500 Class 04 (Zoom)

https://thomaselove.github.io/500-2025/

2025-02-06

Agenda for Zoom Call

Thursday 2025-02-06 from 10 to 11 AM. Zoom details in your email and on Canvas.

- Wrapup and questions about the toy example?
- Normand 2001
  - A matched analysis using propensity scores
  - Inspiration for the Love plot
- Rosenbaum, Chapter 5

The `toy` example

Today's class involves a walk-through of the `toy` example, which is a simple simulated observational study of a treatment on three outcomes (one quantitative, one binary, and one time-to-event) which we will use to demonstrate the completion of 13 tasks using R, which include:

- Fitting a propensity score model
- Assessing pre-adjustment balance of covariates
- Estimating the effects of our treatment on our outcomes ...
  - Using matching on the propensity score
  - Using subclassification on the propensity score
  - Using direct adjustment for the propensity score
  - Using weighting on the propensity score

Note we have three other (more realistic) examples we'll share in time: `lindner`, `dm2200` and `rhc`.

The `toy` example

The `toy` example presents methods for doing 1:1 greedy matching without replacement using the `Match` function from the `Matching` package, and for evaluating the balance before and after matching with `cobalt` and with an alternative strategy for obtaining Love plots.

- The example uses 3 Rules I attribute to Rubin (2001) for determining when a sample comparison shows sufficient balance to allow for a reasonable regression model for the outcome.
  - **Please read** Rubin (2001) in advance of Class 06, which will mostly be about that example.
- What to do in terms of a sensitivity analysis is discussed in the final section of that example, and we'll get to that later on.

Normand (2001)

ELSEVIER

Journal of Clinical Epidemiology 54 (2001) 387–398

Journal of Clinical Epidemiology

Validating recommendations for coronary angiography following acute myocardial infarction in the elderly: A matched analysis using propensity scores

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Normand (2001) Abstract

We determined whether adherence to recommendations for coronary angiography more than 12 h after symptom onset but prior to hospital discharge after acute myocardial infarction (AMI) resulted in better survival. Using propensity scores, we created a matched retrospective sample of 19,568 Medicare patients hospitalized with AMI during 1994–1995 in the United States. Twenty-nine percent, 36%, and 34% of patients were judged necessary, appropriate, or uncertain, respectively, for angiography while 60% of those judged necessary received the procedure during the hospitalization. The 3-year survival benefit was largest for patients rated necessary [mean survival difference (95% CI): 17.6% (15.1, 20.1)] and smallest for those rated uncertain [8.8% (6.8, 10.7)]. Angiography recommendations appear to select patients who are likely to benefit from the procedure and the consequent interventions. Because of the magnitude of the benefit and of the number of patients involved, steps should be taken to replicate these findings.

Normand (2001) Statistical Analysis (section 2.4)

Because we collected detailed clinical information describing admission severity of the patient and characteristics of the hospital to which the patient was admitted, **we assumed that treatment (angiography vs. no angiography) was randomly assigned with probabilities that depended on the observed covariates alone**.

We then employed a propensity score approach to compare survival between those receiving angiography ("cathed") and those who did not ("not cathed") within each category of appropriateness. The propensity score is a measure of the likelihood that a patient would have undergone angiography using the patient's covariate scores.

Normand (2001) Creating the matched sample

To estimate the propensity scores, we fitted a logistic regression model in which the outcome was the log-odds of undergoing angiography more than 12 h after symptom onset but prior to discharge.

{The covariates used in the propensity score} consisted of patient (demographic, comorbidity, admission severity) and hospital characteristics as well as interactions among the covariates.

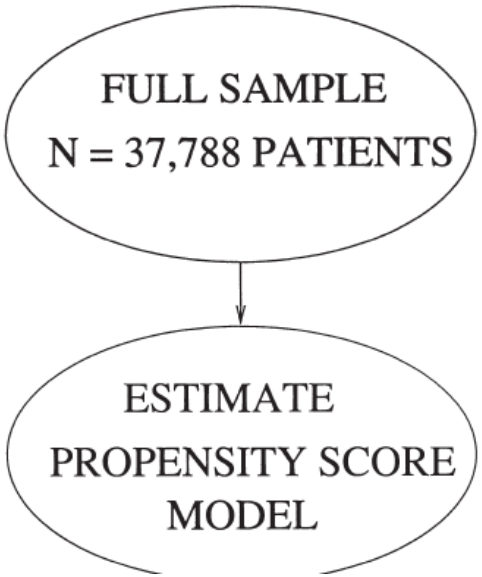
We assumed that missing observations were missing at random, implying that the mechanism by which data were missing is unrelated to information not contained in our observed data. For discrete-valued variables, we included a binary variable that represented "missing." In the case of continuous-valued variables, we created two variables: a binary variable indicating whether the variable was measured and if measured, a continuous variable indicating the value of the variable.

Normand (2001) Creating the matched sample

Once the model was estimated, we stratified the cohort by clinical indication, and within an indication, matched each patient who underwent angiography to a patient with closest estimated propensity score who did not. We included in our analyses only those matches that were within 0.60 of the pooled standard error of q(X) where q(X) is the estimated logit. This method of defining the closeness of a match is referred to caliper matching and is the observational study analogue of randomization in a clinical trial.

Fig. 1 (next two slides) summarizes our methods for identifying and creating the matched sample.

Normand (2001) Figure 1 (steps 1-2 of 4)



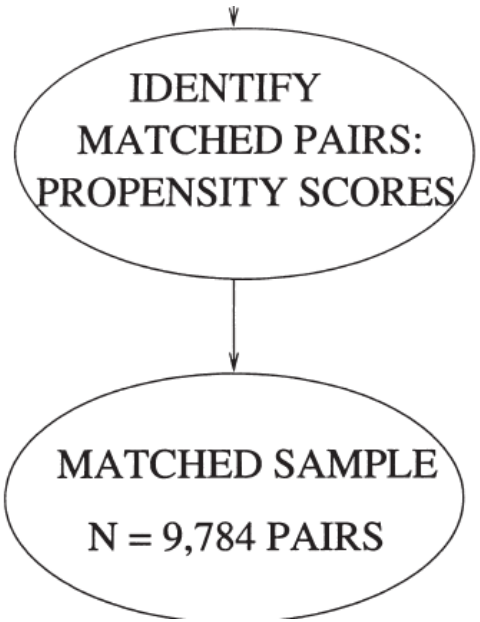
Step 1

Full sample of Medicare patients discharged with AMI: 17,304 cathed & 20,484 not cathed.

Step 2

Estimate probability of undergoing angiography (Equation 1) using patient and hospital characteristics. Calculate the predicted log-odds of cath from the model for each of the 37,788 patients.

Normand (2001) Figure 1 (steps 3-4 of 4)



Step 3

Stratify the 37,788 patients into the 28 clinical indications* defined by the updated angiography recommendations. Within each indication, match a cathed patient with the "closest" non-cathed patient (Equation 2). Close is defined using the distance between the predicted log-odds from Step 2.

*Recommendations based on an independent source and developed prior to collecting patient data.

Step 4

Matched sample: 9,784 cathed and 9,784 not cathed.
Assess appropriateness of matches using standardized difference statistics (Equation 3). Estimate differences in survival using the matched pairs.

Normand (2001) Table 1

Table 1
Characteristics and unadjusted survival in full and matched study cohorts

	Characteristic, *N*(%)	
	Full	Matched
Number of patients	37,788	19,568
Age (years)		
65–69	8,271 (22)	4,504 (23)
70–74	9,735 (26)	6,599 (34)
75–79	8,730 (23)	3,958 (20)
80–84	7,121 (19)	3,393 (17)
85–89	3,931 (10)	1,114 (6)
Race		
White	34,091 (90)	17,593 (90)
Black	1,857 (5)	989 (5)
Other/unknown	1,840 (5)	986 (5)
Female	17,547 (46)	8,892 (45)
State		
California	5,179 (14)	2,815 (14)
Florida	6,454 (17)	3,439 (18)
Massachusetts	3,030 (8)	1,343 (7)
New York	6,439 (17)	3,266 (17)
Ohio	4,387 (12)	2,225 (11)
Pennsylvania	7,627 (20)	3,937 (20)
Texas	4,672 (12)	2,543 (13)
Angiography	17,304 (46)	9,784 (50)
Appropriateness category		
Necessary	10,218 (27)	5,760 (29)
Appropriate, not necessary	14,317 (38)	7,104 (36)
Uncertain	13,253 (35)	6,704 (34)
Survival		
1-Year	30,094 (80)	15,943 (82)

Normand (2001) (from section 3.2)

We matched 57% of the 17,304 cathed patients to noncathed patients using estimated propensity scores.

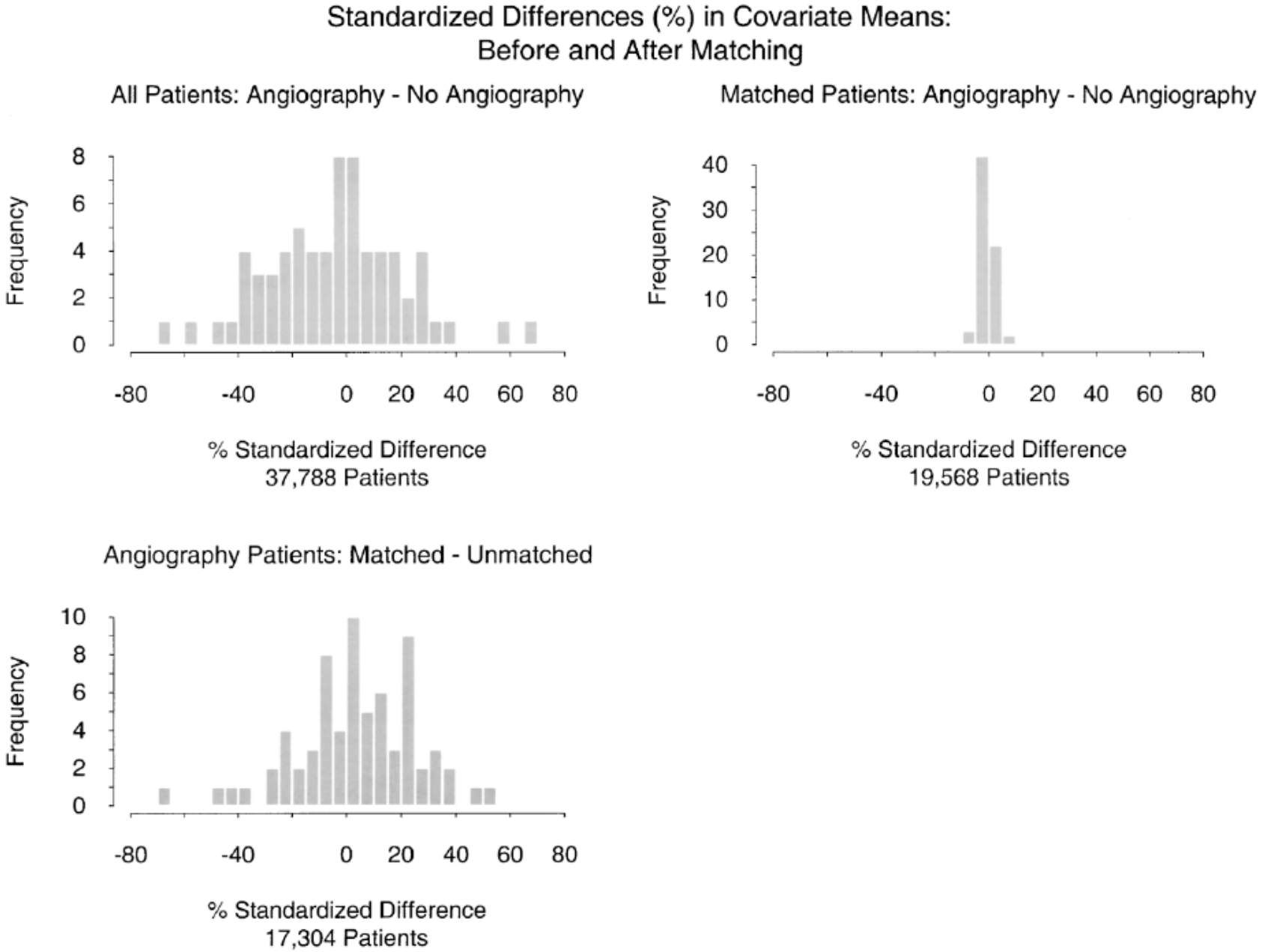
The unmatched angiography patients were more likely to be admitted to large, teaching, urban hospitals with the capability to perform invasive cardiac procedures; were younger; were less sick; and had less comorbid disease compared to the angiography patients for whom we found matches. Prior to matching, the average predicted propensities to undergo angiography were 65% and 30% in the two groups; after matching, the propensities were within 4 percentage points.

Normand (2001) Start of Table 3

Table 3
Characteristics of all patients, matched cathed and noncathed patients, and unmatched cathed patients

	All Patients			Matched Patients			All Cathed Patients		
Characteristic	Cathed	Not Cathed	d_i	Cathed	Not Cathed	d_i	Matched	Unmatched	d_i
No. of patients	17,304	20,484		9,784	9,784		9,784	7,520	
Prop. Score (%)	64.8	29.7	147.8	51.3	47.9	14.1	51.3	82.5	−131.5
Age (mean years)	73.2	77.4	−69.3	74.6	74.7	−2.2	74.6	71.3	53.3
At hospital arrival									
Duration of pain:									
<6 h	54.0	50.1	7.7	54.9	55.4	−1.0	54.9	52.8	4.2
6–12 h	9.6	8.9	2.4	9.5	9.3	0.8	9.5	9.6	−0.4
>12 h	21.1	14.5	17.5	17.8	17.4	0.9	17.8	25.5	−20.2
No pain	15.4	26.6	−27.8	17.9	17.9	−0.2	17.9	12.1	14.2
Shock	1.2	1.7	−4.5	1.4	1.5	−0.5	1.4	0.9	4.4
CHF	31.3	49.9	−38.7	38.6	40.2	−3.2	38.6	21.7	35.2
Thrombolytics									
Contraindicated	39.4	62.7	−48.1	47.3	48.2	−1.9	47.3	29.1	37.3
Received	22.7	12.0	28.4	18.7	18.7	−0.1	18.7	27.9	−24.6

Normand (2001) Figure 3



Normand (2001) Table 4

Table 4
Survival stratified according to recommendation category

%	Necessary (No. pairs = 2880)			Appropriate (No. pairs = 3553)			Uncertain (No. pairs = 3352)		
Survival	Cathed	Not cathed	Diff. (95% CI)	Cathed	Not cathed	Diff. (95% CI)	Cathed	Not cathed	Diff. (95% CI)
2-day	99.7	98.2	1.5 (1.0, 2.0)	99.4	97.7	1.8 (1.2, 2.3)	99.9	99.5	0.4 (0.1, 0.7)
In-hospital	96.5	91.7	4.8 (3.6, 6.0)	93.8	90.3	3.5 (2.3, 4.8)	98.9	98.1	0.8 (0.3, 1.3)
1-year	85.3	72.8	12.5 (10.4, 14.7)	80.8	69.1	11.7 (9.7, 13.8)	92.3	88.7	3.6 (2.2, 4.9)
2-year	79.1	62.8	16.3 (13.9, 18.7)	73.9	59.1	14.8 (12.6, 17.0)	88.0	81.3	6.8 (5.0, 8.5)
3-year	73.2	55.6	17.6 (15.1, 20.1)	67.9	50.7	17.2 (14.9, 19.5)	83.4	74.6	8.8 (6.8, 10.7)

Diff. = percent of angiography patients surviving − percent of patients not undergoing angiography surviving. Positive differences indicate a benefit of angiography. Estimates based on the matched sample.

Normand (2001) Discussion

The propensity score approach, a technique that has been employed in other recent medical studies, reduces the collection of many confounding variables to a single variable that permits easy comparisons of group differences. Although we were successful in reducing the bias that may have resulted from inexact matching on observed covariates, we were only able to adequately match 57% of all patients who underwent angiography. The unmatched angiography patients were generally younger and healthier than the matched angiography patients and if included in the comparisons would have biased the effect of angiography towards a larger benefit. Although the exclusion of the unmatched patients may have introduced a bias, their inclusion would have also compromised the comparability of the final matched groups. Because it is difficult to completely rule out all these biases, it is important for others to validate our findings.

Normand (2001) Discussion (last paragraph)

In conclusion, coronary angiography following AMI was associated with increased survival for a relatively contemporary cohort of Medicare beneficiaries who had an AMI. The benefit was present in all categories of appropriateness that applied to these patients. Because of the magnitude of the benefit, the recent experiences of the patients, and the size of the group involved, the data suggest that not only is underuse of this procedure after AMI prevalent but may explain the lack of long-term survival differences between high-use regions and low-use regions. Because we were unable to match all patients who underwent coronary angiography, research should be undertaken to replicate our findings.

Rosenbaum Chapter 5

Sensitivity to Unmeasured Covariates

For Discussion

- What was the most **important** thing you learned from reading Chapter 5?
- What was the **muddiest**, least clear thing that arose in your reading?