient/family decision, 40% proximity

results



would regionalizing improve survival?

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Table 2. Between-Group Differences in Operative Mortality and Overall Survival for Comparison of Transfer and Regionalization

Operative Mortality	**Transferred vs. Stayed (reference)**			**Rerouted vs. Not Rerouted (reference)***		
Group Contrast Measure	Estimate	95% CI	P Value	Estimate	95% CI	P Value
Absolute Risk Difference (%)	-0.62	-2.6 - 1.34	0.57	-7.5	-10.6 - -4.4	<0.001
Odds Ratio	0.97	0.87 - 1.08	0.55	0.68	0.57 - 0.80	<0.001
Number Needed to Treat (no.)	-	-	-	14	9 - 23	-
Overall Survival	**Transferred vs. Stayed (reference)**			**Rerouted vs. Not Rerouted (reference)**		
Group Contrast Measure	Estimate	95% CI	P Value	Estimate	95% CI	P Value
Hazard Ratio (PH model)	1.02	0.94 - 1.11	0.64	0.8	0.74 - 0.86	<0.001
Restricted Mean Survival Time		15 years			15 years	
Difference (days)	-44.9	-141.2 - 51.5	0.36	232.2	105.2 - 359.1	<0.001
Ratio	0.98	0.94 - 1.02	0.36	1.12	1.05 - 1.18	<0.001
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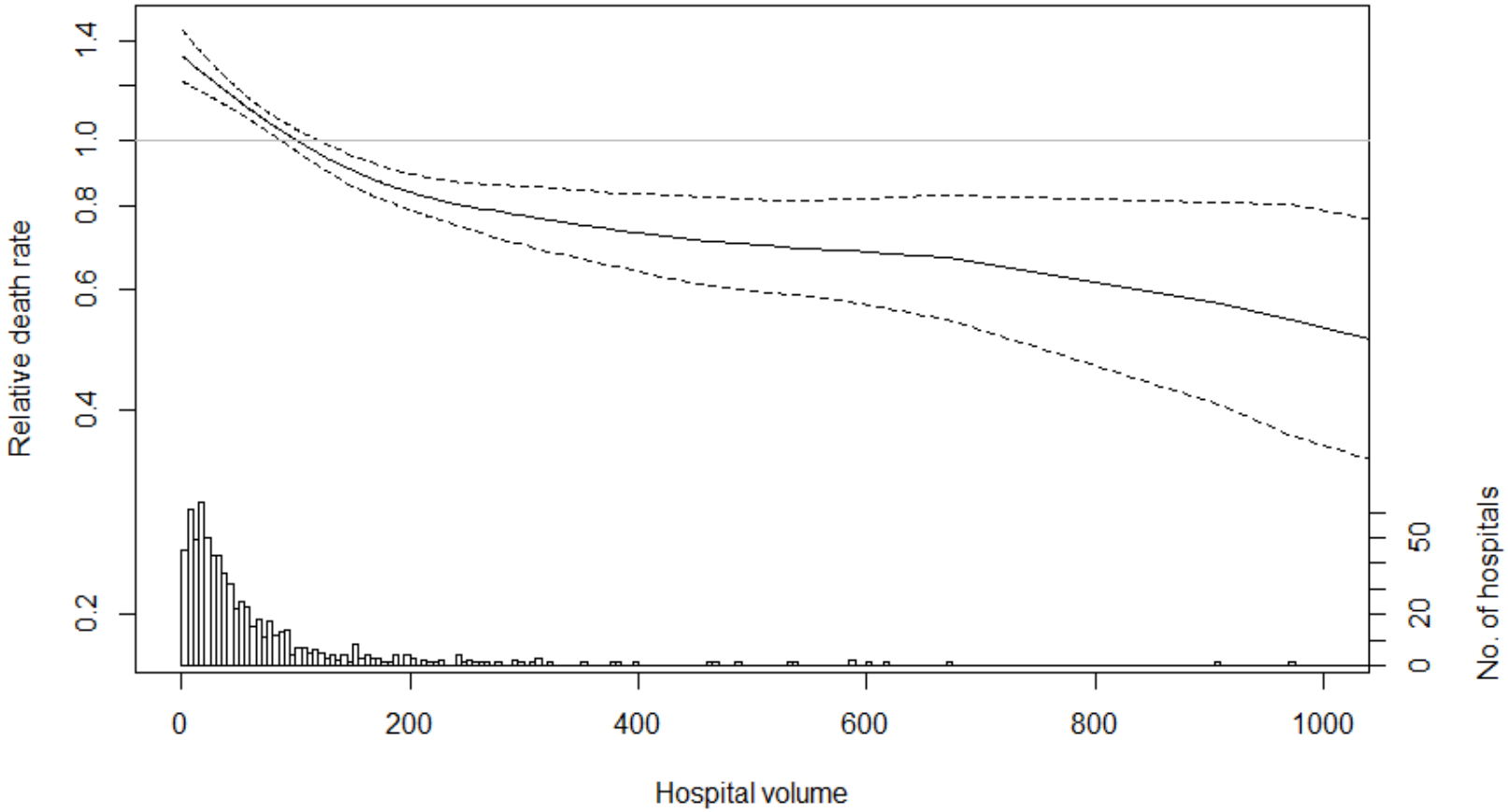

careful reasoning: the effect of transfer

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What if we didn’t use our study design?

(a)

(b)

(c)

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Using “all of the data.”

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Table S7. Propensity Score Analsyis - Between-Group Differences in Operative Mortality and Overall Survival for Comparison of Transfer and Regionalization

Operative Mortality	**Transferred vs. Stayed (reference)**			**High-Volume vs. Low-Volume (reference)***			**Rerouted vs. Not Rerouted (reference)****		
Group Contrast Measure	Estimate	95% CI	P Value	Estimate	95% CI	P Value	Estimate	95% CI	P Value
Absolute Risk Difference (%)	-1.7	-3.2 - -0.001	0.03	-6.1	-7.7 - -4.5	<0.001	-9.6	-11.4 - -7.8	<0.001
Odds Ratio	0.9	0.82 - 0.99	0.03	0.73	0.67 - 0.79	<0.001	0.6	0.54 - 0.67	<0.001
Number Needed to Treat (no.)	-	-	-	17	13 - 23	-	11	9 - 13	-
Overall Survival	**Transferred vs. Stayed (reference)**			**High-Volume vs. Low-Volume (reference)***			**Rerouted vs. Not Rerouted (reference)****		
Group Contrast Measure	Estimate	95% CI	P Value	Estimate	95% CI	P Value	Estimate	95% CI	P Value
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Restricted Mean Survival Time		15 years			15 years			15 years	
Difference (days)	-44.9	-141.2 - 51.5	0.36	300.6	206.4 - 394.7	<0.001	232.2	105.2 - 359.1	<0.001
Ratio	0.98	0.94 - 1.02	0.36	1.15	1.10 - 1.20	<0.001	1.12	1.05 - 1.18	<0.001
Ratio of Restricted Mean Time Lost	1.02	0.98 - 1.05	0.36	0.9	0.88 - 0.93	<0.001	0.93	0.89 - 0.97	<0.001

* Gamma = 1.31

** Gamma = 1.44

Using “all of the data.”

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Restricted Mean Survival Time		15 years			15 years			15 years	
Difference (days)	-44.9	-141.2 - 51.5	0.36	300.6	206.4 - 394.7	<0.001	232.2	105.2 - 359.1	<0.001
Ratio	0.98	0.94 - 1.02	0.36	1.15	1.10 - 1.20	<0.001	1.12	1.05 - 1.18	<0.001
Ratio of Restricted Mean Time Lost	1.02	0.98 - 1.05	0.36	0.9	0.88 - 0.93	<0.001	0.93	0.89 - 0.97	<0.001

* Gamma = 1.31

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Using “all of the data.”

would regionalizing improve survival?

Table S7. Propensity Score Analsyis - Between-Group Differences in Operative Mortality and Overall Survival for Comparison of Transfer and Regionalization

Operative Mortality	**Transferred vs. Stayed (reference)**			High-Volume vs. Low-Volume (reference)*			Rerouted vs. Not Rerouted (reference)**		
Group Contrast Measure	Estimate	95% CI	P Value	Estimate	95% CI	P Value	Estimate	95% CI	P Value
Absolute Risk Difference (%)	-1.7	-3.2 - -0.001	0.03	-6.1	-7.7 - -4.5	<0.001	-9.6	-11.4 - -7.8	<0.001
Odds Ratio	0.9	0.82 - 0.99	0.03	0.73	0.67 - 0.79	<0.001	0.6	0.54 - 0.67	<0.001
Number Needed to Treat (no.)	-	-	-	17	13 - 23	-	11	9 - 13	-
Overall Survival	**Transferred vs. Stayed (reference)**			**High-Volume vs. Low-Volume (reference)***			**Rerouted vs. Not Rerouted (reference)****		
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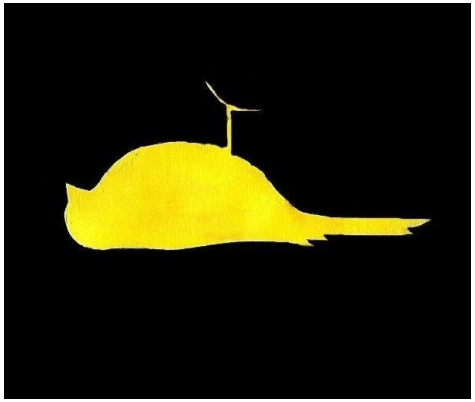

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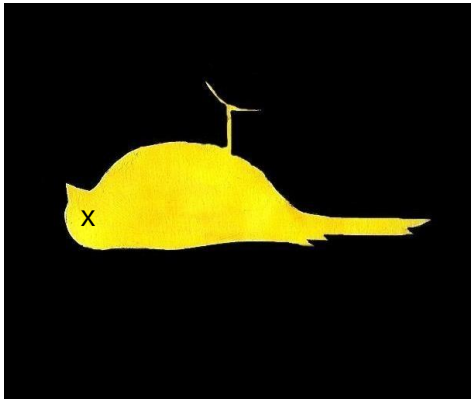

Stanford University

https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.038867

fin.

difference-in-differences

diff-in-diff

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diff-in-diff

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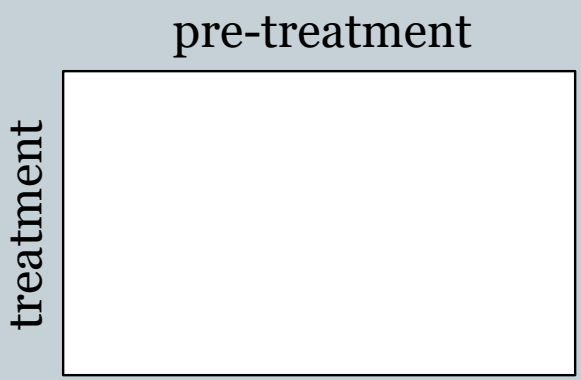
diff-in-diff



diff-in-diff

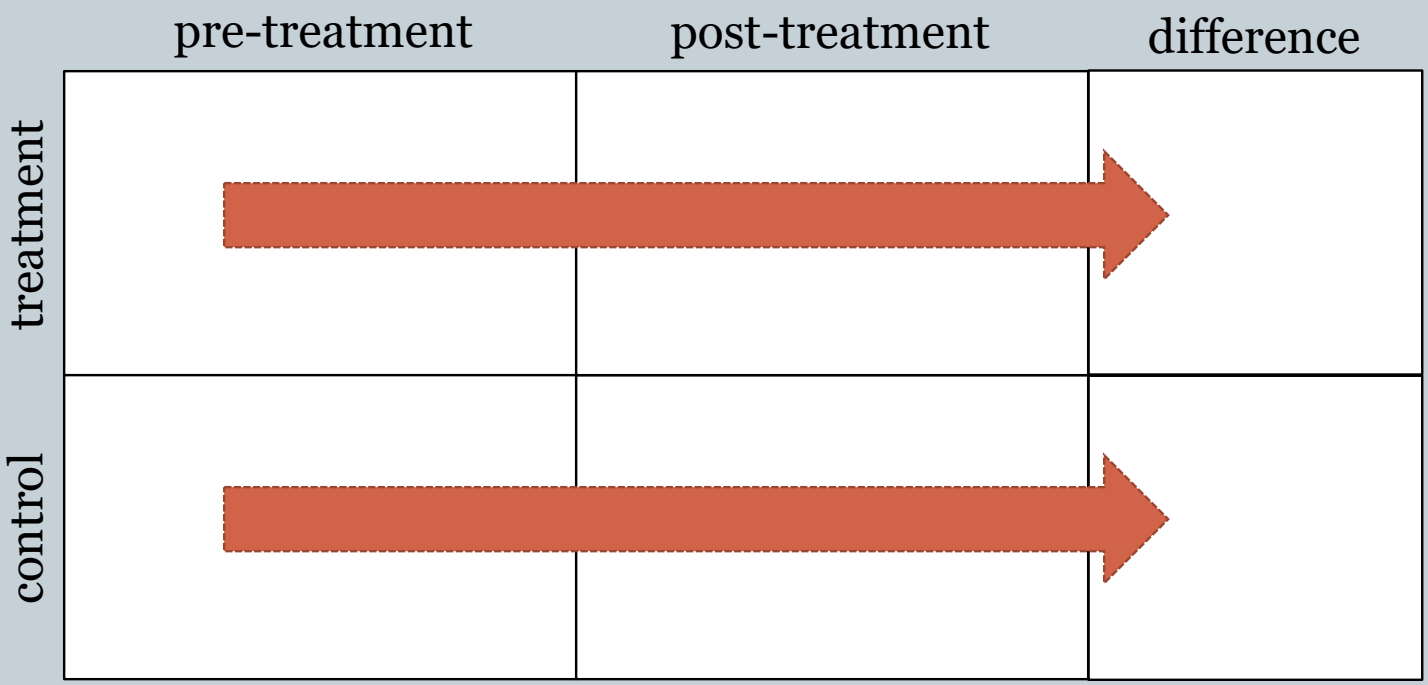
	pre-treatment	post-treatment
treatment		

diff-in-diff

	pre-treatment	post-treatment
treatment		
control		

diff-in-diff

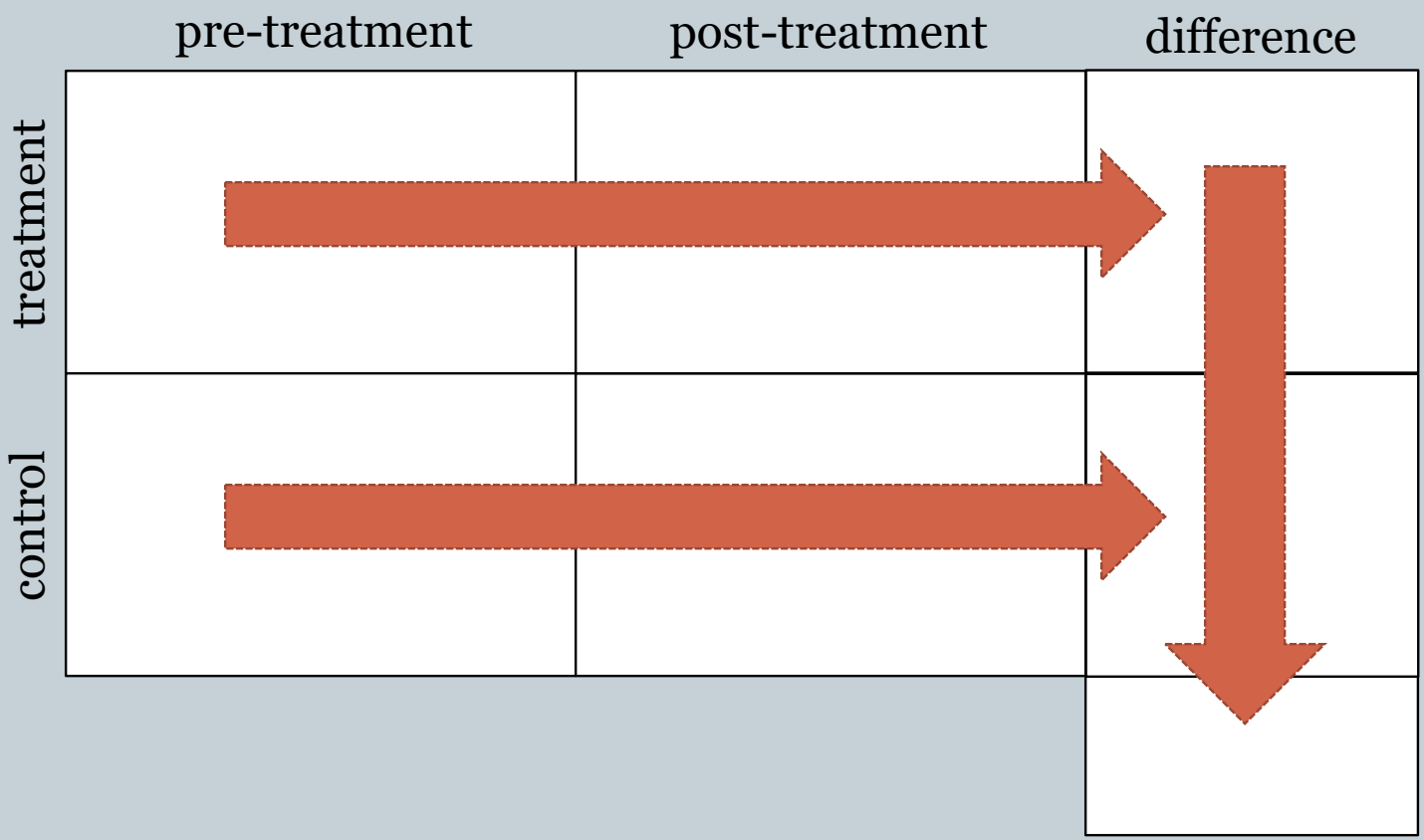
diff-in-diff


pre-treatment
post-treatment
difference
treatment
control

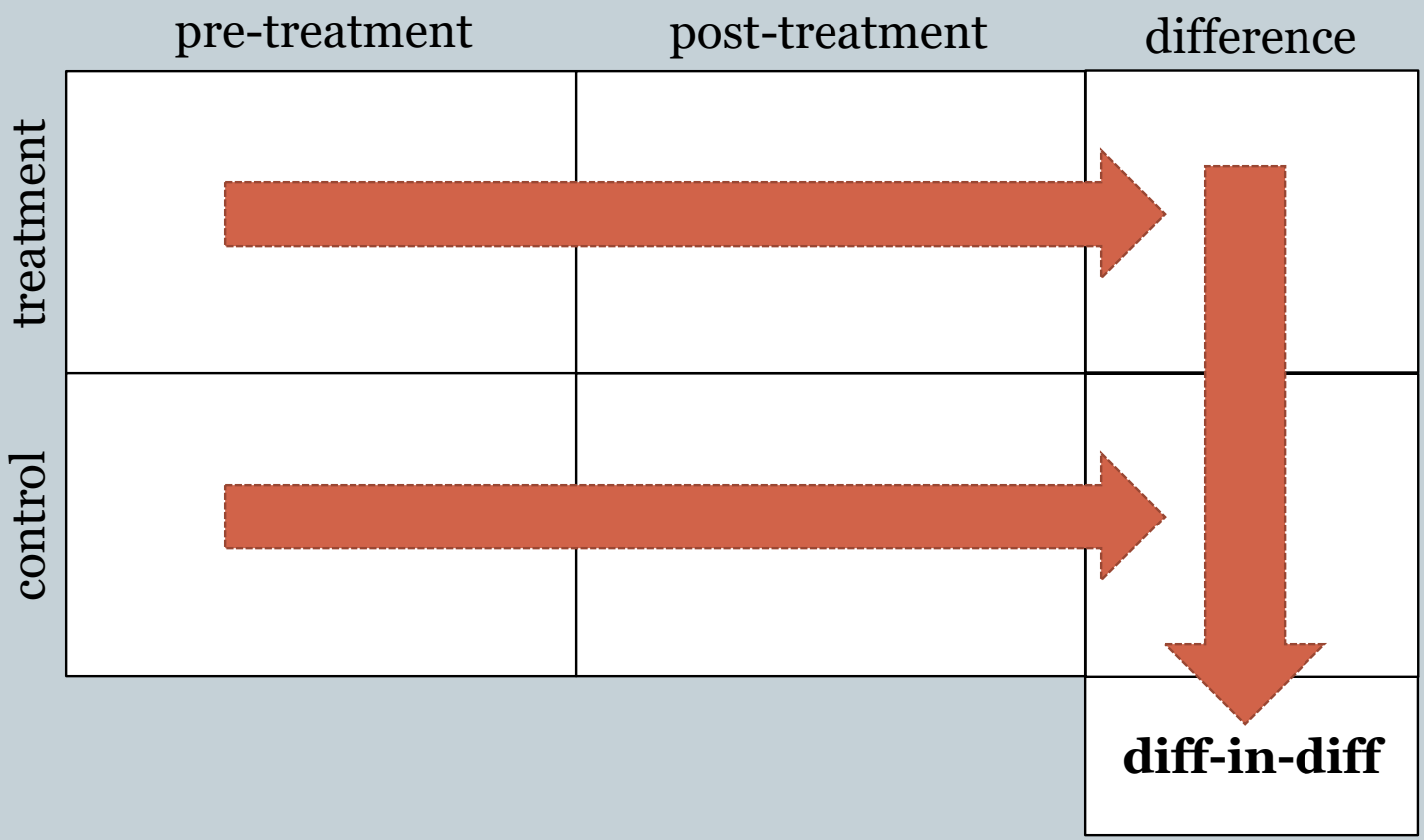
diff-in-diff


pre-treatment
post-treatment
difference
treatment
control

diff-in-diff


pre-treatment
post-treatment
difference
treatment
control

diff-in-diff


pre-treatment
post-treatment
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diff-in-diff

diff-in-diff: inference

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- Inference: When someone invoke a “diff-in-diff design” they haven’t necessarily identified their source of randomization.

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diff-in-diff: inference

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- Design consideration: try to look at "burn in" period prior to the intervention. The more you can get the two groups similar prior, the easier your case will be.
  - Researchers end up using matching a lot in diff-in-diff designs.

diff-in-diff: inference

- In a structural equation model approach:

diff-in-diff: inference

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$$y_{i,t} = \beta_0 + \beta_t * t_i + \beta_d * d_i + \beta_{t*d} t_i * d_i + \varepsilon_{i,t}$$

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where t is time (pre=0, post=1) and d is the intervention (control=0,intervention=1) and $t_i * d_i$ is an interaction term.

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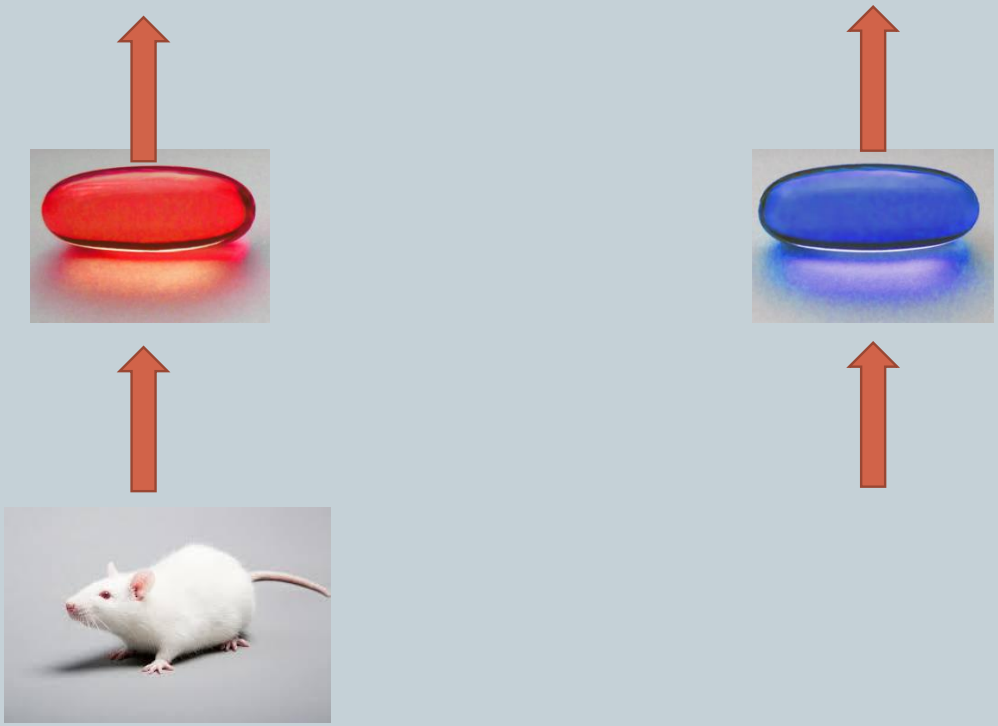
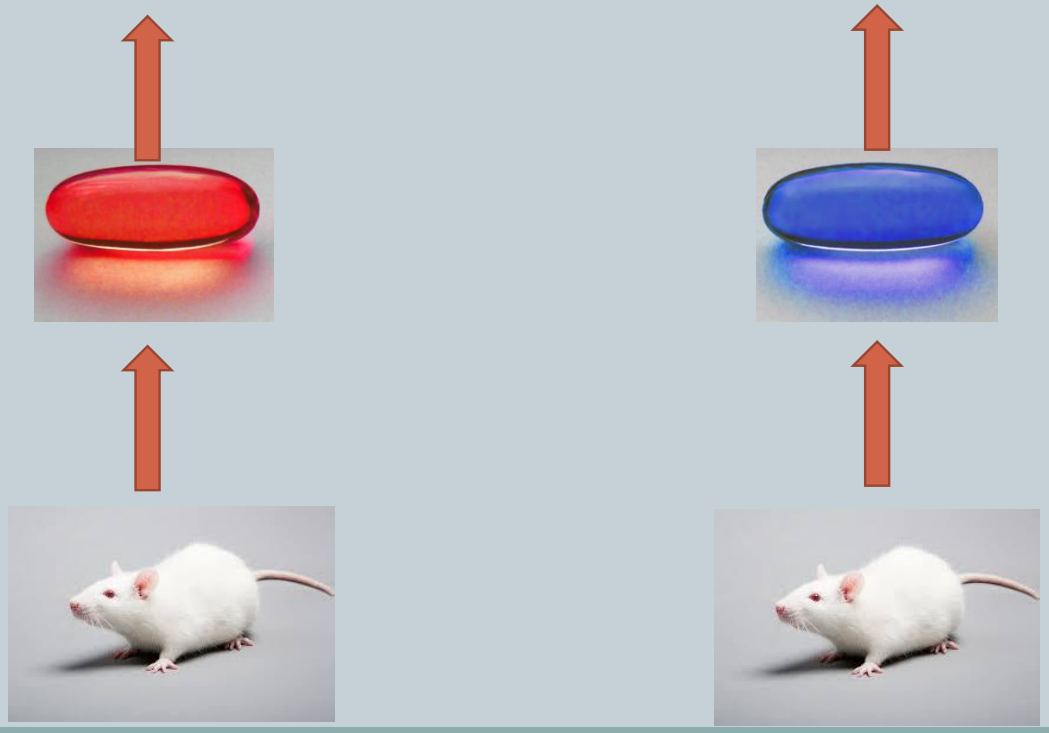
method of difference

method of difference



method of difference



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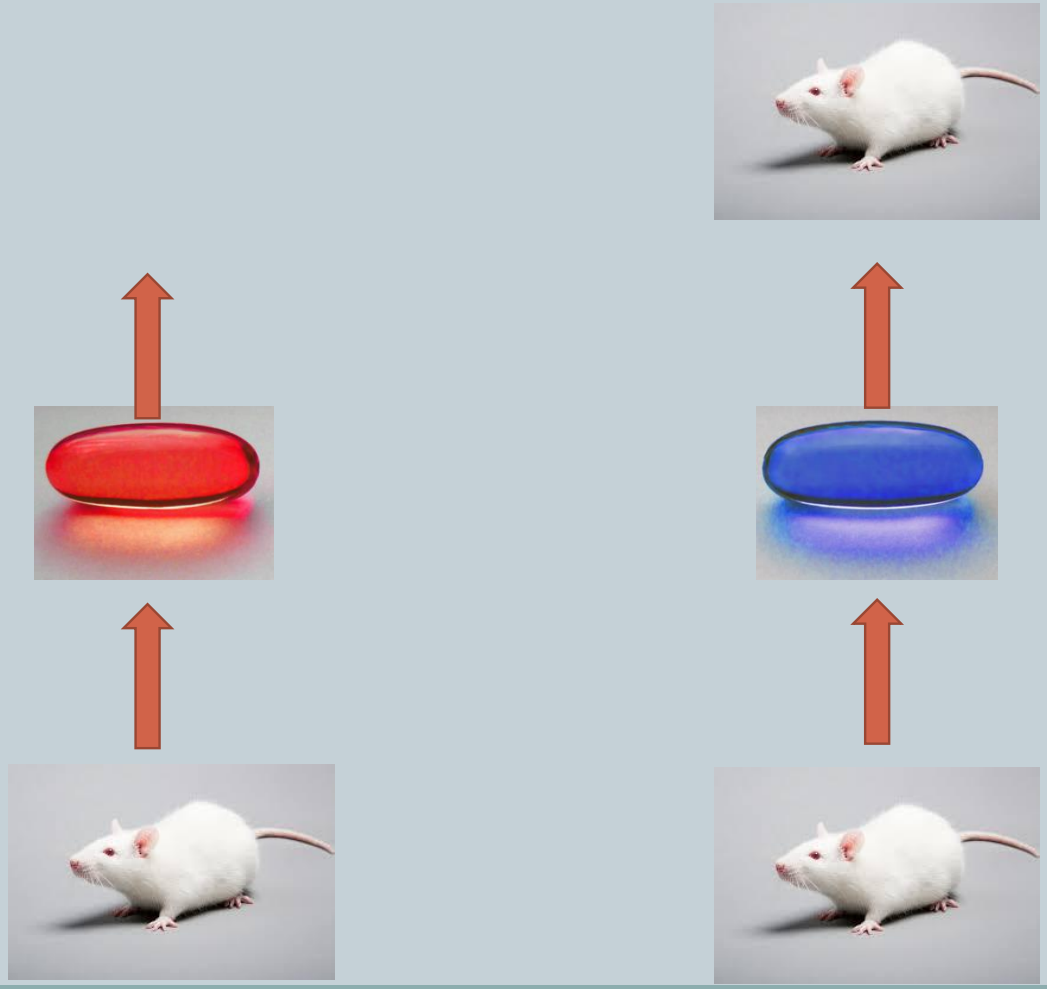

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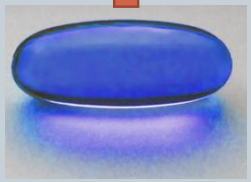

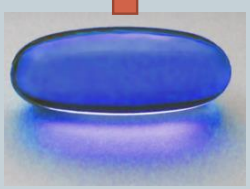

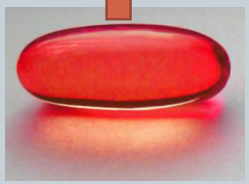

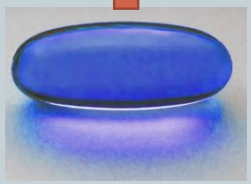

$x =$

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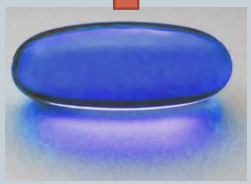

$x' =$

$$\mathrm{r_T} = f(d = 1, X = x)$$

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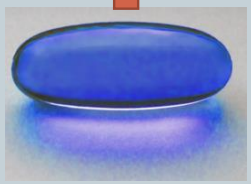

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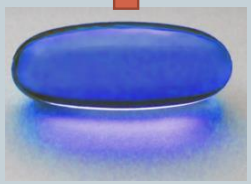

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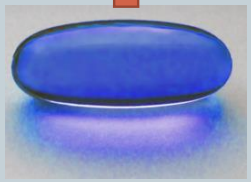

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The only difference

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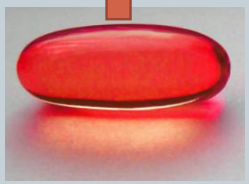

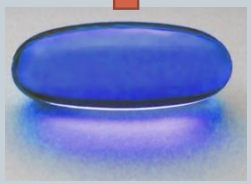

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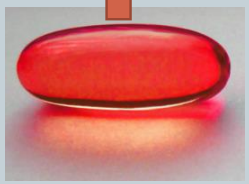

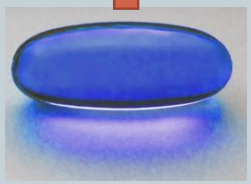

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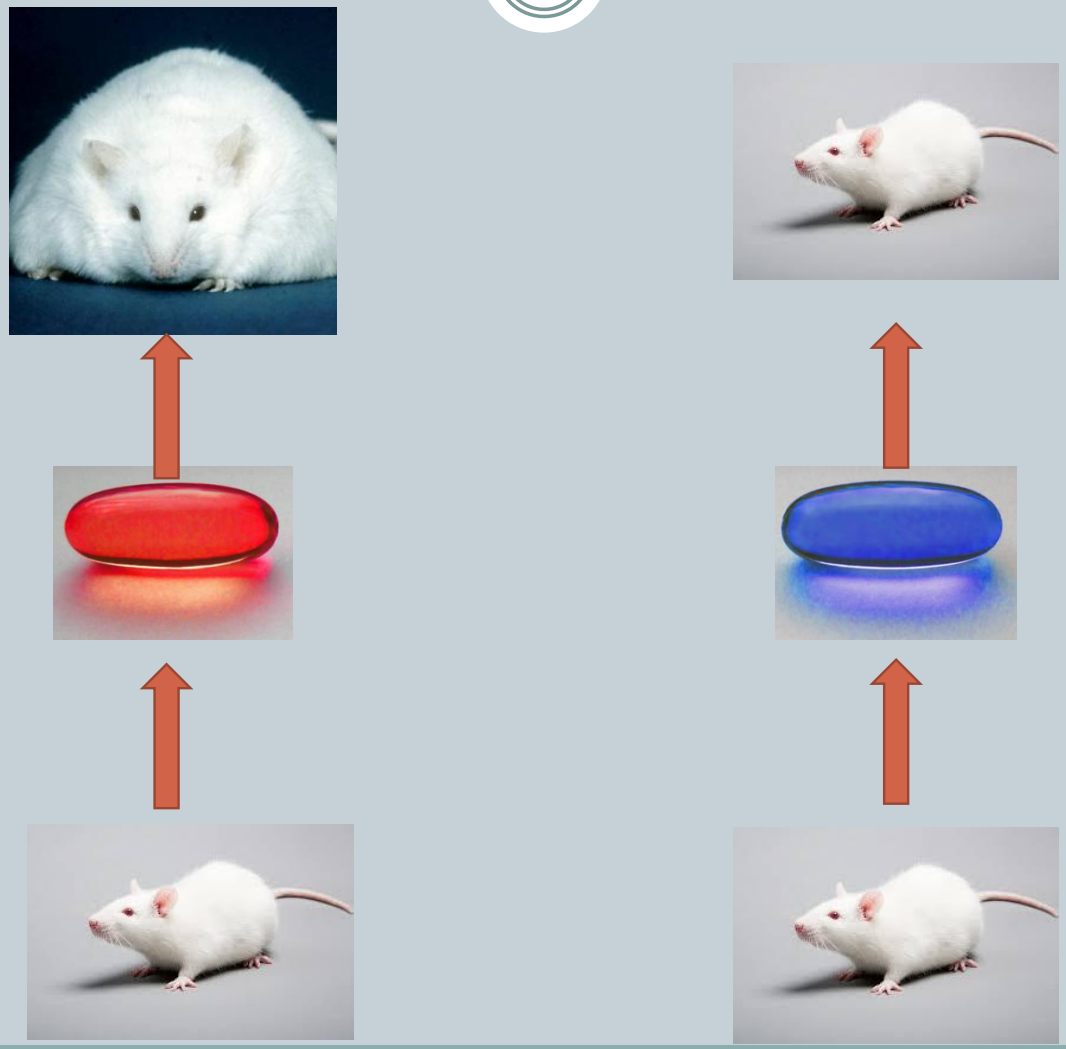
diff-in-diff



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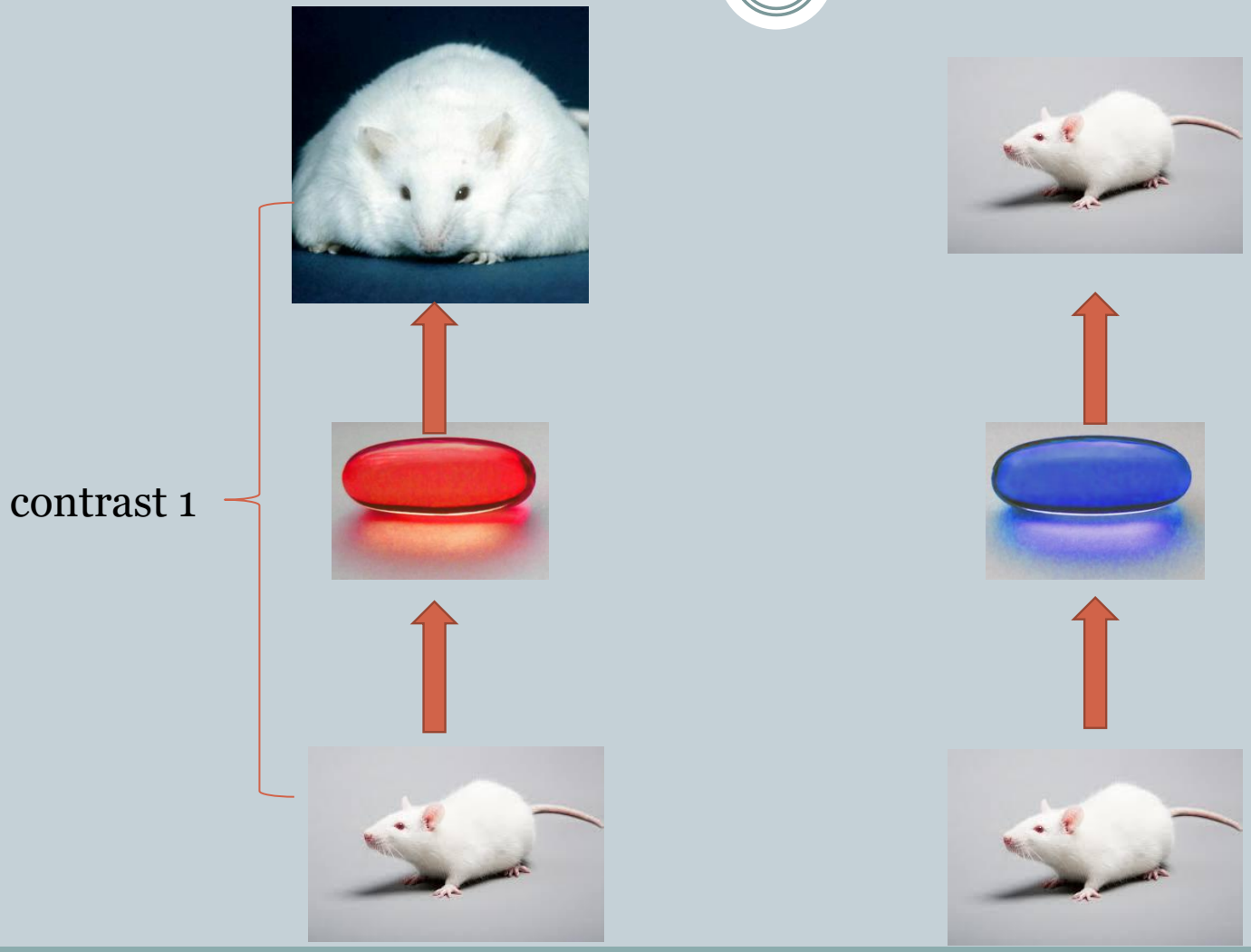

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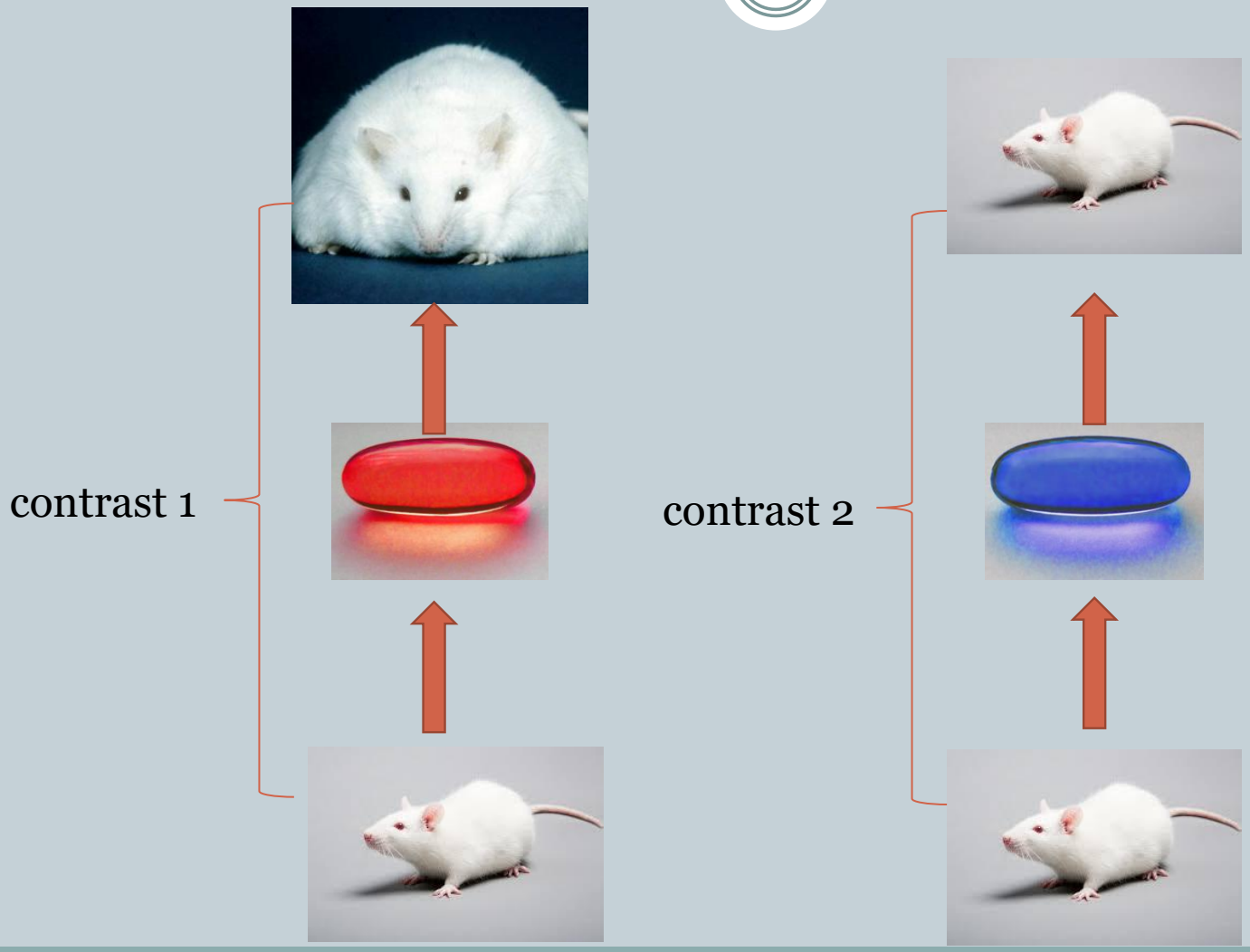
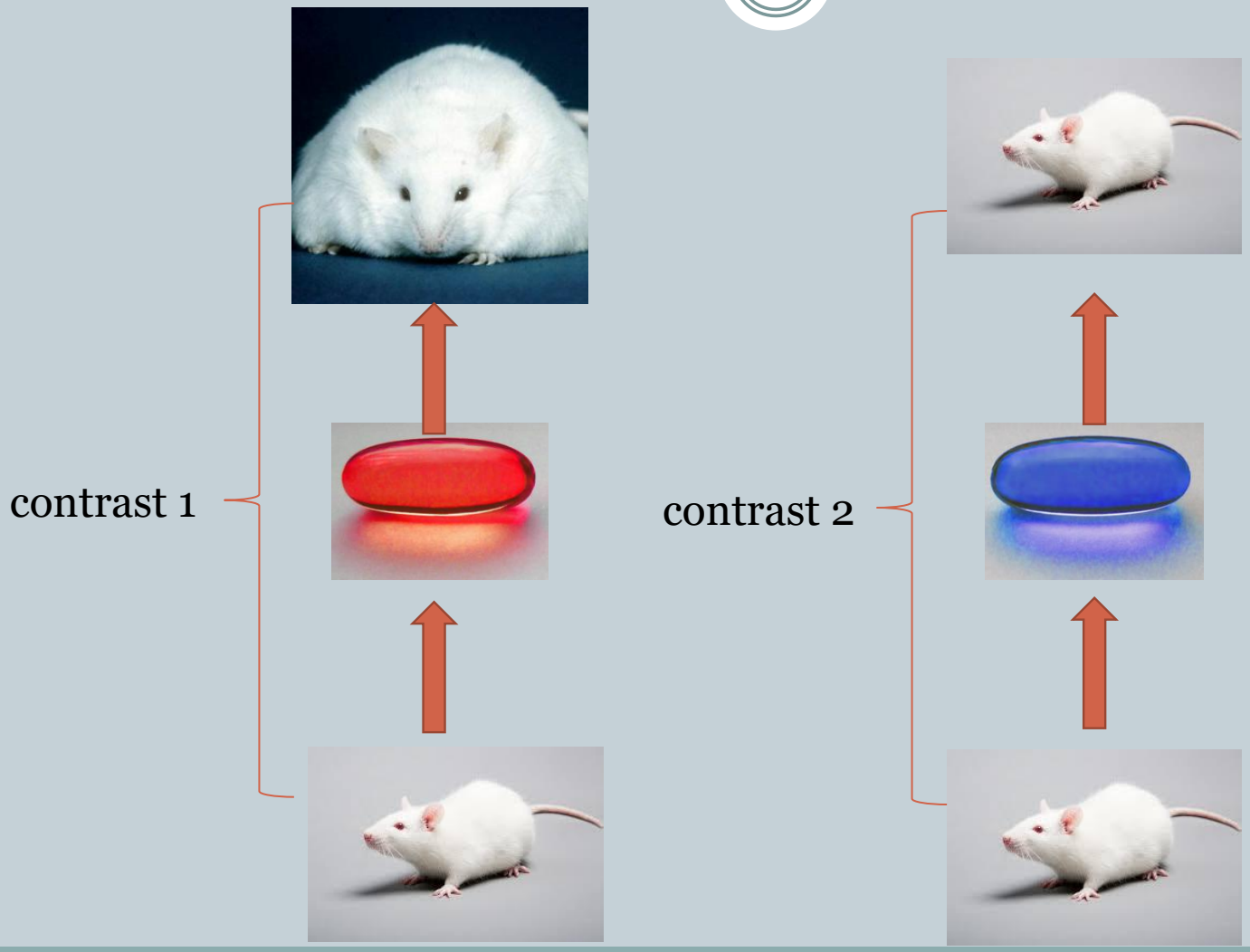


(contrast 1) – (contrast 2) = difference-in-differences



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