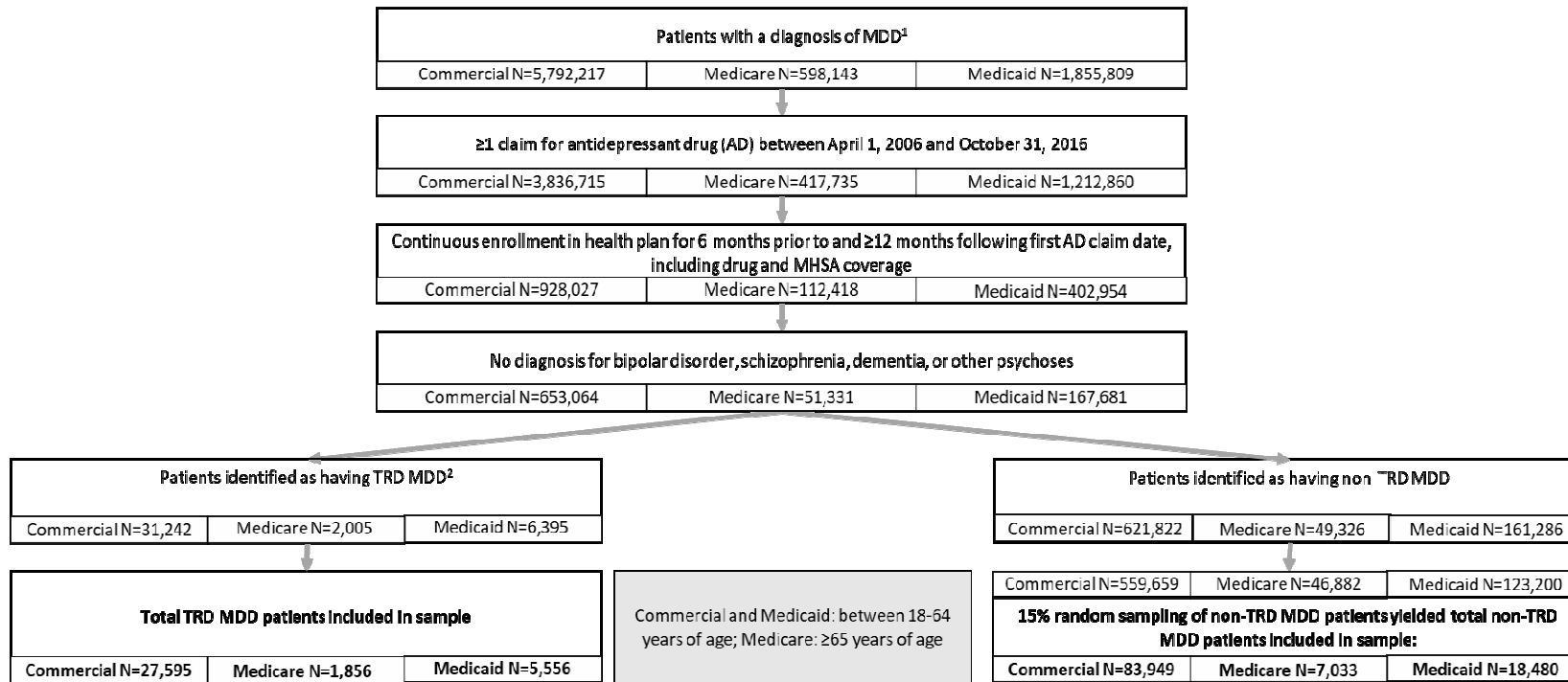


**CONSORT diagram of study sample**



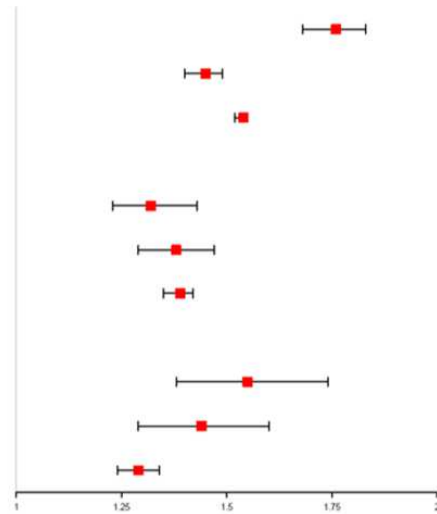
<sup>1</sup> MDD diagnosis codes: ICD-9-CM: 296.2x, 296.3x; ICD-10-CM: F32.x, F33.x

<sup>2</sup> Identification of TRD patients: ≥3 lines of therapy (LOT), ≥2 LOT with adequate dose and duration, subsequent unique LOT after 2 failed lines (i.e. TRD date), AND gap between each LOT prior to TRD date is <90 days; adequate duration: ≥6 weeks of treatment in each LOT with <14 day gap; adequate dose: ≥starting daily dose recommended by APA

## Incremental healthcare utilization of treatment-resistant depression in patients with major depressive disorder treated across national U.S. payers

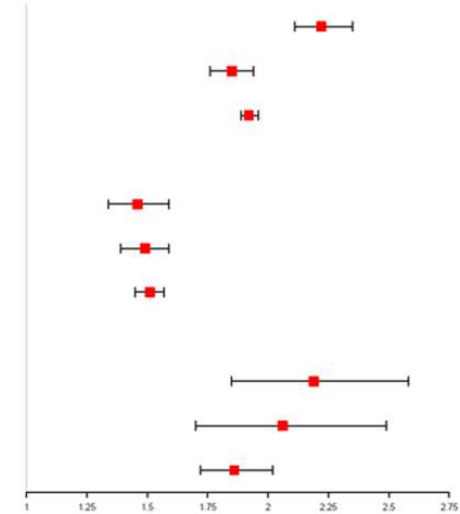
### All Cause Healthcare Utilization

Commercial	OR/IRR	Lower	Upper
Hospitalization	1.76	1.68	1.83
ED	1.45	1.4	1.49
Outpatient	1.54	1.52	1.55
Medicaid	OR/IRR	Lower	Upper
Hospitalization	1.32	1.23	1.43
ED	1.38	1.29	1.47
Outpatient	1.39	1.35	1.42
Medicare	OR/IRR	Lower	Upper
Hospitalization	1.55	1.38	1.74
ED	1.44	1.29	1.6
Outpatient	1.29	1.24	1.34



### Mental Health-Related Healthcare Utilization

Commercial	OR/IRR	Lower	Upper
Hospitalization	2.22	2.11	2.35
ED	1.85	1.76	1.94
Outpatient	1.92	1.89	1.96
Medicaid	OR/IRR	Lower	Upper
Hospitalization	1.46	1.34	1.59
ED	1.49	1.39	1.59
Outpatient	1.51	1.45	1.57
Medicare	OR/IRR	Lower	Upper
Hospitalization	2.19	1.85	2.58
ED	2.06	1.7	2.49
Outpatient	1.86	1.72	2.02



OR: odds ratio; IRR: incident rate ratio  
 Odds ratios are reported for hospitalizations and ED visits; Incident rate ratios are reports for outpatient visits

**Diagnosis codes for excluded comorbidities**

<b>Condition</b>	<b>ICD-9 Code</b>	<b>ICD-10 Code</b>
Bipolar disorder	296.0x-296.9x (except 296.2x, 296.3x)	F30.x, F31.x, F34.8x, F34.9, F39
Schizophrenia	295.x	F20.x, F21, F23, F25.x
Dementia	291.2, 291.1, 292.82, 290.40, 290.41, 290.42, 290.43, 294.10, 294.11, 290.x, 294.2, 294.21	F01.x, F02.x, F03.x, F10.27, F10.97, F13.27, F13.97, F18.17, F18.27, F18.97, F19.17, F19.27, F19.97, G31.0, G31.09, G31.83
Other Psychoses	298.x	F2.x

**Additional baseline characteristics across payers, stratified by TRD status**

Characteristics	Commercial					Medicaid					Medicare				
	No TRD (n=83,949)		TRD (n=27,595)		P-Value <sup>1</sup>	No TRD (n=18,480)		TRD (n=5,556)		P-Value <sup>1</sup>	No TRD (n=7,033)		TRD (n=1,856)		P-Value <sup>1</sup>
	N/Mean	%	N/Mean	%		N/Mean	%	N/Mean	%		N/Mean	%	N/Mean	%	
Pre-index MDD severity, n (%)															
Mild/Remission	1,654	1.97	447	1.62	0.000	307	1.66	63	1.13	0.005	84	1.19	31	1.67	0.107
Moderate	6,347	7.56	1,954	7.08	0.008	1,276	6.90	445	8.01	0.005	288	4.09	84	4.53	0.410
Severe	4,332	5.16	1,529	5.54	0.014	1,201	6.50	378	6.80	0.422	224	3.18	70	3.77	0.209
Unspecified	4,504	5.37	1,161	4.21	0.000	988	5.35	184	3.31	0.000	358	5.09	76	4.09	0.077
Unknown	67,112	79.94	22,504	81.55	0.000	14,708	79.59	4,486	80.74	0.060	6,079	86.44	1,595	85.94	0.579
Baseline MH-related HRU, n (%)															
Number of MH-related hospitalizations ≥ 1	3,175	3.78	1,177	4.27	0.000	1,912	10.35	571	10.28	0.882	341	4.85	115	6.20	0.019
Number of MH-related ED visits ≥ 1	3,177	3.78	1,169	4.24	0.001	3,357	18.17	1,024	18.43	0.654	208	2.96	62	3.34	0.392
Number of MH-related outpatient non-ED visits															
0	49,230	58.64	15,468	56.05	0.000	8,906	48.19	2,504	45.07	0.000	5,034	71.58	1,268	68.32	0.006
1	14,412	17.17	4,615	16.72	0.089	3,658	19.79	1,065	19.17	0.303	995	14.15	255	13.74	0.653
2+	20,307	24.19	7,512	27.22	0.000	5,916	32.01	1,987	35.76	0.000	1,004	14.28	333	17.94	0.000
Baseline all cause HRU, n (%)															
Number of all cause hospitalizations ≥ 1	7,294	8.69	2,848	10.32	0.000	3,571	19.32	1,013	18.23	0.070	1,438	20.45	427	23.01	0.016
Number of all cause ED visits ≥ 1	13,465	16.04	5,023	18.20	0.000	8,134	44.02	2,416	43.48	0.485	1,762	25.05	500	26.94	0.097
Number of all cause outpatient non-ED visits															
0	8,062	9.60	2,128	7.71	0.000	1,310	7.09	426	7.67	0.144	278	3.95	83	4.47	0.314
1	9,803	11.68	2,457	8.90	0.000	1,597	8.64	378	6.80	0.000	313	4.45	89	4.80	0.525
2	9,335	11.12	2,467	8.94	0.000	1,508	8.16	394	7.09	0.010	371	5.28	85	4.58	0.227
3+	56,749	67.60	20,543	74.44	0.000	14,065	76.11	4,358	78.44	0.000	6,071	86.32	1,599	86.15	0.851
Baseline all cause HRU, mean±SD															
Total all cause hospitalizations	0.11±0.40		0.13±0.45		0.000	0.27±0.72		0.26±0.71		0.448	0.25±0.57		0.27±0.56		0.126
Total all cause ED visits	0.24±0.77		0.28±0.83		0.000	1.04±2.05		1.04±2.03		0.969	0.43±0.98		0.47±0.97		0.092
Total all cause outpatient non-ED visits	7.02±8.23		8.76±9.70		0.000	10.38±16.63		11.04±16.38		0.009	13.00±13.11		14.33±13.75		0.000
Baseline MH-related HRU															
Total MH-related hospitalizations	0.04±0.23		0.05±0.25		0.000	0.13±0.47		0.13±0.47		0.933	0.05±0.24		0.07±0.28		0.016
Total MH-related ED visits	0.05±0.28		0.05±0.29		0.013	0.30±0.84		0.31±0.95		0.260	0.04±0.25		0.04±0.25		0.406
Total MH-related outpatient non-ED visits	1.66±4.00		1.92±4.43		0.000	2.89±10.25		3.06±10.56		0.277	0.88±2.72		1.04±2.66		0.026

<sup>1</sup>P-values obtained from a regression of each baseline variable as an outcome of interest on a dummy for TRD status