A Comparison of Sertraline to Duloxetine for the Risk of Stroke in the MDCD Database.

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Abstract

To do

Introduction

This is a very important study. Here's a really cool paper (1).

Methods

The study spanned the period from 2004-08-13 until 2004-08-13.

Data source

Truven Health MarketScan® Medicare Supplemental and Coordination of Benefits Database (MDCR) represents health services of retirees in the United States with primary or Medicare supplemental coverage through privately insured fee-for-service, point-of-service, or capitated health plans. These data include adjudicated health insurance claims (e.g. inpatient, outpatient, and outpatient pharmacy). Additionally, it captures laboratory tests for a subset of the covered lives.

Results

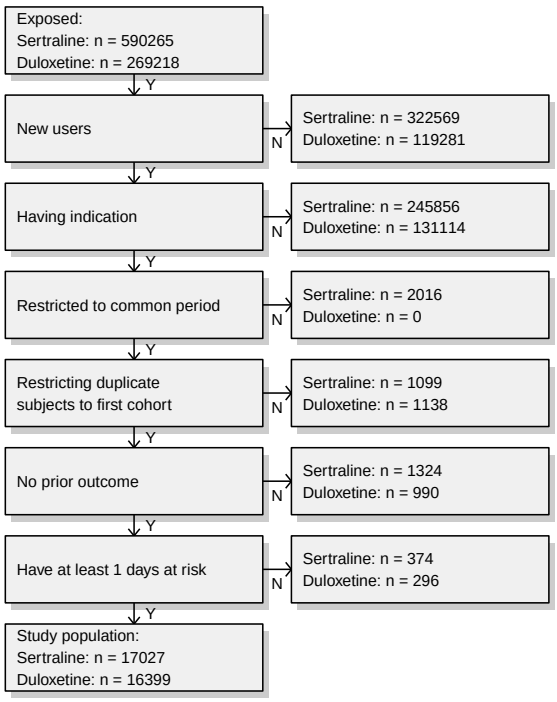

Figure 1. Attrition diagram.

Table 1. Select population characteristics

	Before stratification			After stratification		
	Target	Comparator		Target	Comparator	
Characteristic	%	%	Std. diff	%	%	Std. diff
Age group						
45-49	0.2	0.5	-0.05	0.3	0.4	-0.01
50-54	0.6	1.4	-0.08	0.9	1.2	-0.03
55-59	1.4	2.7	-0.09	1.9	2.3	-0.03
60-64	2.2	3.5	-0.08	2.7	3.0	-0.02
65-69	18.2	22.0	-0.10	21.5	21.2	0.01
70-74	21.4	23.9	-0.06	22.6	22.8	0.00
75-79	19.9	19.5	0.01	19.6	19.1	0.01
80-84	17.1	14.2	0.08	15.2	14.8	0.01
85-89	12.3	8.9	0.11	10.4	10.8	-0.01
90-94	5.3	2.8	0.12	3.9	3.8	0.00
95-99	1.2	0.5	0.08	1.0	0.7	0.03
Gender: female	64.4	69.2	-0.10	67.2	66.7	0.01
Medical history: General						
Acute respiratory disease	29.9	30.2	-0.01	30.0	29.8	0.00
Attention deficit hyperactivity disorder	0.7	0.8	-0.01	0.9	0.7	0.02
Chronic liver disease	1.5	1.5	0.00	1.7	1.5	0.01
Chronic obstructive lung disease	21.3	20.3	0.03	20.2	20.4	0.00
Crohn's disease	0.6	0.7	-0.01	0.7	0.6	0.01
Dementia	19.0	12.1	0.19	14.7	15.0	-0.01
Depressive disorder	86.8	84.6	0.06	86.7	86.5	0.01
Diabetes mellitus	28.5	28.7	0.00	27.5	28.1	-0.01
Gastrointestinal hemorrhage	6.8	6.3	0.02	6.3	6.3	0.00
Human immunodeficiency virus infection	0.2	0.2	0.00	0.2	0.2	0.01
Hyperlipidemia	49.2	44.5	0.09	46.7	47.1	-0.01
Hypertensive disorder	71.0	66.5	0.10	68.1	68.3	-0.01

(continued)

	Before stratification			After stratification		
	Target	Comparator		Target	Comparator	
Lesion of liver	1.7	1.0	0.06	1.4	1.0	0.03
Obesity	8.1	8.2	0.00	8.0	8.5	-0.02
Osteoarthritis	42.6	53.0	-0.21	48.1	47.5	0.01
Pneumonia	13.1	11.6	0.05	11.5	12.2	-0.02
Psoriasis	1.4	1.5	0.00	1.4	1.4	0.01
Renal impairment	19.8	14.6	0.14	16.3	16.5	-0.01
Rheumatoid arthritis	3.0	4.3	-0.07	3.7	3.7	0.00
Ulcerative colitis	0.7	0.8	-0.01	0.7	0.8	-0.02
Urinary tract infectious disease	24.3	22.7	0.04	22.9	23.1	0.00
Viral hepatitis C	0.5	0.4	0.01	0.5	0.4	0.01
Visual system disorder	52.7	51.4	0.02	51.8	51.6	0.00
Medical history: Cardiovascular disease						
Atrial fibrillation	17.9	13.7	0.12	14.8	15.5	-0.02
Cerebrovascular disease	17.5	15.1	0.06	13.7	14.0	-0.01
Coronary arteriosclerosis	27.9	25.6	0.05	25.8	26.0	0.00
Heart disease	57.3	52.4	0.10	53.6	53.7	0.00
Heart failure	19.3	15.7	0.09	16.1	17.0	-0.02
Ischemic heart disease	16.2	14.5	0.05	14.7	14.8	0.00
Peripheral vascular disease	35.7	32.5	0.07	32.5	32.6	0.00
Pulmonary embolism	2.0	2.2	-0.01	1.8	2.1	-0.02
Venous thrombosis	6.6	6.2	0.02	6.0	6.6	-0.02
Medical history: Neoplasms						
Hematologic neoplasm	2.5	2.2	0.02	2.4	2.3	0.01
Malignant lymphoma	1.2	1.1	0.01	1.3	1.1	0.02
Malignant neoplasm of anorectum	0.6	0.4	0.02	0.5	0.4	0.01
Malignant neoplastic disease	20.5	18.7	0.04	19.8	19.5	0.01
Malignant tumor of breast	3.8	3.8	0.00	4.2	3.7	0.02
Malignant tumor of colon	1.1	0.9	0.02	0.9	1.0	-0.01
Malignant tumor of lung	1.1	1.1	0.00	1.0	1.2	-0.02
Malignant tumor of urinary bladder	1.1	1.0	0.02	1.0	1.0	0.00
Primary malignant neoplasm of prostate	2.5	2.4	0.01	2.4	2.6	-0.01
Medication use						
Agents acting on the renin-angiotensin system	51.3	50.3	0.02	50.5	50.1	0.01
Antibacterials for systemic use	68.6	73.0	-0.10	70.7	70.8	0.00
Antiepileptics	33.7	48.6	-0.31	40.7	40.1	0.01
Antiinflammatory and antirheumatic products	29.4	39.3	-0.21	34.8	34.6	0.01
Antineoplastic agents	4.7	5.5	-0.04	5.0	5.3	-0.01
Antipsoriatics	1.1	1.2	-0.01	1.1	1.2	-0.02
Antithrombotic agents	30.6	28.9	0.04	28.0	28.1	0.00
Beta blocking agents	47.6	44.0	0.07	45.0	45.5	-0.01
Calcium channel blockers	32.8	31.5	0.03	31.4	31.4	0.00
Diuretics	45.1	46.1	-0.02	44.9	45.1	-0.01
Drugs for acid related disorders	45.6	51.9	-0.13	48.4	48.1	0.01
Drugs for obstructive airway diseases	35.1	38.2	-0.06	36.5	36.1	0.01
Drugs used in diabetes	22.6	23.5	-0.02	22.4	22.7	-0.01
Immunosuppressants	4.8	6.5	-0.07	5.5	5.8	-0.01
Lipid modifying agents	57.1	57.5	-0.01	56.5	57.0	-0.01
Opioids	36.7	51.0	-0.29	44.2	43.0	0.02
Psycholeptics	64.0	71.2	-0.16	67.9	68.0	0.00

Table 2. Number of subjects, follow-up time (in days), number of outcome events, and event incidence rate (IR) per 1,000 patient years (PY) in the target and comparator group after stratification or matching, as well as the minimum detectable relative risk (MDRR). Note that the IR does not account for any stratification or matching.

	Subjects		PYs		Outcomes		IR (per 1,000 PY)		
Analysis	Target	Comp.	Target	Comp.	Target	Comp.	Target	Comp.	MDRR
PS stratification, on-treatment	16,399	17,027	10,438	9,534	108	104	10.35	10.91	1.47
PS stratification, intent-to-treat	16,690	17,398	48,724	39,581	511	414	10.49	10.46	1.20
PS matching, on-treatment	10,417	16,368	6,046	10,422	64	108	10.58	10.36	1.55
PS matching, intent-to-treat	10,620	16,658	27,549	48,573	293	511	10.64	10.52	1.22

Table 2. Time (days) at risk distribution expressed as minimum (Min), 10th Percentile (P10), 25th percentile (P25), median, 75th percentile (P75), 90th percentile (P90) and maximum (Max) in the target and comparator cohort after stratification.

Cohort	Min	P10	P25	Median	P75	P90	Max
Target	1	30	30	92	397	521	3,490
Comparator	2	30	30	104	451	608	3,883

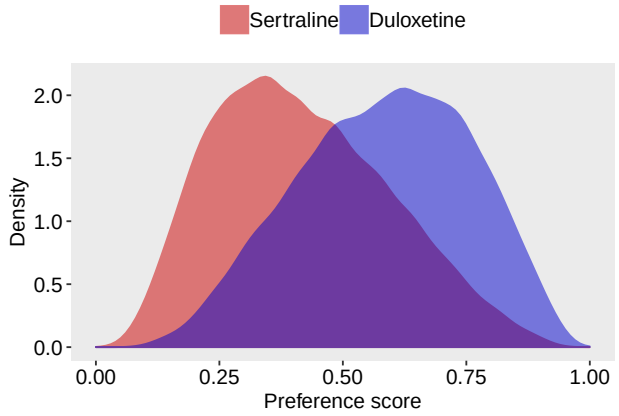

Figure 2. Preference score distribution. The preference score is a transformation of the propensity score that adjusts for differences in the sizes of the two treatment groups. A higher overlap indicates subjects in the two groups were more similar in terms of their predicted probability of receiving one treatment over the other.

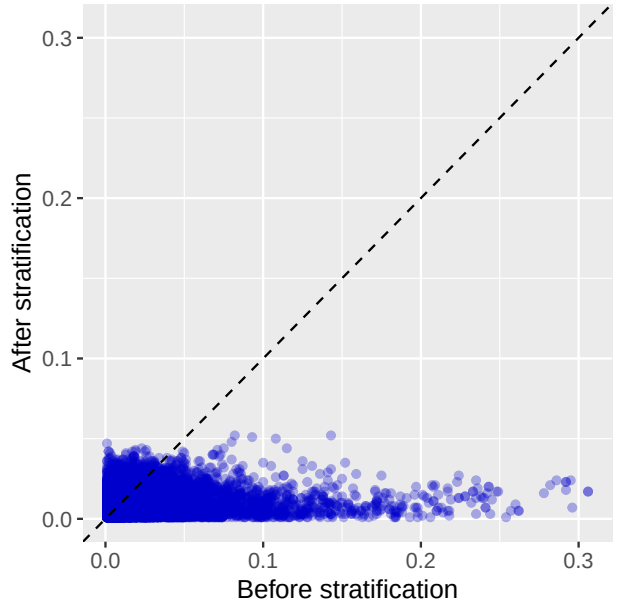

Figure 3. Covariate balance before and after stratification. Each dot represents the standardizes difference of means for a single covariate before and after stratification on the propensity score.

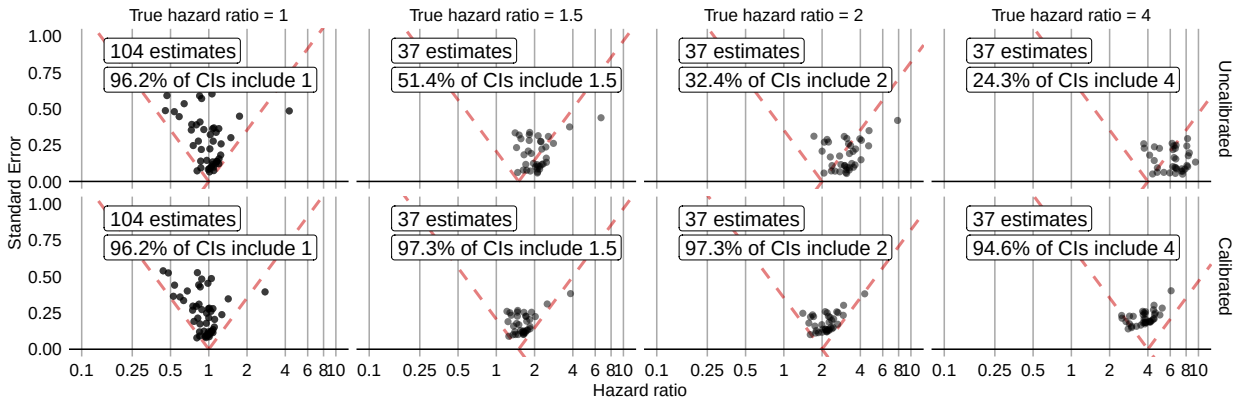

Figure 4. Systematic error

Table 3. Hazard ratios, 95% confidence intervals, uncalibrated and empirically calibrated, for various analyses.

Analysis	HR (95% CI)	P	Cal. HR (95% CI)	Cal. p
PS stratification, on-treatment	0.95 (0.70 - 1.29)	0.74	0.91 (0.71 - 1.18)	0.70
PS stratification, intent-to-treat	1.01 (0.88 - 1.17)	0.87	0.93 (0.77 - 1.12)	0.89
PS matching, on-treatment	1.07 (0.67 - 1.72)	0.77	1.01 (0.69 - 1.50)	0.76
PS matching, intent-to-treat	1.12 (0.92 - 1.36)	0.24	1.03 (0.84 - 1.27)	0.34

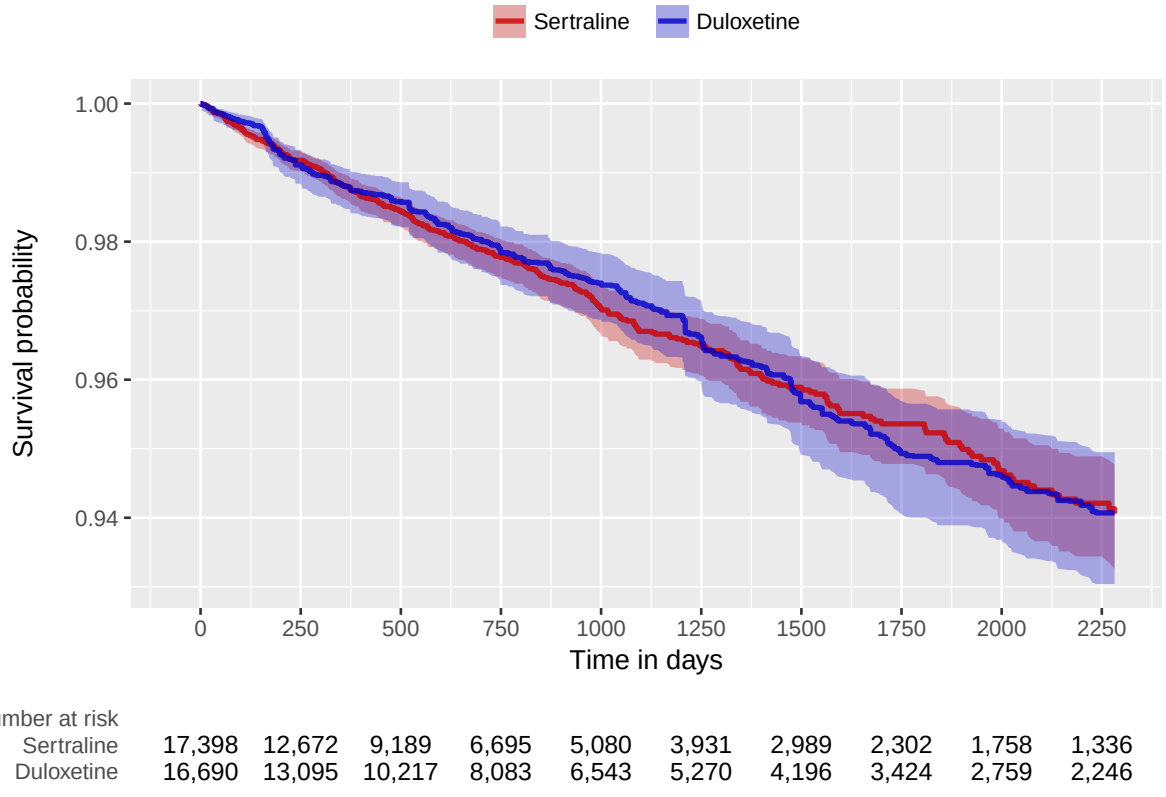

Figure 3. Kaplan Meier plot, showing survival as a function of time. This plot is adjusted for the propensity score stratification: The target curve (Sertraline) shows the actual observed survival. The comparator curve (Duloxetine) applies reweighting to approximate the counterfactual of what the target survival would look like had the target cohort been exposed to the comparator instead. The shaded area denotes the 95 percent confidence interval.

Table 4. Subgroup interactions

	Subjects		On-treatment			Intent-to-treat		
Subgroup	Target	Comparator	HRR (95% CI)	P	Cal. P	HRR (95% CI)	P	Cal. P
Elderly (age $\ge$ 65)	15,009	16,270	0.74 (0.12 - 5.68)	0.76	0.78	1.72 (0.90 - 3.56)	0.12	0.12
Gender = female	11,412	10,987	0.94 (0.53 - 1.67)	0.84	0.90	1.12 (0.85 - 1.48)	0.41	0.42
Hepatic impairment	165	264	1.34 (0.13 - 29.2)	0.83	0.80	0.67 (0.16 - 2.53)	0.56	0.41
Pregnant women	<5	$<$5						
Renal impairment	2,233	3,167	0.83 (0.41 - 1.72)	0.62	0.65	0.74 (0.51 - 1.07)	0.11	0.11

Conclusions

References

1. Schuemie MJ, Ryan PB, DuMouchel W, Suchard MA, Madigan D (2014) Interpreting observational studies: why empirical calibration is needed to correct p-values. *Stat Med* 33(2):209–218.