Cost of illness analysis of self-injection of biologics in patients with rheumatoid arthritis in Japan

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Background

- Self-injection (SI) may reduce: (i) Direct healthcare costs (outpatient visits, drugs[1)]), (ii) Direct non-healthcare costs (transportation[2)]) and (iii) Indirect costs (productivity loss of patients/caregivers)
- Biologic disease-modifying antirheumatic drugs (bDMARDs) have transformed rheumatoid arthritis (RA) care, improving disease control, quality of life, and making remission achievable[3)].Yet, RA still causes major socioeconomic burden through reduced productivity and caregiving needs, increasing indirect costs[4)].
- Our web survey found >80% of Japanese bDMARD users chose SI for convenience. Despite higher per-visit costs, annual out-of-pocket burden was lower[5)].
- Comprehensive cost-of-illness (COI) studies on SI in RA are scarce, especially in Japan. With its aging society, universal healthcare, and SI promotion policies, Japan is a unique case study[6)]. Assessing its societal impact can inform other nations facing similar healthcare challenges.

Aims

- **To compare the annual COI—including both direct and indirect costs—between the SI and non-SI groups among patients with RA in Japan.**

Summary of results

- **SI increased direct medical costs, mainly from higher bDMARD expenses.**
- **Reduced hospital visits lowered some non-medical and indirect costs, but not enough to offset higher drug costs, resulting in a slightly higher total COI in the SI group.**
- **Sensitivity analysis showed that productivity loss from activity impairment was the largest contributor to societal costs in both SI and non-SI groups.**

Methods

- **Study Design & Perspective:**
  - Cross-sectional COI analysis from a societal perspective, based on Larg & Moss framework[7)] and micro-costing approach[8)].
- **Data Sources:**
  - Claims database (DeSC, 2014–2023): 6,784 RA patients (SI: 3,392 / non-SI: 3,392; matched by propensity score).
  - Patient web survey: 79 bDMARD users (travel costs, time, activity impairment)[5)].
  - Official statistics & patient model: Wage surveys and outpatient time (working-age patients only)[9,10)].
- **Study Patients:**
  - The mean weighted age was 57.1 years [11,12)].
- **Costs Evaluated:**
  - Direct medical (Drugs, Hospital, Examination, Rehabilitation, Surgery and Dispensing)
  - Direct non-medical (Traveling)
  - Indirect (productivity/time loss, applied only to employed)
- **Estimation:** Annual per-patient costs in USD (1 USD = 150 JPY).
- **Annual COI** = (Direct Medical Costs [$ / month] × 12)
  + (Traveling Costs × Number of Visits [visits/year])
  + (Time per Visit × Hourly Wage × Number of Visits [visits/year])
  + (Activity Impairment Loss[13,14)] [$ / month] × 12)
  - Subgroups: SI-employed, SI-unemployed, non-SI-employed, non-SI-unemployed.
- **Sensitivity analyses (Tornado diagram):**
  - We conducted sensitivity analyses to examine the robustness of the results by varying key parameters.

Results

Table 1. List of Parameters

Category (Mean,95% CI)		Unit	SI group	non-SI group	p value	Data source
Direct medical cost	Drugs	$/month	701 (689 - 712)	516 (503 - 528)	*<0.05.	1)
	Cost of bDMARDs	$/month	694 (684 - 705)	499 (489 - 508)	*<0.05.	1)
	Number of bDMARDs prescriptions	Units/ month	2.9 (2.9 - 3.0)	1.9 (1.9 - 1.9)	*<0.05.	1)
	Cost of other DMARDs	$/month	7 (5 - 8)	17 (14 - 19)	*<0.05.	1)
	Medical service fees	$/month	73 (69 - 77)	93 (86 - 99)	*<0.05.	1)
	Hospitalization	$/month	16 (15 - 17)	28 (25 - 30)	*<0.05.	1)
	Examination	$/month	22 (22 - 23)	23 (23 - 23)	*<0.05.	1)
	Imaging examination	$/month	13 (13 - 14)	17 (16 - 18)	*<0.05.	1)
	Rehabilitation	$/month	5 (5 - 6)	8 (7 - 9)	*<0.05.	1)
	Surgery	$/month	5 (4 - 6)	6 (4 - 7)	*<0.05.	1)
	Dispensing	$/month	11 (11 - 11)	11 (11 - 11)	*<0.05.	1)
Direct non-medical cost	Traveling cost	$/visit	7 (4 - 9)	3 (2 - 5)	*<0.05.	2)
Indirect cost	Average monthly wage (ages 30–60)	$/month	1,708 (1,448 - 1,967)		N/A	3)
	Average hourly wage (ages 30–60)	$/hr	10 (8 - 11)		N/A	3)
	Productivity loss associated with outpatient visit	$/visit	14 (13 - 15)	13 (12 - 14)	*<0.05.	2)+3)
	Round-trip travel time for outpatient visits	min/visit	38.1 (29.6 - 46.6)	27.9 (19.0 - 36.8)	*<0.05.	2)
	Waiting time before consultation	min/visit	39.1 (1.6 - 76.5)		N/A	3)
	Duration of medical consultation	min/visit	9.7 (0 - 19.9)		N/A	3)
	Total patient time per outpatient visit	hr/visit	1.4 (0.5 - 2.4)	1.3 (0.3 - 2.2)	*<0.05.	2)+3)
	Monthly productivity loss due to activity impairment	$/month	491 (399 - 579)	427 (195 - 626)	> 0.05	2)+3)
	Activity Impairment	%/month	28.8 (23.3 - 33.9)	25.0 (11.4 - 36.7)	> 0.05	2)
Other	Annual frequency of hospital visits	visit/year	9.5(9.4 - 9.6)	25.0 (24.5 - 25.6)	*<0.05.	1)
	J-HAQ	-	0.61(0.48 - 0.74)	0.63 (0.31 - 0.92)	> 0.05	2)

Data sources: 1): Health Insurance Claims Data, 2): Patient Survey [5)],3): Official Statistical Data [9, 10)]
Note: *p value <0.05 indicates statistically significant difference between SI and non-SI groups.

Table 2. Annual Medical Costs for Patients with Rheumatoid Arthritis

Category (Mean,95% CI)		Unit	SI group	non-SI group
Direct medical cost	Annual direct medical costs	$/year	9,280 (9,096 - 9,442)	7,298 (7,072 - 7,448)
	Drug costs	$/year	8,410 (8,273 - 8,545)	6,187 (6,039 - 6,332)
	Medical service fees	$/year	870 (823 - 927)	1,111 (1,033 - 1,186)
Direct non-medical costs	Traveling cost	$/year	64 (37 - 87)	86 (51 - 117)
Indirect costs	Annual productivity loss associated with outpatient visit	$/year	136 (124 - 147)	315 (284 - 645)
	Annual productivity loss due to activity impairment	$/year	5,896 (4,782 - 6,948)	5,123 (2,342 - 7,514)

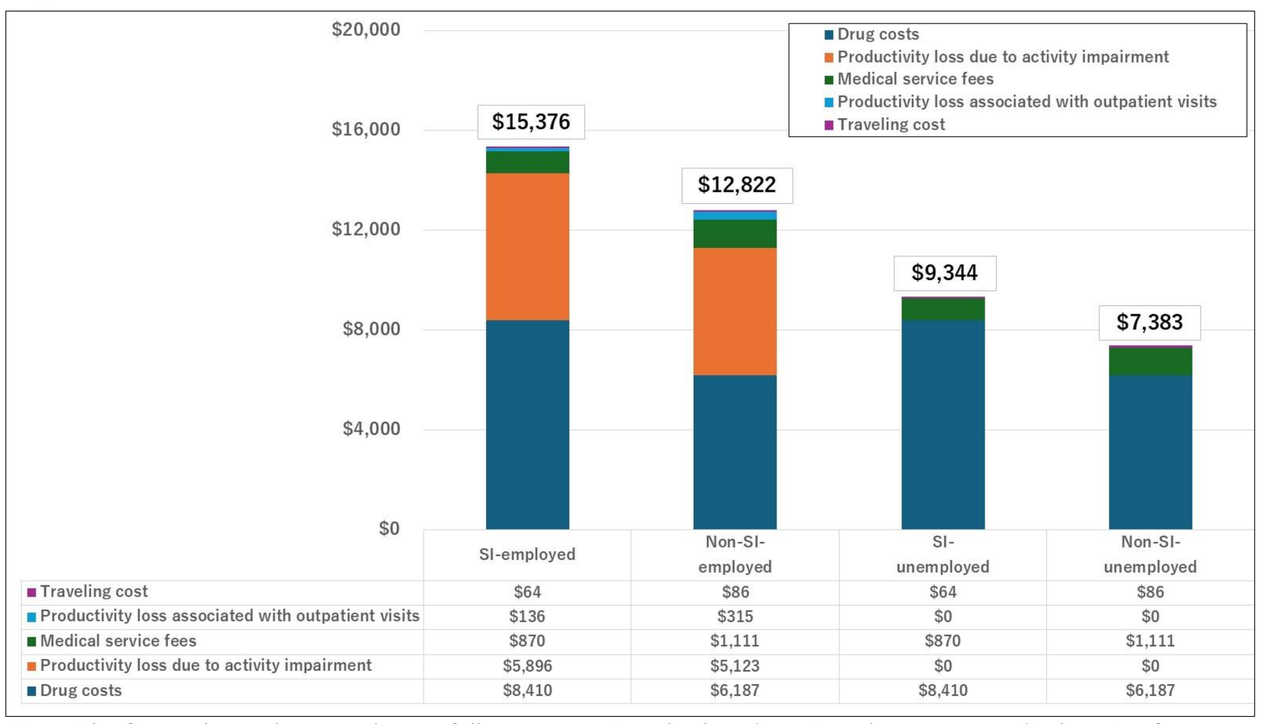
Note: Values are presented as mean (95% confidence interval).

Direct medical costs:
- Annual direct medical costs were higher in the SI group ($9,280 vs. $7,298), mainly due to bDMARDs ($8,410 vs. $6,187).
- Medical service fees were higher in the non-SI group ($1,111 vs. $870) because of more frequent visits.

Direct non-medical costs (travel):
- Lower in the SI group ($64 vs. $86), reflecting fewer visits.

Indirect costs:
- Productivity loss from outpatient visit time was lower in the SI group ($136 vs. $315).
- Productivity loss from activity impairment was slightly higher in the SI group ($5,896 vs. $5,123), but not significant.

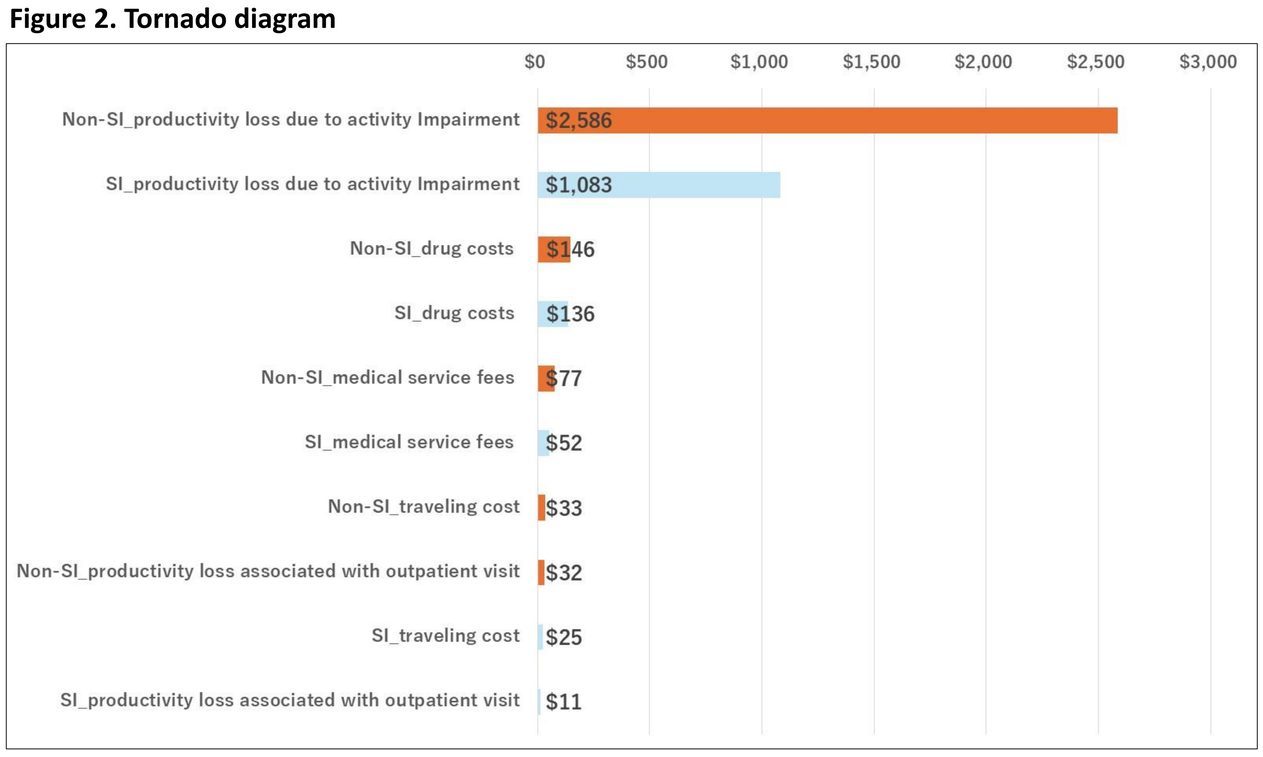
Figure1. Breakdown of annual COI



Note: The figure shows the annual cost of illness per patient, broken down into drug costs, medical service fees, productivity losses (due to activity impairment and outpatient visits), and traveling costs.
Each bar represents the mean total cost for each subgroup.

- Employed patients: SI $15,376 vs non-SI $12,822 → difference $2,554
- Unemployed patients: SI $9,344 vs non-SI $7,383 → difference $1,961
- In employed and unemployed, total COI was consistently higher in the SI group.

Figure 2. Tornado diagram



Note: Tornado diagram showing the contribution of each cost component to the annual cost difference between self-injection (SI) and non-SI groups.

- The largest impact was from productivity loss due to activity impairment in the non-SI group (annual COI variation up to $2,586).
- The second most influential factor was activity impairment in the SI group ($1,083 variation).
- Other factors (outpatient-related productivity loss, drug costs, consultation fees, travel costs) had only minor effects (<$150), supporting robustness of findings.

Limitation

- Study design: Cross-sectional; small non-SI sample may reduce precision
- Residual confounding: Adjusted with propensity scores, but voluntary SI choice may leave bias
- Cost estimation: Travel and time costs approximated by averages; real-world variation not captured
- Productivity loss: Estimated using self-reported scores; subject to reporting bias
- Clinical outcomes: Disease activity, functional status, and QALYs not assessed; cost-effectiveness not evaluated

Conclusion

- **SI was associated with higher drug costs but reduced burdens related to outpatient visit. Productivity loss from activity impairment was the largest contributor to total COI in both groups, emphasizing the importance of labor-related outcomes in RA economic evaluations.**
- **These findings suggest that, regardless of SI, maintaining adequate disease control is crucial to preserving work productivity.**

References
1) Bergqvist V, et al. Aliment Pharmacol Ther. 2022;55(11):1389-401.
2) Di Giorgio L, et al. Contraception. 2018;98(5):396-404.
3) Yamanaka H, et al. Mod Rheumatol. 2020;30(1):1-6.
4) Verstappen SM, et al. Ann Rheum Dis. 2005;64(12):1754-60.
5) Takahata K, et al. BMC Health Serv Res. 2025;25(1):730.
6) Saeki H, et al. J Dermatol. 2023;50(2):e41-e68.
7) Larg A, Moss JR. Pharmacoeconomics. 2011;29(8):653–671.
8) Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. Oxford University Press; 1996.
9) Ministry of Health, Labour and Welfare. The 2023 Basic Survey on Wage Structure.
10) Ministry of Health, Labour and Welfare. Overview of the 2020 Patient Survey (Preliminary Figures).
11) Nakajima A, et al. Int J Rheum Dis. 2020;23(12):1676–84.
12) Nakajima A, et al. Clin Rheumatol Rel Res. 2021;33(1):6–13.
13) Ford et al. Journal of Patient-Reported Outcomes. 2023(7):34.
14) Forman-Hoffman et al. JOEM. 2024;66(3):99-105.

CONFLICT OF INTEREST
- Kazuhiko Takahata is employee of Kyowa Kirin Co., Ltd. and he has received part of his doctoral degree program tuition support from his company.
- Eiichi Tanaka has received lecture fees or consulting fees from AbbVie Japan GK, Asahi Kasei Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Co., Boehringer Ingelheim Japan, Inc., Bristol Myers Squibb Co., Ltd., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Eli Lilly Japan K.K., Gilead Sciences, Inc., GlaxoSmithKline K.K., Mikasa Seiyaku co., Ltd., Mitsubishi Tanabe Pharma Co., Nichi-Iko Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., Pfizer Japan Inc, Sandoz K.K., Taisho Pharmaceutical Co., Ltd, Takeda Pharmaceutical Co., Ltd, Towa Pharmaceutical Co., Ltd., UCB Japan Co. Ltd. and Viatris Inc.
- Eiichi Tanaka has received research funding from Pfizer Inc..
- Ryoko Sakai has received consulting fees from Nippon Kayaku Co., Ltd.
- Manabu Akazawa has received lecture fees or consulting fees from Astellas Pharma Inc., Mitsubishi Tanabe Pharma Co., GlaxoSmithKline K.K. and Janssen Pharmaceutical K.K.

Study approval was obtained from the Meiji Pharmaceutical University Research Ethics Committee in March 2022 (Approval No. 202144).