

## **SUPPLEMENTARY MATERIAL**

### **Apremilast Prolongs the Time to First Biologic Therapy in Japanese Patients With Psoriasis**

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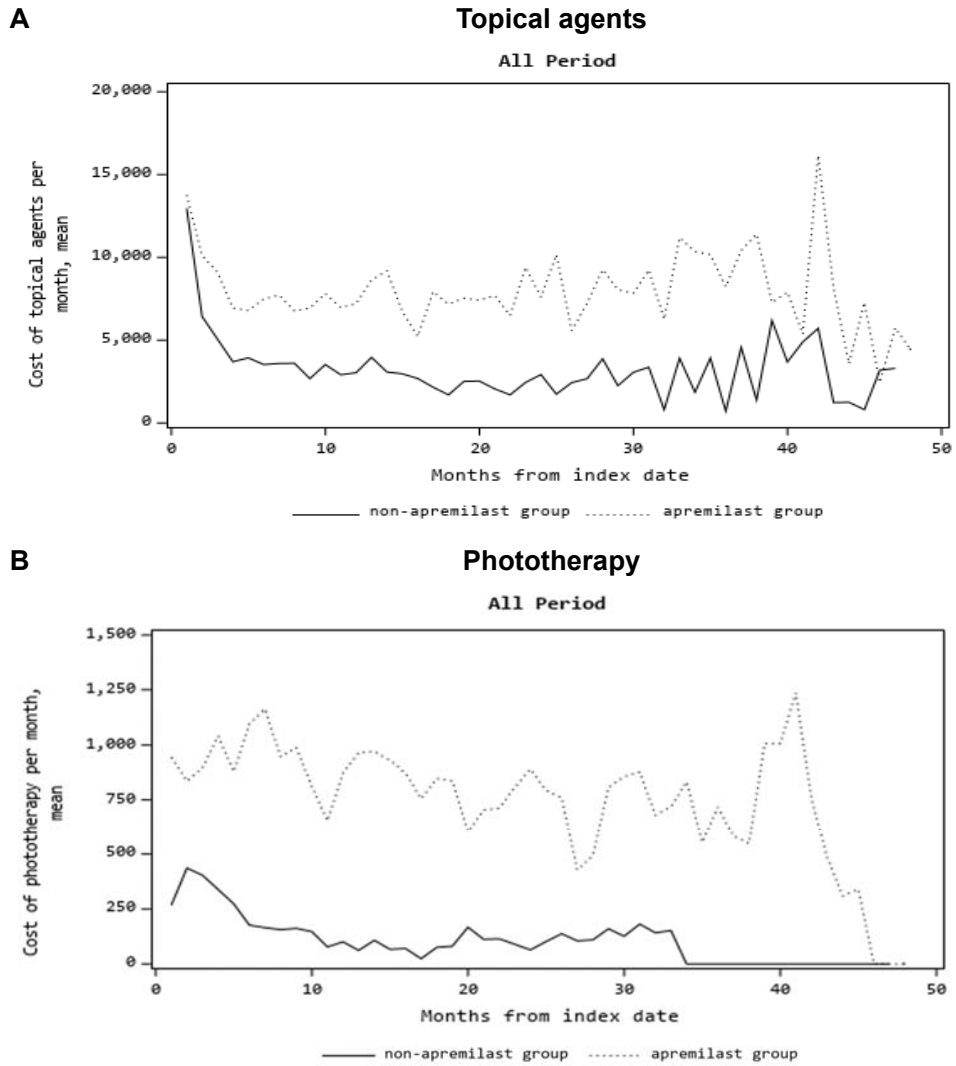
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## **Supplemental Methods**

### **A. Sensitivity Analysis**

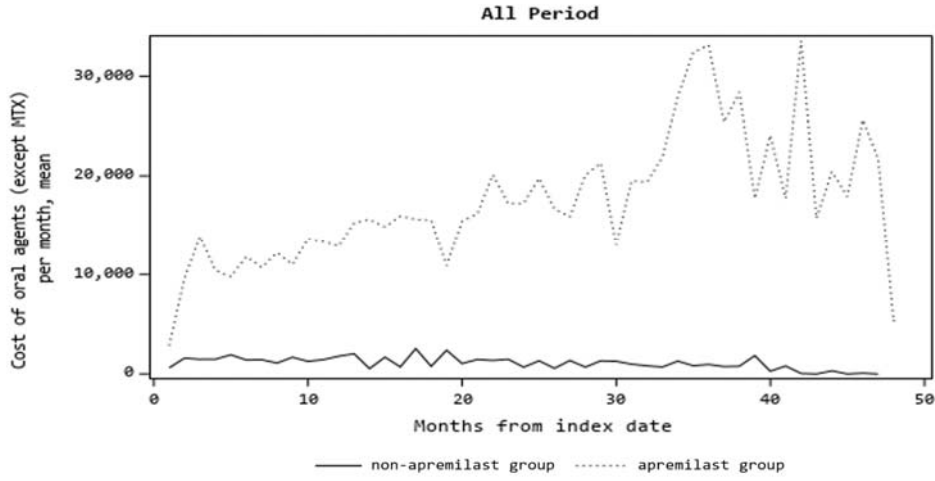
The database does not contain information on disease severity. Disease severity could affect the efficacy and duration of treatment before initiation of biologic therapy, thereby influencing the occurrence and timing of the first biologic therapy use. This could be a major source of bias if the severity was different between the two treatment groups. To help to overcome this bias, the time to first biologic therapy use was analyzed by extracting a subset of eligible patients who were prescribed biologics during the follow-up period from both treatment groups. Instead of matching, an inverse probability of treatment weighting (IPTW) method using propensity scores was also performed as a sensitivity analysis. A stabilization weighting factor, which is the percentage of each group in the overall population multiplied by the IPTW of each group, was used for weighting. The upper limit of the stabilization weighting factor was set to 10, and patients with a propensity score  $<0.005$  or  $>0.9$  were excluded from the analysis to prevent the results from being significantly affected by patients with an extremely large weighting factor.

**Fig. S1.** Mean psoriasis costs per month of (A) topical agents, (B) phototherapy, (C), oral agents, (D) MTX, (E) biologic therapy, (F) other agents for psoriasis, (G) other agents, (H) other treatment procedures, (I) tests, (J) hospitalization, and (K) total medical expenses. *MTX* methotrexate



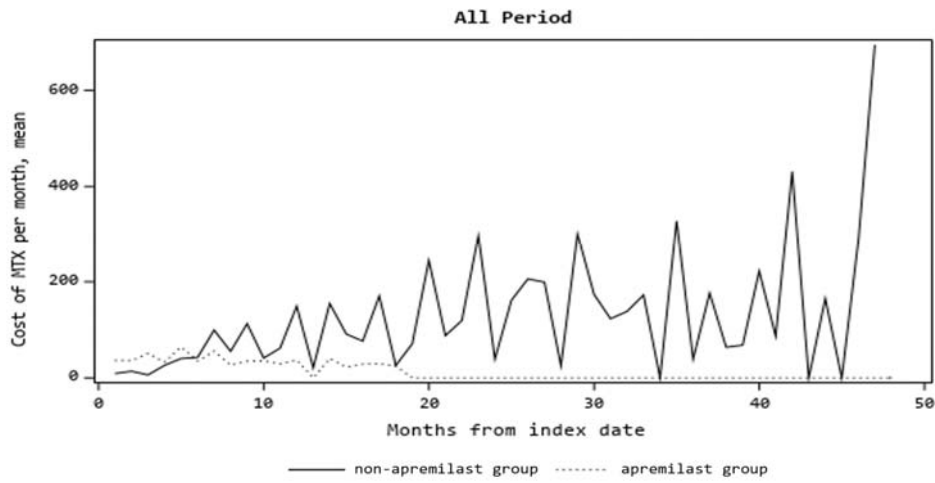
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### Oral agents



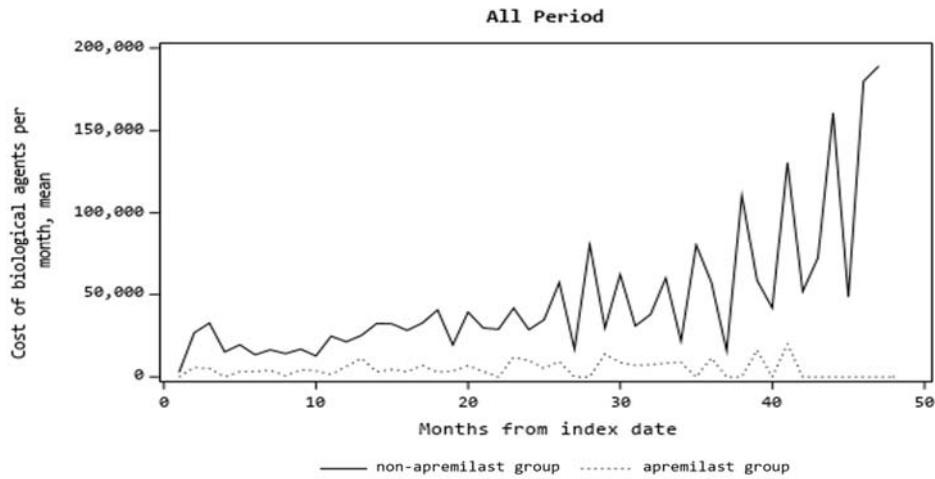
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### MTX



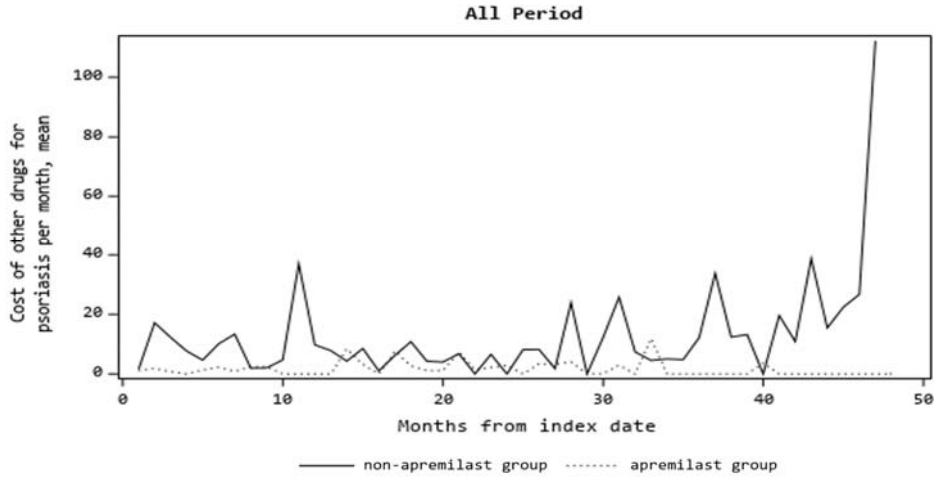
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### Biologic therapy



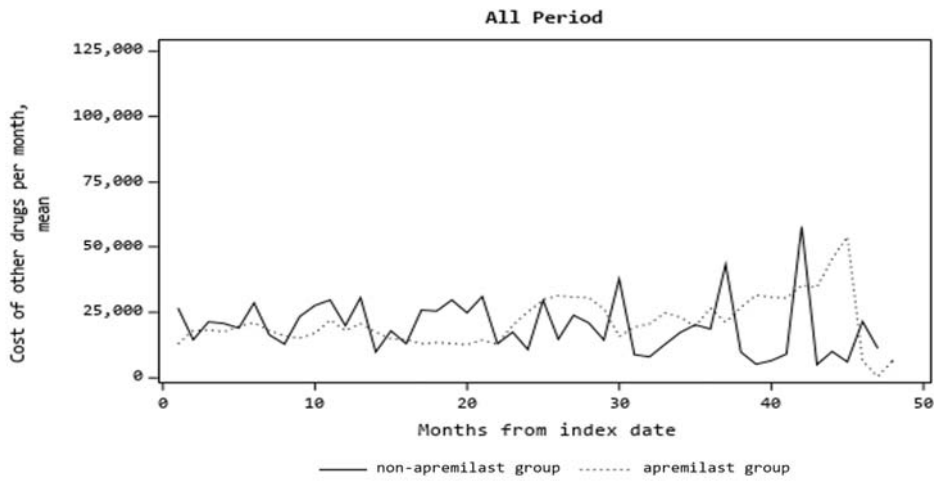
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### Other agents for psoriasis



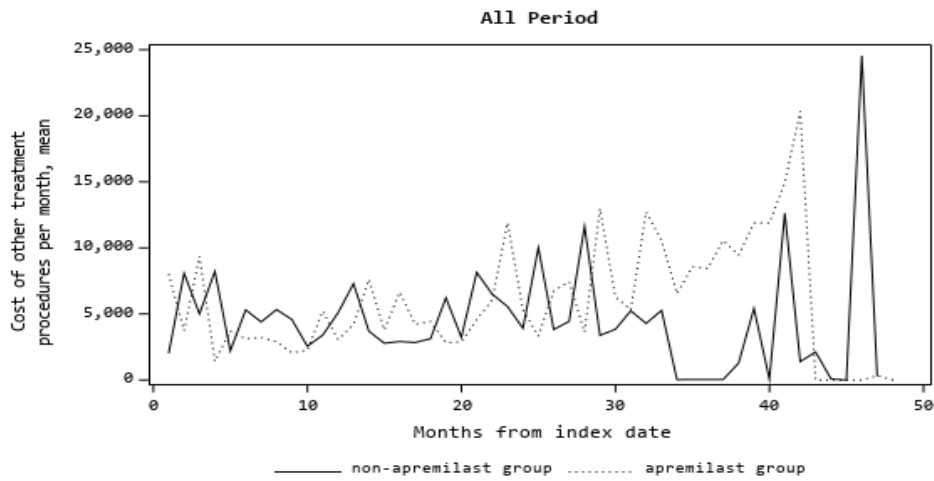
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### Other agents

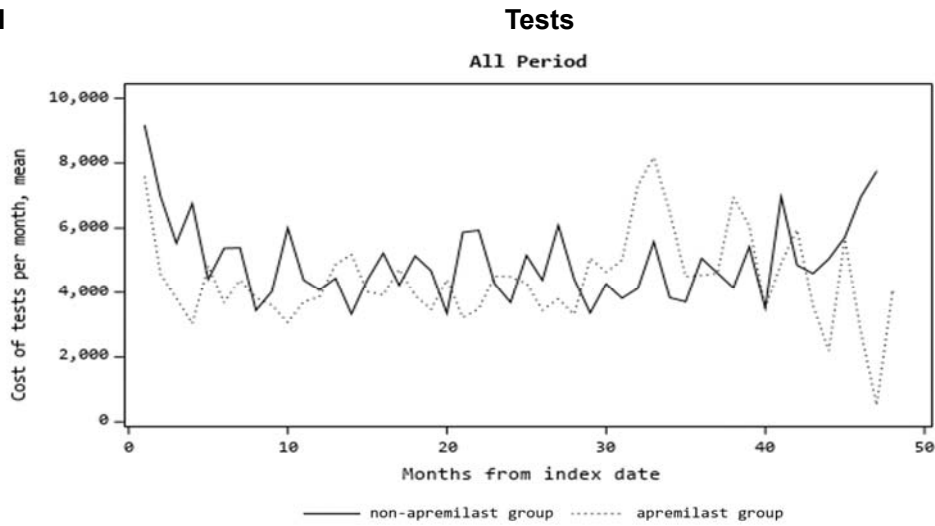


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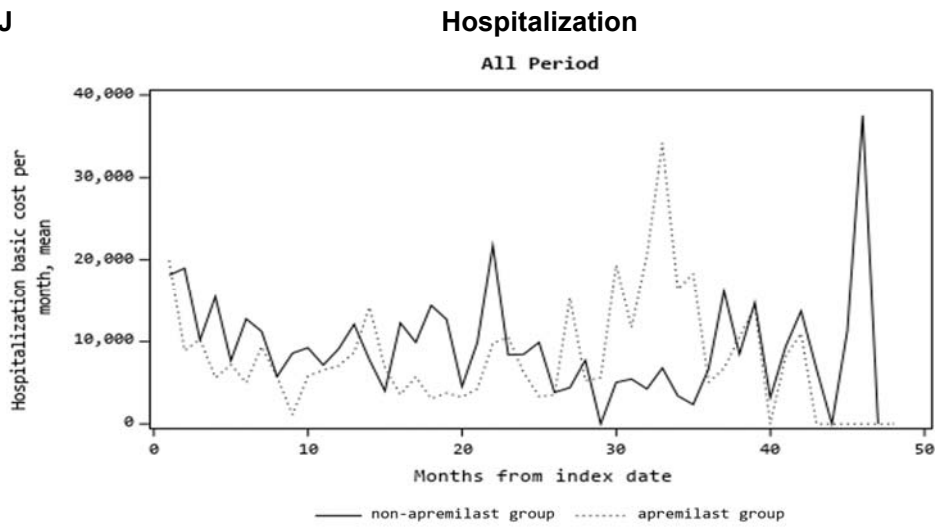
### Other treatment procedures



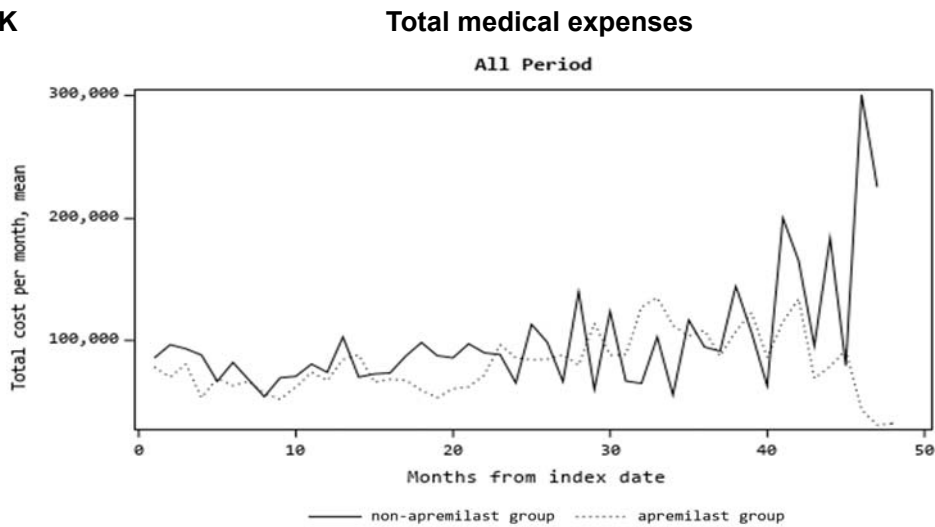
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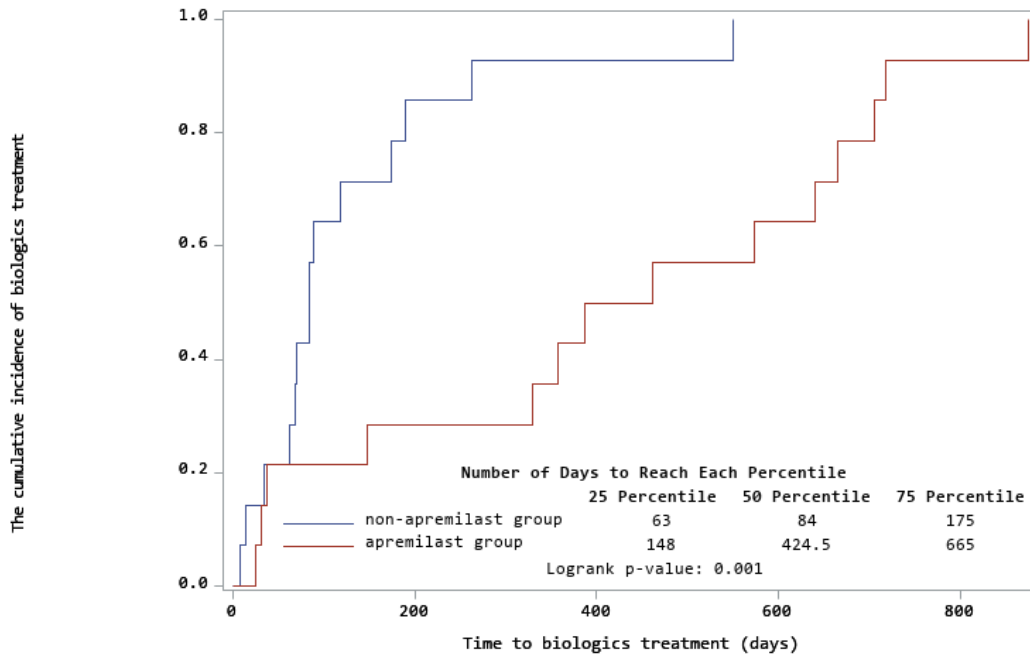
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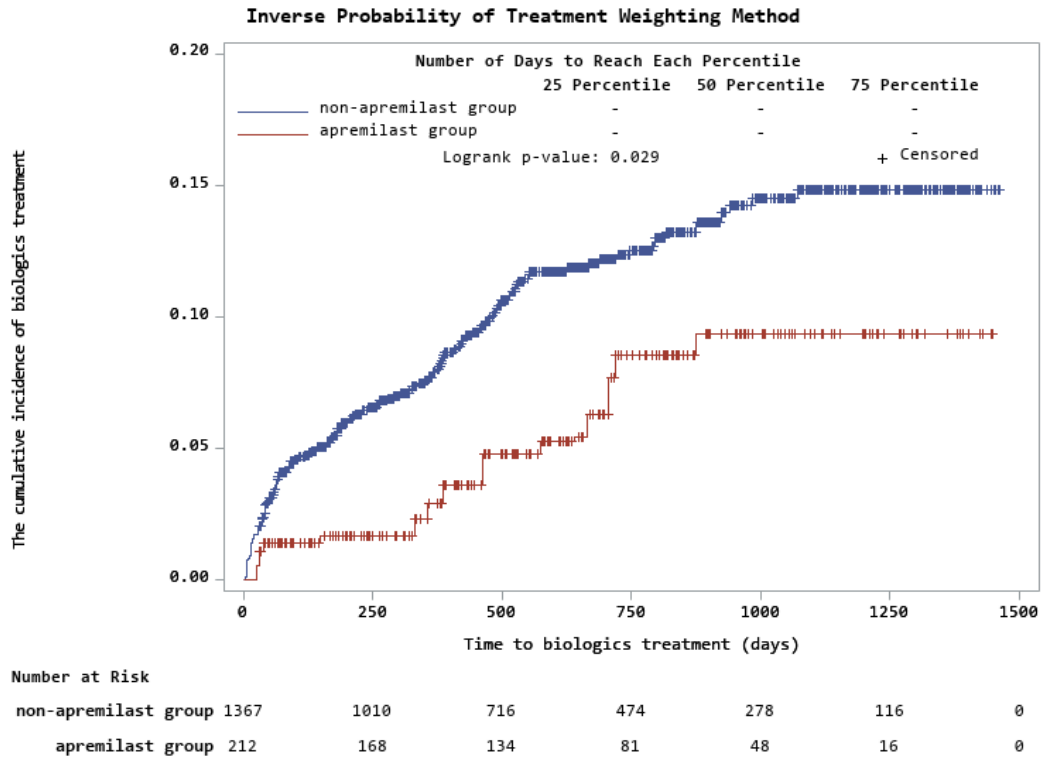


**Fig. S2.** Sensitivity analysis: cumulative incidence of biologic therapy in patients prescribed a biologic during the follow-up period



Number at Risk					
	0	200	400	600	800
non-apremilast group	14	2	1	0	
apremilast group	14	10	7	5	1

**Fig. S3.** Sensitivity analysis: cumulative incidence of biologic therapy using the inverse probability of treatment weighting method





**Table S1.** Patient characteristics before propensity score matching

	Before propensity score matching			SMD <sup>a</sup>
	Apremilast group <i>n</i> = 254	Non-apremilast group <i>n</i> = 1,381	Total <i>n</i> = 1,635	
Age, mean (SD), years, mean (SD)	63.1 (15.9)	65.3 (15.5)	64.9 (15.6)	-0.14
Age category, <i>n</i> (%)				
<50	53 (20.9)	250 (18.1)	303 (18.5)	
50-59	40 (15.7)	188 (13.6)	228 (13.9)	
60-69	56 (22.0)	320 (23.2)	376 (23.0)	
≥70	105 (41.3)	623 (45.1)	728 (44.5)	
Male, <i>n</i> (%)	155 (61.0)	800 (57.9)	955 (58.4)	0.06
Disease type, <i>n</i> (%)				
Psoriasis vulgaris	250 (98.4)	1,346 (97.5)	1,596 (97.6)	-0.07
Psoriatic arthritis	13 (5.1)	77 (5.6)	90 (5.5)	0.02
Diagnosis, <i>n</i> (%)				
Obesity	3 (1.2)	6 (0.4)	9 (0.6)	-0.08
Diabetes	50 (19.7)	407 (29.5)	457 (28.0)	0.23
Hypertension	53 (20.9)	519 (37.6)	572 (35.0)	0.37
Dyslipidaemia	48 (18.9)	354 (25.6)	402 (24.6)	0.16
Treatment information during the baseline period, mean (SD)				
Hospitalization frequency	0.12 (0.40)	0.26 (0.61)	0.24 (0.58)	-0.27
Length of hospital stay, days	0.9 (4.2)	3.7 (14.3)	3.3 (13.3)	-0.26
Number of patients visits	3.4 (6.0)	6.2 (10.5)	5.8 (10.0)	-0.33
Direct medical cost, yen	181,717 (740,750)	441,936 (893,733)	401,511 (876,610)	-0.32
Length of follow-up period, months	20.8 (12.5)	21.7 (13.5)	21.6 (13.3)	-0.07
Period until oral drug or biologic for psoriasis is prescribed, days	289.2 (309.3)	264.4 (284.8)	269.2 (289.8)	0.08
Use of psoriasis drug during the follow-up period				
Use of topical steroid, <i>n</i> (%)	250 (98.4)	1,333 (96.5)	1,583 (96.8)	-0.12
Use of non-steroidal topical agents, <i>n</i> (%)	245 (96.5)	800 (57.9)	1,045 (63.9)	-1.03
Initial dose of steroid topical agents, mean (SD), g <sup>b</sup>	62.2 (53.8)	37.0 (46.3)	40.9 (48.4)	0.50
Maximum dose of steroid topical agents, mean (SD), g <sup>b</sup>	142.9 (125.5)	72.7 (109.9)	83.6 (115.3)	0.59
Average dose of steroid topical agents, mean (SD), g <sup>b</sup>	2.61 (3.27)	1.73 (6.67)	1.86 (6.27)	0.17
Class of steroid topical agents-initial dose <sup>b</sup> , <i>n</i> (%)				
Strongest	46 (18.1)	184 (13.3)	230 (14.1)	
Very strong	193 (76.0)	773 (56.0)	966 (59.1)	
Strong	6 (2.4)	258 (18.7)	264 (16.1)	
Medium	5 (2.0)	114 (8.3)	119 (7.3)	

Weak	0 (0.0)	4 (0.3)	4 (0.2)	
Missing	4 (1.6)	48 (3.5)	52 (3.2)	
Class of steroid topical agents-strongest class <sup>b</sup> , <i>n</i> (%)				
Strongest	106 (41.7)	388 (28.1)	494 (30.2)	
Very strong	141 (55.5)	693 (50.2)	834 (51.0)	
Strong	1 (0.4)	199 (14.4)	200 (12.2)	
Medium	2 (0.8)	52 (3.8)	54 (3.3)	
Weak	0 (0.0)	1 (0.1)	1 (0.1)	
Missing	4 (1.6)	48 (3.5)	52 (3.2)	
Class of steroid topical agents - most frequently used class <sup>b</sup> , <i>n</i> (%)				
Strongest	34 (13.4)	159 (11.5)	193 (11.8)	
Very strong	198 (78.0)	778 (56.3)	976 (59.7)	
Strong	9 (3.5)	263 (19.0)	272 (16.6)	
Medium	5 (2.0)	93 (6.7)	98 (6.0)	
Weak	0 (0.0)	4 (0.3)	4 (0.2)	
Missing	8 (3.1)	84 (6.1)	92 (5.6)	
Initial dose of non-steroidal topical agents, mean (SD), g	56.5 (46.4)	24.0 (42.0)	29.0 (44.3)	0.73
Maximum dose of non-steroidal topical agents, mean (SD), g	109.6 (90.5)	44.2 (106.5)	54.3 (106.8)	0.66
Average dose of non-steroidal topical agents, mean (SD), g	1.96 (2.52)	0.87 (2.60)	1.04 (2.62)	0.43
Total prescription of topical agents, mean (SD), g	1,316.3 (1,777.4)	472.3 (976.9)	603.4 (1,178.4)	0.59
Prescription of topical agents per day, mean (SD), g	2.30 (2.63)	0.95 (1.86)	1.16 (2.06)	
Use of oral etretinate, <i>n</i> (%)	35 (13.8)	102 (7.4)	137 (8.4)	-0.21
Use of oral cyclosporine, <i>n</i> (%)	9 (3.5)	58 (4.2)	67 (4.1)	0.03
Use of biologics, <i>n</i> (%)	14 (5.5)	135 (9.8)	149 (9.1)	0.16

<sup>a</sup>Non-apremilast group as reference. <sup>b</sup>Aggregated period for initial dose, maximum dose, class at the start of use and the strongest class: follow-up period; aggregated period for average dose and the most frequently used class: until oral drugs or biologics for psoriasis were presented during the follow-up period  
*SD* standard deviation; *SMD* standardized mean difference

**Table S2.** Sensitivity analysis: incidence rate for the first biologic therapy use for patients in each treatment group prescribed biologics during the follow-up period, matched by the propensity score

	<i>n</i>	Biologic therapy	Person-years	Biologic treatment incidence rate (per 1,000 person-years)		<i>P</i> -value <sup>b</sup>
				Incidence rate	95% CI <sup>a</sup>	
Apremilast group	14	14	16.4	856.1	507.0, 1,445.5	
Non-apremilast group	14	14	5.0	2,797.6	1,656.9, 4,723.6	NA <sup>†</sup>

<sup>a</sup>95% CI was calculated using Poisson distribution. <sup>b</sup>*P*-value of chi-square test could not be calculated, because all patients in each group were categorized as having an event  
*CI* confidence interval; *NA* not applicable

**Table S3.** Sensitivity analysis: incidence rate for the first biologic therapy use for patients in each treatment group matched by the inverse probability of treatment weighting method

	<i>n</i>	Biologic therapy	Person-years	Biologic treatment incidence rate (per 1,000 person-years)		<i>P</i> -value <sup>b</sup>
				Incidence rate	95% CI <sup>a</sup>	
Apremilast group	253	13	377.5	33.5	19.3, 58.1	
Non-apremilast group	1,361	144	2,230.3	64.7	55.0, 76.2	0.037

<sup>a</sup>95% CI was calculated using Poisson distribution. <sup>b</sup>Chi-square test  
*CI* confidence interval

**Table S4.** Sensitivity analysis: healthcare resource utilization for patients in each treatment group matched by the inverse probability of treatment weighting method

	<b>Apremilast group, mean (SD) n = 253</b>	<b>Non-apremilast group, mean (SD) n = 1,361</b>	<b>Absolute difference</b>	<b>P value<sup>a</sup></b>
Number of outpatient visits/month	1.52 (0.76)	1.37 (1.30)	0.15	0.042
direct medical cost				
Cost of psoriasis drugs/treatment procedure				
Topical agents, yen/month	7,630 (7,497)	2,983 (5,663)	4,647	<0.001
Phototherapy, yen/month	713 (1,796)	183 (969)	530	<0.001
Oral drugs (except methotrexate), yen/month	17,102 (15,239)	941 (3,261)	16,161	<0.001
Methotrexate, yen/month	36 (335)	80 (509)	-44	0.026
Biologic agents, yen/month	5,544 (25,476)	14,396 (52,749)	-8,851	0.023
Other drugs for psoriasis, yen/month	2 (9)	35 (220)	-33	< 0.001
Cost of other drugs, yen/month	18,999 (73,707)	42,180 (104,253)	-23,181	< 0.001
Cost of other treatment procedure, yen/month	2,386 (6,855)	9,735 (46,109)	-7,349	0.001
Cost of tests, yen/month	4,937 (5,067)	9,284 (15,097)	-4,347	< 0.001
Hospitalization basic cost, yen/month	11,656 (27,684)	35,473 (96,946)	-23,817	< 0.001
Total cost, yen/month	79,874 (97,540)	135,923 (228,263)	-56,048	0.004

<sup>a</sup>Wilcoxon rank-sum test

SD standard deviation