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 to 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. 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. Kohno et al. 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. 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
caregiving was an average of 4.5 days/year. A survey was conducted by Fowler et al. 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. reported that the absenteeism per visit for 76 AD patients was 1.1 h, and it increased with severity. Holm et al. 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 use and disease burden 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 Insight were surveyed for self-medication costs and productivity loss (male: female, 1:1; mild: moderate: severe: most severe, 1:1:1:1). The survey period of the physician and patient surveys was 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. 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 ≥10% and <30% of the body surface area, or intense inflammatory rash covering ≥30% of the body surface area). 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. 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 (Al) (%). 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). The productivity loss of housewives was also estimated by multiplying the Al score and its compensation (estimated monetary value of unpaid work [published in June 2013]).

**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) by the prevalence of AD patients (males, 5.4%; females, 8.4%).

**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. 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. 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 distributions\(^3\) 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 weighing the number of AD patients for males and females (males, 1,696 million; female, 2,566 million) by the severity distribution.\(^3\)

**Productivity loss**

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)\(^2\) 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.\(^2\)

\[
PL_{OWI}(\text{JPY/year}) = \sum_{i=1}^{2} N_i \times P_{ADi} \times OWI \times IN_i
\]

\[
OWI = \sum_{j=1}^{8} \sum_{k=1}^{4} OWI_{ijk} \times P_{E_{jk}} \times P_{S_j}
\]

\[
IN_i = \sum_{k=1}^{8} \sum_{l=1}^{4} IN_{ijk} \times P_{E_{jk}}
\]

where \(N_i\) indicates the number of employed workers aged 20-59 in sex of \(i\); \(P_{ADi}\), prevalence of AD in sex of \(i\) (%); \(OWI\), overall work impairment in sex of \(i\) (%); \(IN_i\), annual income in sex of \(i\) (JPY/year); \(OWI_{ijk}\), overall work impairment of working status of \(k\) in sex and severity of \(j\); \(P_{E_{jk}}\), proportion of working status of \(k\) in sex of \(i\) (%); \(P_{S_j}\), proportion of severity of \(j\) (%); \(IN_{ijk}\), annual income of working status of \(k\) in sex and age group of \(i\); \(P_{E_{jk}}\), proportion of working status of \(k\) in sex and age group of \(i\); \(P_{S_j}\), proportion of severity of \(j\) (%); \(IN_{ijk}\), annual income of working status of \(k\) in sex and age group of \(i\); \(P_{E_{jk}}\), proportion of working status of \(k\) in sex and age group of \(i\); \(P_{S_j}\), proportion of severity of \(j\) (%); \(IN_{ijk}\), annual income of working status of \(k\) in sex and age group of \(i\); \(P_{E_{jk}}\), proportion of working status of \(k\) in sex and age group of \(i\); \(P_{S_j}\), proportion of severity of \(j\) (%); \(IN_{ijk}\), annual income of working status of \(k\) in sex and age group of \(i\); \(P_{E_{jk}}\), proportion of working status of \(k\) in sex and age group of \(i\); \(P_{S_j}\), proportion of severity of \(j\) (%); \(IN_{ijk}\), annual income of working status of \(k\) in sex and age group of \(i\); \(P_{E_{jk}}\), proportion of working status of \(k\) in sex and age group of \(i\); and \(I\), 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...
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.

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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 WPAI/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 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 ± 42† |
| No. of physicians who treat patients at states A through D‡ | State A 74  
State B 99  
State C 99  
State D 89 |

†Mean ± 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 ≥10% but <30% of the body surface area, or marked inflammatory rash covering ≥30% of the body surface area.

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

| | Total | Mild‡ | Moderate‡ | Severe‡ | Most severe‡ |
|---|-------|-------|-----------|---------|-------------|
| | n % | n % | n % | n % | n % |
| 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 ~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.
| Item                                           | Overall | State A† | State B† | State C† | State D† |
|-----------------------------------------------|---------|----------|----------|----------|----------|
|                                              | n        | Mean     | SD       | Median   | n        | Mean     | SD       | Median   | n        | Mean     | SD       | Median   |
| Total cost                                    | 346‡     | 136 501  | 151 041  | 88 945   | 97 691   | 115 892  | 54 905   | 75 371   | 79 015   | 131 037  | 109 111  | 94 779   |
| Outpatient                                    | 132 977  | 21 002   | 9553     | 17 320   | 13 731   | 7680     | 14 400   | 23 058   | 8327     | 28 800   | 27 741   | 9724     |
| Basic medical examination fees§               | 6963     | 14 635   | 967      | 5201     | 12 717   | 2        | 6400     | 11 999   | 733      | 9427     | 18 585   | 3048     |
| Test costs§                                   | 1078     | 3 012    | 0        | 589      | 1547     | 0        | 789      | 2 690    | 0        | 1093     | 2 935    | 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   |
| Drug-related costs§                           | 3524     | 18 410   | 0        | 1657     | 7339     | 0        | 3691     | 27 922   | 0        | 1348     | 6538     | 0        |
| Inpatient basic medical examination fees§     | 3179     | 16 188   | 0        | 1531     | 6778     | 0        | 3189     | 23 581   | 0        | 1150     | 5708     | 0        |
| Test costs§                                   | 243      | 1999     | 0        | 90       | 523      | 0        | 407      | 3618     | 0        | 148      | 728      | 0        |
| Additional treatment costs§                   | 24       | 234      | 0        | 6        | 31       | 0        | 44       | 411      | 0        | 5        | 44       | 0        |
| Drug-related costs§                           | 78       | 381      | 0        | 29       | 154      | 0        | 51       | 367      | 0        | 45       | 279      | 0        |

†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 (IgE) 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/photochemotherapy; "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.
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 428 000/year (mild) to JPY 2506 000/year (most severe), and the productivity loss for OWI of employees 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%) and 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. 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 cost per patient (medication type) (JPY/month)$^3$

| Item                  | n    | Mean  | SD    | Median |
|-----------------------|------|-------|-------|--------|
| Foods                 | 400  | 828.3 | 3479.58| 0      |
| OTC drugs             | 400  | 1076.3| 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  |

$^3$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.

| Item                  | n    | Mean  | SD    | Median |
|-----------------------|------|-------|-------|--------|
| Monthly cost per patient (JPY/month) |      |       |       |        |
| Whole population      | 400  | 4726  | 10 510.93| 1000  |
| Male                  | 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                | 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                  | 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                | 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 |

$^3$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.

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.

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## 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       | Regular                  | 39             | 10  | 0.16     |     | 0          |
|            | Non-regular              | 2              | 20  | 0.28     |     | 20         |
| Moderate   | Regular                  | 38             | 22.6| 0.25     | 10  |
|            | Non-regular              | 5              | 30  | 0.28     |     | 20         |
| Severe     | Regular                  | 38             | 42.9| 0.29     | 40  |
|            | Non-regular              | 0              | NA  | NA       | NA  |
|            | Non-regular              | 7              | 44.8| 0.36     | 50  |
|            | Regular                  | 37             | 51.9| 0.32     | 50  |            |
| Female     | Total                    | Regular        | 45  | 39.7     | 0.34| 40         |
|            |                          | Non-regular    | 50  | 37.6     | 0.33| 30         |
|            | Male                     | Regular        | 152 | 1.4      | 0.07| 0          |
|            |                          | Non-regular    | 14  | 6.2      | 0.23| 0          |
| Mild       | Regular                  | 39             | 1.4 | 0.09     |     | 0          |
|            | Non-regular              | 2              | 0.0 | 0.00     |     | 0          |
| Moderate   | Regular                  | 38             | 2.5 | 0.11     |     | 0          |
|            | Non-regular              | 5              | 0.0 | 0.00     |     | 0          |
| Severe     | Regular                  | 38             | 0.8 | 0.04     |     | 0          |
|            | Non-regular              | 0              | NA  | NA       | NA  |
| Most severe| Regular                  | 37             | 0.8 | 0.03     |     | 0          |
|            | Non-regular              | 7              | 12.4| 0.33     |     | 0          |
| 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       | Regular                  | 39             | 1.4 | 0.09     |     | 0          |
|            | Non-regular              | 2              | 0.0 | 0.00     |     | 0          |
| Moderate   | Regular                  | 38             | 2.5 | 0.11     |     | 0          |
|            | Non-regular              | 5              | 0.0 | 0.00     |     | 0          |
| Severe     | Regular                  | 38             | 0.8 | 0.04     |     | 0          |
|            | Non-regular              | 0              | NA  | NA       | NA  |
| Most severe| Regular                  | 37             | 0.8 | 0.03     |     | 0          |
|            | Non-regular              | 7              | 12.4| 0.33     |     | 0          |
| Female     | Total                    | Regular        | 45  | 4.4      | 0.15| 0          |
|            |                          | Non-regular    | 50  | 5.3      | 0.20| 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       | Regular                  | 39             | 8.6 | 0.14     |     | 0          |
|            | Non-regular              | 2              | 20  | 0.28     |     | 20         |
| Moderate   | Regular                  | 38             | 20.1| 0.22     | 10  |
|            | Non-regular              | 5              | 30  | 0.28     |     | 20         |
| Severe     | Regular                  | 38             | 42.2| 0.29     | 40  |
|            | Non-regular              | 0              | NA  | NA       | NA  |
| Most severe| Regular                  | 37             | 51.1| 0.31     | 50  |
|            | Non-regular              | 7              | 32.4| 0.31     | 30  |
| Female     | Total                    | Regular        | 45  | 35.3     | 0.31| 30         |
A female total medical expenditure of JPY 43.071 trillion in 2017 financial section, self-employed worker and family worker; “non-regular workers”, dispatched worker from temporary labor agency, part-time worker and temporary worker 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.

| Item       | Group (sex and severity) | Working status | n  | Mean (%) | SD | Median (%) |
|------------|--------------------------|----------------|----|----------|----|------------|
|            |                          | Non-regular    | 50 | 32.3     | 0.30| 20         |
|            |                          | Regular        | 6  | 1.7      | 0.04| 0          |
|            |                          | Non-regular    | 10 | 14       | 0.18| 5          |
|            |                          | Regular        | 12 | 39.2     | 0.21| 40         |
|            |                          | Non-regular    | 13 | 22.4     | 0.30| 10         |
|            |                          | Regular        | 17 | 34.8     | 0.35| 30         |
|            |                          | Non-regular    | 10 | 32       | 0.23| 25         |
|            |                          | Regular        | 10 | 51.5     | 0.30| 50         |
|            |                          | Non-regular    | 17 | 50.9     | 0.31| 60         |
|            |                          | Total          | 99 | 39.2     | 0.35| 40         |
| Al Female  |                          | 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         |

1Each 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.

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 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. were 27.00% and 31.77%, respectively. Murota et al.’s 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. In an Internet-based, international population survey, 2013 Japan National Health and Wellness Survey, performed by Arima et al. 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.
The cost of illness with regard to domestic income was assessed using the estimated amount adjusted by GDP. Schofield et al. measured annual losses of arthritis through early retirement equivalent to 0.7% of the GDP. Luboń 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. 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 use for physicians, Igarashi et al. 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 distribution 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. 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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### CONFLICT OF INTEREST

H. M. received consulting fees and/or speaker honoraria from Japan Tobacco, Maruho, Shiseido, Kaken Pharmaceutical, Sanofi Genzyme, Mitsubishi Tanabe Pharma, Kyowa Kirin, Torii Pharmaceutical, Lilly, Abbvie, Taiho Pharma, Bristol-Myers Squibb, Kao, Novartis, Kracie, NAOs, Sato Pharmaceutical, Tokai Pharmaceutical, Sumitomo Dainippon Pharma, Nippon Zoki Pharmaceutical and Pola Pharma. S. I. is an employee of CRECON Medical Assessment. CRECON Medical Assessment was paid by Japan Tobacco and Torii Pharmaceutical to conduct analyses for the study. K. Y. and A. I. are employees of Japan Tobacco.

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**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 |

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