




# BURDEN OF PNEUMONIA IN RHEUMATOID ARTHRITIS PATIENTS

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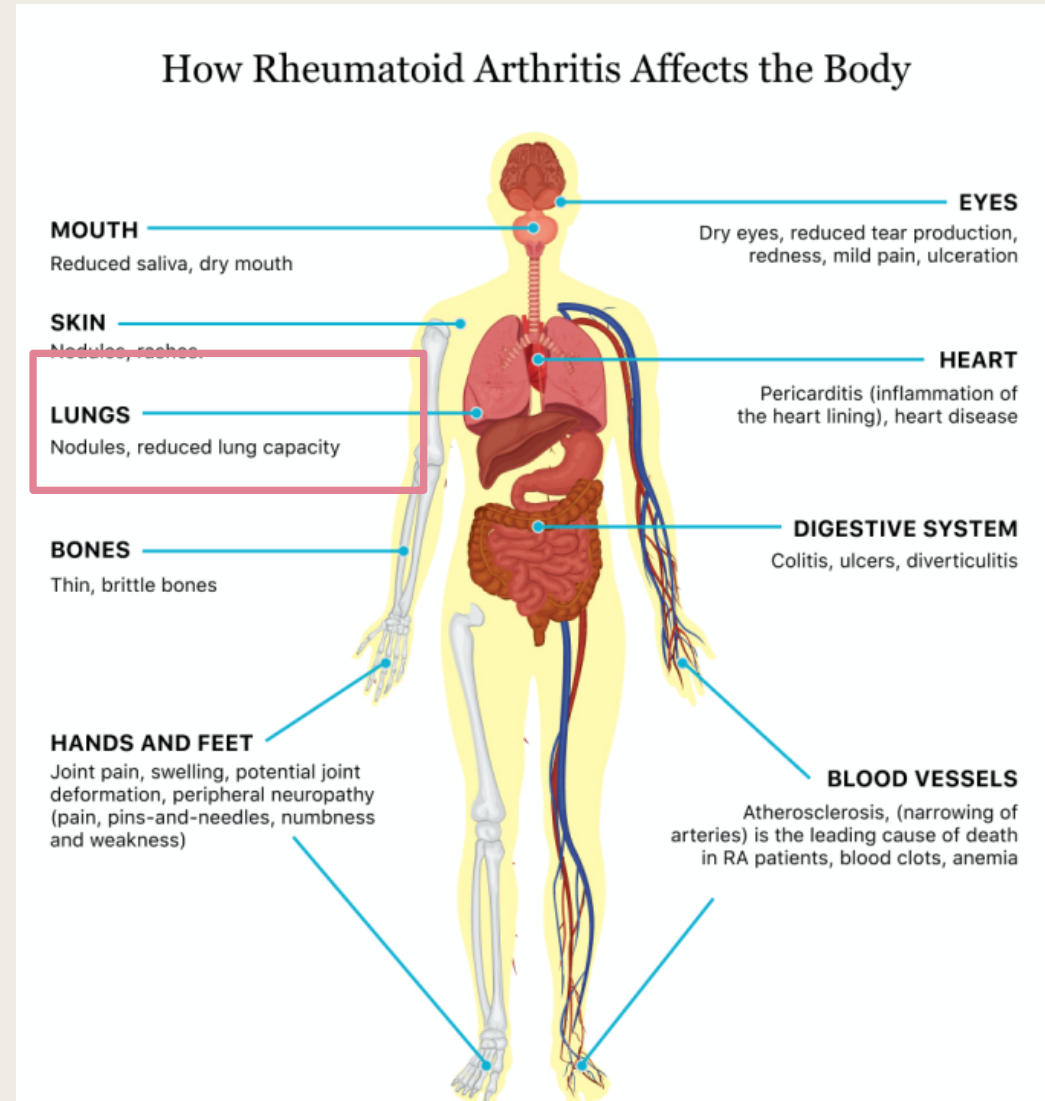
Case Western Reserve University

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# Pneumonia in RA

- Patients with RA are at an increased risk of pneumonia
  - *Lungs are one of the most common sites for extra-articular disease*
  - *Infection risk with immunomodulators*
- Denmark case control study (N=1712) found the odds of **pneumonia** was **1.84** (95% CI 1.62-2.10) times **higher in RA** patients (year 1996-2005)





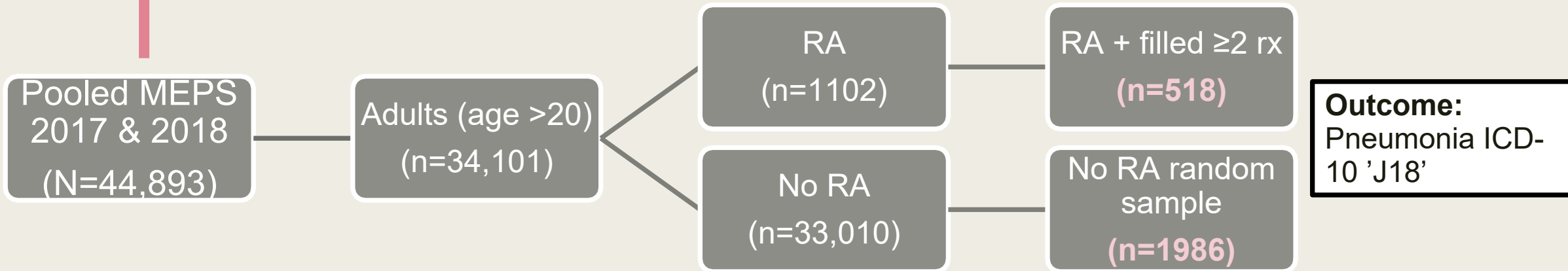
## Research Question & Population

- How does the burden of pneumonia in RA patients compare to non-RA patients in non-institutionalized U.S. adults?

# Study Design: Cross Sectional

- Publicly available & nationally representative
- 5 interviews over 2 yrs about healthcare use
- Can produce “treated” prevalence estimates

- Medical conditions file
- ICD-10 'M06'



# Unadjusted Primary Outcome

Exposure	Pneumonia	No pneumonia
RA	29	487
No-RA	24	1962

Association	Estimate	95% CI
Relative Risk	1.047	1.024-1.070
OR	4.868	2.09-8.437
Probability Difference	0.044	0.026 to 0.068

# Covariates (n=30)

## Demographics

- age , sex , race, marital, region , income, education, insurance, employment

## Past Medical History (MEPS 'Priority' Conditions)

- asthma, diabetes, cancer, bronchitis, emphysema, stroke, hypertension, heart attack, angina, coronary heart disease, other heart problems, high cholesterol

## Functional status & perceived health status

- Perceived physical & mental health, perceived mental health, requires help with IADL or ADL, cognitive difficulties, physical limitations

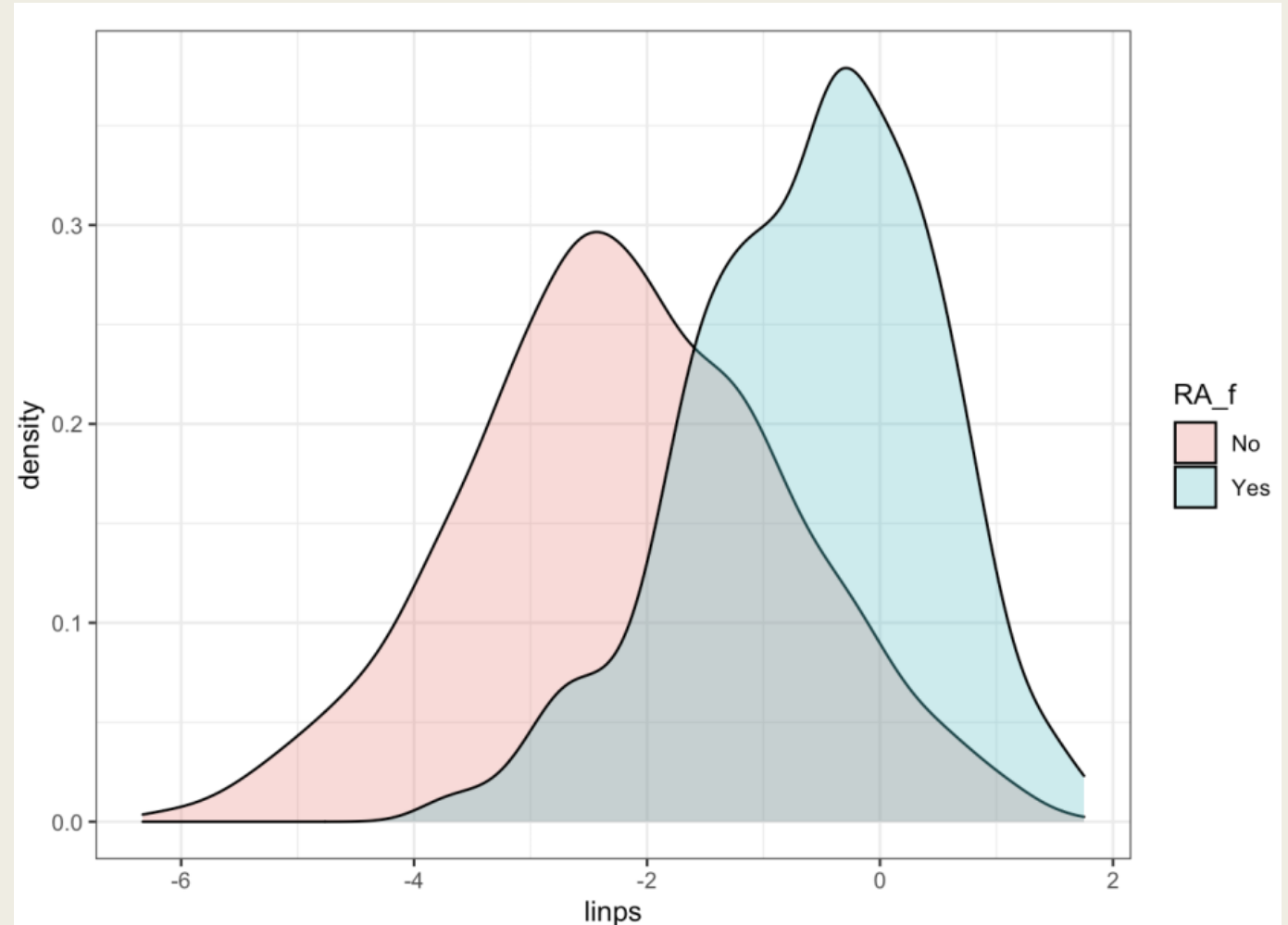
## Other

- Panel number, presence of a usual care provider, current smoker

*\*Single imputation for all covariates except panel, age, sex, race, income, & insurance (max missing 12%)*

# PS Fitting & Results

- 30 covariates to predict exposure status (RA=1)
- PS range:
  - *Non-RA*:
    - 0.002 to 0.841
  - *RA*
    - 0.02 to 0.852



Matching

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graph TD; A[Matching] --> B[Weighting]; B --> C[Sensitivity];
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Weighting

Sensitivity

Statistical  
Analyses



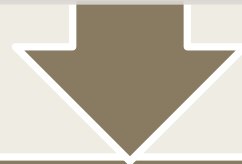
# Matching

'match' function from 'matching' package

1:1

Without replacement

Caliper =0.2



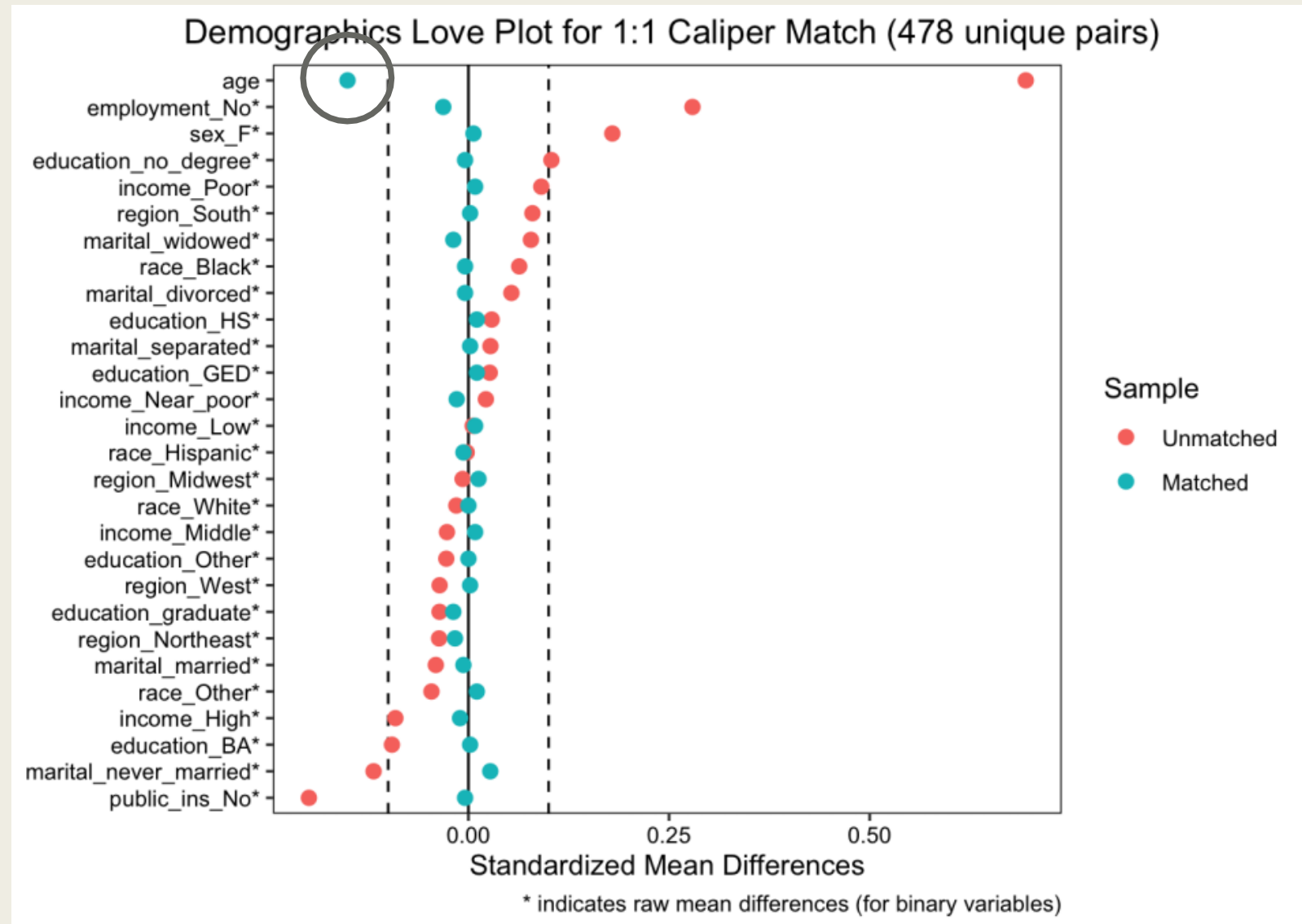
Results

478 unique pairs

38 RA patients dropped

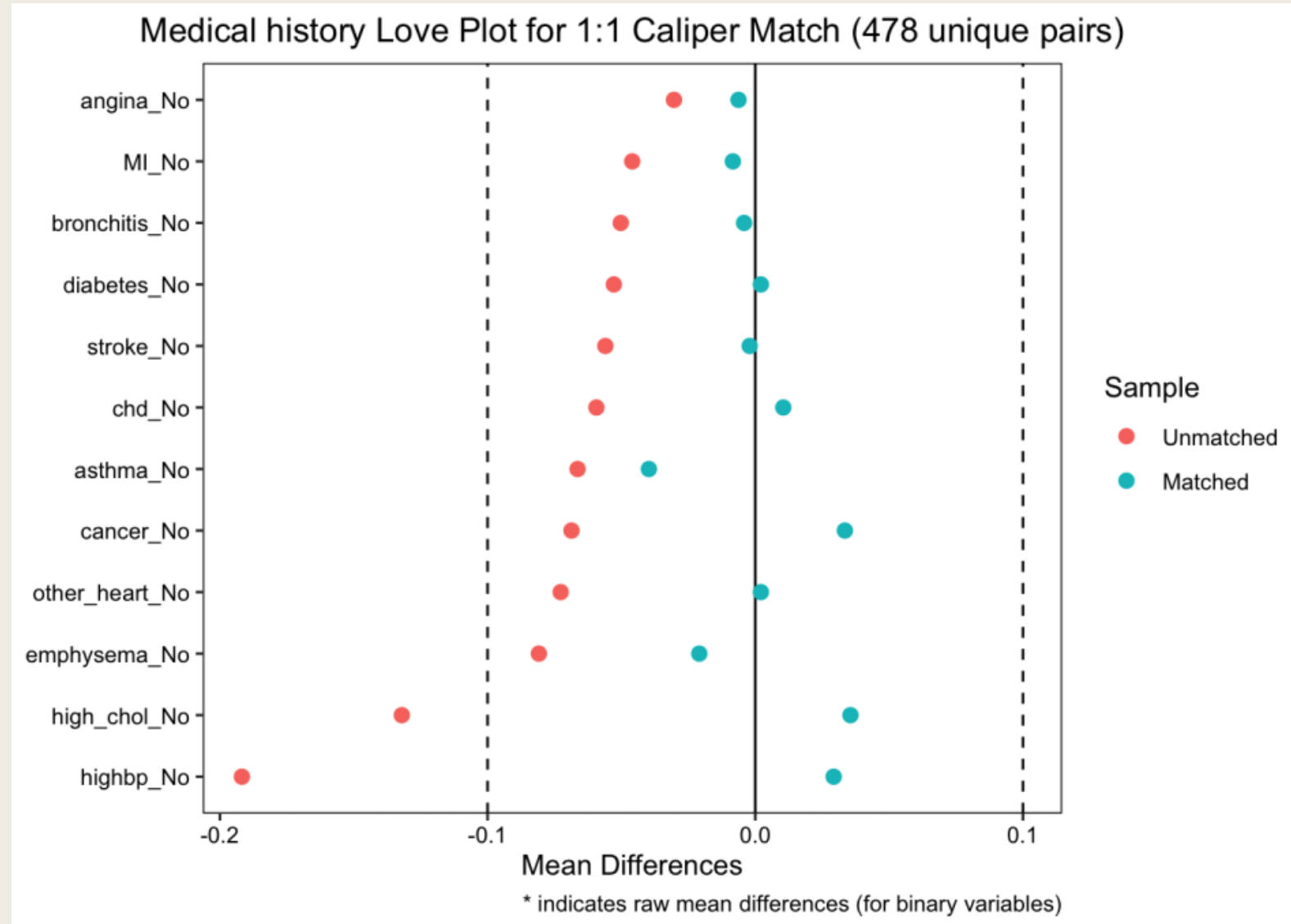
# Standardized Differences: Demographics

- All standardized differences close to 0 after matching
  - *Except age*



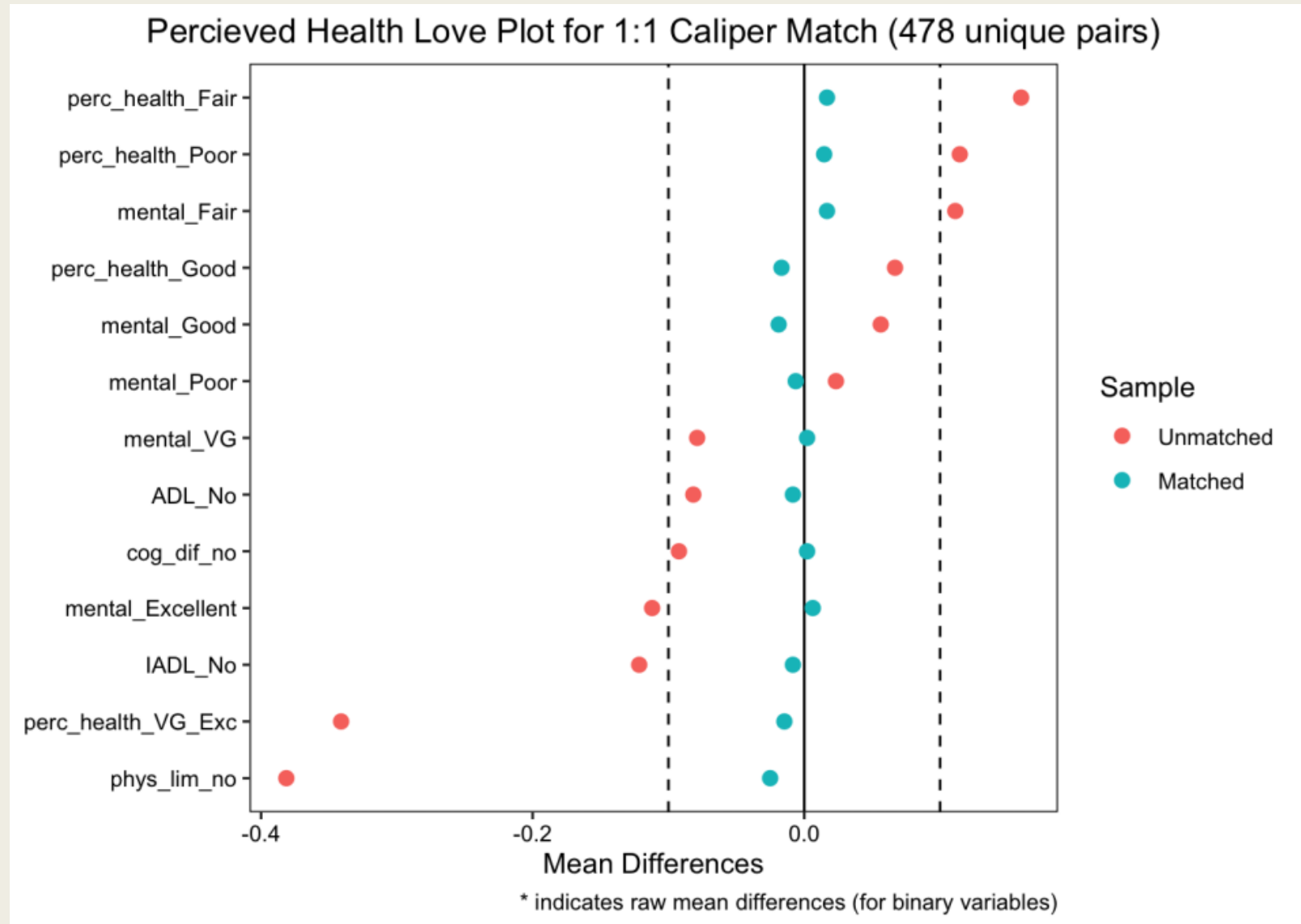
# Past Medical History Standardized Differences

- All within target range after matching



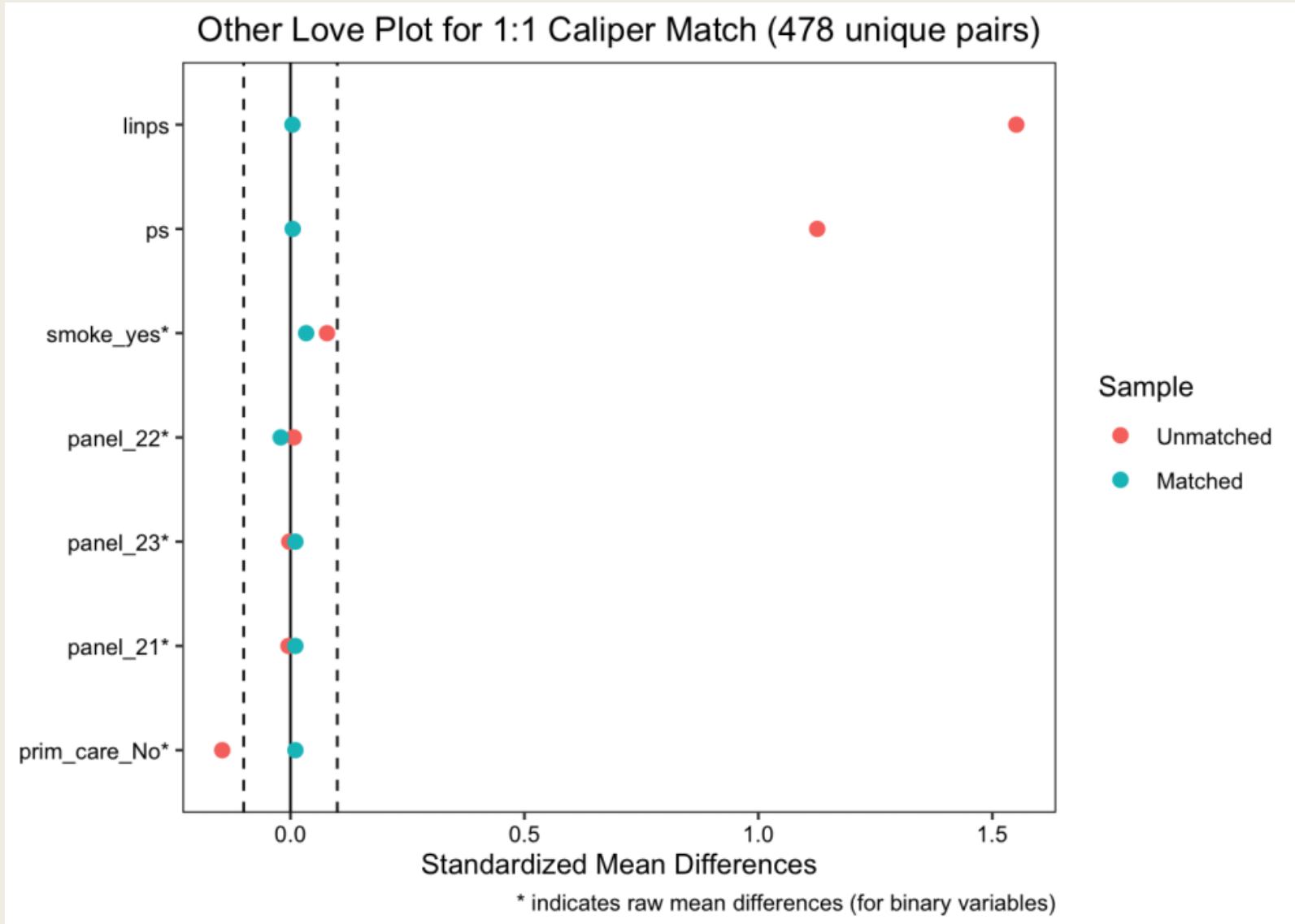
# Health Status Standardized Differences

- All standardized differences close to 0 after matching



# Other Covariates & PS Standardized Differences

- All standardized differences close to 0 after matching



# Rubin's Rules Before and After Matching

- Before matching, we wouldn't have been able to complete an analysis
- 1:1 caliper was the strongest matching method applied
- *Perfectly achieved the target values for balanced groups*

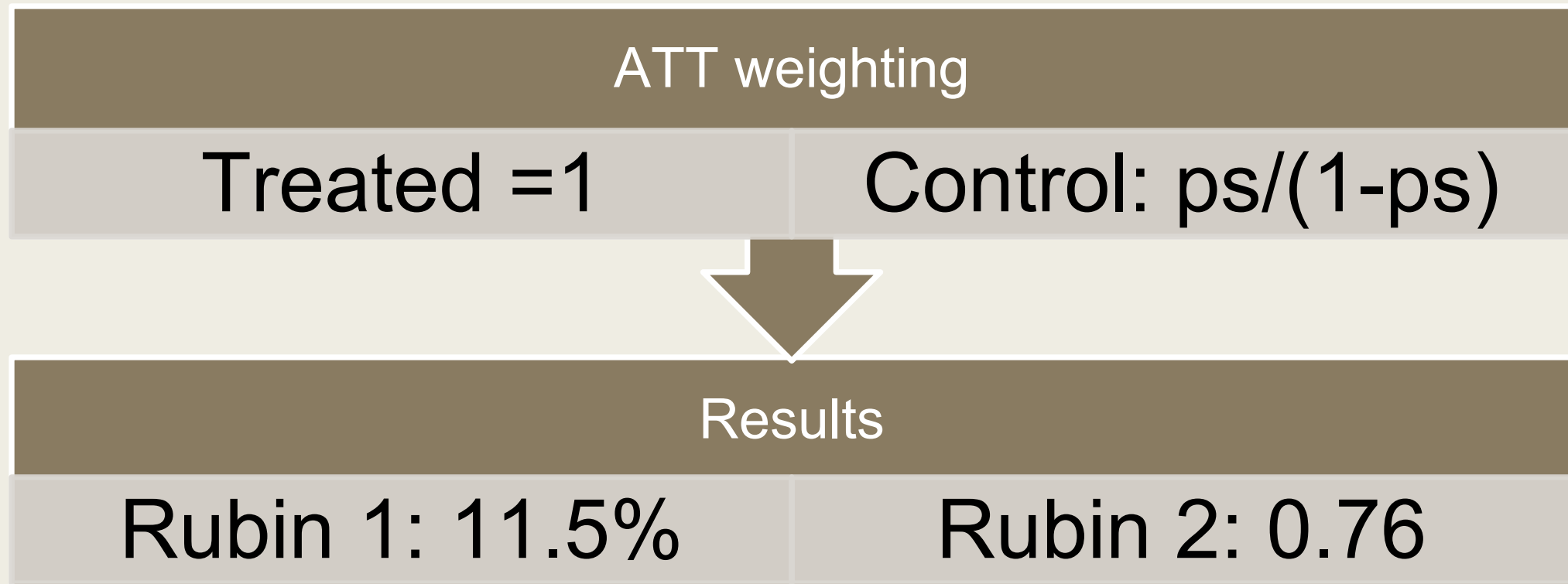
Rubin Rule	Unmatched	Matched
1	155%	0.42%
2	0.57	1.01

# Pneumonia in RA vs Non -RA

- In the **matched** sample (N=956), the odds of having **pneumonia** in **RA** individuals was **2.18** (95%CI: 1.07, 4.45) **times higher** than the odds that a non-RA control had pneumonia

Adjustment	OR	95% CI
None	4.87	2.81, 8.50
Matching	2.18	1.07, 4.45

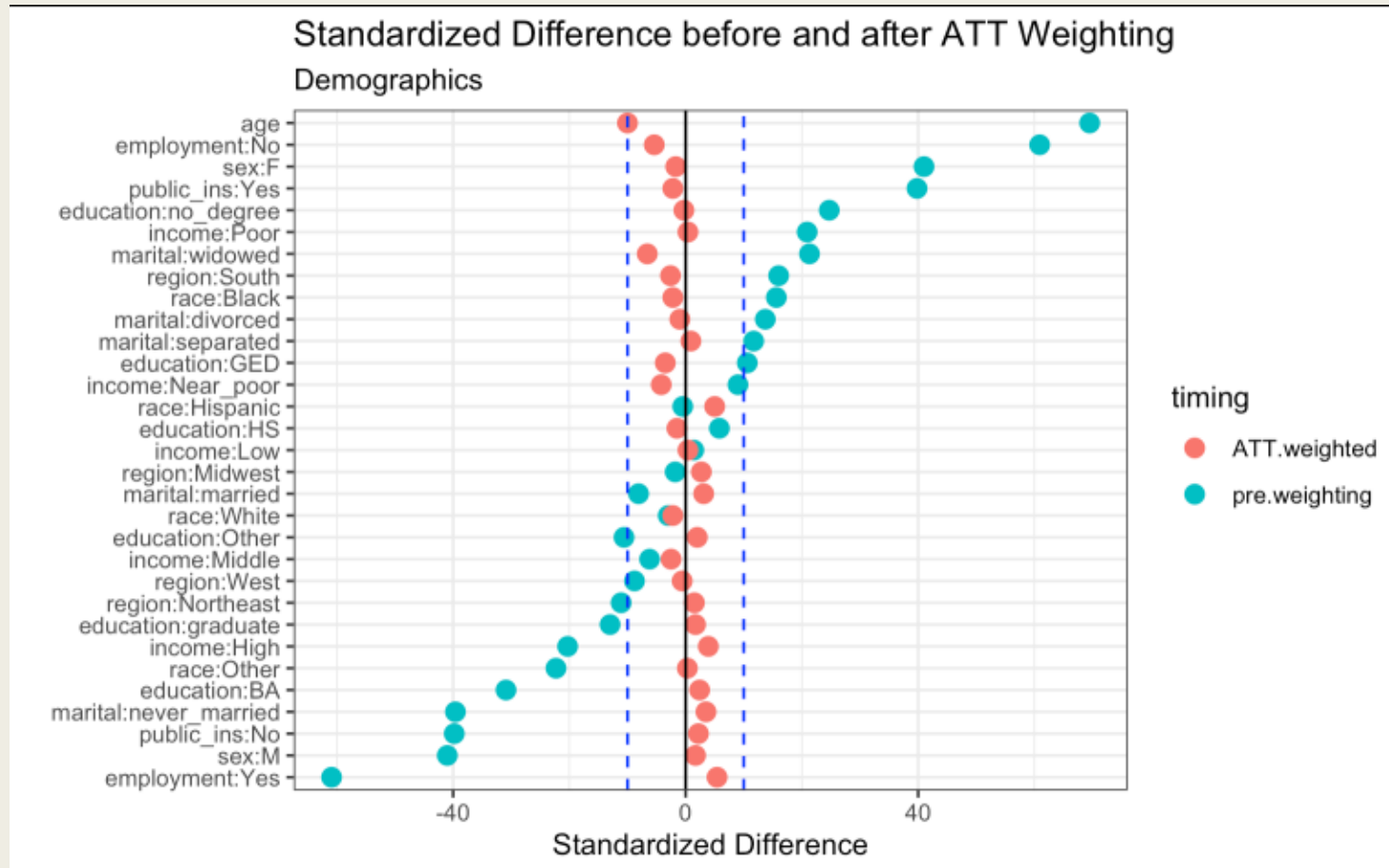
# Weighted Analysis





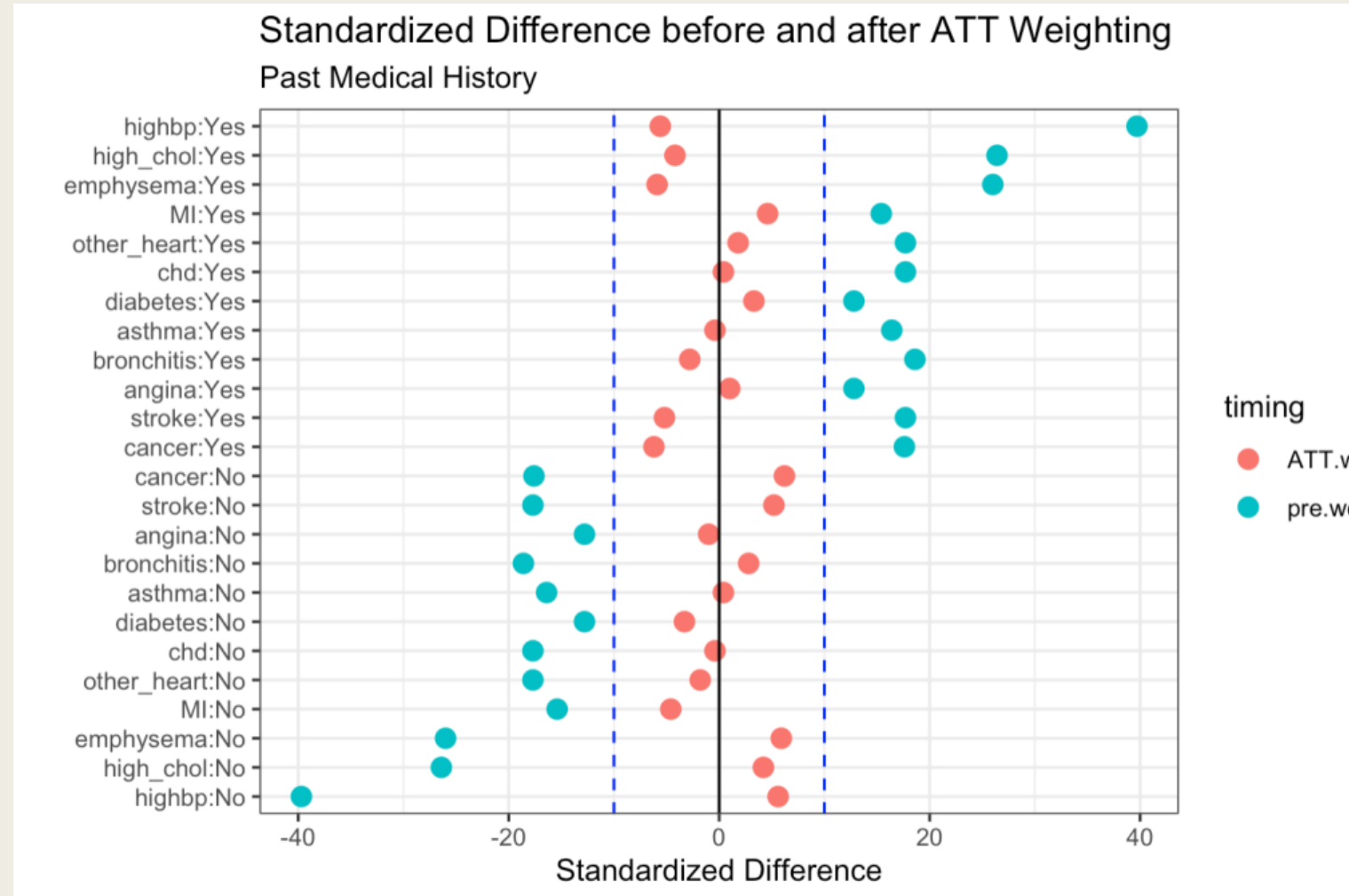
# Covariate Balance after Weighting : Demographics

- All standardized differences within target range after weighting
  - *Except age*



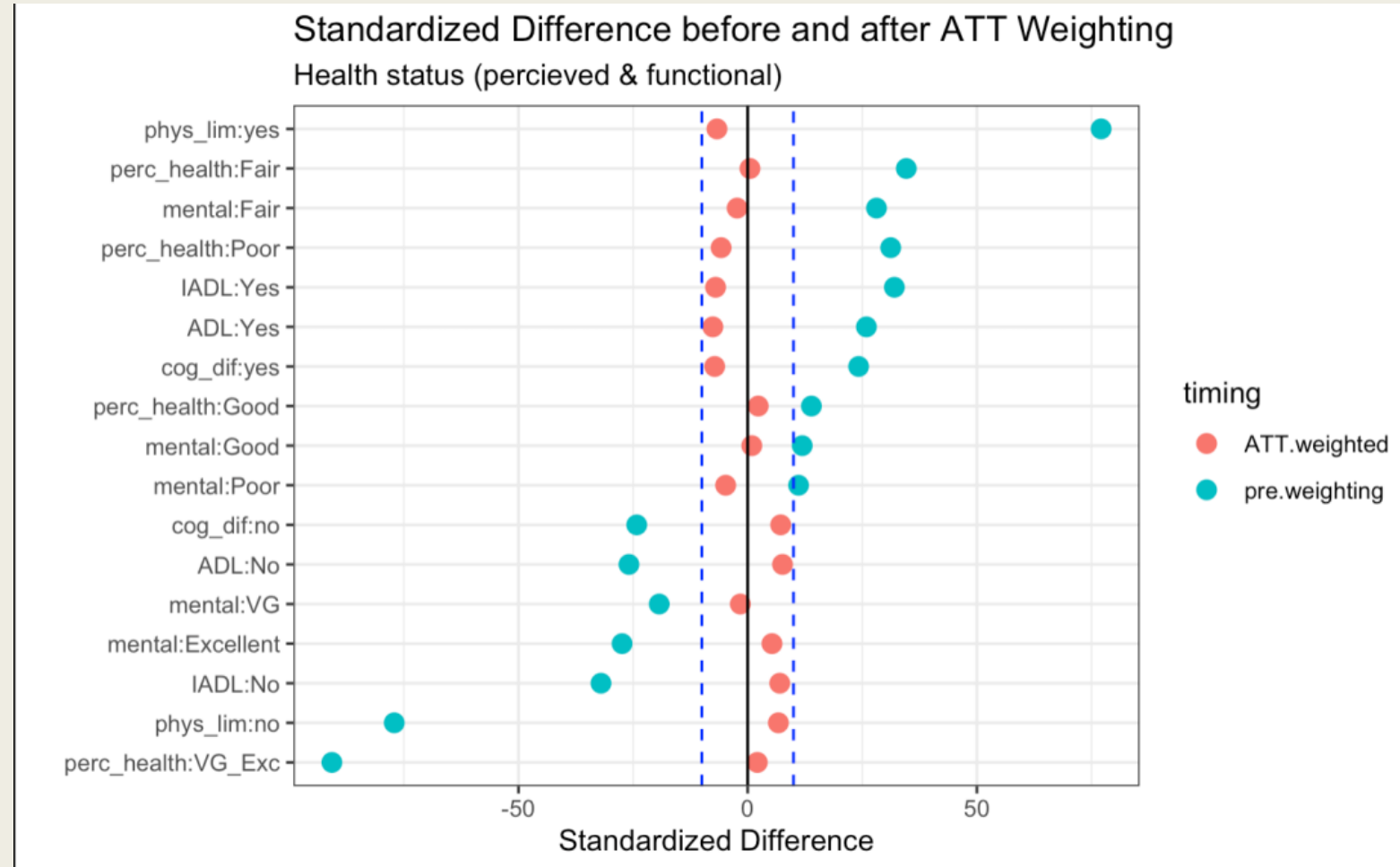
# Covariate Balance after Weighting: **Medical History**

- All standardized differences within target range after weighting



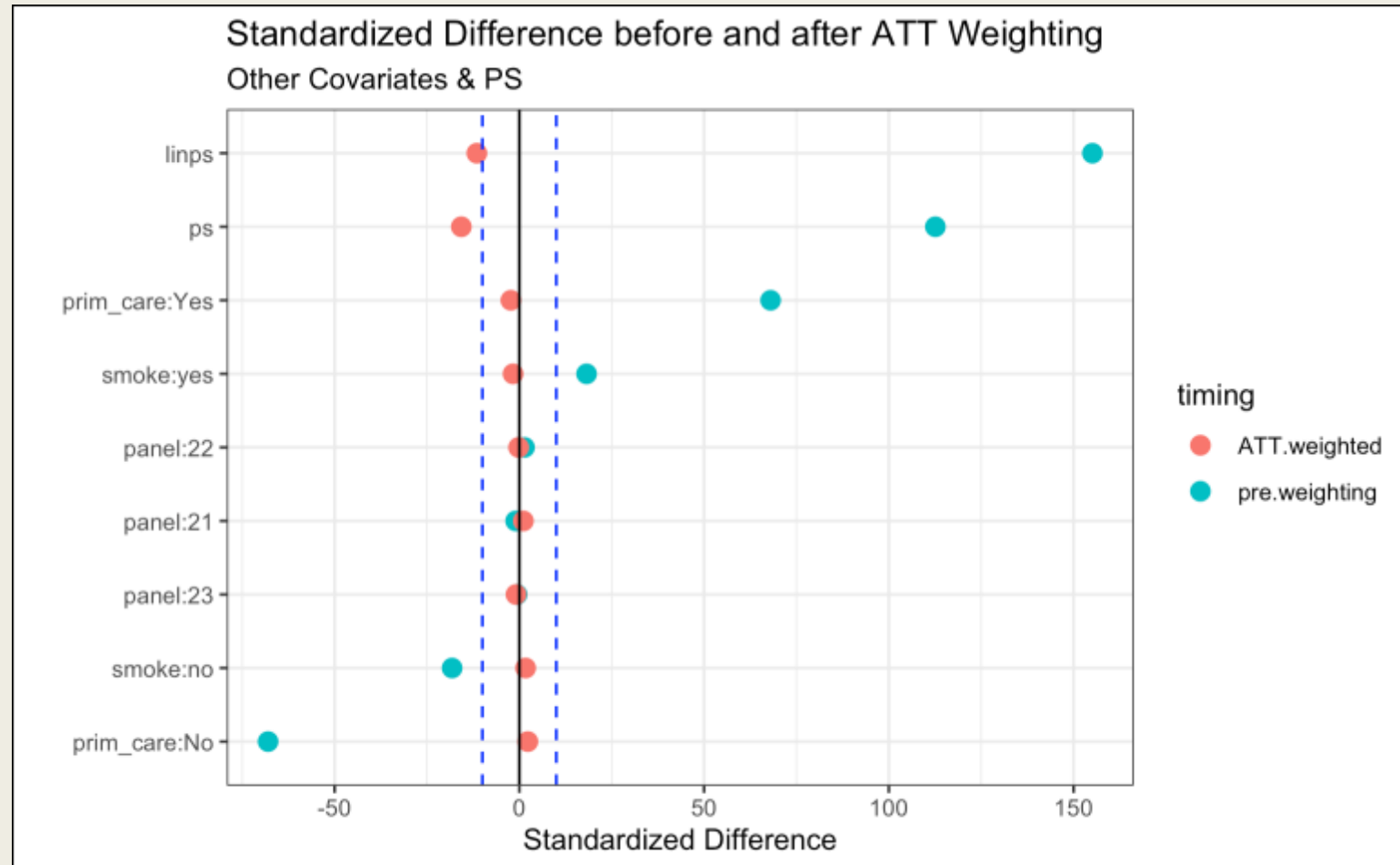
# Covariate Balance after Weighting: Health Status

- All standardized differences within target range after weighting



# Covariate Balance after Weighting: **Other & PS**

- All other covariates were close to 0 after weighting
- PS not within target range



## Pneumonia in RA vs Non-RA: compare PS analyses

- In the **weighted** sample (N=2502), the odds of having **pneumonia** in **RA** individuals was **2.88** (95% CI: 1.39, 5.93) **times higher** than the odds that a non-RA control had pneumonia

Adjustment	OR	95% CI
None	4.87	2.81, 8.50
Matching*	2.18	1.07, 4.45
Double Robust	2.88	1.39, 5.93

\*preferred model based on better covariate balance

# Sensitivity Analysis

- $\Gamma=5.43$
- To attribute the observed significant outcome to an **unobserved covariate** rather than to RA, that observed covariate would have to:
  1. *increase the odds of having RA by a factor of 5.43*
  2. *predict pneumonia quite well*

	RA Pneumonia	RA no Pneumonia	Total
Control, pneumonia	0	11	<b>11</b>
Control, no pneumonia	24	443	<b>467</b>
<b>Total</b>	<b>24</b>	<b>454</b>	<b>478</b>

- Pairs=478 matched pairs overall
- D= 35 discordant pairs (exactly one member had pneumonia)
- T= 24 discordant pairs in which RA had pneumonia

# Conclusion

## Findings

- Among a 2017-2018 nationally representative sample (N=2,502), the odds of pneumonia was higher among adults with RA compared to those without

## Plausibility

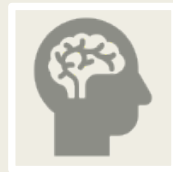
- Consistent with the high infection risks seen in phase III and IV studies
- Slightly higher estimate than the 2005 Denmark study

## Next Steps

- Medication influence
- Exclude other autoimmune diseases
- 2018 & 2019 data (when available) for relevant covariates

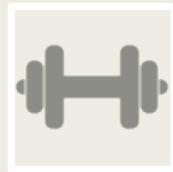
# Statistical Conclusions & Lessons

- All adjustments achieved significant results
- Of all matching methods attempted , 1:1 caliper matching was the strongest



## **Wish I'd known..**

Timing of covariates  
"Group by" function



## **Useful to others**

Try a caliper!  
MEPS is super cool and  
the workshops are  
helpful!



## **Remember next**

Goal is to ~~year~~ **year** up signal!



# QUESTION S



# Appendix

Select Covariates	Description
race	White, Hispanic, Black, Other
marital	married, never_married, divorced, widowed, separated
prim_care	Does a person have a usual care provider (Yes, No)
phys_lim	difficulty in performing certain specific physical actions such as walking, climbing stairs, grasping objects, reaching overhead, lifting, bending or stooping, or standing for long periods of time
cog_dif	difficulty concentrating, remembering or making decisions (Yes,No)

# Appendix

	Stratified by RA_f		p	test
	No	Yes		
n	1986	516		
age (mean (SD))	52.34 (17.13)	61.50 (13.19)	<0.001	
sex = F (%)	1118 (56.3)	383 (74.2)	<0.001	
race (%)			<0.001	
White	1150 (57.9)	291 (56.4)		
Hispanic	366 (18.4)	94 (18.2)		
Black	290 (14.6)	108 (20.9)		
Other	180 ( 9.1)	23 ( 4.5)		
marital (%)			<0.001	
married	1061 (53.7)	256 (49.6)		
never_married	428 (21.7)	51 ( 9.9)		
divorced	267 (13.5)	97 (18.8)		
widowed	158 ( 8.0)	82 (15.9)		
separated	61 ( 3.1)	30 ( 5.8)		
region (%)			0.006	
South	763 (38.7)	241 (46.8)		
West	485 (24.6)	108 (21.0)		
Midwest	405 (20.6)	102 (19.8)		
Northeast	317 (16.1)	64 (12.4)		
income (%)			<0.001	
Poor	320 (16.1)	130 (25.2)		
Near_poor	80 ( 4.0)	32 ( 6.2)		
Low	309 (15.6)	83 (16.1)		
Middle	542 (27.3)	127 (24.6)		
High	735 (37.0)	144 (27.9)		

education (%)			<0.001
no_degree	243 (12.3)	116 (22.7)	
GED	82 ( 4.2)	34 ( 6.7)	
HS	816 (41.4)	226 (44.2)	
BA	397 (20.1)	55 (10.8)	
graduate	235 (11.9)	42 ( 8.2)	
Other	200 (10.1)	38 ( 7.4)	
public_ins = No (%)	1407 (70.8)	263 (51.0)	<0.001
prim_care = No (%)	374 (19.4)	24 ( 4.7)	<0.001
flu_vac = No (%)	456 (48.3)	100 (35.5)	<0.001
asthma = No (%)	1702 (85.9)	409 (79.3)	<0.001
diabetes = No (%)	1653 (83.4)	403 (78.1)	0.006
cancer = No (%)	1745 (88.1)	419 (81.2)	<0.001
bronchitis = No (%)	1902 (97.1)	473 (92.0)	<0.001
emphysema = No (%)	1926 (97.2)	460 (89.1)	<0.001
stroke = No (%)	1870 (94.4)	458 (88.8)	<0.001
perc_health (%)			<0.001
VG_Exc	1003 (51.2)	88 (17.1)	
Good	575 (29.4)	187 (36.4)	
Fair	290 (14.8)	157 (30.5)	
Poor	90 ( 4.6)	82 (16.0)	
mental (%)			<0.001
Excellent	636 (32.5)	109 (21.2)	
VG	570 (29.1)	109 (21.2)	
Good	547 (27.9)	173 (33.7)	
Fair	161 ( 8.2)	100 (19.5)	
Poor	44 ( 2.2)	23 ( 4.5)	

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1001 11 ( 2.2) 25 ( 4.5)
employment = No (%)      822 (42.0)    360 (70.2)    <0.001
IADL = No (%)           1858 (94.8)   426 (82.9)    <0.001
ADL = No (%)            1902 (97.0)   457 (88.9)    <0.001
smoke = yes (%)         285 (16.4)    113 (24.3)    <0.001
phys_lim = no (%)       1587 (81.1)   221 (43.0)    <0.001
cog_dif = no (%)        1802 (91.8)   425 (82.5)    <0.001
highbp = No (%)         1115 (56.3)   191 (37.0)    <0.001
chd = No (%)            1838 (92.9)   448 (87.0)    <0.001
angina = No (%)         1921 (97.0)   485 (94.0)    0.002
MI = No (%)             1876 (94.7)   465 (90.1)    <0.001
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