Outcome versus Exposure Adjustment

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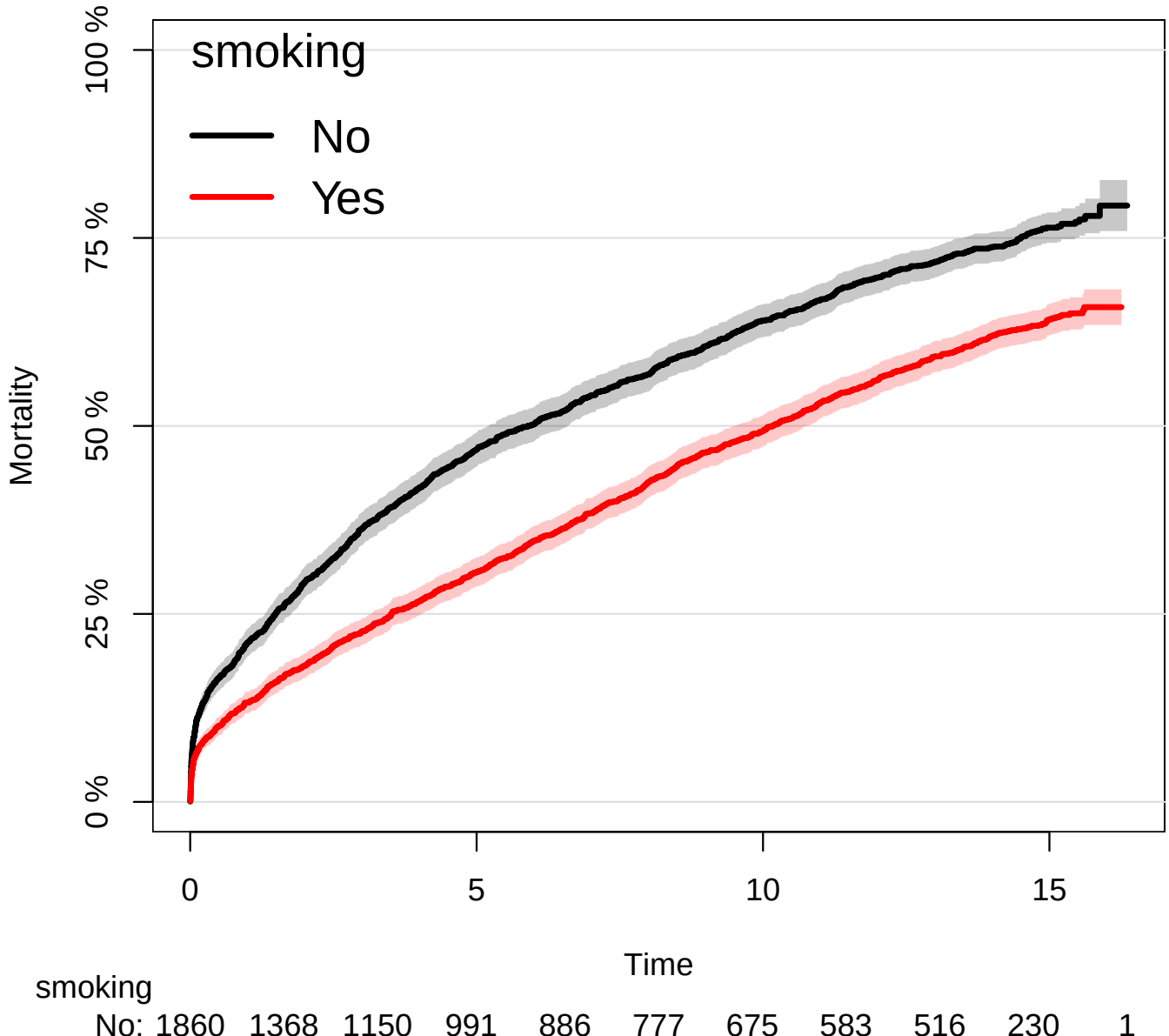
Smoking is good for you??

TRACE screening data

- 6600 patients with AMI 1990-1992
- Follow up - 15 years
- 4000 cases with selected data and complete cases

European Heart Journal (2005)

Survival by smoking



Descriptives by smoking

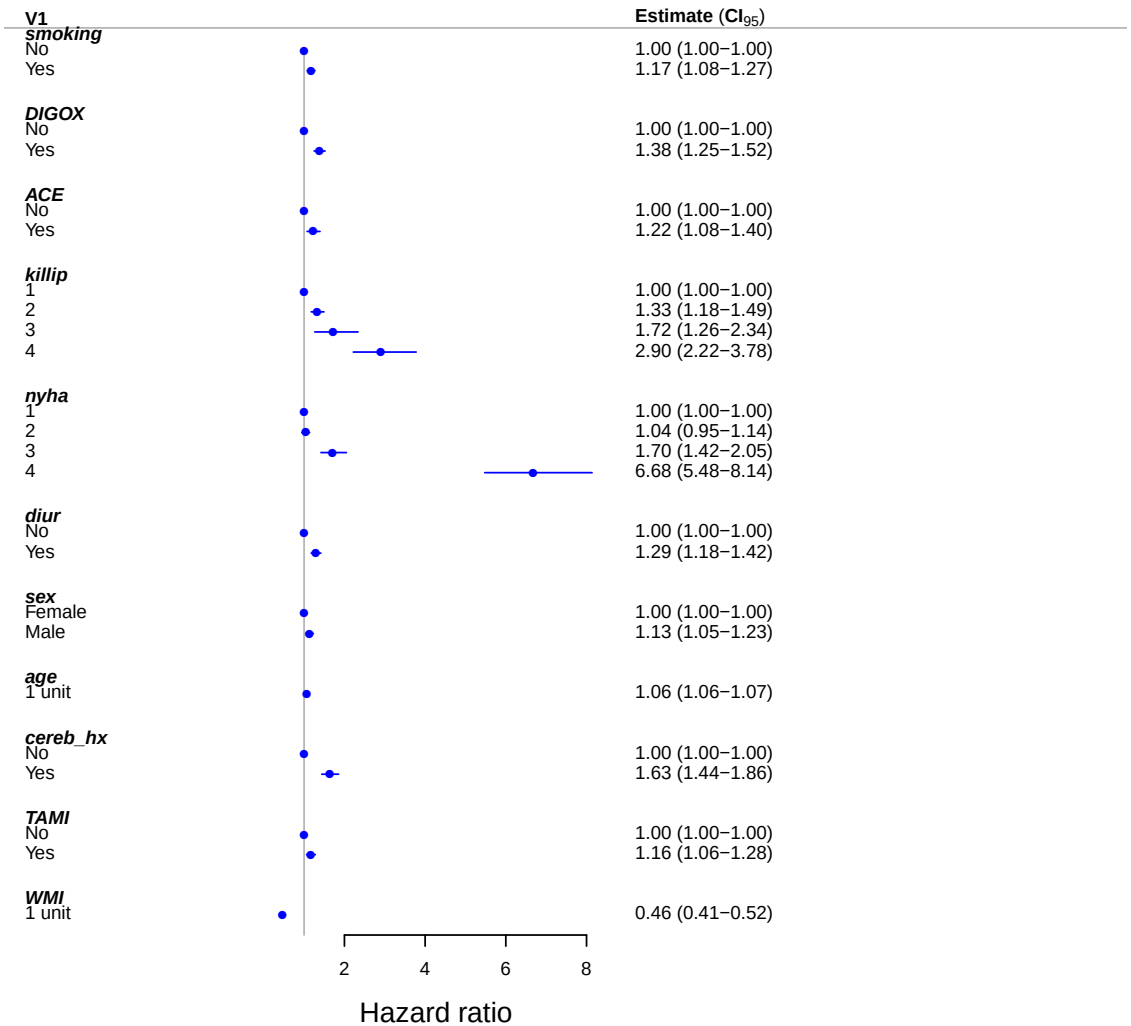
Variable	Level	No (n=1860)	Yes (n=2200)	Total (n=4060)	p-value
DIGOX	No	1445 (77.7)	1947 (88.5)	3392 (83.5)	
	Yes	415 (22.3)	253 (11.5)	668 (16.5)	< 1e-04
ACE	No	1668 (89.7)	2067 (94.0)	3735 (92.0)	
	Yes	192 (10.3)	133 (6.0)	325 (8.0)	< 1e-04
killip	1	1521 (81.8)	1945 (88.4)	3466 (85.4)	
	2	253 (13.6)	195 (8.9)	448 (11.0)	
	3	25 (1.3)	23 (1.0)	48 (1.2)	
	4	61 (3.3)	37 (1.7)	98 (2.4)	< 1e-04
nyha	1	1091 (58.7)	1488 (67.6)	2579 (63.5)	
	2	559 (30.1)	564 (25.6)	1123 (27.7)	
	3	92 (4.9)	62 (2.8)	154 (3.8)	
	4	118 (6.3)	86 (3.9)	204 (5.0)	< 1e-04
diur	No	981 (52.7)	1529 (69.5)	2510 (61.8)	
	Yes	879 (47.3)	671 (30.5)	1550 (38.2)	< 1e-04
sex	Female	716 (38.5)	620 (28.2)	1336 (32.9)	
	Male	1144 (61.5)	1580 (71.8)	2724 (67.1)	< 1e-04
age	mean (sd)	70.6 (10.7)	62.5 (11.5)	66.2 (11.9)	< 1e-04
cereb_{hx}	No	1691 (90.9)	2074 (94.3)	3765 (92.7)	
	Yes	169 (9.1)	126 (5.7)	295 (7.3)	< 1e-04
TAMI	No	1388 (74.6)	1872 (85.1)	3260 (80.3)	
	Yes	472 (25.4)	328 (14.9)	800 (19.7)	< 1e-04
WMI	mean (sd)	1.5 (0.4)	1.6 (0.3)	1.6 (0.4)	< 1e-04

$$h(t) = \lim_{\delta t \to 0} \frac{\text{Observed deaths in}[t, t+\delta t]/N(t)}{\delta t}$$

$$h(t) = h_0(t) e^{smoking\beta 1 + sex\beta_2 + age\beta_3 .....}$$

$$hr_{smoking} = e^{\beta_1}$$

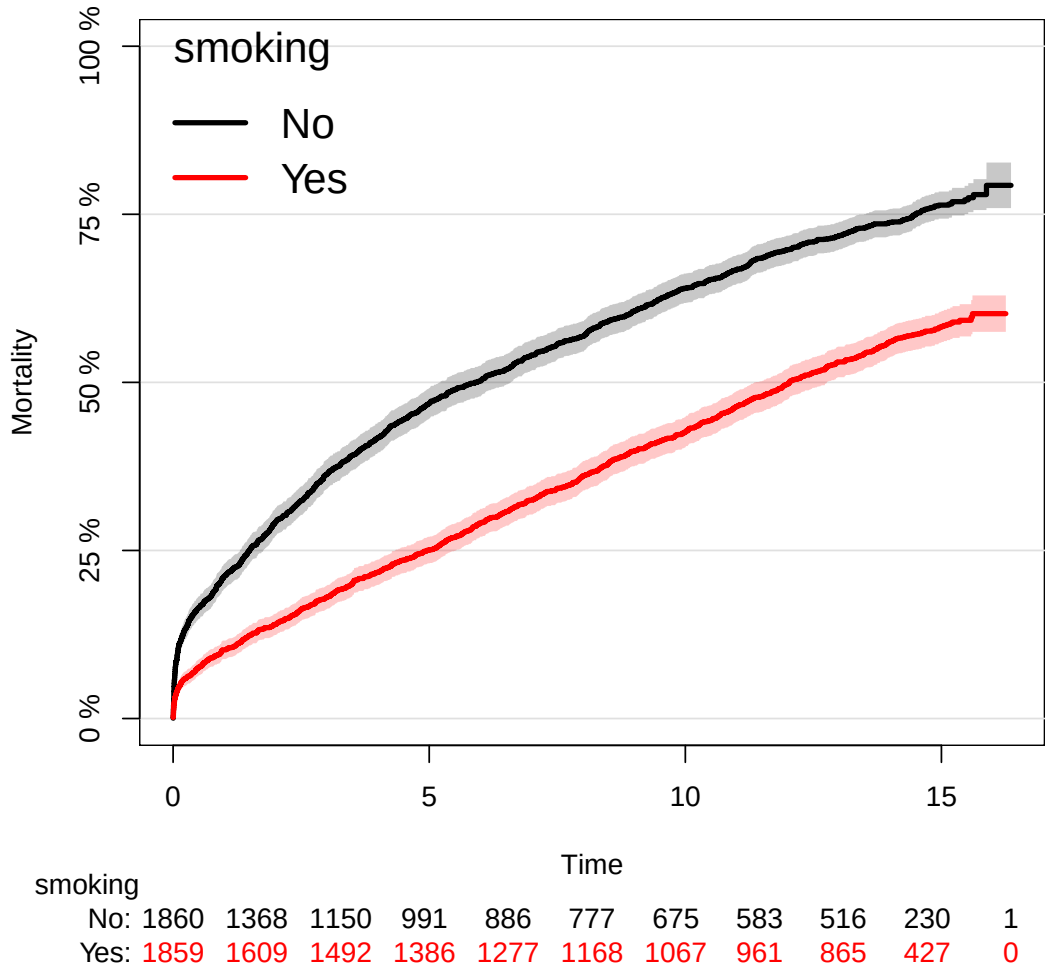
Old fashioned Cox



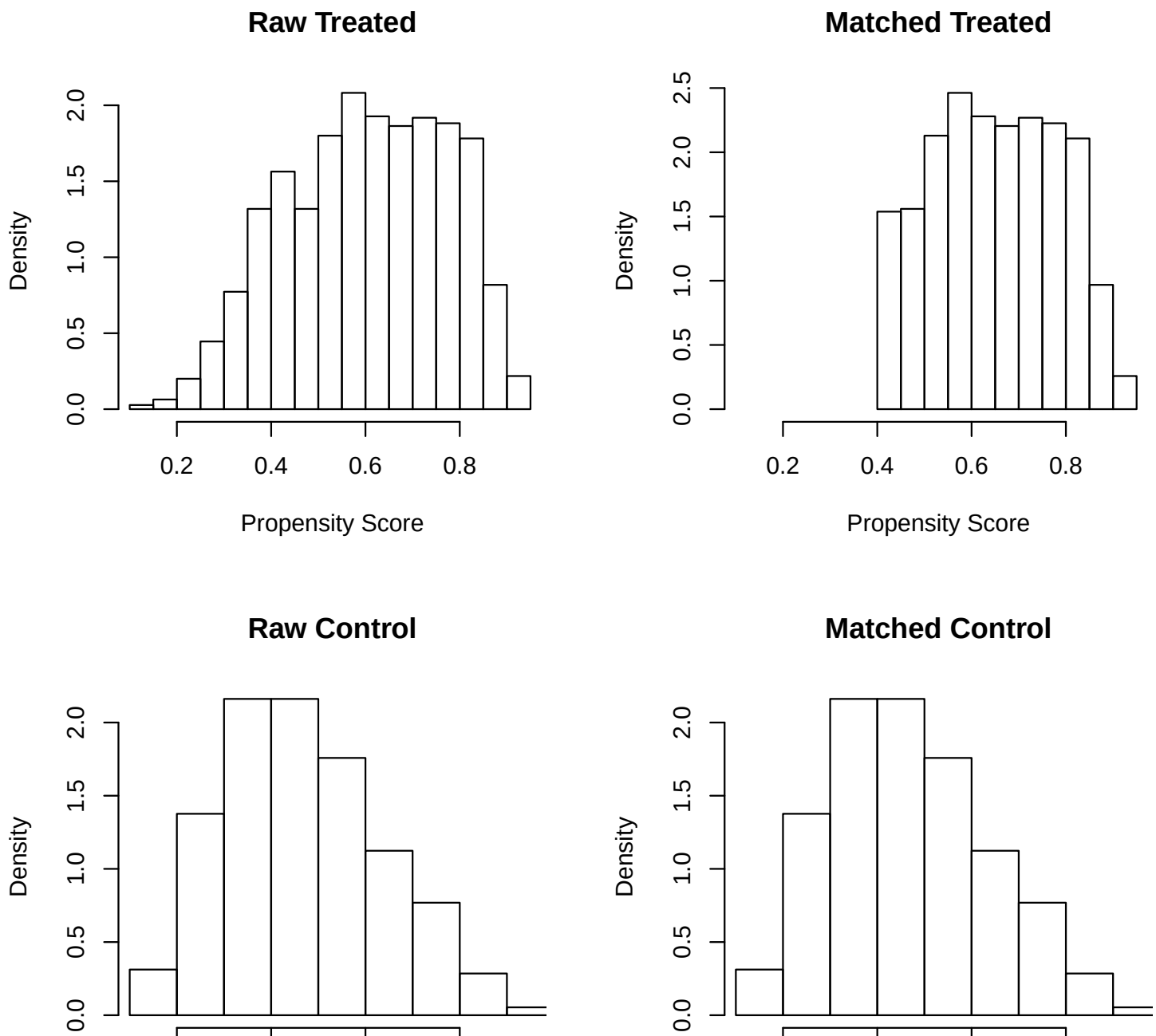
Propensity stratification / matching

- Propensity is probability of smoking
- In propensity stratification analysis is stratified by multiple strata of this propensity to ensure that survival is compared for individual with similar propensity of smoking
- In propensity matching cases are matched with control that have similar probability of smoking. If it works nicely there is apparently a controlled trial.

Propensity matching



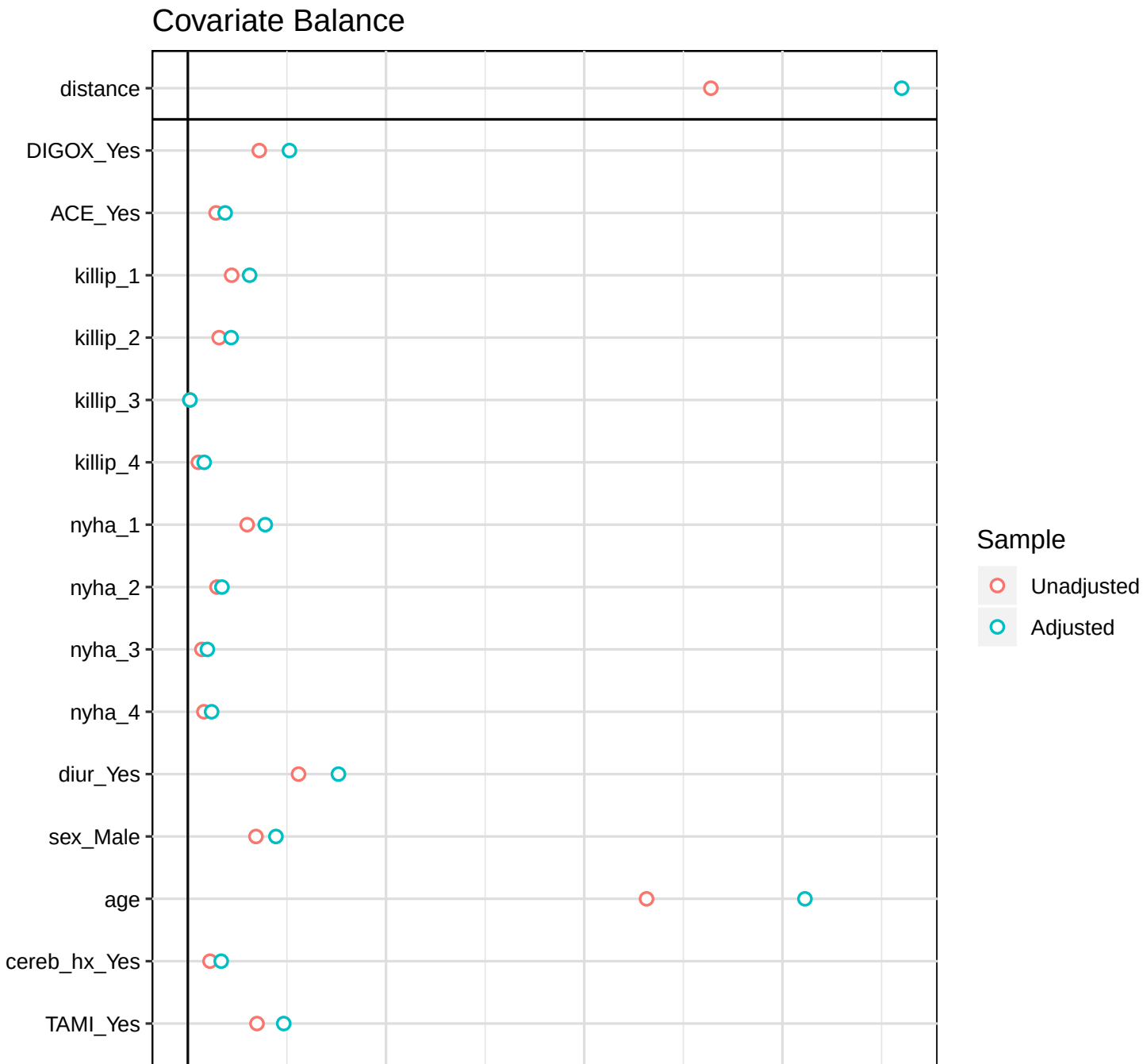
Propensity plot



Descriptives by propensity

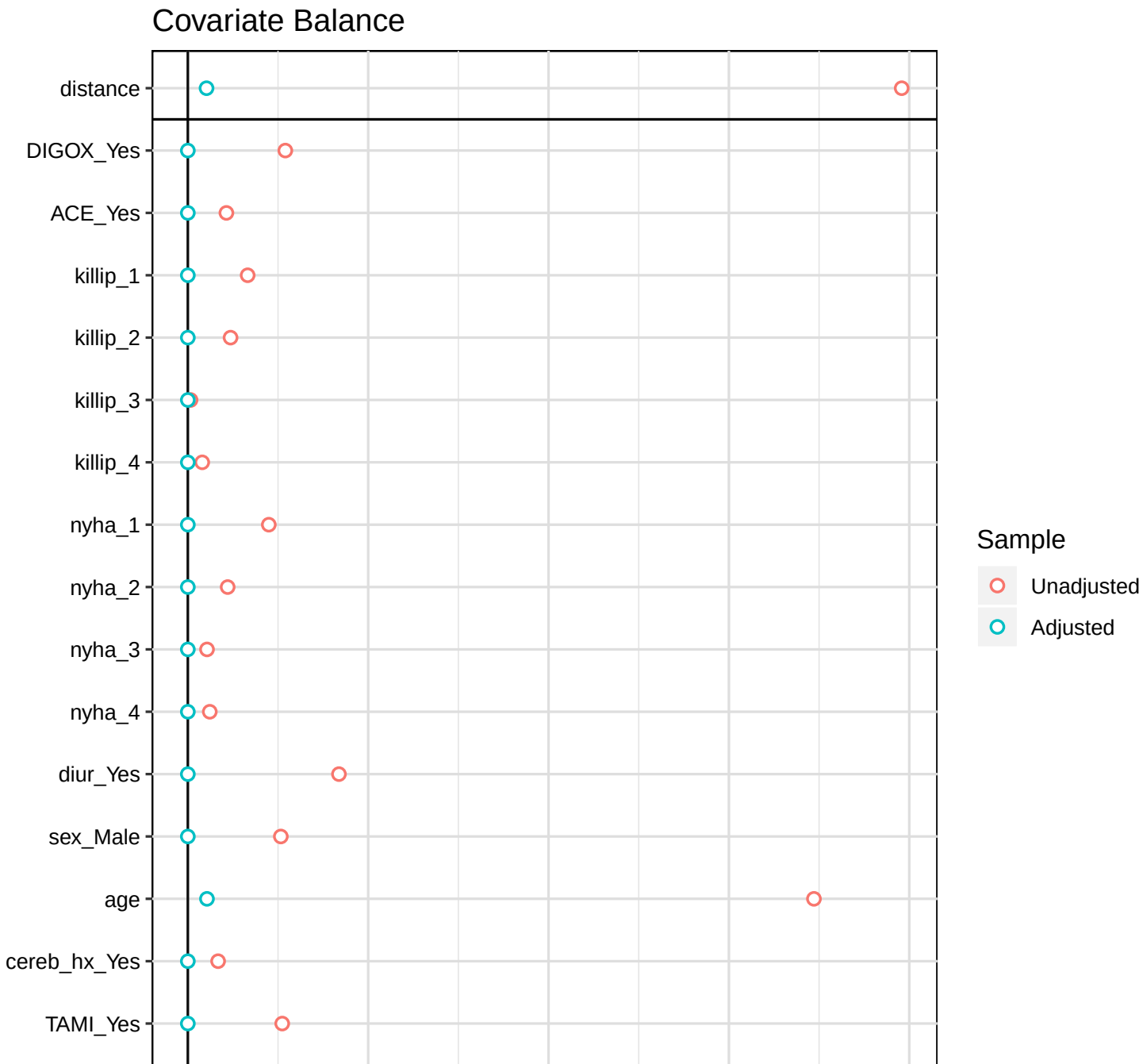
Variable	Level	No (n=1860)	Yes (n=1860)	Total (n=3720)	p-value
DIGOX	No	1445 (77.7)	1731 (93.1)	3176 (85.4)	
	Yes	415 (22.3)	129 (6.9)	544 (14.6)	< 1e-04
ACE	No	1668 (89.7)	1773 (95.3)	3441 (92.5)	
	Yes	192 (10.3)	87 (4.7)	279 (7.5)	< 1e-04
killip	1	1521 (81.8)	1695 (91.1)	3216 (86.5)	
	2	253 (13.6)	131 (7.0)	384 (10.3)	
	3	25 (1.3)	19 (1.0)	44 (1.2)	
	4	61 (3.3)	15 (0.8)	76 (2.0)	< 1e-04
nyha	1	1091 (58.7)	1309 (70.4)	2400 (64.5)	
	2	559 (30.1)	463 (24.9)	1022 (27.5)	
	3	92 (4.9)	37 (2.0)	129 (3.5)	
	4	118 (6.3)	51 (2.7)	169 (4.5)	< 1e-04
diur	No	981 (52.7)	1405 (75.5)	2386 (64.1)	
	Yes	879 (47.3)	455 (24.5)	1334 (35.9)	< 1e-04
sex	Female	716 (38.5)	468 (25.2)	1184 (31.8)	
	Male	1144 (61.5)	1392 (74.8)	2536 (68.2)	< 1e-04
age	mean (sd)	70.6 (10.7)	59.8 (10.1)	65.2 (11.7)	< 1e-04
cereb_{hx}	No	1691 (90.9)	1785 (96.0)	3476 (93.4)	
	Yes	169 (9.1)	75 (4.0)	244 (6.6)	< 1e-04
TAMI	No	1388 (74.6)	1658 (89.1)	3046 (81.9)	
	Yes	472 (25.4)	202 (10.9)	674 (18.1)	< 1e-04
WMI	mean (sd)	1.5 (0.4)	1.6 (0.3)	1.6 (0.3)	< 1e-04

Love plot

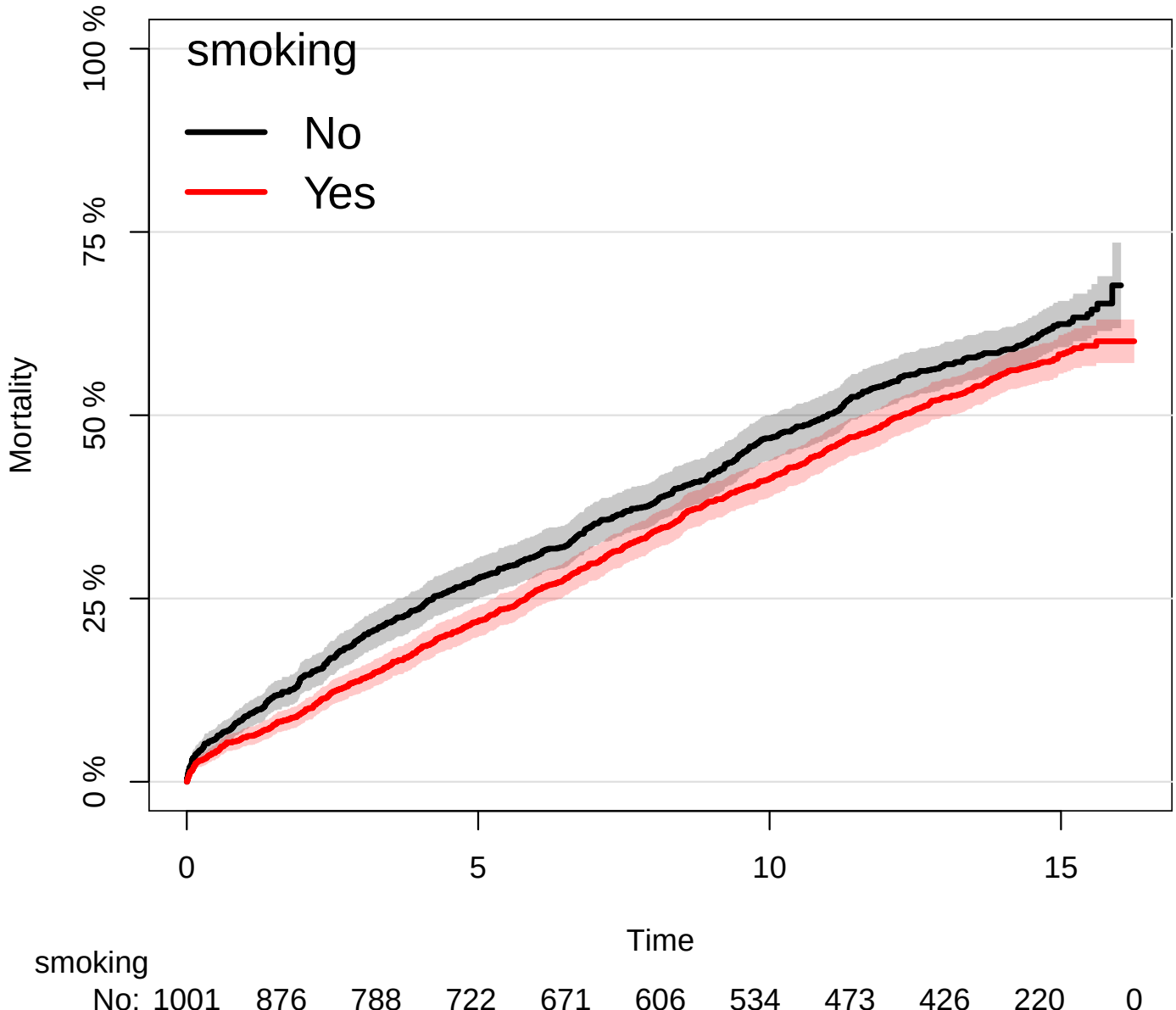

Covariate Balance
distance
DIGOX_Yes
ACE_Yes
killip_1
killip_2
killip_3
killip_4
nyha_1
nyha_2
nyha_3
nyha_4
diur_Yes
sex_Male
age
cereb_hx_Yes
TAMI_Yes
Sample
Unadjusted
Adjusted

Other Matching?

Course Exact Matching



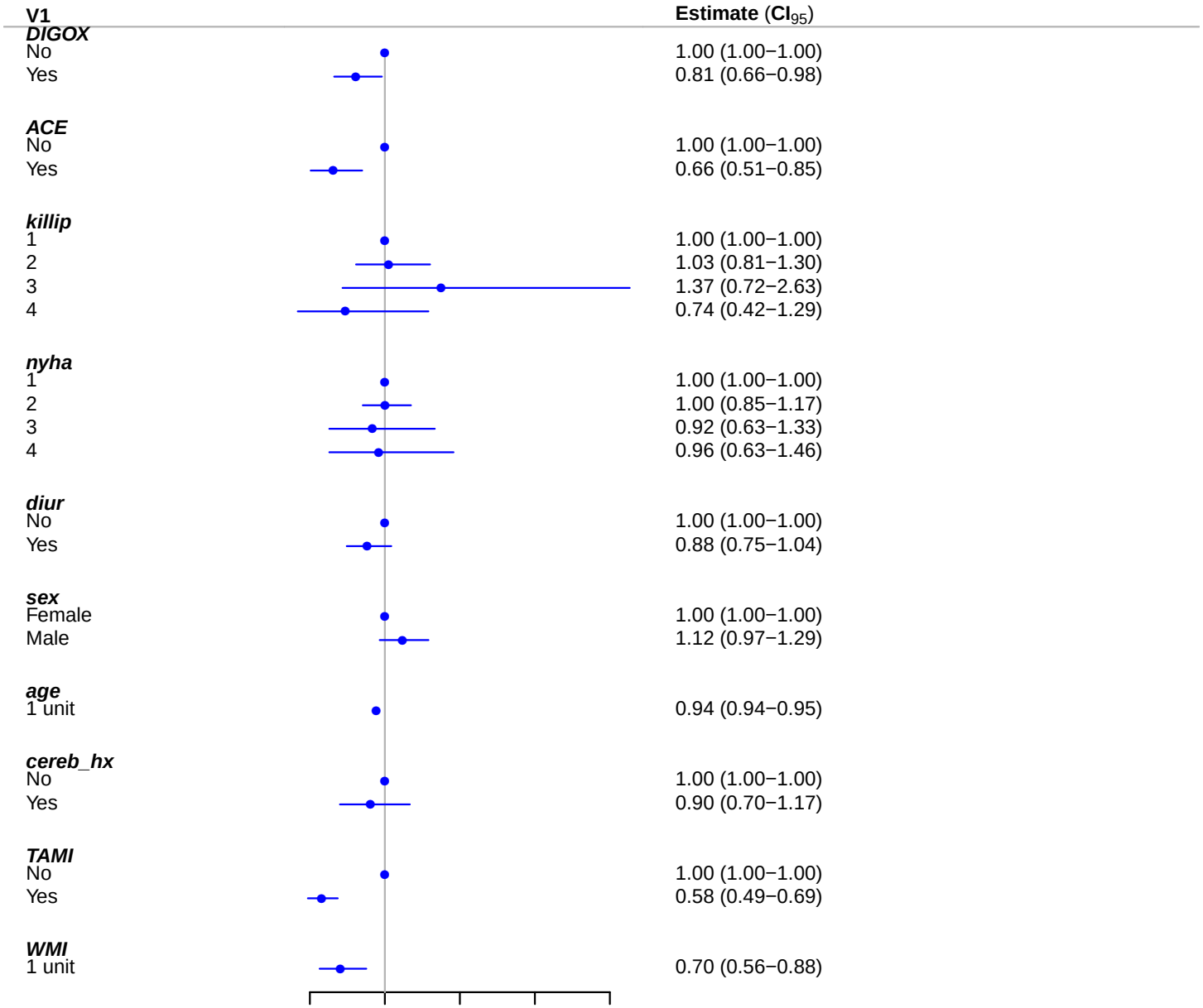
Survival by CEM-matching



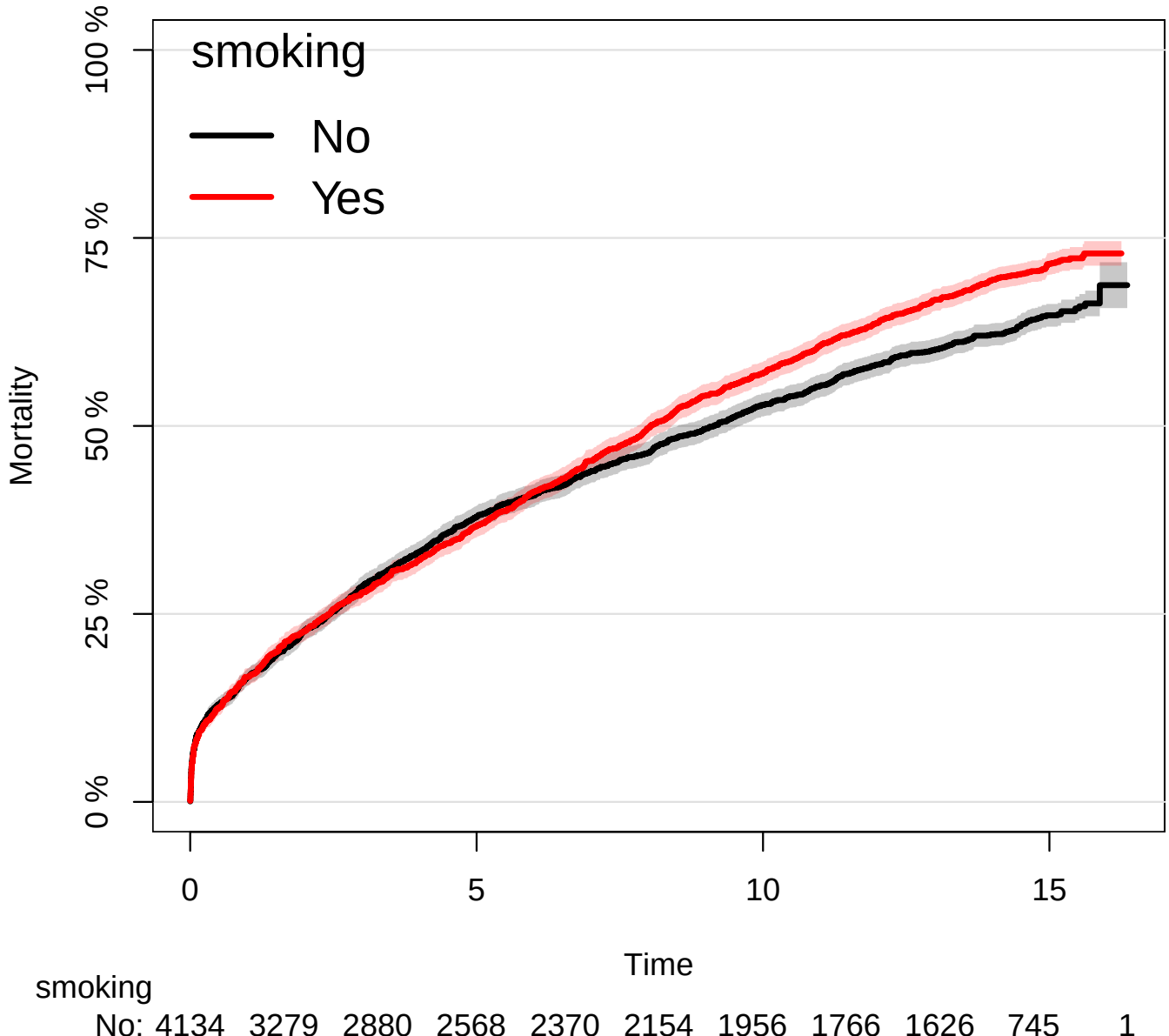
Descriptives by CEM

Variable	Level	No (n=1001)	Yes (n=1462)	Total (n=2463)	p-value
DIGOX	No	927 (92.6)	1396 (95.5)	2323 (94.3)	
	Yes	74 (7.4)	66 (4.5)	140 (5.7)	0.0032658
ACE	No	991 (99.0)	1449 (99.1)	2440 (99.1)	
	Yes	10 (1.0)	13 (0.9)	23 (0.9)	0.9481526
killip	1	969 (96.8)	1428 (97.7)	2397 (97.3)	
	2	29 (2.9)	32 (2.2)	61 (2.5)	
	3	0 (0.0)	0 (0.0)	0 (0.0)	
	4	3 (0.3)	2 (0.1)	5 (0.2)	NA
nyha	1	770 (76.9)	1174 (80.3)	1944 (78.9)	
	2	223 (22.3)	281 (19.2)	504 (20.5)	
	3	4 (0.4)	4 (0.3)	8 (0.3)	
	4	4 (0.4)	3 (0.2)	7 (0.3)	0.1989648
diur	No	768 (76.7)	1210 (82.8)	1978 (80.3)	
	Yes	233 (23.3)	252 (17.2)	485 (19.7)	0.0002614
sex	Female	281 (28.1)	359 (24.6)	640 (26.0)	
	Male	720 (71.9)	1103 (75.4)	1823 (74.0)	0.0564162
age	mean (sd)	67.2 (10.4)	62.2 (10.9)	64.2 (11.0)	< 1e-04
cereb_{hx}	No	983 (98.2)	1443 (98.7)	2426 (98.5)	
	Yes	18 (1.8)	19 (1.3)	37 (1.5)	0.4062322
TAMI	No	862 (86.1)	1317 (90.1)	2179 (88.5)	
	Yes	139 (13.9)	145 (9.9)	284 (11.5)	0.0030339
WMI	mean (sd)	1.7 (0.2)	1.7 (0.2)	1.7 (0.2)	0.9361005

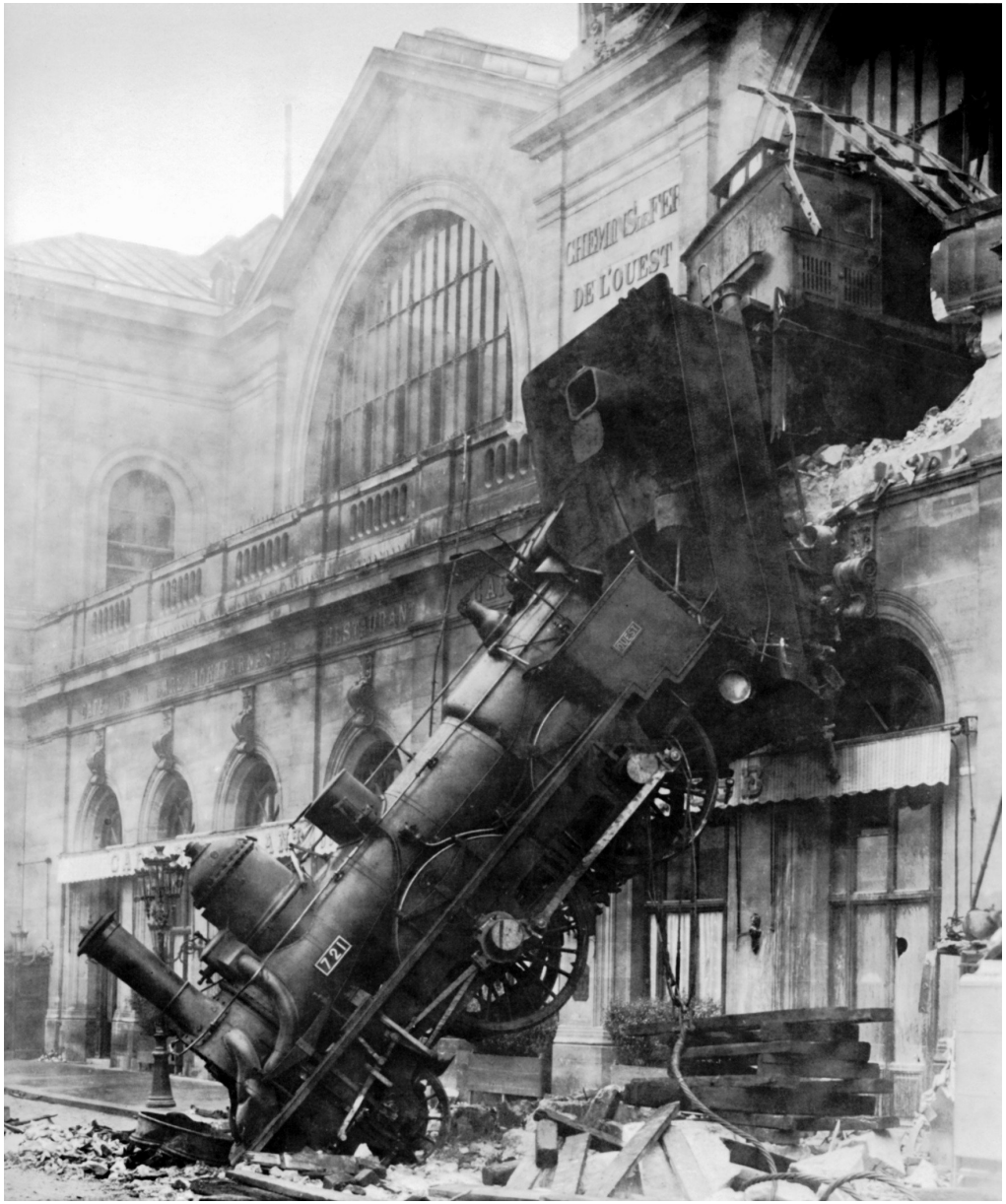
Determinants of smoking



Inverse probability score

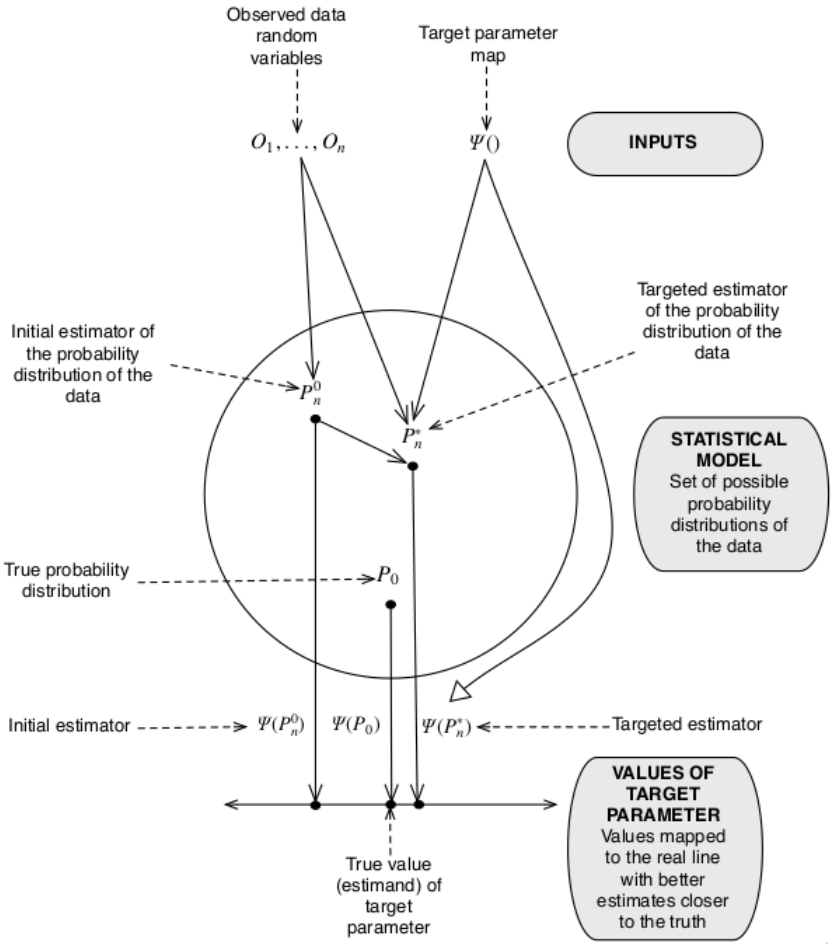


Navigate with care!



Double Robust Methods

Estimating and Targeting



Rose van der Laan, Targeted Learning 2011