

Supplementary Online Content

Dommasch ED, Kim SC, Lee MP, Gagne JJ. Risk of serious infection in patients receiving systemic medications for the treatment of psoriasis. *JAMA Dermatol*. Published online May 10, 2019. doi:10.1001/jamadermatol.2019.1121

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. ICD-CM-9 codes for serious infection and associated positive predictive values (PPV)^a

Serious Infection Type	Primary Discharge ICD-CM-9 Codes ^b	PPV (%)
Pneumonia-primary definition	003.22, 480.x*, 481, 482.x, 483.x, 484.x, 485.x, 486.x, 487.0	96.5
Pneumonia-secondary definition (primary diagnosis code with pneumonia diagnosis (above) in any other diagnosis field)	510.x, 038.x, 790.7, 995.91, 995.92	
Meningitis/encephalitis	003.21, 036.0, 047.x, 049.x, 053.0, 054.72, 072.1, 091.81, 094.2, 098.82, 100.81, 320.x, 036.1, 054.3, 056.01, 058.21, 058.29, 062.x, 063.x, 064.x, 066.41, 072.2, 094.81, 130.0, 323.x	50.0
Bacteremia/Sepsis ^c	038.x, 790.7, 995.91, 995.92	82.6
Cellulitis/Soft-Tissue Infections	035, 040.0, 569.61, 681.x, 682.x, 728.86, 785.4	91.1
Endocarditis	036.42, 074.22, 093.2x, 098.84, 421.x, 422.92	75.0
Pyelonephritis	590.x	87.6
Septic Arthritis/Osteomyelitis	003.23, 056.71, 098.5x, 711.0, 711.00–711.07, 711.09, 711.9x, 003.24, 376.03, 526.4, 730.0x, 730.1x, 730.2x	75.9

^a Table adapted from: Wiese, A. D., Griffin, M. R., Stein, C. M., Schaffner, W., Greevy, R. A., Mitchel, E. F., Jr., & Grijalva, C. G. (2018). Validation of discharge diagnosis codes to identify serious infections among middle age and older adults. *BMJ Open*, 8(6), e020857.

^b x indicates numeric values 0-9

^c Without a diagnosis of pneumonia in any other field

eTable 2. Patient flow chart for Optum© Clinformatics® Data Mart

Psoriasis Parent Cohort																	
	Less Excluded Patients	Remaining Patients															
All patients		68,328,408															
Did not meet cohort entry criteria	-68,151,390	177,018															
Excluded due to insufficient enrollment	-8,473	168,545															
Excluded based on Age	-4,772	163,773															
Excluded based on use of other systemic meds	-17,680	146,093															
Excluded based on other autoimmune conditions	-8,150	137,943															
Excluded based on history of malignancy	-2,712	135,231															
Excluded based on history serious infections	-386	134,845															
Psoriasis Cohort		134,845															
	Acitretin vs MTX^a		Adalimumab vs MTX		Apremilast vs MTX		Etanercept vs MTX		Infliximab vs MTX		Ustekinumab vs MTX						
Psoriasis Cohort		134,845		134,845		134,845		134,845		134,845		134,845					
Not exposed to medication	-117,763	17,082		-112,226	22,619		-119,542	15,303		-109,578	25,267		-120,823	14,022		-116,286	18,559
Excluded due to insufficient enrollment	-201	16,881		-295	22,324		-200	15,103		-286	24,981		-167	13,855		-259	18,300
Excluded due to prior use of referent	-3,983	12,898		-3,716	18,608		-3,930	11,173		-3,778	21,203		-3,971	9,884		-3,822	14,478
Excluded due to prior use of exposure	-1,117	11,781		-2,927	15,681		-160	11,013		-5,611	15,592		-93	9,791		-1,214	13,264

Excluded because patient qualified in >1 exposure category	-1	11,780		-1	15,680		0	11,013		-1	15,591		0	9,791		0	13,264
Final cohort		11,780			15,680			11,013			15,591			9,791			13,264

^a MTX,

methotrexate

eTable 3. Patient flow chart for Truven MarketScan

	Psoriasis Parent Cohort											
	Less Excluded Patients	Remaining Patients										
All patients		185,306,593										
Did not meet cohort entry criteria	-184,835,058	471,535										
Excluded due to insufficient enrollment	-23,390	448,145										
Excluded based on Age	-13,910	434,235										
Excluded based on use of other systemic meds	-22,058	412,177										
Excluded based on other autoimmune conditions	-26,749	385,428										
Excluded based on history of malignancy	-7,181	378,247										
Excluded based on history serious infections	-510	377,737										
Psoriasis Cohort		377,737										
	Acitretin vs MTX^a		Adalimumab vs MTX		Apremilast vs MTX		Etanercept vs MTX		Infliximab vs MTX		Ustekinumab vs MTX	
Psoriasis Cohort		377,737		377,737		377,737		377,737		377,737		377,737
Not exposed to medication	-335,350	42,387	-321,499	56,238	-340,071	37,666	-319,189	58,548	-343,762	33,975	-335,195	42,542
Excluded due to insufficient enrollment	-631	41,756	-950	55,288	-553	37,113	-1,061	57,487	-518	33,457	-642	41,900
Excluded due to prior use of referent	-9,498	32,258	-8,611	46,677	-9,279	27,834	-8,797	48,690	-9,519	23,938	-9,114	32,786
Excluded due to prior use of exposure	-2,819	29,439	-8,092	38,585	-327	27,507	-10,961	37,729	-230	23,708	-2,339	30,447
Excluded because patient qualified in >1 exposure category	-2	29,437	-2	38,583	0	27,507	-2	37,727	0	23,708	-1	30,446

Final cohort		29,437		38,583		27,507		37,727		23,708		30,446
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^a MTX, methotrexate

eTable 4. Censoring reasons for medication cohorts for Optum© Clinformatics® Data Mart and Truven MarketScan for systemic medications compared to methotrexate

	Reference group: Methotrexate Users (compared to adalimumab)	Adalimumab users	Acitretin users	Apremilast users	Etanercept users	Infliximab Users	Ustekinumab Users
Optum© Clinformatics® Data Mart							
No. of patients	8,470	7,181	2,726	1,623	7,102	408	4,085
Median Follow-Up Time (Days) [IQR]	215 [146, 399]	257 [146, 463]	188 [148, 312]	169 [98, 275]	287 [173, 537]	217 [119, 377]	251 [146, 437]
Censoring Reasons							
Outcome	112 (1.3%)	79 (1.1%)	30 (1.1%)	4 (0.2%)	68 (1.0%)	6 (1.5%)	21 (0.5%)
Start of an additional exposure (crossover)	695 (8.2%)	366 (5.1%)	137 (5.0%)	39 (2.4%)	289 (4.1%)	43 (10.5%)	121 (3.0%)
End of index exposure	4,300 (50.8%)	3,004 (41.8%)	1,792 (65.7%)	538 (33.1%)	3,694 (52.0%)	199 (48.8%)	1,542 (37.7%)
Specified date reached (10/01/2015)	918 (10.8%)	1,044 (14.5%)	138 (5.1%)	502 (30.9%)	388 (5.5%)	44 (10.8%)	796 (19.5%)
Death/Disenrollment	2445 (28.9%)	2688 (37.4%)	629 (23.1%)	540 (33.3%)	2663 (37.5%)	116 (28.4%)	1605 (39.3%)
Truven MarketScan							
No. of patients	20,609	17,912	7,456	4,476	16,791	1,027	7,841
Median Follow-Up Time (Days) [IQR]	209 [146, 391]	278 [153, 503]	202 [148, 328]	148 [73, 239]	313 [188, 587]	273 [147, 481]	262 [146, 458]
Censoring Reasons							
Outcome	426 (1.1%)	229 (1.1%)	81 (1.1%)	11 (0.2%)	168 (1.0%)	20 (1.9%)	56 (0.7%)
Start of an additional exposure (crossover)	3,286 (8.5%)	2,249 (10.9%)	418 (5.6%)	85 (1.9%)	672 (4.0%)	265 (25.8%)	244 (3.1%)
End of index exposure	17,282 (44.9%)	10,156 (49.3%)	4,946 (66.3%)	889 (19.9%)	8,682 (51.7%)	579 (56.4%)	2,755 (35.1%)
Specified date reached (10/01/2015)	4,810 (12.5%)	2,021 (9.8%)	369 (4.9%)	1,588 (35.5%)	1,420 (8.5%)	63 (6.1%)	1,774 (22.6%)
Death/Disenrollment	5954 (28.9%)	6763 (37.8%)	1642 (22.0%)	1903 (42.5%)	5849 (34.9%)	100 (9.74%)	3012 (38.4%)

eTable 5. Matched cohorts for systemic medications compared to methotrexate in Optum© Clinformatics® Data Mart and Truven MarketScan

Variable	Optum CDM			Truven Marketscan		
	Methotrexate Users	Acitretin users	Abs Std Dif ^a	Methotrexate Users	Acitretin users	Abs Std Dif
Number of patients	2,722	2,722		7,454	7,454	
Overweight/obesity; n (%)	114 (4.2%)	137 (5.0%)	0.04	242 (3.2%)	256 (3.4%)	0.01
Gender						
...M = MALE; n (%)	1,601 (58.8%)	1,578 (58.0%)	0.017	4,286 (57.5%)	4,220 (56.6%)	0.018
...F = FEMALE; n (%)	1,121 (41.2%)	1,144 (42.0%)		3,168 (42.5%)	3,234 (43.4%)	
Smoking; n (%)	135 (5.0%)	148 (5.4%)	0.022	252 (3.4%)	284 (3.8%)	0.023
CCI Combined Comorbidity Score (180 days)						
...mean (sd)	0.14 (1.03)	0.13 (1.06)	0.003	0.07 (0.83)	0.08 (0.91)	0.012
...median [IQR] ^b	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]		0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Influenza vaccination; n (%)	247 (9.1%)	283 (10.4%)	0.045	584 (7.8%)	639 (8.6%)	0.027
Lipid screening; n (%)	21 (0.8%)	23 (0.8%)	0.008	38 (0.5%)	46 (0.6%)	0.014
Nursing home; n (%)	10 (0.4%)	8 (0.3%)	0.013	4 (0.1%)	9 (0.1%)	0.023
Any office visit; n (%)	2,651 (97.4%)	2,654 (97.5%)	0.007	7,250 (97.3%)	7,259 (97.4%)	0.007
ER visit; n (%)	217 (8.0%)	236 (8.7%)	0.025	676 (9.1%)	717 (9.6%)	0.019
Occurrence of inpatient hospitalization; n (%)	111 (4.1%)	125 (4.6%)	0.025	306 (4.1%)	334 (4.5%)	0.019
Occurrence of laboratory tests; n (%)	2,043 (75.1%)	2,042 (75.0%)	0.001	5,457 (73.2%)	5,463 (73.3%)	0.002
Use of a statin; n (%)	655 (24.1%)	694 (25.5%)	0.033	1,837 (24.6%)	1,948 (26.1%)	0.034
Use of ACE-inhibitors; n (%)	262 (9.6%)	279 (10.2%)	0.021	739 (9.9%)	800 (10.7%)	0.027
Use of antidepressants; n (%)	97 (3.6%)	124 (4.6%)	0.05	334 (4.5%)	357 (4.8%)	0.015
Use of any anticoagulant; n (%)	45 (1.7%)	54 (2.0%)	0.025	130 (1.7%)	149 (2.0%)	0.019
Use of ARBs; n (%)	130 (4.8%)	140 (5.1%)	0.017	288 (3.9%)	326 (4.4%)	0.026
Use of Aspirin/dipyridamole; n (%)	3 (0.1%)	4 (0.1%)	0.01	5 (0.1%)	7 (0.1%)	0.009
Use of beta blockers; n (%)	279 (10.2%)	309 (11.4%)	0.036	853 (11.4%)	939 (12.6%)	0.035

Use of calcium channel blockers; n (%)	52 (1.9%)	57 (2.1%)	0.013	147 (2.0%)	187 (2.5%)	0.036
Use of diabetes medications, except insulin; n (%)	158 (5.8%)	159 (5.8%)	0.002	403 (5.4%)	464 (6.2%)	0.035
Use of diclofenac, ibuprofen, indomethacin, ketoprofen, or naproxen; n (%)	210 (7.7%)	203 (7.5%)	0.01	563 (7.6%)	613 (8.2%)	0.025
Use of other antiplatelet agents; n (%)	3 (0.1%)	3 (0.1%)	0	10 (0.1%)	11 (0.1%)	0.004
Use of other hypertension drugs; n (%)	265 (9.7%)	287 (10.5%)	0.027	719 (9.6%)	798 (10.7%)	0.035
Use of other lipid-lowering drugs; n (%)	151 (5.5%)	165 (6.1%)	0.022	38 (0.5%)	46 (0.6%)	0.017
Medicare/Commercial				436 (5.8%)	467 (6.3%)	
...Commercial; n (%)	2,364 (86.8%)	2,367 (87.0%)	0.003	6,389 (85.7%)	6,295 (84.5%)	0.035
...Medicare; n (%)	358 (13.2%)	355 (13.0%)		1,065 (14.3%)	1,159 (15.5%)	
Region						
...Northeast; n (%)	283 (10.4%)	304 (11.2%)	0.037	1,257 (16.9%)	1,322 (17.7%)	0.029
...Midwest; n (%)	591 (21.7%)	582 (21.4%)		1,584 (21.3%)	1,610 (21.6%)	
...South; n (%)	1,418 (52.1%)	1,385 (50.9%)		3,111 (41.7%)	3,022 (40.5%)	
...West; n (%)	425 (15.6%)	447 (16.4%)		1,424 (19.1%)	1,420 (19.1%)	
...Other; n (%)	5 (0.2%)	4 (0.1%)		78 (1.0%)	80 (1.1%)	
Age						
...mean (sd)	52.16 (14.31)	52.29 (13.88)	0.009	52.58 (13.16)	52.99 (12.99)	0.032
...median [IQR]	52.00 [42.00, 61.00]	53.00 [43.00, 61.00]		54.00 [44.00, 61.00]	54.00 [45.00, 61.00]	
Depression; n (%)	41 (1.5%)	45 (1.7%)	0.012	288 (3.9%)	319 (4.3%)	0.021
Use of antibiotics; n (%)	1,074 (39.5%)	1,125 (41.3%)	0.038	3,140 (42.1%)	3,212 (43.1%)	0.02
	Optum CDM			Truven MarketScan		
Variable	Methotrexate Users	Adalimumab users	Abs Std Dif	Methotrexate Users	Adalimumab users	Abs Std Dif
Number of patients	5,798	5,798		15,699	15,699	

Overweight/obesity; n (%)	328 (5.7%)	315 (5.4%)	0.01	660 (4.2%)	648 (4.1%)	0.004
Gender						
...M = MALE; n (%)	3,067 (52.9%)	3,076 (53.1%)	0.003	8,077 (51.4%)	8,121 (51.7%)	0.006
...F = FEMALE; n (%)	2,731 (47.1%)	2,722 (46.9%)		7,622 (48.6%)	7,578 (48.3%)	
Smoking; n (%)	275 (4.7%)	285 (4.9%)	0.008	627 (4.0%)	627 (4.0%)	0
CCI Combined Comorbidity Score (180 days)						
...mean (sd)	0.08 (0.87)	0.07 (0.81)	0.007	0.05 (0.74)	0.06 (0.73)	0.008
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]		0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Influenza vaccination; n (%)	607 (10.5%)	618 (10.7%)	0.006	1,374 (8.8%)	1,420 (9.0%)	0.01
Lipid screening; n (%)	63 (1.1%)	62 (1.1%)	0.002	132 (0.8%)	125 (0.8%)	0.005
Nursing home; n (%)	5 (0.1%)	4 (0.1%)	0.006	9 (0.1%)	9 (0.1%)	0
Any office visit; n (%)	5,679 (97.9%)	5,682 (98.0%)	0.004	15,422 (98.2%)	15,431 (98.3%)	0.004
ER visit; n (%)	485 (8.4%)	463 (8.0%)	0.014	1,591 (10.1%)	1,582 (10.1%)	0.002
Occurrence of inpatient hospitalization; n (%)	215 (3.7%)	211 (3.6%)	0.004	585 (3.7%)	583 (3.7%)	0.001
Occurrence of laboratory tests; n (%)	4,549 (78.5%)	4,542 (78.3%)	0.003	12,930 (82.4%)	12,904 (82.2%)	0.004
Use of a statin; n (%)	1,176 (20.3%)	1,171 (20.2%)	0.002	3,145 (20.0%)	3,143 (20.0%)	0
Use of ACE-inhibitors; n (%)	489 (8.4%)	494 (8.5%)	0.003	1,332 (8.5%)	1,351 (8.6%)	0.004
Use of antidepressants; n (%)	247 (4.3%)	245 (4.2%)	0.002	734 (4.7%)	746 (4.8%)	0.004
Use of any anticoagulant; n (%)	62 (1.1%)	68 (1.2%)	0.01	185 (1.2%)	194 (1.2%)	0.005
Use of ARBs; n (%)	206 (3.6%)	197 (3.4%)	0.008	513 (3.3%)	527 (3.4%)	0.005
Use of Aspirin/dipyridamole; n (%)	9 (0.2%)	8 (0.1%)	0.005	22 (0.1%)	20 (0.1%)	0.003
Use of beta blockers; n (%)	574 (9.9%)	565 (9.7%)	0.005	1,505 (9.6%)	1,523 (9.7%)	0.004
Use of calcium channel blockers; n (%)	72 (1.2%)	55 (0.9%)	0.028	142 (0.9%)	144 (0.9%)	0.001
Use of diabetes medications, except insulin; n (%)	304 (5.2%)	308 (5.3%)	0.003	753 (4.8%)	738 (4.7%)	0.004
Use of diclofenac, ibuprofen, indomethacin, ketoprofen, or naproxen; n (%)	688 (11.9%)	684 (11.8%)	0.002	1,820 (11.6%)	1,842 (11.7%)	0.004

Use of other antiplatelet agents; n (%)	0 (0.0%)	2 (0.0%)	0.026	15 (0.1%)	12 (0.1%)	0.007
Use of other hypertension drugs; n (%)	464 (8.0%)	459 (7.9%)	0.003	1,229 (7.8%)	1,276 (8.1%)	0.011
Use of other lipid-lowering drugs; n (%)	313 (5.4%)	296 (5.1%)	0.013	132 (0.8%)	125 (0.8%)	0.005
Medicare/Commercial						
...Commercial; n (%)	5,353 (92.3%)	5,357 (92.4%)	0.003	14,729 (93.8%)	14,683 (93.5%)	0.012
...Medicare; n (%)	445 (7.7%)	441 (7.6%)		970 (6.2%)	1,016 (6.5%)	
Region						
...Northeast; n (%)	500 (8.6%)	502 (8.7%)	0.017	2,307 (14.7%)	2,313 (14.7%)	0.009
...Midwest; n (%)	1,512 (26.1%)	1,510 (26.0%)		3,704 (23.6%)	3,760 (24.0%)	
...South; n (%)	2,812 (48.5%)	2,777 (47.9%)		6,949 (44.3%)	6,906 (44.0%)	
...West; n (%)	968 (16.7%)	1,003 (17.3%)		2,481 (15.8%)	2,461 (15.7%)	
...Other; n (%)	6 (0.1%)	6 (0.1%)		258 (1.6%)	259 (1.6%)	
Age						
...mean (sd)	48.17 (13.32)	48.16 (12.67)	0.001	47.60 (12.86)	47.57 (12.65)	0.003
...median [IQR]	49.00 [39.00, 57.00]	49.00 [39.00, 57.00]		49.00 [39.00, 57.00]	49.00 [39.00, 57.00]	
Depression; n (%)	144 (2.5%)	143 (2.5%)	0.001	777 (4.9%)	769 (4.9%)	0.002
Use of antibiotics; n (%)	2,261 (39.0%)	2,243 (38.7%)	0.006	6,255 (39.8%)	6,295 (40.1%)	0.005
	Optum CDM			Truven MarketScan		
Variable	Methotrexate Users	Apremilast users	Abs Std Dif	Methotrexate Users	Apremilast users	Abs Std Dif
Number of patients	1,623	1,623		4,470	4,470	
Overweight/obesity; n (%)	82 (5.1%)	87 (5.4%)	0.014	213 (4.8%)	242 (5.4%)	0.03
Gender						
...M = MALE; n (%)	808 (49.8%)	820 (50.5%)	0.015	2,178 (48.7%)	2,173 (48.6%)	0.002
...F = FEMALE; n (%)	815 (50.2%)	803 (49.5%)		2,292 (51.3%)	2,297 (51.4%)	
Smoking; n (%)	63 (3.9%)	57 (3.5%)	0.02	213 (4.8%)	242 (5.4%)	0.03
CCI Combined Comorbidity Score (180 days)						
...mean (sd)	0.14 (0.93)	0.14 (0.85)	0.008	0.07 (0.78)	0.08 (0.81)	0.02
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]		0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	

Influenza vaccination; n (%)	190 (11.7%)	223 (13.7%)	0.061	427 (9.6%)	487 (10.9%)	0.044
Lipid screening; n (%)	9 (0.6%)	11 (0.7%)	0.016	31 (0.7%)	38 (0.9%)	0.018
Nursing home; n (%)	2 (0.1%)	4 (0.2%)	0.029	3 (0.1%)	5 (0.1%)	0.015
Any office visit; n (%)	1,602 (98.7%)	1,605 (98.9%)	0.017	4,417 (98.8%)	4,421 (98.9%)	0.008
ER visit; n (%)	106 (6.5%)	131 (8.1%)	0.059	410 (9.2%)	471 (10.5%)	0.046
Occurrence of inpatient hospitalization; n (%)	64 (3.9%)	63 (3.9%)	0.003	160 (3.6%)	191 (4.3%)	0.036
Occurrence of laboratory tests; n (%)	1,089 (67.1%)	1,142 (70.4%)	0.07	3,193 (71.4%)	3,261 (73.0%)	0.034
Use of a statin; n (%)	333 (20.5%)	373 (23.0%)	0.06	992 (22.2%)	1,060 (23.7%)	0.036
Use of ACE-inhibitors; n (%)	137 (8.4%)	156 (9.6%)	0.041	387 (8.7%)	437 (9.8%)	0.039
Use of antidepressants; n (%)	18 (1.1%)	15 (0.9%)	0.018	28 (0.6%)	30 (0.7%)	0.006
Use of any anticoagulant; n (%)	25 (1.5%)	30 (1.8%)	0.024	54 (1.2%)	83 (1.9%)	0.053
Use of ARBs; n (%)	41 (2.5%)	47 (2.9%)	0.023	135 (3.0%)	151 (3.4%)	0.02
Use of Aspirin/dipyridamole; n (%)	4 (0.2%)	5 (0.3%)	0.012	14 (0.3%)	15 (0.3%)	0.004
Use of beta blockers; n (%)	190 (11.7%)	200 (12.3%)	0.019	470 (10.5%)	531 (11.9%)	0.043
Use of calcium channel blockers; n (%)	16 (1.0%)	16 (1.0%)	0	35 (0.8%)	30 (0.7%)	0.013
Use of diabetes medications, except insulin; n (%)	88 (5.4%)	95 (5.9%)	0.019	208 (4.7%)	219 (4.9%)	0.012
Use of diclofenac, ibuprofen, indomethacin, ketoprofen, or naproxen; n (%)	195 (12.0%)	215 (13.2%)	0.037	465 (10.4%)	506 (11.3%)	0.029
Use of other antiplatelet agents; n (%)	1 (0.1%)	2 (0.1%)	0.02	2 (0.0%)	2 (0.0%)	0
Use of other hypertension drugs; n (%)	168 (10.4%)	182 (11.2%)	0.028	404 (9.0%)	453 (10.1%)	0.037
Use of other lipid-lowering drugs; n (%)	53 (3.3%)	74 (4.6%)	0.067	203 (4.5%)	229 (5.1%)	0.027
Medicare/Commercial						
...Commercial; n (%)	1,378 (84.9%)	1,389 (85.6%)	0.019	4,034 (90.2%)	3,990 (89.3%)	0.032
...Medicare; n (%)	245 (15.1%)	234 (14.4%)		436 (9.8%)	480 (10.7%)	
Region						

...Northeast; n (%)	232 (14.3%)	209 (12.9%)	0.047	944 (21.1%)	989 (22.1%)	0.039
...Midwest; n (%)	389 (24.0%)	380 (23.4%)		950 (21.3%)	986 (22.1%)	
...South; n (%)	685 (42.2%)	706 (43.5%)		1,979 (44.3%)	1,928 (43.1%)	
...West; n (%)	315 (19.4%)	326 (20.1%)		585 (13.1%)	553 (12.4%)	
...Other; n (%)	2 (0.1%)	2 (0.1%)		12 (0.3%)	14 (0.3%)	
Age						
...mean (sd)	51.07 (14.80)	51.37 (13.77)	0.021	50.18 (13.02)	50.51 (12.84)	0.025
...median [IQR]	51.00 [40.00, 61.00]	52.00 [42.00, 61.00]		52.00 [41.00, 59.00]	52.00 [42.00, 59.00]	
Depression; n (%)	32 (2.0%)	27 (1.7%)	0.023	126 (2.8%)	140 (3.1%)	0.018
Use of antibiotics; n (%)	587 (36.2%)	617 (38.0%)	0.038	1,841 (41.2%)	1,890 (42.3%)	0.022
	Optum CDM			Truven MarketScan		
Variable	Methotrexate Users	Etanercept users	Abs Std Dif	Methotrexate Users	Etanercept users	Abs Std Dif
Number of patients	5,715	5,715	0.005	15,493	15,493	
Overweight/obesity; n (%)	308 (5.4%)	301 (5.3%)		578 (3.7%)	581 (3.8%)	0.001
Gender						
...M = MALE; n (%)	2,954 (51.7%)	2,971 (52.0%)	0.006	8,127 (52.5%)	8,078 (52.1%)	0.006
...F = FEMALE; n (%)	2,761 (48.3%)	2,744 (48.0%)		7,366 (47.5%)	7,415 (47.9%)	
Smoking; n (%)	292 (5.1%)	275 (4.8%)	0.014	525 (3.4%)	525 (3.4%)	0
CCI Combined Comorbidity Score (180 days)						
...mean (sd)	0.07 (0.87)	0.07 (0.84)	0.006	0.06 (0.74)	0.06 (0.73)	0
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]		0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Influenza vaccination; n (%)	543 (9.5%)	544 (9.5%)	0.001	1,207 (7.8%)	1,232 (8.0%)	0.006
Lipid screening; n (%)	65 (1.1%)	68 (1.2%)	0.005	95 (0.6%)	105 (0.7%)	0.008
Nursing home; n (%)	6 (0.1%)	4 (0.1%)	0.012	7 (0.0%)	7 (0.0%)	0
Any office visit; n (%)	5,569 (97.4%)	5,574 (97.5%)	0.006	7 (0.0%)	7 (0.0%)	0
ER visit; n (%)	423 (7.4%)	430 (7.5%)	0.005	1,552 (10.0%)	1,565 (10.1%)	0.003
Occurrence of inpatient hospitalization; n (%)	237 (4.1%)	219 (3.8%)	0.016	636 (4.1%)	643 (4.2%)	0.002
Occurrence of laboratory tests; n (%)	4,351 (76.1%)	4,347 (76.1%)	0.002	12,148 (78.4%)	12,143 (78.4%)	0.001
Use of a statin; n (%)	1,101 (19.3%)	1,080 (18.9%)	0.009	2,972 (19.2%)	2,995 (19.3%)	0.004
Use of ACE-inhibitors; n (%)	454 (7.9%)	462 (8.1%)	0.005	1,279 (8.3%)	1,322 (8.5%)	0.01

Use of antidepressants; n (%)	303 (5.3%)	272 (4.8%)	0.025	762 (4.9%)	797 (5.1%)	0.01
Use of any anticoagulant; n (%)	72 (1.3%)	72 (1.3%)	0	205 (1.3%)	210 (1.4%)	0.003
Use of ARBs; n (%)	207 (3.6%)	180 (3.1%)	0.026	545 (3.5%)	562 (3.6%)	0.006
Use of Aspirin/dipyridamole; n (%)	5 (0.1%)	5 (0.1%)	0	16 (0.1%)	14 (0.1%)	0.004
Use of beta blockers; n (%)	551 (9.6%)	549 (9.6%)	0.001	1,572 (10.1%)	1,562 (10.1%)	0.002
Use of calcium channel blockers; n (%)	79 (1.4%)	73 (1.3%)	0.009	231 (1.5%)	232 (1.5%)	0.001
Use of diabetes medications, except insulin; n (%)	278 (4.9%)	284 (5.0%)	0.005	760 (4.9%)	765 (4.9%)	0.001
Use of diclofenac, ibuprofen, indomethacin, ketoprofen, or naproxen; n (%)	688 (12.0%)	665 (11.6%)	0.012	1,704 (11.0%)	1,723 (11.1%)	0.004
Use of other antiplatelet agents; n (%)	0 (0.0%)	2 (0.0%)	0.026	7 (0.0%)	10 (0.1%)	0.008
Use of other hypertension drugs; n (%)	427 (7.5%)	418 (7.3%)	0.006	1,241 (8.0%)	1,271 (8.2%)	0.007
Use of other lipid-lowering drugs; n (%)	260 (4.5%)	265 (4.6%)	0.004	770 (5.0%)	787 (5.1%)	0.005
Medicare/Commercial						
...Commercial; n (%)	5,341 (93.5%)	5,333 (93.3%)	0.006	14,272 (92.1%)	14,270 (92.1%)	0
...Medicare; n (%)	374 (6.5%)	382 (6.7%)		1,221 (7.9%)	1,223 (7.9%)	
Region						
...Northeast; n (%)	495 (8.7%)	495 (8.7%)	0.025	2,248 (14.5%)	2,260 (14.6%)	0.015
...Midwest; n (%)	1,483 (25.9%)	1,436 (25.1%)		3,810 (24.6%)	3,791 (24.5%)	
...South; n (%)	2,785 (48.7%)	2,787 (48.8%)		6,608 (42.7%)	6,695 (43.2%)	
...West; n (%)	944 (16.5%)	988 (17.3%)		2,556 (16.5%)	2,480 (16.0%)	
...Other; n (%)	8 (0.1%)	9 (0.2%)		271 (1.7%)	267 (1.7%)	
Age						
...mean (sd)	47.63 (13.15)	47.55 (12.76)	0.006	47.66 (13.29)	47.63 (13.05)	0.002
...median [IQR]	48.00 [38.00, 57.00]	48.00 [38.00, 56.00]		49.00 [38.00, 57.00]	49.00 [38.00, 57.00]	
Depression; n (%)	144 (2.5%)	124 (2.2%)	0.023	762 (4.9%)	749 (4.8%)	0.004
Use of antibiotics; n (%)	2,225 (38.9%)	2,223 (38.9%)	0.001	6,178 (39.9%)	6,144 (39.7%)	0.004
	Optum CDM			Truven MarketScan		

Variable	Methotrexate Users	Infliximab users	Abs Std Dif	Methotrexate Users	Infliximab users	Abs Std Dif
Number of patients	406	406		1,027	1,027	
Overweight/obesity; n (%)	26 (6.4%)	27 (6.7%)	0.01	67 (6.5%)	59 (5.7%)	0.032
Gender						
...M = MALE; n (%)	212 (52.2%)	201 (49.5%)	0.054	450 (43.8%)	474 (46.2%)	0.047
...F = FEMALE; n (%)	194 (47.8%)	205 (50.5%)		577 (56.2%)	553 (53.8%)	
Smoking; n (%)	28 (6.9%)	24 (5.9%)	0.04	49 (4.8%)	50 (4.9%)	0.005
CCI Combined Comorbidity Score (180 days)						
...mean (sd)	0.10 (0.97)	0.20 (1.07)	0.104	0.17 (0.96)	0.18 (1.04)	0.007
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]		0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Influenza vaccination; n (%)	62 (15.3%)	61 (15.0%)	0.007	89 (8.7%)	105 (10.2%)	0.053
Lipid screening; n (%)	4 (1.0%)	4 (1.0%)	0	8 (0.8%)	10 (1.0%)	0.021
Nursing home; n (%)	0 (0.0%)	2 (0.5%)	0.1	2 (0.2%)	2 (0.2%)	0
Any office visit; n (%)	399 (98.3%)	400 (98.5%)	0.02	1,020 (99.3%)	1,018 (99.1%)	0.022
ER visit; n (%)	53 (13.1%)	43 (10.6%)	0.076	146 (14.2%)	148 (14.4%)	0.006
Occurrence of inpatient hospitalization; n (%)	34 (8.4%)	30 (7.4%)	0.037	70 (6.8%)	69 (6.7%)	0.004
Occurrence of laboratory tests; n (%)	360 (88.7%)	362 (89.2%)	0.016	902 (87.8%)	907 (88.3%)	0.015
Use of a statin; n (%)	77 (19.0%)	85 (20.9%)	0.049	189 (18.4%)	217 (21.1%)	0.069
Use of ACE-inhibitors; n (%)	39 (9.6%)	36 (8.9%)	0.026	77 (7.5%)	93 (9.1%)	0.057
Use of antidepressants; n (%)	20 (4.9%)	25 (6.2%)	0.054	61 (5.9%)	72 (7.0%)	0.044
Use of any anticoagulant; n (%)	5 (1.2%)	4 (1.0%)	0.024	8 (0.8%)	16 (1.6%)	0.073
Use of ARBs; n (%)	15 (3.7%)	18 (4.4%)	0.037	31 (3.0%)	41 (4.0%)	0.053
Use of Aspirin/dipyridamole; n (%)	0 (0.0%)	0 (0.0%)	-	1 (0.1%)	1 (0.1%)	0
Use of beta blockers; n (%)	36 (8.9%)	43 (10.6%)	0.058	100 (9.7%)	118 (11.5%)	0.057
Use of calcium channel blockers; n (%)	4 (1.0%)	5 (1.2%)	0.024	6 (0.6%)	14 (1.4%)	0.079
Use of diabetes medications, except insulin; n (%)	17 (4.2%)	24 (5.9%)	0.079	54 (5.3%)	63 (6.1%)	0.038
Use of diclofenac, ibuprofen, indomethacin, ketoprofen, or naproxen; n (%)	44 (10.8%)	48 (11.8%)	0.031	138 (13.4%)	127 (12.4%)	0.032

Use of other antiplatelet agents; n (%)	0 (0.0%)	0 (0.0%)	-	0 (0.0%)	0 (0.0%)	-
Use of other hypertension drugs; n (%)	38 (9.4%)	41 (10.1%)	0.025	89 (8.7%)	98 (9.5%)	0.03
Use of other lipid-lowering drugs; n (%)	20 (4.9%)	24 (5.9%)	0.044	71 (6.9%)	77 (7.5%)	0.023
Medicare/Commercial						
...Commercial; n (%)	355 (87.4%)	350 (86.2%)	0.036	953 (92.8%)	935 (91.0%)	0.064
...Medicare; n (%)	51 (12.6%)	56 (13.8%)		74 (7.2%)	92 (9.0%)	
Region						
...Northeast; n (%)	29 (7.1%)	34 (8.4%)	0.057	169 (16.5%)	158 (15.4%)	0.052
...Midwest; n (%)	131 (32.3%)	135 (33.3%)		223 (21.7%)	244 (23.8%)	
...South; n (%)	204 (50.2%)	195 (48.0%)		540 (52.6%)	531 (51.7%)	
...West; n (%)	42 (10.3%)	42 (10.3%)		88 (8.6%)	87 (8.5%)	
...Other; n (%)	0 (0.0%)	0 (0.0%)		7 (0.7%)	7 (0.7%)	
Age						
...mean (sd)	49.81 (14.56)	50.15 (14.60)	0.023	47.50 (13.19)	48.18 (12.47)	0.053
...median [IQR]	50.00 [40.00, 60.00]	50.00 [40.00, 59.00]		48.00 [38.00, 57.00]	49.00 [40.00, 57.00]	
Depression; n (%)	15 (3.7%)	12 (3.0%)	0.041	61 (5.9%)	65 (6.3%)	0.016
Use of antibiotics; n (%)	161 (39.7%)	159 (39.2%)	0.01	490 (47.7%)	473 (46.1%)	0.033
	Optum CDM			Truven MarketScan		
Variable	Methotrexate Users	Ustekinumab users	Abs Std Dif	Methotrexate Users	Ustekinumab users	Abs Std Dif
Number of patients	4,037	4,037		7,838	7,838	
Overweight/obesity; n (%)	235 (5.8%)	247 (6.1%)	0.013	336 (4.3%)	377 (4.8%)	0.025
Gender						
...M = MALE; n (%)	2,250 (55.7%)	2,259 (56.0%)	0.023	4,273 (54.5%)	4,300 (54.9%)	0.007
...F = FEMALE; n (%)	1,787 (44.3%)	1,777 (44.0%)		3,565 (45.5%)	3,538 (45.1%)	
Smoking; n (%)	184 (4.6%)	183 (4.5%)	0.001	332 (4.2%)	356 (4.5%)	0.015
CCI Combined Comorbidity Score (180 days)						
...mean (sd)	0.08 (0.83)	0.08 (0.78)	0.001	0.03 (0.69)	0.05 (0.77)	0.022
...median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]		0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	
Influenza vaccination; n (%)	458 (11.3%)	485 (12.0%)	0.021	656 (8.4%)	734 (9.4%)	0.035

Lipid screening; n (%)	31 (0.8%)	33 (0.8%)	0.006	61 (0.8%)	65 (0.8%)	0.006
Nursing home; n (%)	7 (0.2%)	6 (0.1%)	0.006	9 (0.1%)	9 (0.1%)	0
Any office visit; n (%)	3,981 (98.6%)	3,978 (98.5%)	0.006	7,734 (98.7%)	7,732 (98.6%)	0.002
ER visit; n (%)	322 (8.0%)	311 (7.7%)	0.01	682 (8.7%)	754 (9.6%)	0.032
Occurrence of inpatient hospitalization; n (%)	112 (2.8%)	115 (2.8%)	0.004	239 (3.0%)	259 (3.3%)	0.015
Occurrence of laboratory tests; n (%)	3,165 (78.4%)	3,197 (79.2%)	0.019	6,322 (80.7%)	6,329 (80.7%)	0.002
Use of a statin; n (%)	728 (18.0%)	786 (19.5%)	0.037	1,483 (18.9%)	1,619 (20.7%)	0.044
Use of ACE-inhibitors; n (%)	333 (8.2%)	342 (8.5%)	0.008	609 (7.8%)	706 (9.0%)	0.045
Use of antidepressants; n (%)	88 (2.2%)	94 (2.3%)	0.01	220 (2.8%)	248 (3.2%)	0.021
Use of any anticoagulant; n (%)	61 (1.5%)	59 (1.5%)	0.004	78 (1.0%)	94 (1.2%)	0.02
Use of ARBs; n (%)	99 (2.5%)	111 (2.7%)	0.019	208 (2.7%)	240 (3.1%)	0.025
Use of Aspirin/dipyridamole; n (%)	4 (0.1%)	7 (0.2%)	0.02	12 (0.2%)	16 (0.2%)	0.012
Use of beta blockers; n (%)	322 (8.0%)	324 (8.0%)	0.002	683 (8.7%)	777 (9.9%)	0.041
Use of calcium channel blockers; n (%)	21 (0.5%)	17 (0.4%)	0.014	37 (0.5%)	34 (0.4%)	0.006
Use of diabetes medications, except insulin; n (%)	190 (4.7%)	197 (4.9%)	0.008	362 (4.6%)	416 (5.3%)	0.032
Use of diclofenac, ibuprofen, indomethacin, ketoprofen, or naproxen; n (%)	336 (8.3%)	345 (8.5%)	0.008	694 (8.9%)	691 (8.8%)	0.001
Use of other antiplatelet agents; n (%)	1 (0.0%)	1 (0.0%)	0	2 (0.0%)	2 (0.0%)	0
Use of other hypertension drugs; n (%)	278 (6.9%)	307 (7.6%)	0.028	602 (7.7%)	684 (8.7%)	0.038
Use of other lipid-lowering drugs; n (%)	180 (4.5%)	185 (4.6%)	0.006	61 (0.8%)	65 (0.8%)	0.006
Medicare/Commercial				377 (4.8%)	426 (5.4%)	0.028
...Commercial; n (%)	3,763 (93.2%)	3,759 (93.1%)	0.004	7,355 (93.8%)	7,296 (93.1%)	0.03
...Medicare; n (%)	274 (6.8%)	278 (6.9%)		483 (6.2%)	542 (6.9%)	
Region						
...Northeast; n (%)	387 (9.6%)	409 (10.1%)	0.022	1,422 (18.1%)	1,492 (19.0%)	0.049
...Midwest; n (%)	983 (24.3%)	971 (24.1%)		1,649 (21.0%)	1,595 (20.3%)	
...South; n (%)	1,991 (49.3%)	1,997 (49.5%)		3,593 (45.8%)	3,560 (45.4%)	

...West; n (%)	671 (16.6%)	656 (16.2%)		1,043 (13.3%)	1,016 (13.0%)	
...Other; n (%)	5 (0.1%)	4 (0.1%)		131 (1.7%)	175 (2.2%)	
Age						
...mean (sd)	46.50 (13.49)	46.67 (12.79)	0.013	46.45 (13.08)	46.89 (12.86)	0.035
...median [IQR]	46.00 [37.00, 56.00]	47.00 [38.00, 55.00]		47.00 [37.00, 56.00]	48.00 [38.00, 56.00]	
Depression; n (%)	74 (1.8%)	76 (1.9%)	0.004	333 (4.2%)	363 (4.6%)	0.019
Use of antibiotics; n (%)	1,466 (36.3%)	1,491 (36.9%)	0.013	2,939 (37.5%)	3,013 (38.4%)	0.019

^a Absolute standardized difference

^b Interquartile range

eTable 6. Overall and subtypes of serious infections in patient with psoriasis on systemic medications compared to methotrexate in Optum© Clinformatics® Data Mart

Exposure	No. of Patients in Reference Group (MTX) ^a	Events in Reference Group (MTX) ^b	Incidence Rate ^c in Reference Group	No. of Patients in Exposure Group	Events in Exposure Group	Incidence Rate in Exposure Group	Rate Difference (95% CI) ^d	Unadjusted HR ^e (95% CI)	p	PS-Adjusted HR (95% CI)	p
Acitretin											
Overall Serious Infection	9048	127	14.46	2726	30	14.44	-0.02 (-5.76, 5.73)	1.00 (0.67, 1.50)	0.99	1.33 (0.78, 2.27)	0.29
Bacteremia/Sepsis		28	3.17		8	3.83	0.66 (-2.24, 3.56)	1.19 (0.54, 2.63)	0.66	1.49 (0.51, 4.32)	0.46
Cellulitis/soft-tissue infection		36	4.07		17	8.16	4.09 (-0.01, 8.19)	1.87 (1.05, 3.33)	0.03	2.11 (0.93, 4.79)	0.08
Endocarditis		0	0		0	0	0	1.00 (1.00, 1.00)	* ^f	1.00 (1.00, 1.00)	*
Meningitis/Encephalitis		4	0.45		1	0.48	0.03 (-1.01, 1.06)	1.36 (0.15, 12.37)	0.79	*	0.90
Pneumonia		51	5.78		6	2.87	-2.91 (-5.70, -0.12)	0.52 (0.22, 1.22)	0.13	0.79 (0.28, 2.22)	0.65
Pyelonephritis		6	0.68		0	0	-0.68 (-1.22, -0.14)	*	*	*	*
Septic arthritis/osteomyelitis		6	0.68		0	0	-0.68 (-1.22, -0.14)	*	*	*	*
Adalimumab											
Overall Serious Infection	8470	112	14.24	7181	79	10.33	-3.91 (-7.39, -0.42)	0.73 (0.55, 0.98)	0.03	1.26 (0.86, 1.85)	0.23
Bacteremia/Sepsis		26	3.29		18	2.34	-0.94 (-2.61, 0.72)	0.70 (0.38, 1.27)	0.24	1.98 (0.77, 5.12)	0.16
Cellulitis/soft-tissue infection		28	3.54		36	4.69	1.15 (-0.86, 3.17)	1.39 (0.84, 2.27)	0.2	1.93 (1.03, 3.63)	0.04
Endocarditis		0	0		0	0	0	1.00 (1.00, 1.00)	*	1.00 (1.00, 1.00)	*
Meningitis/Encephalitis		2	0.25		0	0	-0.25 (-0.60, 0.10)	*	*	*	*
Pneumonia		48	6.07		23	2.99	-3.08 (-5.19, -0.97)	0.49 (0.30, 0.81)	<0.01	0.94 (0.49, 1.79)	0.84
Pyelonephritis		5	0.63		4	0.52	-0.11 (-0.86, 0.64)	0.83 (0.22, 3.10)	0.78	0.81 (0.11, 5.83)	0.84
Septic arthritis/osteomyelitis		7	0.88		2	0.26	-0.62 (-1.37, 0.12)	0.29 (0.06, 1.41)	0.13	0.32 (0.06, 1.67)	0.18
Apremilast											
Overall Serious Infection	9383	134	14.62	1623	4	4.36	-10.27 (-15.20, -5.33)	0.30 (0.11, 0.80)	0.02	0.39 (0.13, 1.20)	0.10

Bacteremia/Sepsis		30	3.25		1	1.09	-2.17 (-4.60, 0.26)	0.34 (0.05, 2.52)	0.29	1.12 (0.07, 17.95)	0.94
Cellulitis/soft-tissue infection		38	4.12		2	2.17	-1.95 (-5.23, 1.34)	0.45 (0.11, 1.88)	0.28	0.41 (0.08, 2.02)	0.27
Endocarditis		0	0		0	0	0	*	*	*	*
Meningitis/Encephalitis		4	0.43		0	0	0	*	0.86	*	*
Pneumonia		54	5.86		1	1.09	-4.78 (-7.42, -2.13)	0.18 (0.03, 1.31)	0.09	0.28 (0.03, 2.42)	0.25
Pyelonephritis		6	0.65		0	0	0	*	*	*	*
Septic arthritis/osteomyelitis		7	0.76		0	0	-0.76 (-1.32, -0.20)	*	*	*	*
Etanercept											
Overall Serious Infection	8475	118	14.98	7102	68	8.05	-6.94 (-10.25, -3.63)	0.54 (0.40, 0.72)	<0.01	0.78 (0.54, 1.15)	0.21
Bacteremia/Sepsis		27	3.41		9	1.06	-2.35 (-3.81, -0.89)	0.31 (0.14, 0.65)	<0.01	0.64 (0.24, 1.67)	0.36
Cellulitis/soft-tissue infection		33	4.16		35	4.13	-0.03 (-2.00, 1.94)	1.02 (0.63, 1.64)	0.93	1.16 (0.65, 2.07)	0.61
Endocarditis		0	0.5		1	0	-0.50 (-1.00, -0.01)	*	*	*	*
Meningitis/Encephalitis		4	0.5		0	0	-0.50 (-1.00, -0.01)	*	*	*	*
Pneumonia		50	6.32		19	2.24	-4.08 (-6.10, -2.06)	0.36 (0.21, 0.60)	<0.01	0.61 (0.30, 1.21)	0.15
Pyelonephritis		4	0.5		2	0.24	-0.27 (-0.86, 0.32)	0.42 (0.08, 2.30)	0.32	0.64 (0.09, 4.59)	0.66
Septic arthritis/osteomyelitis		5	0.63		4	0.47	-0.16 (-0.88, 0.56)	0.74 (0.20, 2.79)	0.66	0.53 (0.09, 3.21)	0.49
Infliximab											
Overall Serious Infection	9378	132	14.58	408	6	17.67	3.09 (-11.27, 17.45)	1.22 (0.54, 2.76)	0.62	2.01 (0.50, 8.02)	0.32
Bacteremia/Sepsis		30	3.29		1	2.93	-0.36 (-6.23, 5.50)	0.91 (0.12, 6.67)	0.93	*	*
Cellulitis/soft-tissue infection		39	4.28		1	2.94	-1.35 (-7.26, 4.57)	0.64 (0.09, 4.68)	0.66	1.01 (0.06, 16.08)	1.00
Endocarditis		0	0		0	0	0	*	*	*	*
Meningitis/Encephalitis		3	0.33		1	2.93	2.60 (-3.15, 8.36)	10.24 (1.06, 98.78)	0.04	*	*
Pneumonia		52	5.72		2	5.86	0.14 (-8.12, 8.41)	1.02 (0.25, 4.17)	0.98	0.98 (0.14, 6.94)	0.98
Pyelonephritis		6	0.66		1	2.93	2.27 (-3.50, 8.04)	4.36 (0.52, 36.36)	0.17	*	*
Septic arthritis/osteomyelitis		7	0.77		0	0	-0.77 (-1.34, -0.20)	*	0.85	*	*
Ustekinumab											
Overall Serious Infection	9167	133	14.95	4085	21	5.57	-9.37 (-12.86, -5.89)	0.38 (0.24, 0.61)	<0.01	0.54 (0.32, 0.92)	0.02

Bacteremia/Sepsis		30	3.35		6	1.59	-1.76 (-3.51, -0.02)	0.48 (0.20, 1.15)	0.1	1.42 (0.40, 5.04)	0.59
Cellulitis/soft-tissue infection		37	4.13		9	2.38	-1.75 (-3.80, 0.30)	0.55 (0.26, 1.13)	0.11	0.73 (0.31, 1.73)	0.47
Endocarditis		0	0		0	0	0	*	*	*	*
Meningitis/Encephalitis		4	0.45		0	0	-0.45 (-0.88, -0.01)	*	*	*	*
Pneumonia		54	6.04		5	1.32	-4.71 (-6.70, -2.73)	0.24 (0.09, 0.59)	<0.01	0.36 (0.13, 0.99)	0.05
Pyelonephritis		6	0.67		0	0	-0.67 (-1.20, -0.13)	*	*	*	*
Septic arthritis/osteomyelitis		7	0.78		2	0.53	-0.25 (-1.19, 0.68)	0.76 (0.16, 3.70)	0.73	0.52 (0.09, 2.83)	0.45

^a MTX, methotrexate

^b The sum of events in the sub analyses of serious infections may be greater than the number of events in the overall serious infection analysis if a patient experienced greater than one serious infectious event.

^c Incident rate in 1000 person-years

^d CI, confidence interval

^e HR, hazard ratio

^f HR not calculated due to zero events in either exposure or reference group

eTable 7. Overall and subtypes of serious infections in patient with psoriasis on systemic medications compared to methotrexate in Truven MarketScan

Exposure	No. of Patients in Reference Group (MTX ^a)	Events in Reference Group (MTX) ^b	Incidence Rate ^c in Reference Group	No. of Patients in Exposure Group	Events in Exposure Group	Incidence Rate in Exposure Group	Rate Difference (95% CI ^d)	Unadjusted HR ^e (95% CI)	p	PS-Adjusted HR (95% CI)	p
Acitretin											
Overall Serious Infection	21,935	258	12.11	7,456	81	13.68	1.57 (-1.75, 4.90)	1.14 (0.89, 1.46)	0.31	1.02 (0.76, 1.38)	0.87
Bacteremia/Sepsis		60	2.79		15	2.52	-0.28 (-1.74, 1.18)	0.92 (0.52, 1.63)	0.79	0.79 (0.41, 1.50)	0.46
Cellulitis/soft-tissue infection		74	3.45		36	6.05	2.60 (0.48, 4.73)	1.72 (1.15, 2.56)	<0.01	1.65 (0.99, 2.73)	0.05
Endocarditis		0	0		0	0	*	* ^f	*	*	*
Meningitis/Encephalitis		4	0.19		0	0	-0.19 (-0.37, -0.00)	*	*	*	*
Pneumonia		117	5.46		30	5.04	-0.42 (-2.48, 1.63)	0.95 (0.64, 1.43)	0.82	0.87 (0.54, 1.39)	0.56
Pyelonephritis		6	0.28		2	0.34	0.06 (-0.46, 0.57)	1.24 (0.25, 6.17)	0.79	1.46 (0.21, 10.41)	0.70
Septic arthritis/osteomyelitis		6	0.28		3	0.5	0.22 (-0.39, 0.83)	1.73 (0.43, 6.95)	0.44	1.22 (0.24, 6.09)	0.81
Adalimumab											
Overall Serious Infection	20,609	229	12.14	17,912	197	9.75	-2.39 (-4.47, -0.31)	0.80 (0.66, 0.97)	0.02	1.02 (0.82, 1.28)	0.84
Bacteremia/Sepsis		52	2.74		37	1.82	-0.91 (-1.86, 0.03)	0.67 (0.44, 1.02)	0.06	0.90 (0.55, 1.46)	0.66
Cellulitis/soft-tissue infection		69	3.63		81	3.99	0.36 (-0.86, 1.58)	1.14 (0.83, 1.57)	0.42	1.19 (0.82, 1.72)	0.36
Endocarditis		0	0		0	0	*	*	*	*	*
Meningitis/Encephalitis		4	0.21		2	0.1	-0.11 (-0.36, 0.14)	0.46 (0.08, 2.52)	0.37	0.78 (0.11, 5.63)	0.81
Pneumonia		103	5.43		75	3.69	-1.74 (-3.08, -0.40)	0.66 (0.49, 0.88)	<0.01	0.94 (0.66, 1.34)	0.74
Pyelonephritis		4	0.21		4	0.2	-0.01 (-0.30, 0.27)	0.88 (0.22, 3.51)	0.85	1.40 (0.26, 7.64)	0.70
Septic arthritis/osteomyelitis		6	0.32		6	0.29	-0.02 (-0.37, 0.33)	0.94 (0.30, 2.93)	0.92	1.20 (0.34, 4.26)	0.78
Apremilast											
Overall Serious Infection	22,987	288	12.72	4,476	11	5.35	-7.37 (-10.86, -3.88)	0.45 (0.25, 0.82)	<0.01	0.54 (0.27, 1.09)	0.09
Bacteremia/Sepsis		64	2.8		4	1.94	-0.86 (-2.88, 1.17)	0.71 (0.25, 1.98)	0.51	0.83 (0.24, 2.84)	0.77

Cellulitis/soft-tissue infection		85	3.73		4	1.94	-1.78 (-3.85, 0.28)	0.49 (0.18, 1.36)	0.17	0.58 (0.18, 1.84)	0.35
Endocarditis		0	0		1	0.49	0.49	*	*	*	*
Meningitis/Encephalitis		4	0.17		0	0	*	*	*	*	*
Pneumonia		132	5.8		4	1.94	-3.86 (-6.00, -1.71)	0.39 (0.14, 1.07)	0.07	0.47 (0.15, 1.44)	0.19
Pyelonephritis		6	0.26		0	0	-0.26 (-0.47, -0.05)	*	*	*	*
Septic arthritis/osteomyelitis		6	0.26		0	0	-0.26 (-0.47, -0.05)	*	*	*	*
Etanercept											
Overall Serious Infection	20,878	224	11.6	16,791	168	7.66	-3.95 (-5.86, -2.03)	0.66 (0.54, 0.80)	<0.01	0.74 (0.59, 0.93)	0.01
Bacteremia/Sepsis		51	2.62		28	1.27	-1.35 (-2.21, -0.49)	0.44 (0.27, 0.70)	<0.01	0.48 (0.29, 0.79)	<0.01
Cellulitis/soft-tissue infection		60	3.09		71	3.23	0.14 (-0.95, 1.22)	1.12 (0.79, 1.58)	0.52	1.16 (0.79, 1.72)	0.45
Endocarditis		0	0		1	0.49	0.49 (-0.47, 1.44)	*	*	*	*
Meningitis/Encephalitis		4	0.17		0	0	-0.17 (-0.35, -0.00)	*	*	*	*
Pneumonia		132	5.8		4	1.94	-3.86 (-6.00, -1.71)	0.39 (0.14, 1.07)	0.07	0.47 (0.15, 1.44)	0.19
Pyelonephritis		6	0.26		0	0	-0.26 (-0.47, -0.05)	*	*	*	*
Septic arthritis/osteomyelitis		6	0.26		0	0	-0.26 (-0.47, -0.05)	*	*	*	*
Infliximab											
Overall Serious Infection	22,642	253	11.68	1,027	20	17.08	5.41 (-2.22, 13.03)	1.44 (0.91, 2.27)	0.12	1.36 (0.67, 2.73)	0.39
Bacteremia/Sepsis		59	2.7		3	2.54	-0.16 (-3.12, 2.80)	0.90 (0.28, 2.87)	0.86	1.29 (0.21, 7.78)	0.78
Cellulitis/soft-tissue infection		68	3.12		9	7.65	4.53 (-0.52, 9.58)	2.51 (1.25, 5.04)	<0.01	1.95 (0.60, 6.35)	0.27
Endocarditis		0	0		1	0.49	0.49 (-0.47, 1.44)	*	*	*	*
Meningitis/Encephalitis		4	0.18		0	0	-0.18 (-0.36, -0.00)	*	*	*	*
Pneumonia		118	5.42		6	5.1	-0.32 (-4.52, 3.87)	0.91 (0.40, 2.07)	0.82	0.75 (0.25, 2.25)	0.61
Pyelonephritis		6	0.27		2	1.7	1.42 (-0.94, 3.79)	6.68 (1.35, 33.15)	0.02	*	*
Septic arthritis/osteomyelitis		5	0.22		1	0.97	0.75 (-1.67, 3.18)	3.79 (0.44, 32.40)	0.22	*	*
Ustekinumab											
Overall Serious Infection	22,556	280	12.7	7,841	56	7.06	-5.63 (-8.01, -3.26)	0.56 (0.42, 0.75)	<0.01	0.70 (0.49, 0.99)	0.05

Bacteremia/Sepsis		62	2.79		10	1.62	-1.53 (-2.57, -0.49)	0.48 (0.24, 0.93)	0.03	0.66 (0.29, 1.49)	0.32
Cellulitis/soft-tissue infection		84	3.78		22	2.77	-1.02 (-2.43, 0.40)	0.73 (0.46, 1.18)	0.2	0.95 (0.52, 1.72)	0.86
Endocarditis		0	0		0	0	0	*	*	*	*
Meningitis/Encephalitis		4	0.18		0	0	-0.18 (-0.36, -0.00)	*	*	*	*
Pneumonia		127	5.73		23	2.89	-2.84 (-4.38, -1.29)	0.51 (0.32, 0.79)	<0.01	0.59 (0.35, 1.00)	0.05
Pyelonephritis		6	0.27		3	0.38	0.11 (-0.37, 0.58)	1.35 (0.34, 5.41)	0.67	1.32 (0.22, 7.93)	0.76
Septic arthritis/osteomyelitis		6	0.27		0	0	-0.27 (-0.48, -0.05)	*	*	*	*

^a MTX, methotrexate

^b The sum of events in the sub analyses of serious infections may be greater than the number of events in the overall serious infection analysis if a patient experienced greater than one serious infectious event.

^c Incident rate in 1000 person-years

^d CI, confidence interval

^e HR, hazard ratio

^f HR not calculated due to zero events in either exposure or reference group

eTable 8. Overall serious infections in patients with psoriasis and psoriatic arthritis on systemic medications compared to methotrexate in Optum© Clinformatics® Data Mart

Exposure	No. of Patients in Reference Group (MTX)^a	Events in Reference Group (MTX)	No. of Patients in Exposure Group	Events in Exposure Group	Unadjusted HR	p	PS-Adjusted HR	p
Acitretin	10,241	147	2800	33	1.06 (0.73, 1.56)	0.75	1.33 (0.81, 2.19)	0.26
Adalimumab	9,467	126	7,792	85	0.73 (0.55, 0.96)	0.02	1.23 (0.86, 1.75)	0.25
Apremilast	10,553	155	1,758	5	0.34 (0.14, 0.83)	0.02	0.43 (0.16, 1.19)	0.11
Etanercept	9,442	137	7,657	74	0.53 (0.40, 0.70)	<0.01	0.76 (0.53, 1.08)	0.13
Infliximab	10,509	151	601	7	0.92 (0.43, 1.96)	0.83	1.56 (0.49, 4.92)	0.45
Ustekinumab	10,332	154	4,283	22	0.38 (0.24, 0.60)	<0.01	0.57 (0.34, 0.96)	0.03

^a MTX, methotrexate

eTable 9. Overall risk of serious infection compared to methotrexate in patients with psoriasis by age and gender in Optum© Clinformatics® Data Mart

Exposure	PS-adjusted HR ^a (95% CI)		Gender PS-adjusted HR (95% CI)			
	Overall	p	Male	p	Female	p
Acitretin	1.33 (0.78, 2.27)	0.29	1.12 (0.57, 2.21)	0.73	1.41 (0.64, 3.12)	0.40
Adalimumab	1.26 (0.86, 1.85)	0.23	1.16 (0.70, 1.95)	0.56	0.90 (0.52, 1.56)	0.71
Apremilast	0.39 (0.13, 1.20)	0.10	0.52 (0.13, 2.03)	0.35	0.36 (0.04, 3.31)	0.37
Etanercept	0.78 (0.54, 1.15)	0.21	0.78 (0.47, 1.31)	0.35	0.68 (0.38, 1.22)	0.19
Infliximab	2.01 (0.50, 8.02)	0.32	4.21 (0.43, 40.99)	0.22	1.53 (0.25, 9.15)	0.64
Ustekinumab	0.54 (0.32, 0.92)	0.02	0.54 (0.25, 1.13)	0.10	0.69 (0.31, 1.54)	0.36

Exposure	Age Category PS-adjusted HR (95% CI)							
	18-54	p	55-64	p	65-74	p	>=75	p
Acitretin	0.64 (0.27, 1.52)	0.31	0.94 (0.37, 2.40)	0.90	2.00 (0.64, 6.18)	0.23	0.60 (0.18, 2.06)	0.42
Adalimumab	1.34 (0.77, 2.35)	0.30	1.29 (0.68, 2.45)	0.43	1.80 (0.54, 5.98)	0.34	0.66 (0.12, 3.74)	0.64
Apremilast	0.32 (0.04, 2.90)	0.31	0.63 (0.11, 3.47)	0.59	0.51 (0.05, 5.60)	0.58	* ^b	*
Etanercept	0.75 (0.43, 1.32)	0.32	1.18 (0.58, 2.40)	0.64	0.40 (0.12, 1.32)	0.13	1.66 (0.30, 9.11)	0.56
Infliximab	4.00 (0.45, 35.76)	0.22	*	*	3.57 (0.29, 43.94)	0.32	*	*
Ustekinumab	0.53 (0.25, 1.16)	0.53	0.84 (0.31, 2.27)	0.73	2.12 (0.39, 11.61)	0.39	*	*

^a PS-adjusted HR, propensity score adjusted hazard ratio

^b PS-adjusted HR could not be calculated due to low sample size

eTable 10. Censoring reasons for medication cohorts for Optum© Clinformatics® Data Mart and Truven MarketScan for systemic medications compared to adalimumab

	Reference group: Adalimumab Users (compared to methotrexate)	Methotrexate users	Acitretin users	Apremilast users	Etanercept users	Infliximab Users	Ustekinumab Users
United Optum CRD							
No. of patients	7,181	8,470	2,835	1,573	7,698	458	3,254
Median Follow-Up Time (Days) [IQR]	257 [146, 463]	215 [146, 399]	181 [148, 295]	154 [84, 270]	258 [146, 500]	148 [57, 307]	227 [145, 414]
Censoring Reasons							
Outcome	79 (1.1%)	112 (1.3%)	29 (1.0%)	2 (0.1%)	67 (0.9%)	6 (1.3%)	18 (0.6%)
Start of an additional exposure (crossover)	366 (5.1%)	695 (8.2%)	108 (3.8%)	65 (4.1%)	871 (11.3%)	17 (3.7%)	76 (2.3%)
End of index exposure	3,004 (41.8%)	4,300 (50.8%)	1,757 (62.0%)	444 (28.2%)	3,005 (39.0%)	164 (35.8%)	1,083 (33.3%)
Specified date reached (10/01/2015)	1,044 (14.5%)	918 (10.8%)	136 (4.8%)	476 (30.3%)	373 (4.8%)	36 (7.9%)	649 (19.9%)
Death/Disenrollment	2688 (37.4%)	2445 (28.9%)	612 (21.6%)	490 (31.2%)	2638 (34.3%)	109 (23.8%)	1234 (37.9%)
Methotrexate added	*	*	193 (6.8%)	96 (6.1%)	744 (9.7%)	126 (27.5%)	194 (6.0%)
Truven MarketScan							
No. of patients	17,912	20,609	7,883	4,344	18,719	1,332	6,028
Median Follow-Up Time (Days) [IQR]	278 [153, 503]	209 [146, 391]	189 [148, 313]	148 [65, 233]	284 [146, 551]	158 [34, 358]	245 [145, 444]
Censoring Reasons							
Outcome	197 (1.1%)	229 (1.1%)	78 (1.0%)	8 (0.2%)	176 (0.9%)	22 (1.7%)	41 (0.7%)
Start of an additional exposure (crossover)	1,037 (5.8%)	2,249 (10.9%)	339 (4.3%)	115 (2.6%)	1,852 (9.9%)	92 (6.9%)	179 (3.0%)
End of index exposure	7,126 (39.8%)	10,156 (49.3%)	4,858 (61.6%)	719 (16.6%)	7,396 (39.5%)	430 (32.3%)	1,907 (31.6%)
Specified date reached (10/01/2015)	2,789 (15.6%)	2,021 (9.8%)	367 (4.7%)	1,503 (34.6%)	1,419 (7.6%)	61 (4.6%)	1,325 (22.0%)
Death/Disenrollment ^a	6763 (37.8%)	5954 (28.9%)	1163 (21.1%)	1752 (40.3%)	5992 (32.0%)	85 (6.4%)	2201 (36.5%)
Methotrexate added	*	*	578 (7.3%)	247 (5.7%)	1,884 (10.1%)	642 (48.2%)	375 (6.2%)

eTable 11. Meta-analysis of pooled hazard risk of serious infection in patients with psoriasis on systemic medications compared to adalimumab

Exposure	No. of Pooled Patients in Reference Group (adalimumab)	No. Pooled Events in Reference Group (adalimumab) ^a	No. of Pooled Patients in Exposure Group	Events in Exposure Group	Pooled Hazard Ratio ^b (95% CI ^c)	Test for Overall Effect, P
Acitretin						
Overall Serious Infection	30,236	288	10,718	107	1.06 (0.79, 1.43)	0.71
Bacteremia/Sepsis		65		21	0.85 (0.45, 1.61)	0.63
Cellulitis/soft-tissue infection		117		45	1.27 (0.80, 2.01)	0.31
Endocarditis		0		0	*	*
Meningitis/Encephelitis		3		1	*	*
Pneumonia		100		39	0.98 (0.59, 1.65)	0.94
Pyelonephritis		7		3	2.82 (0.42, 18.77)	0.29
Septic arthritis/osteomyelitis		8		4	0.60 (0.10, 3.64)	0.59
Apremilast						
Overall Serious Infection	31,385	319	5,917	10	0.31 (0.15, 0.65)	<0.01
Bacteremia/Sepsis		65		2	0.28 (0.05, 1.42)	0.14
Cellulitis/soft-tissue infection		137		4	0.27 (0.08, 0.86)	0.03
Endocarditis		0		1	*	*
Meningitis/Encephelitis		4		0	*	*
Pneumonia		108		5	0.59 (0.19, 1.78)	0.36
Pyelonephritis		8		0	*	*
Septic arthritis/osteomyelitis		9		0	*	*
Etanercept						
Overall Serious Infection	22,987	202	26,417	243	0.76 (0.61, 0.94)	0.01
Bacteremia/Sepsis		47		40	0.52 (0.30, 0.87)	0.02
Cellulitis/soft-tissue infection		77		103	0.92 (0.66, 1.30)	0.64
Endocarditis		0		0	*	*
Meningitis/Encephelitis		4		7	1.15 (0.30, 4.38)	0.85
Pneumonia		68		83	0.62 (0.42, 0.91)	0.02
Pyelonephritis		7		6	0.62 (0.17, 2.23)	0.48
Septic arthritis/osteomyelitis		7		12	1.20 (0.43, 3.39)	0.74
Infliximab						
Overall Serious Infection	31,427	309	1,790	28	1.92 (1.01, 3.62)	0.04
Bacteremia/Sepsis		64		5	1.16 (0.26, 5.11)	0.86
Cellulitis/soft-tissue infection		132		13	1.46 (0.61, 3.49)	0.40

Endocarditis		0		0	*	*
Meningitis/Encephelitis		4		1	*	*
Pneumonia		105		9	2.18 (0.60, 7.97)	0.24
Pyelonephritis		7		1	*	*
Septic arthritis/osteomyelitis		9		0	*	*
Methotrexate						
Overall Serious Infection	25,093	276	29,079	341	0.93 (0.75, 1.14)	0.51
Bacteremia/Sepsis		55		78	0.93 (0.58, 1.48)	0.77
Cellulitis/soft-tissue infection		117		97	0.74 (0.53, 1.05)	0.08
Endocarditis		0		0	*	*
Meningitis/Encephelitis		2		6	1.28 (0.16, 10.28)	0.83
Pneumonia		98		151	1.09 (0.78, 1.52)	0.63
Pyelonephritis		8		9	0.90 (0.22, 3.66)	0.89
Septic arthritis/osteomyelitis		8		13	1.37 (0.46, 4.07)	0.58
Ustekinumab						
Overall Serious Infection	30,942	306	9,282	59	0.70 (0.49, 1.00)	0.05
Bacteremia/Sepsis		62		12	0.77 (0.32, 1.86)	0.57
Cellulitis/soft-tissue infection		133		26	0.69 (0.40, 1.19)	0.18
Endocarditis		0		0	*	*
Meningitis/Encephelitis		4		1	*	*
Pneumonia		105		18	0.64 (0.34, 1.20)	0.17
Pyelonephritis		7		2	1.08 (0.14, 8.56)	0.95
Septic arthritis/osteomyelitis		7		1	*	*

^a The sum of events in the sub analyses of serious infections may be greater than the number of events in the overall serious infection analysis if a patient experienced greater than one serious infectious event.

^b Adjusted for 20% overlap of patients between United Optum CDM and Truven MarketScan

^c CI, confidence interval

* Pooled HRs not calculated when HR not calculated in either Optum or MarketScan due to zero events in exposure or reference groups.