

ORIGINAL ARTICLE

Cost of illness study for adult atopic dermatitis in Japan: A cross-sectional Web-based survey

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ABSTRACT

Atopic dermatitis is a pruritic, eczematous dermatitis, the symptoms of which chronically fluctuate with remissions and relapses. Although a high psychosomatic and economic burden caused by atopic dermatitis is expected, few studies have been conducted estimating the cost of illness, including the self-medication costs and productivity loss due to atopic dermatitis. The aim of this study was to conduct a cross-sectional, Web-based survey of the direct medical costs, self-medication costs and productivity loss for adult atopic dermatitis patients, and estimate the burden of Japanese adult atopic dermatitis patients by disease severity. In a physician survey, the medical resource consumption related to medical treatments was surveyed by disease severity. The direct medical costs were calculated by multiplying the medical resource consumption and medical fee corresponding to each treatment. Based on the results of a patient survey, the self-medication costs and productivity loss were estimated by sex and disease severity. Atopic dermatitis-related productivity loss was calculated based on absenteeism, presenteeism, overall work impairment for employed workers and activity impairment for housewives. The nationwide estimations were calculated based on the estimated number of atopic dermatitis patients, employed workers with atopic dermatitis, and housewives with atopic dermatitis in their 20s–50s in Japan. Based on the surveys, all costs per patient and the scores increased with disease severity. The cost of illness for adult atopic dermatitis patients in Japan was estimated to be approximately JPY 3 trillion/year. Considering the physical and mental burdens, the burden of illness for adult atopic dermatitis was demonstrated to be vast.

Key words: atopic dermatitis, cost of illness, direct medical cost, overall work impairment, self-medication cost.

INTRODUCTION

Atopic dermatitis (AD) is a common chronic inflammatory dermatosis characterized by recurring exacerbations of red, dry and itchy skin.¹ The prevalence of adult AD was reported to range 2.1–4.9% in an international, cross-sectional, Web-based survey on the prevalence of adult AD (18–65 years old), which was conducted in the USA, Canada, France, Germany, Italy, Spain, UK and Japan between 29 February and 13 April 2016.² Kohno *et al.*³ surveyed 4826 Japanese adults in their 20s–60s between 2000 and 2008, and reported the prevalence of Japanese adult AD to be 6.8%, and that it was slightly lower in males than females and decreased with age. The distribution of adults with mild, moderate, severe and most severe AD was 80.1%, 17.7%, 1.5% and 0.6%, respectively, and mild cases accounted for 80%.³

Atopic dermatitis often affects everyday life, and it commonly requires regular treatments to repair the skin barrier using moisturizers and topical anti-inflammatory management by using corticosteroids to control inflammation.^{4,5} In addition,

there are out-of-pocket expenses for self-medication such as moisturizing creams, hygiene products and laundry costs.

Furthermore, the AD condition also reduces the health-related quality of life (HRQoL) due to itching, appearance problems and treatment burden for AD. Poole *et al.*⁶ reported that the quality of life (QOL) score decreased with disease severity in a HRQoL study using EuroQoL 5 Dimension and Short Form 6 Dimension for AD patients. A HRQoL survey using time trade-off conducted in Germany revealed that the QOL score of patients with uncontrolled AD was lower than that of those with controlled AD, being 0.65 and 0.96, respectively.⁷ Furthermore, 62.2% of AD patients have sleep disorders,⁸ and AD is expected to cause a high psychosomatic and economic burden.

Several studies have evaluated the economic burden of AD. Kim *et al.*⁹ surveyed 34 AD patients who visited dermatologists at three universities in Korea between 1 June 2010 and 31 August 2010. They found that the annual total direct medical cost for AD patients was KRW 457 038, and the absenteeism for their families and guardians due to informal

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caregiving was an average of 4.5 days/year. A survey was conducted by Fowler *et al.*¹⁰ using claims data of 13 749 patients diagnosed with AD between 1 January 1998 and 31 January 2005. The increase in direct and indirect medical costs in the AD patient group aged 0–64 years compared with those in control group was USD 88/month and USD 64/month, respectively. Barbeau *et al.*¹¹ reported that the absenteeism per visit for 76 AD patients was 1.1 h, and it increased with severity. Holm *et al.*¹² also reported that the absenteeism of AD patients for the past 6 months was an average of 5.8 days.

However, in Japan, although the health-care resource use¹³ and disease burden¹⁴ related to AD treatment in AD patients have been reported, few studies have estimated the cost of illness, including the self-medication costs and productivity loss due to AD.

The aim of this study was to conduct a cross-sectional, Web-based survey on the direct medical costs, self-medication costs and productivity loss for adult AD patients (aged ≥ 16 years) and estimate the burden of Japanese adult AD patients by disease severity.

METHODS

Study design and participants

Direct medical costs, self-medication costs and productivity loss were estimated as the burden of AD. A cross-sectional, Web-based survey was performed. Participants were 100 Japanese physicians registered with M3¹⁵ who regularly treat AD patients for the direct medical costs, and 400 Japanese AD patients aged 16–59 years registered with Rakuten Insight¹⁶ were surveyed for self-medication costs and productivity loss (male : female, 1:1; mild : moderate : severe : most severe, 1:1:1:1).¹ The survey period of the physician and patient surveys was 25–28 March 2019 and 25–27 April 2018, respectively.

Direct medical costs

The direct medical cost was assessed using the prevalence method, a widely used cost of illness approach. The medical resource consumption related to the following medical treatments was surveyed between inpatients and outpatients: prescriptions of topical and oral medicines and injections; prescription rate; dose and dosing period; rate and frequency of ultraviolet therapy/photochemotherapy and each test; frequency of outpatient visits; and frequency and length of hospitalization. The annual direct medical cost was estimated by multiplying the medical resource consumption and medical fee corresponding to each treatment.¹⁷ The medical resource consumption was surveyed by AD severity and calculated by the following four states: state A (no symptoms, minimal symptoms), state B (only mild rash regardless of area), state C (marked inflammatory rash covering <10% of the body surface area) and state D (severe inflammatory rash covering $\geq 10\%$ and <30% of the body surface area, or intense inflammatory rash covering $\geq 30\%$ of the body surface area).¹ The distributions of the calculated direct medical costs were confirmed, and the respondents whose total cost was within the top 5% in each state were excluded as outliers.

Self-medication costs and productivity loss

The self-medication costs and productivity loss were estimated by sex and severity (mild/moderate/severe/most severe). For the self-medication costs, the participants responded for each severity defined as follows: mild, state with skin that dries out with no marked change in the skin color or condition, or reddish skin that dries out; moderate, state with remaining scratch marks or solidified swelling on the skin due to worsening of drying, redness and roughness; severe, state with worsened symptoms covering approximately 10% of all skin such as raised skin with reddish swelling, flaky skin and skin peeling; and most severe, state with worsened symptoms covering more than 10% of all skin such as raised skin with reddish swelling, flaky skin and skin peeling.

As self-medication costs, the annual cost was calculated by investigating the approximate payment per month for the following items purchased due to AD: foods (including drinks); over the counter (OTC) drugs and supplements; cosmetics; body cleaning agents, such as soap, shampoo and body soap; clothes; bedding; and other. AD-related productivity loss was estimated following the human capital approach and evaluated using the work productivity and activity impairment (WPAI)/AD.¹⁸ The productivity loss of employed workers was calculated based on absenteeism (%), presenteeism (%) and overall work impairment (OWI) (%). The productivity loss of housewives was calculated based on activity impairment (AI) (%). The annual productivity loss was estimated from each score, and the annual wage by corresponding occupational information on each patient based on age and sex (Wage Census).¹⁹ The productivity loss of housewives was also estimated by multiplying the AI score and its compensation (estimated monetary value of unpaid work [published in June 2013])²⁰.

Nationwide estimation

The number of nationwide AD patients was calculated as 4.262 million people (males, 1.696 million; females, 2.566 million) by multiplying the total population in their 20s–50s (20–59 years) in 2018, 61.96 million people (males, 31.41 million; females, 30.55 million)²¹ by the prevalence of AD patients (males, 5.4%; females, 8.4%).³

Direct medical costs

The nationwide direct medical cost was estimated by multiplying the number of AD patients of each severity and the estimated annual direct medical costs for each severity. The number of AD patients was calculated by weighting the estimated number of AD patients by the severity distribution.³ It was 3.417 million for mild, 0.755 million for moderate, 64 000 for severe and 26 000 people for most severe. The severity distribution used in the calculation was adjusted by the sum of the distribution to be 100% because the total of the reported values by Kohno *et al.*³ was 99.9%. The average cost of state A and state B was assigned for the direct medical costs for mild cases, the medical cost of state C for moderate cases, and the medical cost of state D for all severe and most severe cases.

Self-medication costs

Based on the assumption that the severity distributions³ were the same regardless of sex, the nationwide self-medication cost was estimated by multiplying the number of AD patients of each sex and severity with the estimated annual self-medication costs for each sex and severity. The number of AD patients of each sex and severity was calculated by weighting the number of AD patients for males and females (males, 1.696 million; female, 2.566 million) by the severity distribution.³

Productivity loss

Productivity loss for OWI. The nationwide productivity loss for OWI was estimated based on the number of employed workers with AD by sex (males, 1.527 million; females, 1.94 million). It was calculated by multiplying the number of employed workers in the same age group (20s–50s) in 2018 (51.37 million people)²² with the prevalence of AD. Assuming that the severity distributions were the same regardless of sex, it was estimated by multiplying the number of employed workers with AD of each sex and severity with the annual productivity loss for OWI for each sex and severity. The number of employed workers with AD was weighted by the severity distribution,³ and the annual productivity loss was weighted by the proportion of regular or non-regular workers:²²

$$PL_{OWI}(\text{JPY/year}) = \sum_{i=1}^2 N_{E_i} \times P_{AD_i} \times OWI_i \times IN_i$$

$$OWI_i = \sum_{j=1}^4 \sum_{k=1}^2 OWI_{i,j,k} \times P_{E_{i,k}} \times P_{S_j}$$

$$IN_i = \sum_{k=1}^2 \sum_{l=1}^8 IN_{i,k,l} \times P_{E_{i,k,l}}$$

where N_{E_i} indicates the number of employed workers aged 20–59 in sex of i ; P_{AD_i} , prevalence of AD in sex of i (%); OWI_i , overall work impairment in sex of i (%); IN_i , annual income in sex of i (JPY/year)*; $OWI_{i,j,k}$, overall work impairment of working status of k in sex and severity of i, j (%); $P_{E_{i,k}}$, proportion of working status of k in sex of i (%); P_{S_j} , proportion of severity of j (%); $IN_{i,k,l}$, annual income of working status of k in sex and age group of i, l (JPY/year); $P_{E_{i,k,l}}$, proportion of working status of k in sex and age group of i, l (%); l , sex (1, male; 2, female); j , 4 severity grades (1, mild; 2, moderate; 3, severe; 4, most severe); k , working status (1, regular; 2, non-regular); and l , 8 age groups divided into 5 years from 20–59 years old.

Productivity loss for AI. The nationwide productivity loss for AI was estimated based on the number of housewives with AD of 499 000 people, which was calculated by multiplying the number of housewives (5.943 million people) with the prevalence of AD. The number of housewives with AD was calculated by multiplying the female population in the same age group

(20s–50s) in 2018,²¹ the percentage of houseworkers in females²³ and the prevalence of AD. The productivity loss of housewives was estimated by multiplying the number of housewives with AD of each severity and the estimated annual productivity loss for AI for each severity. The number of housewives with AD of each severity was weighted by the severity distribution:³

$$PL_{AI}(\text{JPY/year}) = N_{HW} \times P_{AD_2} \times AI \times UW$$

$$N_{HW} = \sum_{l=1}^8 N_{2,l} \times P_{HW_l}$$

$$AI = \sum_{j=1}^4 AI_j \times P_{S_j}$$

$$UW = \sum_{l=1}^8 UW_l \times P_{HW_l}$$

where N_{HW} indicates the number of housewives aged 20–59; P_{AD_2} , prevalence of AD in females (%); AI, activity impairment (%); UW, value of unpaid work by unemployed female spouse (JPY/year); $N_{2,l}$: the number of females in age group of l ; P_{HW_l} , percentage of houseworkers in females in age group of l (%); AI_j , activity impairment at severity of j (%); P_{S_j} , proportion of severity of j (%); UW_l , value of unpaid work by unemployed female spouse in age group of l (%); j , 4 severity grades (1, mild; 2, moderate; 3, severe; 4, most severe); and l , 8 age groups divided into 5 years from 20–59 years old.

RESULTS

Sample characteristics

The characteristics of the 100 physicians enrolled in the Web-based survey of the direct medical cost are summarized in Table 1. Approximately half of the responding physicians worked at clinics (bedless medical facilities), and regularly treated approximately 90 cases of adult AD per month. The number of physicians who answered that they treat patients in each state, namely who answered questions related to the cost of each state, was 74 for state A, 99 for states B and C, and 89 for state D.

The characteristics of the 400 patients enrolled in the Web-based survey of the self-medication costs and productivity loss are summarized in Table 2. Although they were allocated to be equal in sex ratio and severity ratio, there was no significant imbalance in the age distribution among the severity groups. Similarly, although there was no significant imbalance among the severity groups in terms of employment status, the proportion of part-time workers was slightly higher in the most severe group.

Direct medical costs

The calculation results of the annual direct medical cost per patient by state are summarized in Table 3. The mean annual

Table 1. Characteristics of physicians ($n = 100$) who participated in the physician survey (direct medical cost)

Item	Value
Specialty	
General internal medicine	8
Dermatology	80
Pediatrics	12
Other	0
No. of beds in the medical facility	
≥ 400	30
200–399	14
100–199	6
20–99	1
1–19	2
0 (bedless)	47
No. of AD patients aged ≥ 16 years (/month)	$88 \pm 42^\dagger$
No. of physicians who treat patients at states A through D [‡]	
State A	74
State B	99
State C	99
State D	89

[†]Mean \pm standard deviation. [‡]Each state was defined as follows: state A, minimal symptoms; state B, only mild rash regardless of area; state C, marked inflammatory rash covering $<10\%$ of the body surface area; and state D, severe inflammatory rash covering $\geq 10\%$ but $<30\%$ of the body surface area, or marked inflammatory rash covering $\geq 30\%$ of the body surface area.

expected cost per patient of adult AD was JPY 136 501 (median, JPY 88 945). By severity, it was estimated as JPY 97 691 (median, JPY 54 905) for state A, JPY 96 531 (JPY 79 015) for state B, JPY 131 037 (JPY 94 779) for state C and

JPY 219 699 (JPY 131 874) for state D. It increased as the condition deteriorated by 1.36 times from state B to state C, and by 1.68 times from state C to state D.

In terms of cost breakdown, outpatient medical costs accounted for over 95% of the total, and the proportions were similar regardless of severity. The proportions of drug-related costs and hospitalization fees were the highest among outpatient costs and in hospitalization costs, respectively, and the drug-related costs accounted for 78% of outpatient costs. The outpatient drug-related costs increased by 1.47 times from state B to state C and by 1.75 times from state C to state D.

Self-medication costs

The mean expected self-medication cost per patient was JPY 4726/month. The cost of OTC drugs was the highest (JPY 1077/month), followed by cosmetics (JPY 915/month) and foods (JPY 828/month) (Table 4).

The calculation results of the self-medication cost by sex and severity are summarized in Table 5. The mean expected self-medication cost per adult AD patient by sex was estimated to be JPY 3796/month (JPY 45 547/year) for males and JPY 5657/month (JPY 67 883/year) for females, and the cost for females was higher. On comparison by severity, the self-medication costs approximately increased with severity in both sexes, and the self-medication costs in most severe cases were JPY 92 414/year for males and JPY 133 644/year for females.

Productivity losses

The results of the survey on productivity loss using WPAl/AD are summarized in Table 6. The OWI (%) of adult AD patients was 33.4% for regular workers and 37.2% for non-regular

Table 2. Characteristics of patients who participated in patient survey (self-medication cost and productivity loss)

	Total		Mild [†]		Moderate [†]		Severe [†]		Most severe [†]	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Whole population	400	100	100	100	100	100	100	100	100	100
Sex										
Male	200	50	50	50	50	50	50	50	50	50
Female	200	50	50	50	50	50	50	50	50	50
Age group										
20s	38	9.5	5	5	11	11	15	15	7	7
30s	126	31.5	33	33	34	34	26	26	33	33
40s	153	38.3	40	40	32	32	38	38	43	43
50s	83	20.8	22	22	23	23	21	21	17	17
Employment status										
Regular employee	167	62.8	38	64	44	63	44	68	41	57
Executive of company or corporation	7	2.6	1	2	3	4	1	2	2	3
Self-employed worker and family worker	27	10.2	8	14	5	7	10	15	4	6
Dispatched worker from temporary labor agency	11	4.1	4	7	1	1	2	3	4	6
Part-time worker, temporary worker	54	20.3	8	14	17	24	8	12	21	29

[†]Each severity was defined as follows: mild, state with skin that dries out with no marked change in skin color or condition, or reddish skin that dries out; moderate, state with remaining scratched marks or solidified swelling on skin due to worsening of drying-out, redness and roughness; severe, state with worsened symptoms covering $\sim 10\%$ of all skin such as raised skin with reddish swelling, flaky skin and skin peeling; and most severe, state with worsened symptoms covering $>10\%$ of all skin such as raised skin with reddish swelling, flaky skin and skin peeling.

Table 3. Direct medical cost (annual medical cost per patient by severity) (JPY/year)

Item	State A [†]					State B [†]					State C [†]					State D [†]				
	n	Mean	SD	Median	n	Mean	SD	Median	n	Mean	SD	Median	n	Mean	SD	Median	n	Mean	SD	Median
Total cost	346 [‡]	136 501	151 041	88 945	71 [‡]	97 691	115 892	54 905	95 [‡]	96 531	75 371	79 015	95 [‡]	131 037	109 111	94 779	85 [‡]	219 699	229 581	131 874
Outpatient		132 977	149 138	86 986		96 034	115 209	54 905		92 840	69 695	79 015		129 688	109 039	94 779		212 371	228 438	126 188
Basic		21 002	9953	17 320		13 731	7680	14 400		18 352	8570	14 460		23 058	8327	28 800		27 741	9724	28 800
medical examination fees [§]		6963	14 635	967		5201	12 717	2		6400	11 999	733		6636	14 310	1602		9427	18 585	3048
Test costs [§]		1078	3 012	0		589	1547	0		789	2 690	0		1093	2 935	0		1792	4088	0
Additional treatment costs [§]		103 935	143 599	56 272		76 514	113 110	35 643		67 298	65 555	47 119		98 902	103 649	66 238		173 410	223 905	89 866
Drug-related costs [§]		3524	18 410	0		1657	7339	0		3691	27 922	0		1348	6538	0		7328	20 095	0
Inpatient		3179	16 188	0		1531	6778	0		3189	23 581	0		1150	5708	0		6812	18 945	0
Basic medical examination fees [§]		243	1999	0		90	523	0		407	3618	0		148	728	0		294	938	0
Test costs [§]		24	234	0		6	31	0		44	411	0		5	44	0		37	180	0
Additional treatment costs [§]		78	381	0		29	154	0		51	367	0		45	279	0		185	567	0
Drug-related costs [§]																				

[†]Each state was defined as follows: state A, minimal symptoms; state B, only mild rash regardless of area; state C, marked inflammatory rash covering <10% of the body surface area; and state D, severe inflammatory rash covering ≥10% but <30% of the body surface area, or marked inflammatory rash covering ≥30% of the body surface area. [‡]The respondents whose total cost was within the top 5% were excluded in each state. [§]The cost details included were as follows: “basic medical examination fees”, (outpatient) revisit fee, prescription fee, injection fee and (inpatient) hospitalization basic fee; “test costs”, biochemical test (I), non-specific immunoglobulin (Ig)E test, specific IgE test, eosinophil blood count test, thymus and activation-regulated chemokine test, patch test, prick (scratch) test and histamine-release test; “additional treatment costs”, ultraviolet therapy/phototherapy, “drug-related costs”, each drug cost, (outpatient) dispensation fee, dispensation basic fee, pharmaceutical management fee, (inpatient) dispensation fee and dispensing technology basic fee. SD, standard deviation.

Table 4. Self-medication cost (monthly cost per patient by medication type) (JPY/month)[†]

Item	<i>n</i>	Mean	SD	Median
Foods	400	828.3	3479.58	0
OTC drugs	400	1076.5	3773.15	0
Cosmetics	400	915.1	2745.66	0
Body cleaning agents	400	705.6	1505.79	0
Clothes	400	423.3	1533.87	0
Bedding	400	431.3	2559.44	0
Other	400	346.3	2831.00	0
Total amount	400	4726.2	10 510.93	1000

[†]Question: Approximately how much did you pay per month for the items purchased due to AD in the past 3 months? AD, atopic dermatitis; OTC, over-the-counter; SD, standard deviation.

workers (median, 30% for both), and the OWI (%) increased with severity for both males and females. The absenteeism (%) for regular workers and non-regular workers was 2.1% and 5.5%, respectively, and the presenteeism (%) was 31.4% and 31.8%, respectively, demonstrating that the majority of OWI is due to the presenteeism. The AI (%) for housewives also increased with severity.

Nationwide estimation

The estimation results of the annual cost of illness per patient for adult AD in Japan and the nationwide cost of illness are

summarized in Table 7. The direct medical costs per patient ranged from JPY 97 111/year (mild) to JPY 219 699/year (severe/most severe), the self-medication costs ranged from JPY 13 494/year (mild) to JPY 117 238/year (most severe), the productivity loss for OWI of employees ranged from JPY 428 000/year (mild) to JPY 2506 000/year (most severe), and the productivity loss for AI of housewives ranged from JPY 643 000/year (mild) to JPY 2512 000/year (most severe). The nationwide disease burden for adult AD in 2018 was estimated at JPY 3036.9 billion, of which the direct medical cost was JPY 450.5 billion (14.8%), the self-medication cost was JPY 86.3 billion (2.8%), the OWI was JPY 2117.2 billion (69.7%) and the AI was JPY 382.9 billion (12.6%).

DISCUSSION

In our study, the disease burden for adult AD in Japan in 2018 was estimated at approximately JPY 3 trillion, corresponding to 0.55% of Japan's nominal gross domestic product (GDP) in 2018.²⁴ All items comprising the cost per patient for adult AD (direct medical costs, self-medication cost and productivity loss) increased with disease severity. To the best of our knowledge, this is the first report of a cross-sectional Web-based survey of the cost of illness for adult AD patients in Japan focusing on disease severity.

The direct medical cost of adult AD patients was estimated at JPY 450 billion/year based on the survey of medical

Table 5. Self-medication cost (monthly and annual cost per patient by sex and severity)[†]

Item	Group (sex and severity) [‡]		<i>n</i>	Mean	SD	Median
Monthly cost per patient (JPY/month)	Whole population		400	4726	10 510.93	1000
	Male	Total	200	3796	9744.39	600
		Mild	50	750	1489.43	0
		Moderate	50	4062	12 342.31	500
		Severe	50	2669	5638.40	700
		Most severe	50	7701	13 148.61	3000
	Female	Total	200	5657	11 172.31	1500
		Mild	50	1372	2616.04	0
		Moderate	50	3413	8515.43	300
		Severe	50	6706	13 921.56	2250
Most severe		50	11 137	13 345.98	6750	
Annual cost per patient (JPY/year)	Whole population		400	56 715	126 131.16	12 000
	Male	Total	200	45 547	116 932.63	7200
		Mild	50	9000	17 873.16	0
		Moderate	50	48 744	148 107.72	6000
		Severe	50	32 028	67 660.76	8400
		Most severe	50	92 414	157 783.28	36 000
	Female	Total	200	67 883	134 067.69	18 000
		Mild	50	16 464	31 392.54	0
		Moderate	50	40 950	102 185.13	3600
		Severe	50	80 472	167 058.78	27 000
Most severe		50	133 644	160 151.76	81 000	

[†]Question: Approximately how much did you pay per month for the items purchased due to AD in the past 3 months? [‡]Each severity was defined as follows: mild, state with skin that dries out with no marked change in skin color or condition or reddish skin that dries out; moderate, state with remaining scratch marks or solidified swelling on skin due to worsening of drying-out, redness and roughness; severe, state with worsened symptoms covering ~10% of the whole skin such as raised skin with reddish swelling, flaky skin and skin peeling; most severe, state with worsened symptoms covering >10% of the whole skin such as raised skin with reddish swelling, flaky skin and skin peeling. AD, atopic dermatitis; SD, standard deviation.

Table 6. WPAI calculation

Item	Group (sex and severity [†])		Working status [‡]	n	Mean (%)	SD	Median (%)
OWI	Overall population		Regular	197	33.4	0.32	30
			Non-regular	64	37.2	0.33	30
	Male	Total	Regular	152	31.6	0.31	20
			Non-regular	14	36.0	0.32	35
	Mild	Moderate	Regular	39	10	0.16	0
			Non-regular	2	20	0.28	20
	Severe	Most severe	Regular	38	22.6	0.25	10
			Non-regular	5	30	0.28	20
	Female	Total	Regular	38	42.9	0.29	40
			Non-regular	0	NA	NA	NA
	Mild	Moderate	Regular	37	51.9	0.32	50
			Non-regular	7	44.8	0.36	50
	Severe	Most severe	Regular	45	39.7	0.34	40
			Non-regular	50	37.6	0.33	30
	Mild	Moderate	Regular	6	1.7	0.04	0
			Non-regular	10	14	0.18	5
	Severe	Most severe	Regular	12	42.5	0.23	40
			Non-regular	13	28.8	0.37	10
	Mild	Moderate	Regular	17	36.8	0.35	30
			Non-regular	10	32	0.23	25
Severe	Most severe	Regular	10	64	0.35	70	
		Non-regular	17	61.5	0.30	70	
Absenteeism [§]	Overall population		Regular	197	2.1	0.10	0
			Non-regular	64	5.5	0.20	0
	Male	Total	Regular	152	1.4	0.07	0
			Non-regular	14	6.2	0.23	0
	Mild	Moderate	Regular	39	1.4	0.09	0
			Non-regular	2	0.0	0.00	0
	Severe	Most severe	Regular	38	2.5	0.11	0
			Non-regular	5	0.0	0.00	0
	Female	Total	Regular	38	0.8	0.04	0
			Non-regular	0	NA	NA	NA
	Mild	Moderate	Regular	37	0.8	0.03	0
			Non-regular	7	12.4	0.33	0
	Severe	Most severe	Regular	45	4.4	0.15	0
			Non-regular	50	5.3	0.20	0
	Mild	Moderate	Regular	6	0.0	0.00	0
			Non-regular	10	0.0	0.00	0
	Severe	Most severe	Regular	12	3.2	0.11	0
			Non-regular	13	6.5	0.19	0
	Mild	Moderate	Regular	17	2.0	0.07	0
			Non-regular	10	0.0	0.00	0
Severe	Most severe	Regular	10	12.5	0.26	0	
		Non-regular	17	10.6	0.29	0	
Presenteeism [§]	Overall population		Regular	197	31.4	0.30	20
			Non-regular	64	31.8	0.29	20
	Male	Total	Regular	152	30.2	0.30	20
			Non-regular	14	29.8	0.28	25
	Mild	Moderate	Regular	39	8.6	0.14	0
			Non-regular	2	20	0.28	20
	Severe	Most severe	Regular	38	20.1	0.22	10
			Non-regular	5	30	0.28	20
	Female	Total	Regular	38	42.2	0.29	40
			Non-regular	0	NA	NA	NA
	Mild	Moderate	Regular	37	51.1	0.31	50
			Non-regular	7	32.4	0.31	30
	Severe	Most severe	Regular	45	35.3	0.31	30
			Non-regular				

Table 6. (continued)

Item	Group (sex and severity [†])	Working status [‡]	<i>n</i>	Mean (%)	SD	Median (%)	
AI	Mild	Non-regular	50	32.3	0.30	20	
		Regular	6	1.7	0.04	0	
	Moderate	Non-regular	10	14	0.18	5	
		Regular	12	39.2	0.21	40	
	Severe	Non-regular	13	22.4	0.30	10	
		Regular	17	34.8	0.35	30	
	Most severe	Non-regular	10	32	0.23	25	
		Regular	10	51.5	0.30	50	
	Female	Total	–	99	39.2	0.35	40
		Mild	–	33	16.4	0.25	0
		Moderate	–	22	29.1	0.27	25
		Severe	–	22	58.6	0.29	60
		Most severe	–	22	64.1	0.32	70

[†]Each severity was defined as follows: mild, state with skin that dries out with no marked change in skin color or condition, or reddish skin that dries out; moderate, state with remaining scratched marks or solidified swelling on skin due to worsening of drying-out, redness and roughness; severe, state with worsened symptoms covering ~10% of the whole skin such as raised skin with reddish swelling, flaky skin and skin peeling; most severe, state with worsened symptoms covering >10% of the whole skin such as raised skin with reddish swelling, flaky skin and skin peeling. [‡]Regular worker and non-regular workers include the following statuses in employment: “regular workers”, regular employee, executive of company or corporation, self-employed worker and family worker; “non-regular workers”, dispatched worker from temporary labor agency, part-time worker and temporary worker. [§]The questions related to absenteeism and presenteeism were calculated for employed workers. Non-responders and those who answered that the actual number of working hours was excluded. AI, activity impairment; OWI, overall work impairment; SD, standard deviation; WPAI, work productivity and activity impairment.

resource consumption for 100 Japanese physicians who regularly treat AD patients. It accounted for approximately 80% of the medical cost of JPY 565.1 billion categorized as “XII. Skin and subcutaneous tissue disease (classification by the name of the main injuries or diseases determined according to International Statistical Classification of Diseases and Related Health Problems (ICD)-10)”²⁵ among the Japanese national medical expenditure of JPY 43.071 trillion in 2017 financial year.²⁶

The WPAI survey confirmed that even in mild cases, accounting for 80% of adult AD patients, the performance decreased by approximately 10% during working hours (weighted average value of presenteeism by sex and working status in mild cases). The productivity loss per year caused by OWI, including absenteeism and presenteeism, in mild cases was estimated at approximately JPY 430 000 per patient and JPY 1.2 trillion as a whole in Japan (56% of the total productivity loss for adult AD patients). Similarly, in moderate cases, accounting for 17.7% of adult AD patients, the performance decreased by approximately 25%. The productivity loss per year was estimated at approximately JPY 1 290 000/patient and JPY 792.0 billion as a whole (37% of the total productivity loss for adult AD patients).

Although severe and most severe cases only account for 2% of all patients, the decrease in performance during working hours became as high as approximately 44%. Comparing the costs per patient in moderate cases, the direct medical cost increased by 1.7 times, the productivity loss for OWI increased by 1.3 times and 1.9 times, and the productivity loss for AI increased by 2 times and 2.2 times in severe and most severe cases, respectively. Many clinical studies have

investigated the efficacy and safety of topical corticosteroids and topical calcineurin inhibitors among drugs for ameliorating inflammation due to AD.¹ The use of different topical corticosteroids depending on AD severity based on the steroid strength is recommended. In addition to treatment with these drugs, administration of cyclosporin, oral steroids, dupilumab and so forth will be also considered at the time of exacerbation. Disease severity-based nationwide estimation of the disease burden for adult AD was JPY 1823.6 billion (mild), JPY 1025.2 billion (moderate), JPY 119.8 billion (severe) and JPY 68.3 billion (more severe), respectively. In the viewpoint of the impact of nationwide expenditure, more efficient treatment interventions, namely efficient selection of more effective and less expensive treatment, are expected for mild and moderate AD patients, which account for the majority of AD patients.

Although caution is needed when comparing the disease burden among countries, the mean WPAI and AI scores in a WPAI survey of 1860 AD patients conducted by Eckert *et al.*²⁷ were 27.00% and 31.77%, respectively. Murota *et al.*'s²⁸ reported mean overall WPAI score of 31 AD patients was 40.4%. These results are consistent with our findings (34.3% and 39.2%, respectively). Furthermore, in the patients with a Dermatology Life Quality Index of more than 10 (corresponding to severe and most severe), it was 57.11% and 51.72%, respectively, also consistent with our findings.²⁷ In an Internet-based, international population survey, 2013 Japan National Health and Wellness Survey, performed by Arima *et al.*²⁹ using data of 634 registered Japanese AD patients, the mean OWI and AI scores were 30.61% and 32.18%, respectively, consistent with our survey results.

Table 7. Estimation of annual cost of illness for adult AD in Japan

	Cost per patient (JPY/year)	Total cost (JPY)
Direct medical cost		
Mild	97 111 [†]	331.9 billion
Moderate	131 037	99.0 billion
Severe	219 699 [‡]	14.1 billion
Most severe	219 699 [‡]	5.6 billion
Total	–	450.5 billion (14.8%)
Self-medication cost		
Mild	13 494	46.1 billion
Moderate	44 051	33.3 billion
Severe	61 195	3.9 billion
Most severe	117 238	3.0 billion
Total	–	86.3 billion (2.8%)
OWI[§]		
Mild	427 551	1188.4 billion
Moderate	1 289 522	792.0 billion
Severe	1 625 220	84.6 billion
Most severe	2 506 167	52.2 billion
Total	–	2117.2 billion (69.7%)
AI[§]		
Mild	642 666	257.2 billion
Moderate	1 140 340	100.9 billion
Severe	2 296 355	17.2 billion
Most severe	2 511 884	7.5 billion
Total	–	382.9 billion (12.6%)
Total amount	–	3036.9 billion/year

[†]The direct medical cost per patient for mild AD was the mean of the costs for state A and state B. [‡]The direct medical cost per patient for severe and most severe AD was the costs for state D. [§]The annual wage used to calculate productivity loss was estimated as “contractual monthly cash earnings” (including overtime worked) × 12 + “annual special earnings”.¹⁹ OWI = estimated wage × OWI (%). Absenteeism = estimated wage × absenteeism (%). Presenteeism = estimated w × (OWI [%] – absenteeism [%]). AI = estimated wage × AI (%). AD, atopic dermatitis; AI, activity impairment; OWI, overall work impairment; SD, standard deviation; WPAI, work productivity and activity impairment.

The cost of illness with regard to domestic income was assessed using the estimated amount adjusted by GDP. Schofield *et al.*³⁰ measured annual losses of arthritis through early retirement was equivalent to 0.7% of the GDP. Lubloy³¹ reported that the economic burden of migraine in Latvia and Lithuania was equivalent to 0.42% and 0.35%, respectively. The cost of illness of adult AD patients (0.55% against the GDP) estimated in our analysis cannot be considered inconsequential. Villacorta *et al.*³² conducted a survey on total work productivity loss (WPL) in 936 patients with psoriasis in France, Germany, Spain, the UK, Italy and the USA. Average indirect costs associated with total WPL for patients with mild (body surface area [BSA], 0–2%), moderate (BSA, 3–10%) and severe (BSA, >10%) psoriasis were USD 3592, USD 7478 and USD 12 194, respectively. According to the survey for health-care resource utilization of chronic spontaneous urticaria (CSU) in France (the ASSURE-CSU study), the mean total direct costs of CSU was EUR 2397 per patient per year and the indirect costs for 4 weeks were mainly driven by presenteeism

(EUR 421) and work productivity loss (EUR 420).³³ Although it requires attention to compare those estimates conducted in other countries due to differences in the medical environments and economic situations, they tended to be smaller than our estimates for AD patients.

Several limitations in the present study need to be considered. First, the direct medical cost was based on the Web survey of health-care resource use for physicians. Igarashi *et al.*¹³ estimated the value related to AD for outpatient visits to be 6.324 times per year in a retrospective claims database analysis of health-care resource use. On the other hand, in our Web survey, the mean number of outpatient visits per year for states A through D was 4.6 times, 6.7 times, 8 times and 12 times, respectively. The weighted average by the severity distribution³ was 5.07 times per year. These values were mostly within acceptable range considering the uncertainty of the consistency of disease severity and age distributions with those of Igarashi *et al.*¹³ The validity of the physicians’ answers in this survey was confirmed to some extent. Second, the reliability of the survey results on self-medication costs is uncertain. As no previous studies on self-medication costs were available, sufficient validation was unable to be performed. However, as the proportion of overall cost of illness was 2.8%, it was considered to have little influence on the estimation results. To reduce the uncertainty of the nationwide estimation, further verification of the robustness of the results is expected using statistical inference methods such as bootstrap method or Monte Carlo method.

Conclusion

In the present study, the cost of illness of adult AD patients in Japan was estimated to be approximately JPY 3 trillion/year. The cost per patient increased with disease severity. The OWI for adult AD patients was 34.3%, demonstrating the degree of impairment to increase with severity. Considering the physical and mental burdens, the burden of illness for adult AD was considered to be vast.

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