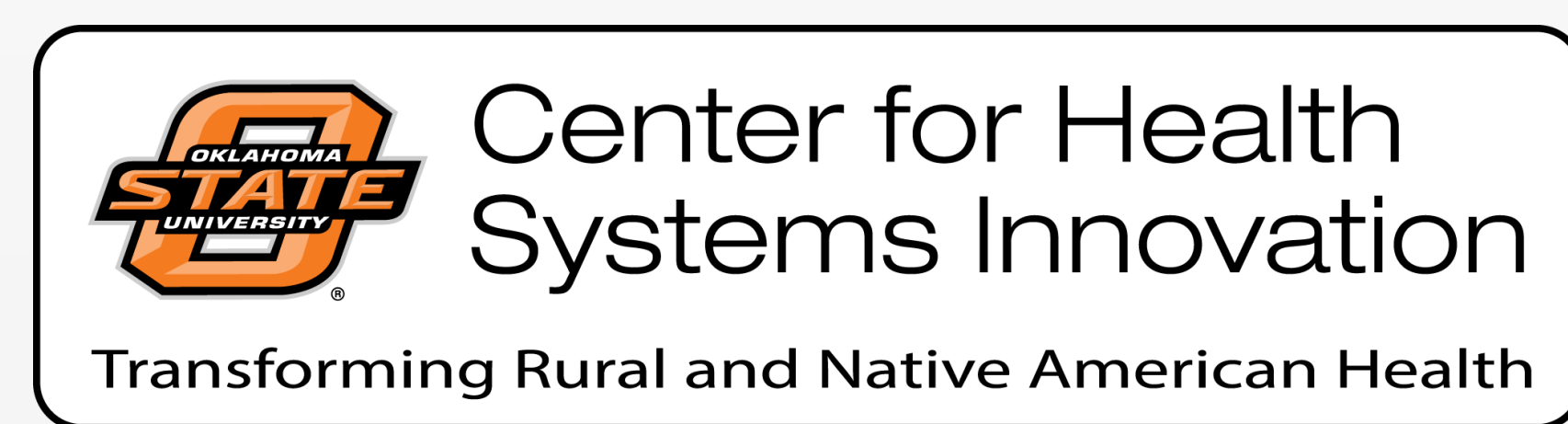


# A Retrospective, Matched Cohort Study of the Effectiveness of Common COPD Drug Treatments on 30-Day Readmissions

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## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent and progressive lung disease<sup>1</sup> and represents an important public health challenge<sup>2</sup>. Pharmacological treatment of COPD continues to be a challenging problem for clinicians in the US, especially in rural areas<sup>3</sup>. In spite of various treatment combinations, high 30-day readmissions for this disease continue to be a problem for hospitals facing penalties under Medicare Hospital Readmissions Reduction Program (HRRP)<sup>4</sup>. The most common pharmacological treatment combinations, fluticasone/salmeterol (Advair) and budesonide/formoterol (Symbicort), appear to be effective treatment options. However, an independent validation of the effectiveness of these treatments, and their combination with tiotropium (Spiriva), on controlling early hospital readmission is needed. Our study on the readmission rates between these combination and triple combination treatments will fill this gap.

## Descriptive Statistics

Table 1

Population	Drug Treatment	Total No. of Patients	No. of Patients Readmitted	Readmission %	P value
Drug Type	Fluticasone/salmeterol	8502	1323	7.78%	0.087
	Budesonide/formoterol	8502	1243	7.31%	
African American	Fluticasone/salmeterol	1273	202	8.22%	0.133
	Budesonide/formoterol	1185	215	8.75%	
Asian	Fluticasone/salmeterol	51	4	3.88%	0.056
	Budesonide/formoterol	52	11	10.68%	
Caucasian	Fluticasone/salmeterol	6693	1050	7.74%	0.004
	Budesonide/formoterol	6877	959	7.07%	
Hispanic	Fluticasone/salmeterol	62	11	10.19%	0.81
	Budesonide/formoterol	46	9	8.33%	
Native American	Fluticasone/salmeterol	53	5	5.32%	0.958
	Budesonide/formoterol	41	4	4.26%	
Biracial/Other	Fluticasone/salmeterol	171	27	8.36%	0.436
	Budesonide/formoterol	152	29	8.98%	
Divorced	Fluticasone/salmeterol	1689	264	8.34%	0.783
	Budesonide/formoterol	1476	236	7.46%	
Married	Fluticasone/salmeterol	3011	437	8.88%	0.578
	Budesonide/formoterol	3146	441	7.51%	
Single	Fluticasone/salmeterol	1923	317	8.35%	0.145
	Budesonide/formoterol	1874	277	7.30%	
Widowed	Fluticasone/salmeterol	1598	272	8.17%	0.088
	Budesonide/formoterol	1730	257	7.72%	
Self-Pay	Fluticasone/salmeterol	248	36	8.08%	0.008
	Budesonide/formoterol	197	13	2.92%	
Medicare/ Medicaid	Fluticasone/salmeterol	4839	842	8.68%	0.019
	Budesonide/formoterol	4857	759	7.83%	
Private Insurance	Fluticasone/salmeterol	522	54	5.90%	0.690
	Budesonide/formoterol	394	44	4.80%	
Female	Fluticasone/salmeterol	4787	750	7.94%	0.072
	Budesonide/formoterol	4663	669	7.08%	
Male	Fluticasone/salmeterol	3715	573	7.59%	0.568
	Budesonide/formoterol	3839	574	7.60%	
Rural Location	Fluticasone/salmeterol	1313	218	6.32%	0.915
	Budesonide/formoterol	2138	352	10.20%	
Urban Location	Fluticasone/salmeterol	7189	1105	8.15%	0.025
	Budesonide/formoterol	6364	891	6.57%	

Table 2

Population	Drug Treatment	Total No. of Patients	No. of Patients Readmitted	Readmission %	P value
Drug Type	Fluticasone/Salmeterol/Tiotropium	5553	1008	9.08%	0.045
	Budesonide/formoterol/Tiotropium	5553	928	8.36%	
African American	Fluticasone/salmeterol/Tiotropium	831	145	9.21%	0.030
	Budesonide/formoterol/Tiotropium	743	162	10.29%	
Asian	Fluticasone/salmeterol/Tiotropium	35	9	16.98%	0.560
	Budesonide/formoterol/Tiotropium	18	6	11.32%	
Caucasian	Fluticasone/salmeterol/Tiotropium	4351	804	9.09%	0.0008
	Budesonide/formoterol/Tiotropium	4493	710	8.03%	
Hispanic	Fluticasone/salmeterol/Tiotropium	44	8	9.41%	0.444
	Budesonide/formoterol/Tiotropium	41	5	5.88%	
Native American	Fluticasone/salmeterol/Tiotropium	27	3	6.00%	0.834
	Budesonide/formoterol/Tiotropium	23	3	6.00%	
Biracial/Other	Fluticasone/salmeterol/Tiotropium	127	22	9.57%	0.341
	Budesonide/formoterol/Tiotropium	103	23	10.00%	
Divorced	Fluticasone/salmeterol/Tiotropium	922	185	9.50%	0.088
	Budesonide/formoterol/Tiotropium	1026	175	8.98%	
Married	Fluticasone/salmeterol/Tiotropium	2057	362	8.88%	0.035
	Budesonide/formoterol/Tiotropium	2020	306	7.51%	
Single	Fluticasone/salmeterol/Tiotropium	893	139	6.72%	0.125
	Budesonide/formoterol/Tiotropium	1175	213	10.30%	
Widowed	Fluticasone/salmeterol/Tiotropium	1146	225	9.82%	0.489
	Budesonide/formoterol/Tiotropium	1146	212	9.25%	
Self-Pay	Fluticasone/salmeterol/Tiotropium	130	14	5.98%	0.589
	Budesonide/formoterol/Tiotropium	104	9	3.85%	
Medicare/ Medicaid	Fluticasone/salmeterol/Tiotropium	3065	632	10.00%	0.043
	Budesonide/formoterol/Tiotropium	3258	606	9.58%	
Private Insurance	Fluticasone/salmeterol/Tiotropium	378	60	9.45%	0.434
	Budesonide/formoterol/Tiotropium	257	35	5.51%	
Female	Fluticasone/salmeterol/Tiotropium	2883	517	8.93%	0.181
	Budesonide/formoterol/Tiotropium	2909	483	8.34%	
Male	Fluticasone/salmeterol/Tiotropium	2670	291	9.24%	0.136
	Budesonide/formoterol/Tiotropium	2644	445	8.37%	
Rural Location	Fluticasone/salmeterol/Tiotropium	677	124	6.16%	0.711
	Budesonide/formoterol/Tiotropium	1337	254	12.61%	
Urban Location	Fluticasone/salmeterol/Tiotropium	4876	884	9.72%	0.007
	Budesonide/formoterol/Tiotropium	4216	674	7.41%	

Tables 1 and 2 above show the total number of patients, the number of patients readmitted, and the 30-day readmission rates for each category.

Table 1: Chi-square analyses on readmission rates for combination therapies indicate that there is a significant difference in the 30-day readmission rates for Caucasians, patients who self-pay or utilize Medicare/Medicaid, and patients in urban locations.

Table 2: Chi-square analyses on readmission rates for triple therapies indicate that there is a significant difference in the 30-day readmission rates between drug types, as well as patients who are African Americans, Caucasians, married, utilize Medicare/Medicaid, and patients in urban locations.

The p-values are obtained from the association test indicating that if  $p < 0.05$  then there is a significant association between the categories and 30-day readmission (indicated in red).

## Methods

In this study, we conducted a phase IV (after market release) retrospective drug trial of combination treatments: fluticasone/salmeterol and budesonide/formoterol; triple combination treatments: budesonide/formoterol/tiotropium and fluticasone/salmeterol/tiotropium. Patient data came from a clinical dataset donated to Oklahoma State University by the Cerner Corporation. Data was utilized to compare 30-day readmission rates among COPD patients prescribed these common COPD treatment options. Using propensity score matching and chi-square analysis on patient demographics and hospital-associated variables, we tested for differences in readmission rates among patient populations in this matched cohort study. Relative risks (RR) and confidence interval (CI) estimates were also obtained and compared. Covariates used for these analyses were drug type, ethnicity, marital status, payer type, gender, and hospital location.

## Results

Figure 1

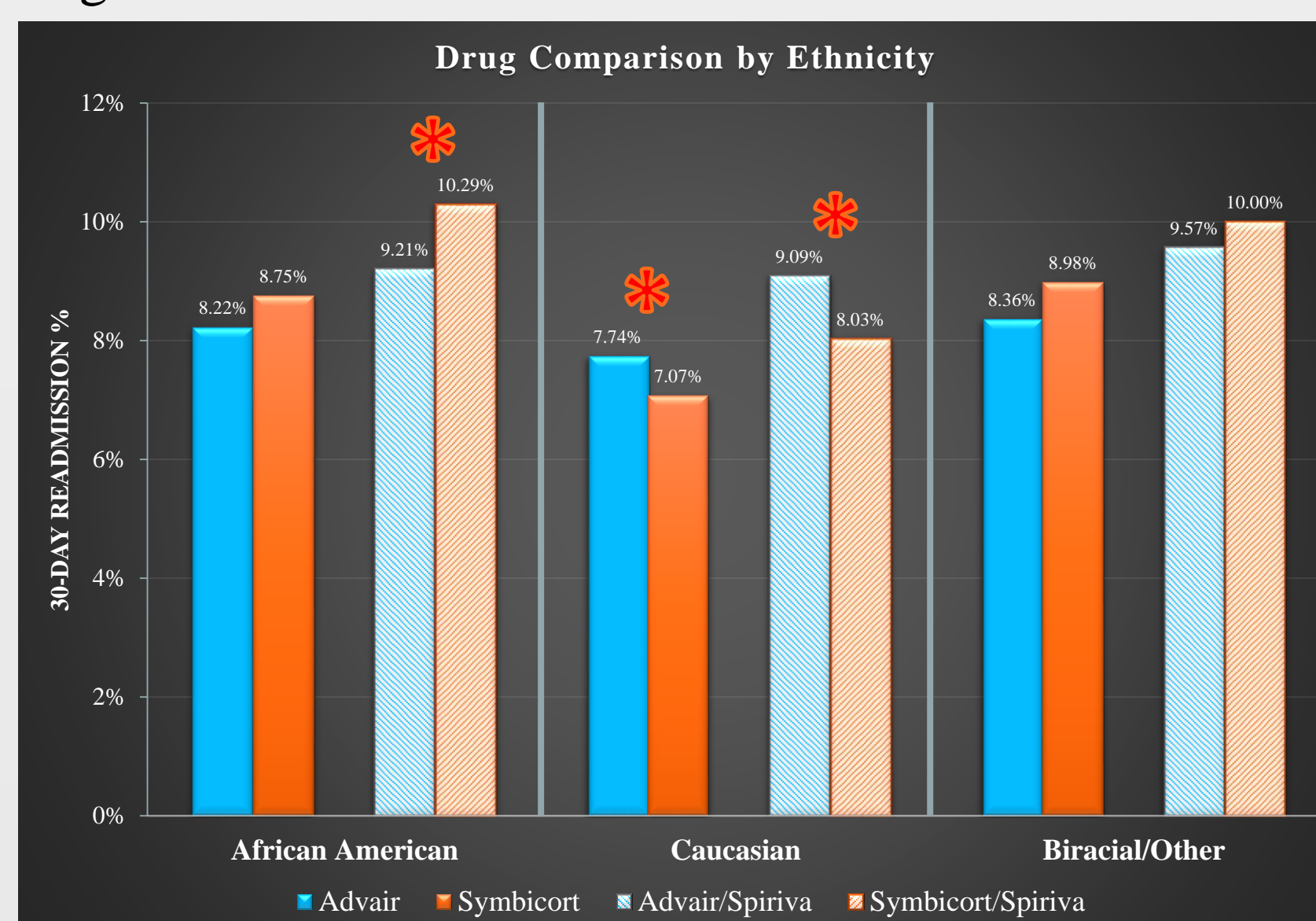


Figure 2

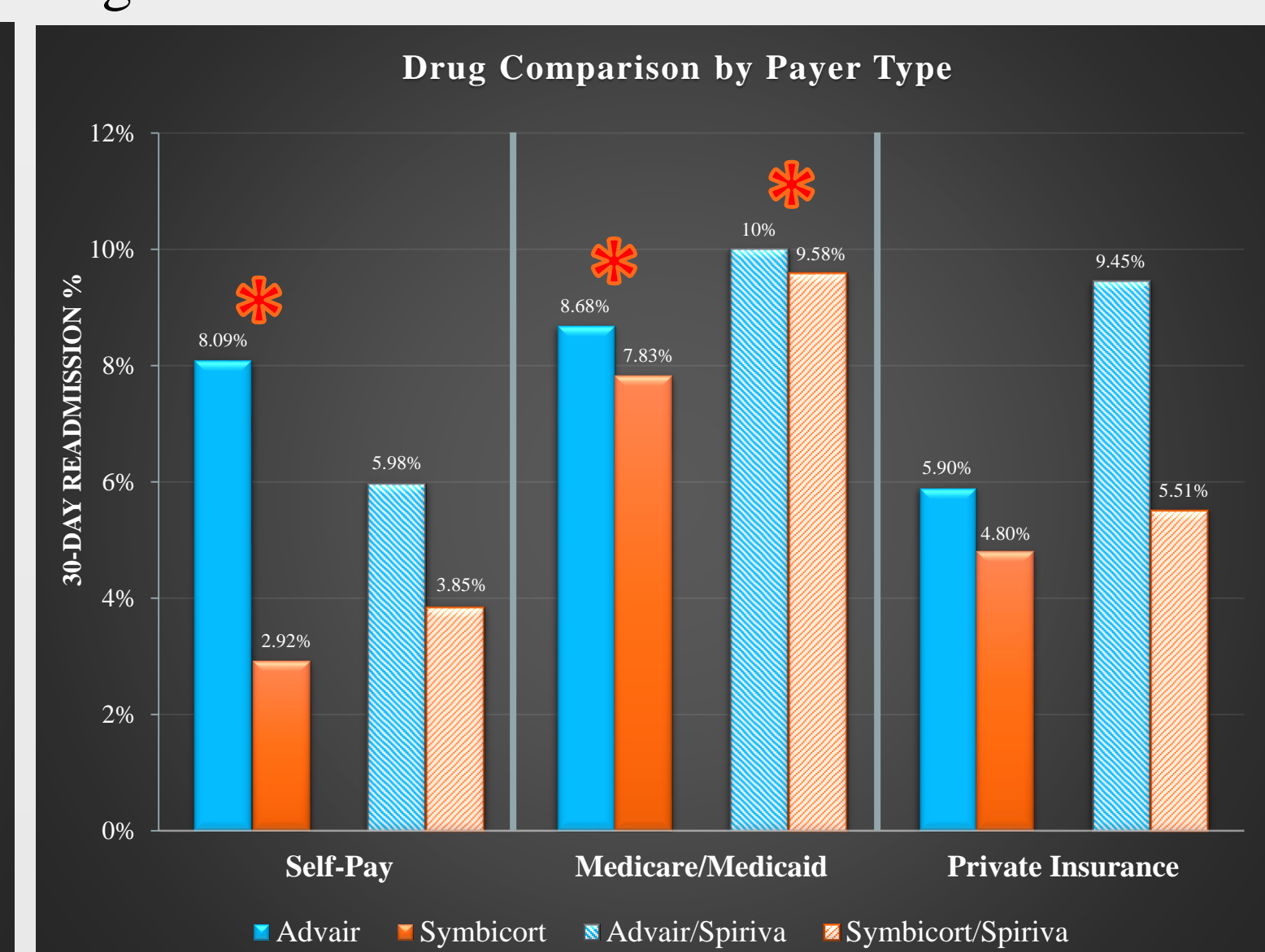


Figure 3

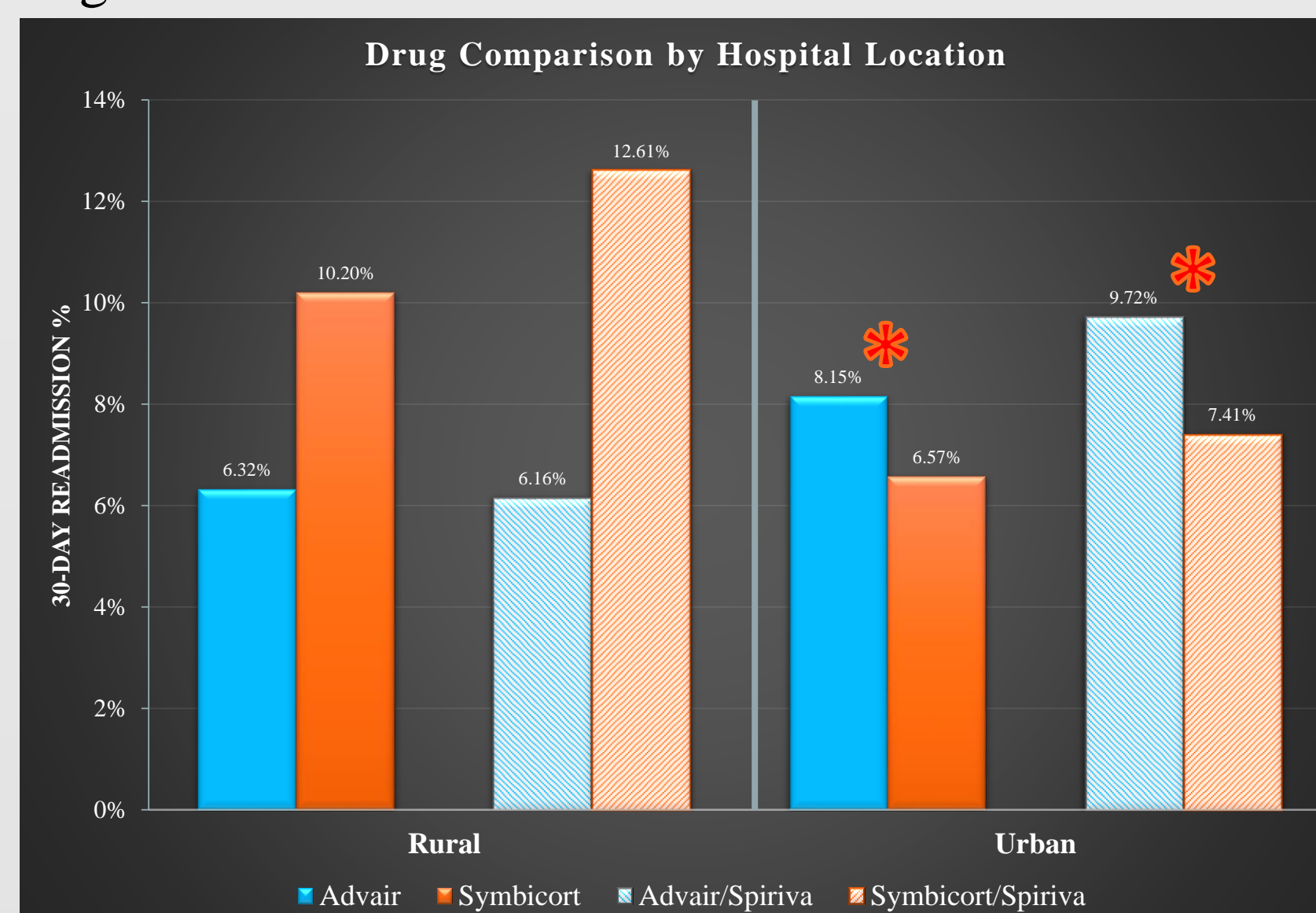
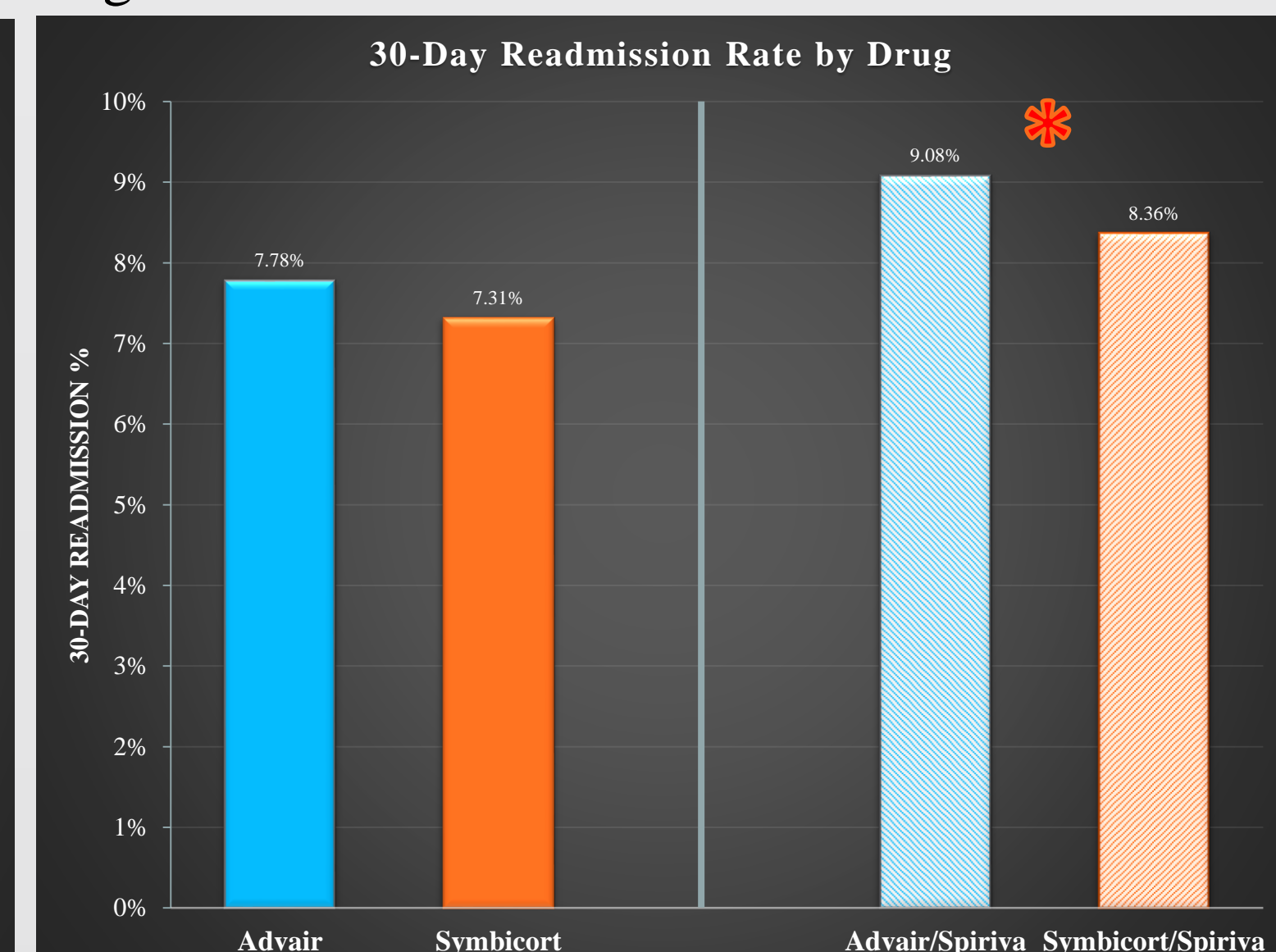


Figure 4



30-day readmission rates for different ethnicities, payers and hospital locations for combination and triple combination drugs are shown in Figure 1 - 3. Figure 4 represents the difference in 30-day readmission rates for combination and triple combination drugs. Advair = fluticasone/salmeterol (blue/blue striped bars); Symbicort = budesonide/formoterol (orange/orange striped bars); Spiriva = Tiotropium.  $P < 0.05$  was considered significant (\*).

Chi-square analysis showed that number of 30-day readmissions between combination drugs were significantly different in Caucasians [7.74 vs 7.07%; RR 1.13; CI 1.04-1.22;  $p < 0.05$ ], patients who self-pay [8.09 vs 2.92%; RR 2.2; CI 1.2-4.03;  $p < 0.05$ ], utilize Medicare/Medicaid [8.68 vs 7.83%; RR 1.114; CI 1.018-1.22;  $p < 0.05$ ] and patients in urban hospital locations [8.15 vs 6.57%; RR 1.1; CI 1.012-1.19;  $p < 0.05$ ]. Triple combination therapies had significantly different number of 30-day readmissions in African Americans [9.21 vs 10.29%; RR 1.25; CI 1.02-1.53;  $p < 0.05$ ], Caucasians [9.09 vs 8.03%; RR 1.17; CI 1.07-1.28;  $p < 0.001$ ], patients who utilize Medicare/Medicaid [10.0 vs 9.58%; RR 1.11; CI 1.0003-1.23;  $p < 0.05$ ] and patients in urban hospital locations [9.72 vs 7.41%; RR 1.13; CI 1.04-1.24;  $p < 0.05$ ]. No significant differences in number of 30-day readmissions between combination drugs (Advair vs Symbicort) were found. In contrast, separate chi-square analysis revealed significant differences in number of 30-day readmissions between triple combination therapies (Advair/Spiriva vs Symbicort/Spiriva) [9.08 vs 8.36%; RR 1.09; CI 1.002-1.18;  $p < 0.05$ ].

## Conclusion

Analysis of 30-day readmission rates between triple therapies showed that Fluticasone/salmeterol/tiotropium readmission rates were significantly higher than Budesonide/formoterol/tiotropium readmission rates. However, differences in rates were non-significant for combination therapies. When other covariates were considered further differences were highlighted, with budesonide/formoterol and budesonide/formoterol/tiotropium having lower readmission rates except in African Americans. Identifying drug therapies that have lower 30-day readmission among COPD patients could influence clinical decisions as providers make choices regarding patient care such as hospital length of stay and discharge options. However, due to the observational nature we cannot conclude with certainty that medication was the only factor responsible for any differences observed in this study. Further studies are needed to confirm and could provide information to guide further research for therapeutics and tools to better patient management post discharge.

## References

- Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of COPD 2017 Report [Internet]. 2017[cited 2018 Nov 6]. Available from: <http://goldcopd.org>.
- World Health Organization. Chronic obstructive pulmonary disease (COPD) fact sheet [Internet]. 2016 [cited 2018 Nov 6]. Available from: <http://www.who.int/mediacentre/factsheets/fs315/en/>.
- Croft JB, Wheaton AG, Liu Y, Xu F, Lu H, Matthews KA, Cunningham TJ, Wang Y, Holt JB. Urban-Rural county and state differences in chronic obstructive pulmonary disease-united states, 2015. *Morbidity and Mortality Weekly Report* 2018;67(7):205.
- Centers for Medicare & Medicaid Services. Readmissions reduction program (HRRP) [Internet]. Baltimore: CMS.gov; 2016 [cited 2018 Nov 6]. Available from <https://www.cms.gov/Medicare>.