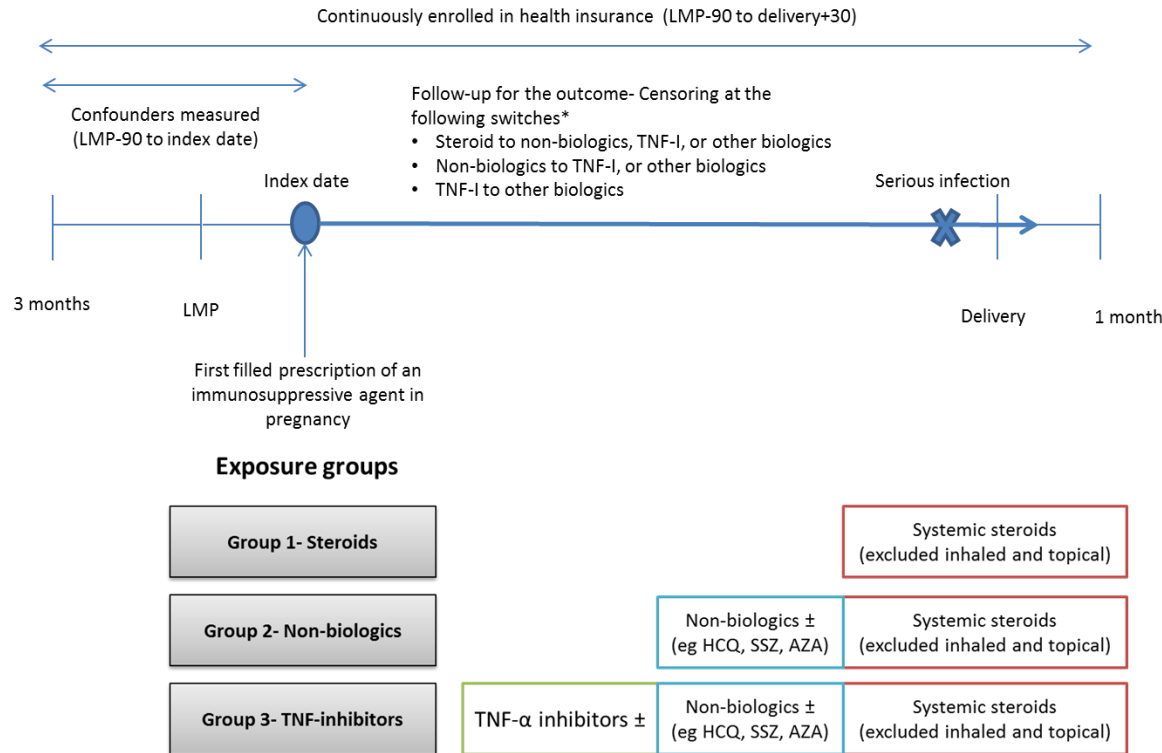


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eFigure 1- Study design



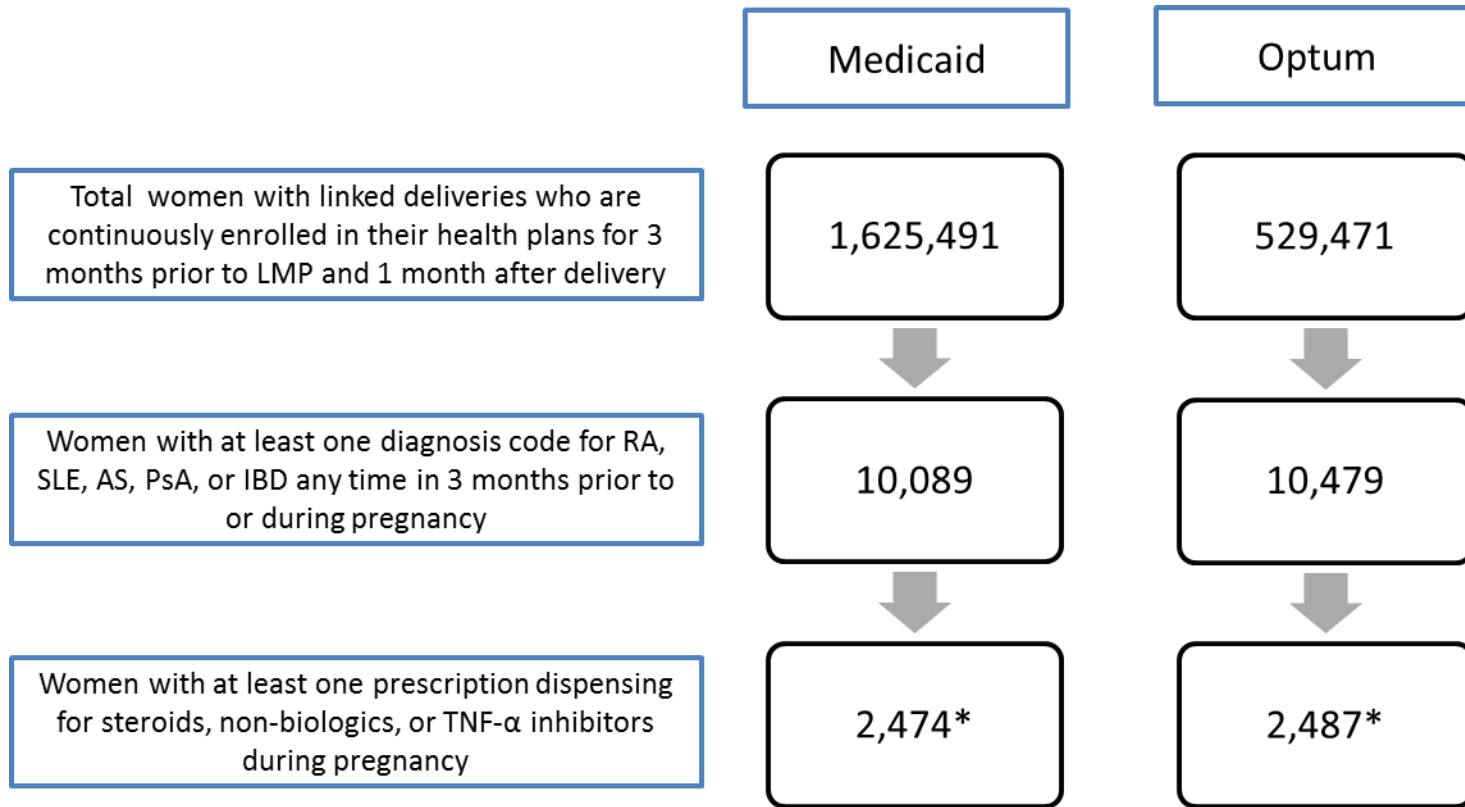
* 277 out of 2,598 steroid users (10.6%) were censored upon filling subsequent prescriptions for non-biologics (234), TNF-inhibitors (37), or other biologics (6). 36 out of 1,587 non-biologic users (2.2%) were censored upon filling subsequent prescriptions for TNF-inhibitors (31), or other biologics (5). None of the TNF-inhibitor users subsequently filled other biologic prescriptions. **Abbreviations:** AZA- azathioprine, HCQ- hydroxychloroquine, LMP- last menstrual period, SSZ- sulfasalazine, TNF-I- Tumor necrosis factor inhibitors.

Immunosuppressive agent use of each treatment group

Treatment group†	Immunosuppressive agent use	No. of patients
Steroids (n=2,598)	Steroids only	2,598
	Non-biologics only	1,013 (63.8%)
Non-biologics (n=1,587)	Non-biologics+steroids	574 (36.2%)
	TNF-inhibitors only	413 (53.2%)
TNF-inhibitors (n=776)	TNF-inhibitors+steroids	218 (28.1%)
	TNF-inhibitors+non-biologics	75 (9.7%)
	TNF-inhibitors+steroids+non-biologics	70 (9.0%)

† Treatment group defined based on the first filled prescription during pregnancy. Subsequent immunosuppressive agent use identified any time in pregnancy based on filling of a prescription of an agent from the respective class after the prescription of the index exposure.

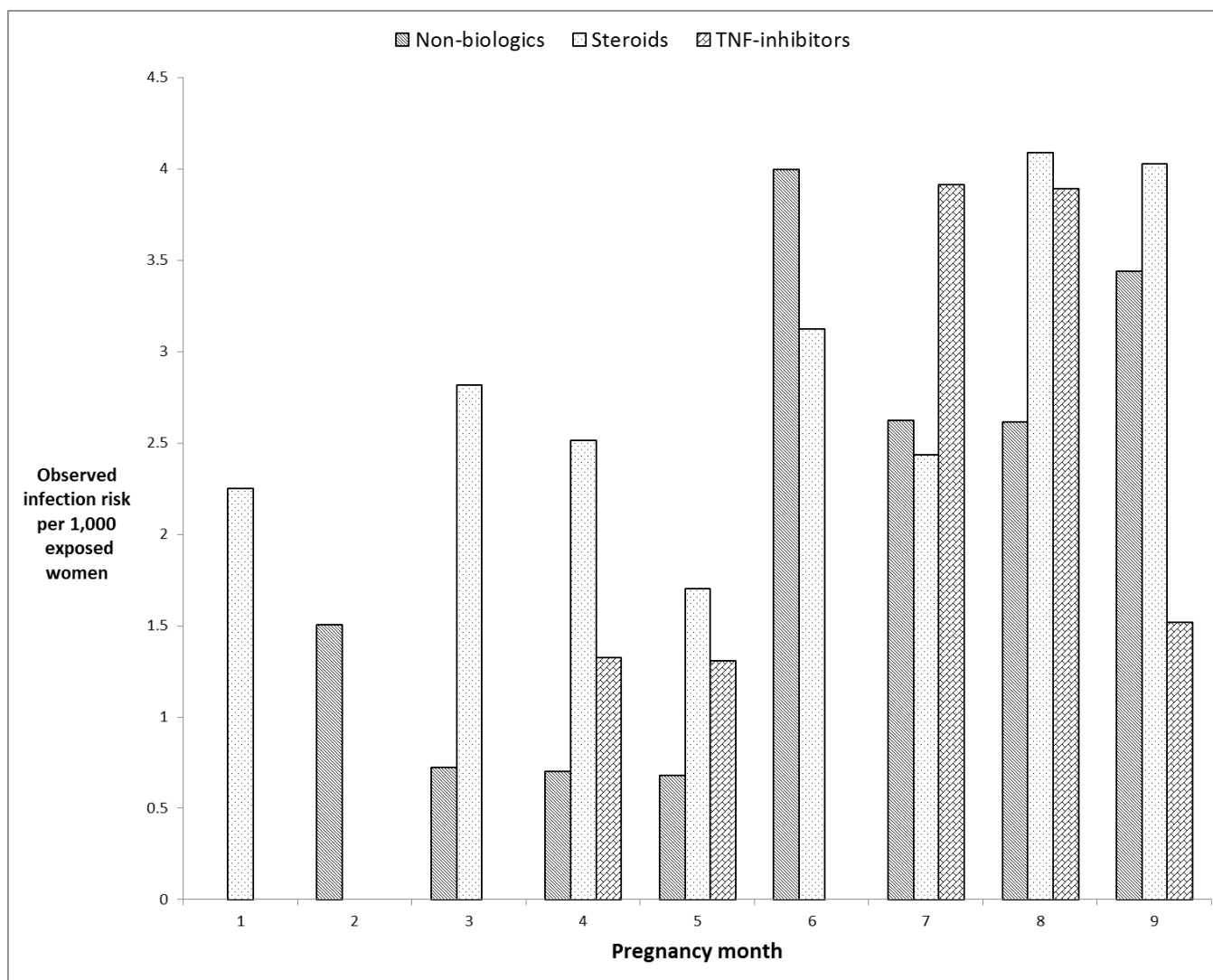
eFigure 2- Patient selection flow-chart



* The total numbers of patients 4,961; of which 776 TNF-inhibitor users, 1,587 non-biologic users, and 2,598 steroid users (Table 1).

Abbreviations: AS- ankylosing spondylitis, IBD- inflammatory bowel disease, PsA- Psoriatic arthritis, RA- rheumatoid arthritis, SLE- systemic lupus erythematosus.

eFigure 3- Patterns of infection risk in each treatment group by the month of pregnancy in women with autoimmune inflammatory conditions, Medicaid data 2000-2010 and Optum Clinformatics data 2004-2015



Infection risks calculated separately in the three treatment groups as a ratio of the total number of serious infection events to the total number of at-risk women under follow-up during each pregnancy month

eTable 1- The list of ICD-9 diagnosis codes and prescription immunosuppressive agents used to determine inclusion in this study

<i>Rheumatoid arthritis</i> diagnosis codes	714.xx
<i>Systemic lupus erythematosus</i> diagnosis codes	710.0x, 695.4x
<i>Ankylosing spondylitis</i> diagnosis codes	720.xx
<i>Psoriatic arthritis</i> diagnosis codes	696.0x
<i>Inflammatory bowel disease</i> diagnosis codes	555.xx, 556.xx
<i>Steroid agents included*</i>	prednisone, hydrocortisone, cortisone, prednisolone, methylprednisolone, dexamethasone, budesonide, triamcinolone, betamethasone
<i>Non-biologic disease modifying agents included</i>	<u>RA, AS, and PsA</u> : methotrexate, hydroxychloroquine, azathioprine, cyclosporine, leflunomide, minocycline, sulfasalazine. <u>SLE</u> : hydroxychloroquine, azathioprine, mycophenolate mofetil. <u>IBD</u> : azathioprine, mercaptopurine
<i>TNF-α inhibitors included</i>	adalimumab, certolizumab pegol, etanercept, golimumab, infliximab

* Only systemically administered steroids included, excluded if route of administration is topical or inhaled

eTable 2- Covariate distribution among patients included in each comparison prior to propensity score weighting, Medicaid data 2000-2010 and Optum Clinformatics data 2004-2015

	Patients with autoimmune inflammatory conditions*			Patients with autoimmune inflammatory conditions* other than SLE			Patients with autoimmune inflammatory conditions* other than SLE		
	<i>Non-biologics (n=1,587)</i>	<i>Steroids (n=2,598)</i>	<i>Std Diff†</i>	<i>TNF-inhibitors (n=776)</i>	<i>Steroids (n=1,879)</i>	<i>Std Diff†</i>	<i>TNF-inhibitors (n=776)</i>	<i>Non-biologics (n=816)</i>	<i>Std Diff†</i>
Demographics									
Age, years (Mean (SD))	29 (6.1)	28 (6.2)	10.7	30 (5.4)	29 (6.2)	28.4	30 (5.4)	30 (5.9)	11.7
Region (n (%))									3
Midwest	426 (26.8)	731 (28.1)	-2.9	235 (30.3)	549 (29.2)	2.3	235 (30.3)	236 (28.9)	-11.1
Northeast	275 (17.3)	394 (15.2)	5.9	104 (13.4)	276 (14.7)	-3.7	104 (13.4)	142 (17.4)	1.4
South	582 (36.7)	983 (37.8)	-2.4	279 (36)	734 (39.1)	-6.4	279 (36)	288 (35.3)	5
West	304 (19.2)	490 (18.9)	0.8	158 (20.4)	320 (17)	8.6	158 (20.4)	150 (18.4)	
Insurance type (n (%))									
Medicaid	744 (46.9)	1534 (59)	-24.6	196 (25.3)	1033 (55)	-63.6	196 (25.3)	352 (43.1)	-38.4
Optum Clinformatics	843 (53.1)	1064 (41)	24.6	580 (74.7)	846 (45)	63.6	580 (74.7)	464 (56.9)	38.4
Autoimmune inflammatory condition diagnoses (n (%))									
AS	45 (2.8)	480 (18.5)	-52.4	58 (7.5)	480 (25.5)	-50.2	58 (7.5)	45 (5.5)	8
PsA	17 (1.1)	44 (1.7)	-5.3	82 (10.6)	44 (2.3)	34	82 (10.6)	17 (2.1)	35.4
RA	496 (31.3)	931 (35.8)	-9.7	370 (47.7)	931 (49.5)	-3.7	370 (47.7)	496 (60.8)	-26.5
SLE	933 (58.8)	880 (33.9)	51.6	13 (1.7)	161 (8.6)	-31.7	13 (1.7)	162 (19.9)	-61.3
IBD	295 (18.6)	494 (19)	-1.1	334 (43)	494 (26.3)	35.8	334 (43)	295 (36.2)	14.1
Immunosuppressive medication use at baseline (n (%))[#]									
Steroids	989 (38.1)	589 (37.1)	2.1	245 (31.6)	720 (38.3)	-14.1	245 (31.6)	285 (34.9)	-7.0
Non-biologics	1,070 (67.4)	280 (10.8)	142.4	133 (17.1)	154 (8.2)	27.2	133 (17.1)	489 (59.9)	-97.9
TNF-inhibitors	43 (2.7)	97 (3.7)	-5.7	682 (87.9)	96 (5.1)	297.6	682 (87.9)	42 (5.1)	297.6
Other medical conditions and medication use at baseline (n (%))									

Anemia	139 (8.8)	229 (8.8)	-0.2		45 (5.8)	155 (8.2)	-9.6		45 (5.8)	71 (8.7)	-11.2
Chronic respiratory conditions	23 (1.4)	107 (4.1)	-16.3		<11 [‡]	86 (4.6)	-20.6		<11 [‡]	11 (1.3)	-1.7
Pre-existing diabetes mellitus	29 (1.8)	78 (3)	-7.7		<11 [‡]	59 (3.1)	-12.6		<11 [‡]	16 (2)	-5.3
Drug abuse or dependence	43 (2.7)	164 (6.3)	-17.4		11 (1.4)	126 (6.7)	-27		11 (1.4)	29 (3.6)	-13.8
Renal disease	80 (5)	72 (2.8)	11.7		<11 [‡]	27 (1.4)	-11.1		<11 [‡]	11 (1.3)	-10.4
Prior infections	17 (1.1)	34 (1.3)	-2.2		<11 [‡]	26 (1.4)	-10.7		<11 [‡]	<11 [‡]	-8.3
Insulin	18 (1.1)	58 (2.2)	-8.5		<11 [‡]	42 (2.2)	-10.7		<11 [‡]	<11 [‡]	-0.8
Oral hypoglycemic medications	27 (1.7)	60 (2.3)	-4.3		<11 [‡]	47 (2.5)	-10		<11 [‡]	16 (2)	-6.5
Opioids	422 (26.6)	1100 (42.3)	-33.6		193 (24.9)	853 (45.4)	-44		193 (24.9)	220 (27)	-4.8
Benzodiazepines	110 (6.9)	304 (11.7)	-16.5		67 (8.6)	236 (12.6)	-12.8		67 (8.6)	61 (7.5)	4.3
Antidepressants	286 (18)	580 (22.3)	-10.7		131 (16.9)	435 (23.2)	-15.7		131 (16.9)	155 (19)	-5.5
Antihypertensive medications	185 (11.7)	241 (9.3)	7.8		34 (4.4)	140 (7.5)	-13		34 (4.4)	67 (8.2)	-15.8
Healthcare use characteristics (Mean (SD))											
Number of distinct prescription medications	3 (2.9)	4 (3.4)	-22		2 (2.8)	4 (3.5)	-38.6		2 (2.8)	3 (2.8)	-10.4
Number of hospitalization	0 (0.3)	0 (0.4)	-18.1		0 (0.2)	0 (0.4)	-22.3		0 (0.2)	0 (0.3)	-6.7
Number of outpatient visits	6 (6.1)	9 (8.3)	-36.5		6 (5.5)	9 (8.5)	-45.5		6 (5.5)	6 (6.3)	-7.4

Abbreviations--: AS- ankylosing spondylitis, IBD- inflammatory bowel disease, PsA- Psoriatic arthritis, RA- rheumatoid arthritis, SLE- systemic lupus erythematosus, Std Diff- Standardized difference, SD- Standard deviation, TNF- tumor necrosis factor

*Autoimmune inflammatory conditions included ankylosing spondylitis, inflammatory bowel disease, psoriatic arthritis, rheumatoid arthritis, and systemic lupus erythematosus (SLE). For the comparisons involving TNF-inhibitors, we excluded patients with only SLE as TNF-inhibitors are not indicated for the treatment of SLE.

†Standardized difference values of 10 or greater indicate substantial imbalance in a particular covariate between the two treatment groups.

‡Actual numbers suppressed as required per data use agreement with the Centers for Medicare and Medicaid Services for counts <11.

Not included in the propensity score models

eTable 3- Crude absolute and relative risk estimates for serious infections in pregnant women treated with immunosuppressive agents stratified by autoimmune conditions, Medicaid data 2000-2010 and Optum Clinformatics data 2004-2015

Population and drug exposure	Number of exposed pregnancies	Person-years	Serious infection events	Incidence rate/100 person-years (95% CI)	Incidence rate difference/100 person-years (95% CI)	Incidence rate ratio (95% CI)
Inflammatory bowel disease						
Steroid	494	196	<11†	<11†	Ref	Ref
Non-biologics	295	180	<11†	<11†	-0.3 (-4.1,3.5)	0.92 (0.31,2.74)
TNF-inhibitors	334	224	<11†	<11†	-1.8 (-5,1.4)	0.5 (0.15,1.71)
Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis						
Steroid	1385	659	22	3.3 (2.1,5.1)	Ref	Ref
Non-biologics	521	329	<11†	<11†	-2.1 (-3.9,-0.3)	0.36 (0.12,1.04)
TNF-inhibitors	442	299	<11†	<11†	-2.0 (-3.9,-0.1)	0.39 (0.13,1.13)
Systemic lupus erythamatosus						
Steroid	719	306	11	3.6 (1.8,6.4)	Ref	Ref
Non-biologics	771	482	13	2.7 (1.4,4.6)	-0.9 (-3.5,1.7)	0.75 (0.34,1.67)

Abbreviations: CI- Confidence interval, IBD- inflammatory bowel disease, RA- rheumatoid arthritis, SpA- Spondyloarthritis (includes Psoriatic arthritis and ankylosing spondylitis), TNF- tumor necrosis factor

*Serious infections- A composite outcome consisting of hospitalized bacterial (meningitis, encephalitis, cellulitis, endocarditis, pneumonia, pyelonephritis, osteomyelitis, and bacteremia) or opportunistic infections (tuberculosis, systemic candidiasis, cryptococcosis, aspergillosis)

† Actual numbers and rates suppressed as required per data use agreement with the Centers for Medicare and Medicaid Services for counts <11.

eTable 4- Covariate distribution among patients included in each comparison for autoimmune condition stratified analysis after to propensity score weighting, Medicaid data 2000-2010 and Optum Clinformatics data 2004-2015

	Non-biologics vs steroids						TNF-inhibitors vs steroids				TNF-inhibitors vs non-biologics			
	IBD		RA, PsA, AS		SLE		IBD		RA, PsA, AS		IBD		RA, PsA, AS	
	Non-biologics	Steroids	Non-biologics	Steroids	Non-biologics	Steroids	TNF-inhibitors	Steroids	TNF-inhibitors	Steroids	TNF-inhibitors	Non-biologics	TNF-inhibitors	Non-biologics
Total	271	444	516	1281	703	704	260	392	441	1186	322	232	402	499
Demographics														
Age (mean years (SD))	29 (6.1)	29 (5.7)	30 (5.8)	31 (6)	28 (6.2)	28 (6.2)	30 (4.9)	29 (5.7)	31 (5.8)	31 (6.1)	29 (5.2)	29 (5.7)	31 (5.9)	31 (5.3)
Region (%)														
Midwest	34.7	35.2	25.4	26.0	25.0	22.9	31.9	33.8	25.6	25.5	34.8	36.6	25.6	25.9
Northeast	17.3	18.8	17.4	17.0	17.4	18.1	12.3	13.0	15.9	17.7	15.7	15.9	15.2	16.5
South	36.9	34.7	34.7	34.6	37.1	36.0	40.0	42.4	32.7	30.6	40.6	36.2	32.8	29.8
West	11.1	11.3	22.5	22.4	20.5	23.0	15.8	10.8	25.9	26.2	8.9	11.2	26.4	27.8
Insurance type (%)														
Medicaid	39.5	38.7	46.1	46.2	53.9	54.4	24.6	28.2	29.0	26.1	36.9	34.5	30.6	31.3
Optum Clinformatics	60.5	61.3	53.9	53.8	46.1	45.6	75.4	71.8	71.0	73.9	63.1	65.5	69.4	68.7
Other medical conditions and medication use at baseline (%)														
Anemia	10.7	10.0	6.0	6.1	8.7	9.0	10.4	9.8	<11†	1.9	14.1	12.1	2.5	2.2
Chronic respiratory conditions	<11†	<11†	<11†	<11†	1.6	2.0	<11†	<11†	<11†	1.2	<11†	<11†	<11†	<11†
Pre-existing diabetes mellitus	<11†	<11†	2.5	3.1	1.6	1.4	<11†	<11†	<11†	1.1	<11†	<11†	<11†	<11†
Drug abuse or dependence	4.8	4.4	2.9	2.8	2.0	1.9	<11†	<11†	<11†	0.9	<11†	<11†	<11†	<11†
Renal disease	<11†	<11†	<11†	2.1	8.3	12.1	<11†	<11†	<11†	<11†	<11†	<11†	<11†	<11†
Prior serious infections	<11†	<11†	<11†	<11†	<11†	2.2	<11†	<11†	<11†	<11†	<11†	<11†	<11†	<11†
Insulin	<11†	<11†	<11†	<11†	<11†	<11†	<11†	<11†	<11†	1.3	<11†	<11†	<11†	<11†
Oral hypoglycemic medications	<11†	<11†	2.3	2.5	<11†	<11†	<11†	<11†	<11†	1.0	<11†	<11†	<11†	<11†
Opioids	21.4	17.5	31.0	31.8	27.3	26.7	27.7	36.8	23.6	22.8	22.1	20.7	23.4	22.1
Benzodiazepines	9.2	6.8	6.6	7.1	6.5	6.4	9.6	11.0	7.9	7.6	9.3	10.8	6.5	7.1
Antidepressants	16.2	17.7	20.5	21.4	17.1	16.2	18.8	18.3	15.4	13.2	17.6	16.8	15.2	15.9

Antihypertensive medications	<11†	<11†	10.5	10.0	15.5	16.5	5.4	7.1	3.6	3.3	2.9	3.4	3.7	3.1
Healthcare use characteristics (mean number (SD))														
distinct prescription medications	2 (2.5)	2 (2.5)	3 (3)	3 (2.8)	3 (3)	3 (2.7)	3 (2.9)	3 (3)	2 (2.8)	2 (2.7)	3 (3.4)	2 (2.5)	2 (2.7)	3 (2.6)
hospitalizations	0.1 (0.4)	0.1 (0.3)	0.1 (0.2)	0 (0.2)	0.1 (0.3)	0.1 (0.3)	0.1 (0.4)	0.1 (0.3)	0.1 (0.1)	0.1 (0.1)	0.1 (0.4)	0.1 (0.4)	0.1 (0.1)	0.1 (0.1)
outpatient visits	6 (6.1)	6 (7)	6 (6.5)	6 (5.9)	6 (6)	6 (6)	7 (5.7)	8 (8.7)	5 (5.5)	5 (5.6)	7 (5.3)	6 (6.3)	5 (5.7)	6 (5.2)

† Actual numbers and proportions suppressed as required per data use agreement with the Centers for Medicare and Medicaid Services for counts <11.