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### Title

Characterization of socioeconomic status of Japanese patients with atopic dermatitis showing poor medical adherence and reasons for drug discontinuation

### Permalink

<https://escholarship.org/uc/item/0v07d95m>

### Journal

Journal of Dermatological Science, 79(3)

### ISSN

0923-1811

### Authors

Murota, Hiroyuki  
Takeuchi, Satoshi  
Sugaya, Makoto  
et al.

### Publication Date

2015-09-01

### DOI

10.1016/j.jdermsci.2015.05.010

Peer reviewed

**Poor adherence to oral and topical medication in 3096 dermatological patients as assessed by the Morisky Medication Adherence Scale-8**

DOI: 10.1111/bjd.13377

DEAR EDITOR, Recent studies have shown that adherence to treatment is an important factor for good therapeutic outcome in various chronic disorders such as hypertension and diabetes.<sup>1,2</sup> In dermatology, patient nonadherence to therapy is also very problematic and has been associated with poor therapeutic outcomes in common skin diseases.<sup>3–5</sup> Although there is no 'gold standard' to measure medication adherence, an eight-item self-reported scale called the Morisky Medication Adherence Scale-8 (MMAS-8) has been developed by Morisky et al.<sup>1</sup> MMAS-8 originally targeted oral medication for hypertensive patients, but it is now applied to measure medication adherence in a wide range of disorders such as diabetes and osteoporosis.<sup>2,6</sup> However, there are no reports of studies investigating dermatological adherence using this scale. Therefore, this study assessed medication adherence for oral and topical remedies using a translated version of MMAS-8 together with other socioeconomic background factors in 3096 Japanese dermatological patients.

This study was conducted among patients registered in a monitoring system established by Macromill Inc. (Tokyo, Japan). The registered individuals ( $n = 4144$ ) were prescreened in terms of skin diseases and their intention to participate in this study. In total 3096 eligible patients were enrolled, 1327 with atopic dermatitis, 751 with urticaria, 237 with psoriasis and 781 with tinea. Our web-based questionnaire included the following items: age, sex, marital status, annual income, employment status, educational status, smoking habit, alcohol consumption, frequency of hospital visits, main healthcare institution, oral or topical medication, experience of the effectiveness of oral medication, experience of the effectiveness of topical medication, experience of adverse events associated with oral medication, experience of adverse events associated with topical medication, overall satisfaction with treatment, MMAS-8 for oral medication and MMAS-8 for topical medication.

The original MMAS-8 was translated into Japanese according to international guidelines.<sup>7</sup> Forward translation of the original questionnaire was undertaken by translation from English into Japanese to produce a version that was semantically and conceptually as close as possible to the original questionnaire. Translation was carried out by two qualified independent linguistic translators; both are native speakers of Japanese and

proficient in English. Back translation from Japanese into English was then carried out by another translator, who is a native speaker of English and proficient in Japanese. The back translation form was sent to the original author. Inconsistencies were resolved after repeated discussion among the original author, the English translator and the Japanese investigators and a final version was generated. According to the MMAS-8 score (range 0–8), adherence was defined as high (score 8), medium (score 6 to < 8) or low (score < 6).<sup>1</sup>

The proportions and frequencies for categorical variables were calculated, while means and SDs were calculated for continuous variables. The characteristics of the whole sample and of the groups with different levels of adherence in terms of the MMAS-8 score are presented. The  $\chi^2$ -test for categorical variables or ANOVA for continuous variables was used to evaluate the differences in the study variables among the three adherence groups. Internal consistency was assessed using Cronbach's  $\alpha$ . An acceptable Cronbach's  $\alpha$  value is considered to be  $\geq 0.7$ .<sup>8</sup> Known group validity was assessed through the association of items and MMAS categories using a correlation coefficient and covariance. All analyses were performed using STATA version 9 (StataCorp, College Station, TX, U.S.A.). The significance level was set at  $P < 0.05$ .

The demographic data of the 3096 patients are summarized in Table 1. The mean age of the subjects was 46.3 years (range 17–85), and 50.4% were male. Among the 3096 participants, 1984 took oral medication and 2763 were treated with topical medication. The mean adherence scores by MMAS-8 were 4.8 for oral and 4.3 for topical medication. The reliability scores (Cronbach's  $\alpha$ ) were 0.710 for oral MMAS-8 and 0.715 for topical MMAS-8,<sup>8</sup> which demonstrates the high reliability of the Japanese version of MMAS-8.

Adherence levels were compared by the type of medication (oral and topical) (Table 2). The percentages of high, medium and low adherence were 9.5%, 24.2% and 66.3% for oral medication, and 6.9%, 17.7% and 75.5% for topical medication, respectively. The overall adherence status was significantly better for oral medication than for topical medication (Table 2).

As shown in Table 3, the adherence to oral medication was significantly associated with age, sex, alcohol consumption, disease classification, frequency of hospital visits, experience of drug effectiveness and overall satisfaction with treatment. Lower adherence was found in younger subjects, female patients, heavier drinkers, cases of atopic dermatitis, those who visited their hospitals less than once per half year or at an unknown frequency, those who had not experienced drug effectiveness and those who were not satisfied with their

Table 1 Basic characteristics of the study subjects (n = 3096)

| Characteristic                            | n                       | %         |
|---|-------------------------|-----------|
| Age (years), mean $\pm$ SD (min–max)      | 46.3 $\pm$ 13.0 (17–85) |           |
| Sex                                       |                         |           |
| Male                                      | 1559                    | 50.4      |
| Female                                    | 1537                    | 49.6      |
| Marital status                            |                         |           |
| Married                                   | 1160                    | 37.5      |
| Unmarried                                 | 1936                    | 62.5      |
| Annual income                             |                         |           |
| $\geq$ 6 million yen <sup>a</sup>         | 1074                    | 39.7      |
| < 6 million yen                           | 1629                    | 60.3      |
| Employment                                |                         |           |
| Employed                                  | 1969                    | 66.8      |
| Unemployed                                | 977                     | 33.2      |
| Education                                 |                         |           |
| University graduate                       | 1524                    | 49.5      |
| Not university graduate                   | 1556                    | 50.5      |
| Smoking                                   |                         |           |
| Smoker                                    | 605                     | 19.6      |
| Nonsmoker                                 | 2480                    | 80.4      |
| Alcohol consumption                       |                         |           |
| More than once per month                  | 1927                    | 62.5      |
| Less than once per month                  | 1158                    | 37.5      |
| Diseases                                  |                         |           |
| Atopic dermatitis                         | 1327                    | 42.9      |
| Urticaria                                 | 751                     | 24.3      |
| Psoriasis                                 | 237                     | 7.7       |
| Tinea                                     | 781                     | 25.2      |
| Frequency of hospital visits              |                         |           |
| At least once per half year               | 2769                    | 89.4      |
| Less than once per half year or unknown   | 327                     | 10.6      |
| Main healthcare institution               |                         |           |
| University hospital                       | 141                     | 4.6       |
| Municipal hospital                        | 555                     | 18.0      |
| Private clinic or other                   | 2381                    | 77.4      |
| Oral medication                           |                         |           |
| Experience of drug effectiveness, yes/no  | 1634/350                | 82.4/17.6 |
| Experience of adverse events, yes/no      | 349/1635                | 17.6/82.4 |
| Topical medication                        |                         |           |
| Experience of drug effectiveness, yes/no  | 2365/398                | 85.6/14.4 |
| Experience of adverse events, yes/no      | 382/2381                | 13.8/86.2 |
| Overall satisfaction with treatment       |                         |           |
| Satisfied                                 | 1798                    | 58.1      |
| Unsatisfied                               | 1298                    | 41.9      |
| Adherence, mean $\pm$ SD (min–max)        |                         |           |
| Oral medication (n = 1984)                | 4.8 $\pm$ 2.0 (0–8)     |           |
| Topical medication (n = 2763)             | 4.3 $\pm$ 2.0 (0–8)     |           |
| Cronbach's $\alpha$ of adherence measures |                         |           |
| Oral medication                           | 0.710                   |           |
| Topical medication                        | 0.715                   |           |

<sup>a</sup>6 million yen is about £34 000.

Table 2 Adherence levels by type of medication

|                               | High, n (%) | Medium, n (%) | Low, n (%)  | P-value |
|-------------------------------|-------------|---------------|-------------|---------|
| Oral medication (n = 1984)    | 188 (9.5)   | 480 (24.2)    | 1316 (66.3) | < 0.001 |
| Topical medication (n = 2763) | 190 (6.9)   | 488 (17.7)    | 2085 (75.5) |         |

treatments. Variables affecting the adherence to topical medication included age, frequency of hospital visits, experience of drug effectiveness and overall satisfaction with treatment. Sex and disease classification tended to be associated with adherence to topical medication; however, they did not reach statistical significance (Table 3).

Poor adherence to treatment may be associated with poor clinical efficacy, increased healthcare costs and unnecessary treatments that include nonstandard folk medicine.<sup>9</sup> In general, a low adherence rate has been reported in patients with chronic dermatological diseases such as atopic dermatitis,<sup>3</sup> psoriasis,<sup>4</sup> urticaria<sup>5</sup> and acne;<sup>9</sup> however, few comparative studies have been performed among dermatological diseases. In the present study, the adherence rates as assessed by MMAS-8 were lower than those in other systemic diseases (Table S1; see Supporting Information). Previous studies have indicated that adherence to topical remedies is poorer than that to systemic drugs.<sup>4,10</sup> The present study supports this.

Younger age was associated with lower adherence in both the oral and topical drug groups. It was also previously implicated in decreased drug adherence in cases of acne.<sup>10,11</sup> As expected, lower adherence was observed in those who had not experienced drug effectiveness and those who were not satisfied with their treatments, both in oral and topical medication. Female sex and heavier drinking were additional factors associated with poorer adherence to oral medication. The adherence to medication tended to be lower in patients with atopic dermatitis than in those with psoriasis or tinea. Although the exact reason for this remains unclear, it is conceivable that topical corticosteroid phobia or anxiety may underlie poor adherence, as suggested by Aubert-Wastiaux et al.<sup>12</sup>

There are many limitations in the present study. Although we checked the diagnosis of patients in the web registration system, the diagnosis was still self-reported. Because of the length of the questionnaire, we did not include items about quality of life, the dosage of topical medications or steroid phobia.

In conclusion, medication adherence, especially to topical drugs, was very poor in 3096 dermatological patients. MMAS-8 is likely to be a reliable tool for comparing adherence in various disorders. Poor adherence to dermatological remedies was variably associated with younger age, female sex, heavier alcohol consumption, atopic dermatitis, no experience of drug effectiveness and dissatisfaction with treatment. Further analyses of disease-specific adherence are warranted in order

Table 3 Prevalence of study variables among the three adherence levels: oral and topical medication

| Characteristic                          | Oral medication (n = 1984) |                             |                           | P-value | Topical medication (n = 2763) |                             |                           | P-value |
|---|----------------------------|-----------------------------|---------------------------|---------|-------------------------------|-----------------------------|---------------------------|---------|
|   | High adherence<br>n = 188  | Medium adherence<br>n = 480 | Low adherence<br>n = 1316 |         | High adherence<br>n = 190     | Medium adherence<br>n = 488 | Low adherence<br>n = 2085 |         |
| Age (years)<br>mean ± SD                | 47.28 ± 13.13              | 46.89 ± 12.27               | 43.75 ± 12.09             | < 0.001 | 48.01 ± 12.97                 | 47.51 ± 13.76               | 45.57 ± 12.98             | 0.001   |
| Sex                                     |                            |                             |                           |         |                               |                             |                           |         |
| Male                                    | 98 (10.7)                  | 239 (26.0)                  | 583 (63.4)                | 0.030   | 105 (7.5)                     | 267 (19.0)                  | 1034 (73.5)               | 0.057   |
| Female                                  | 90 (8.5)                   | 241 (22.7)                  | 733 (68.9)                |         | 85 (6.3)                      | 221 (16.3)                  | 1051 (77.5)               |         |
| Marital status                          |                            |                             |                           |         |                               |                             |                           |         |
| Married                                 | 80 (10.0)                  | 194 (24.3)                  | 523 (65.6)                | 0.757   | 67 (6.4)                      | 205 (19.5)                  | 780 (74.1)                | 0.121   |
| Unmarried                               | 108 (9.1)                  | 286 (24.1)                  | 793 (66.8)                |         | 123 (7.2)                     | 283 (16.5)                  | 1305 (76.3)               |         |
| Annual income                           |                            |                             |                           |         |                               |                             |                           |         |
| ≥ 6 million yen <sup>a</sup>            | 71 (10.6)                  | 170 (25.4)                  | 428 (64.0)                | 0.469   | 70 (7.4)                      | 154 (16.2)                  | 724 (76.4)                | 0.282   |
| < 6 million yen                         | 96 (9.3)                   | 250 (24.1)                  | 692 (66.7)                |         | 98 (6.7)                      | 273 (18.7)                  | 1091 (74.6)               |         |
| Employment                              |                            |                             |                           |         |                               |                             |                           |         |
| Employed                                | 113 (8.8)                  | 314 (24.4)                  | 860 (66.8)                | 0.306   | 122 (7.0)                     | 299 (17.1)                  | 1331 (76.0)               | 0.624   |
| Unemployed                              | 65 (11.0)                  | 137 (23.1)                  | 391 (65.9)                |         | 59 (6.7)                      | 163 (18.6)                  | 655 (74.7)                |         |
| Education                               |                            |                             |                           |         |                               |                             |                           |         |
| University graduate                     | 80 (8.4)                   | 237 (24.8)                  | 637 (66.8)                | 0.264   | 84 (6.1)                      | 245 (17.8)                  | 1046 (76.1)               | 0.283   |
| Not university graduate                 | 107 (10.5)                 | 241 (23.6)                  | 672 (65.9)                |         | 105 (7.6)                     | 242 (17.6)                  | 1027 (74.8)               |         |
| Smoking                                 |                            |                             |                           |         |                               |                             |                           |         |
| Smoker                                  | 39 (9.9)                   | 90 (22.8)                   | 265 (67.3)                | 0.760   | 32 (5.9)                      | 90 (16.6)                   | 421 (77.5)                | 0.380   |
| Nonsmoker                               | 149 (9.4)                  | 389 (24.6)                  | 1044 (66.0)               |         | 158 (7.2)                     | 398 (18.0)                  | 1653 (74.8)               |         |
| Alcohol use                             |                            |                             |                           |         |                               |                             |                           |         |
| More than once per month                | 104 (8.6)                  | 277 (23.0)                  | 825 (68.4)                | 0.033   | 112 (6.5)                     | 298 (17.2)                  | 1325 (76.4)               | 0.244   |
| Less than once per month                | 84 (10.9)                  | 202 (26.2)                  | 484 (62.9)                |         | 78 (7.7)                      | 190 (18.7)                  | 749 (73.7)                |         |
| Diseases                                |                            |                             |                           |         |                               |                             |                           |         |
| Atopic dermatitis                       | 74 (8.1)                   | 181 (19.7)                  | 664 (72.3)                | < 0.001 | 76 (5.9)                      | 223 (17.3)                  | 993 (76.9)                | 0.080   |
| Urticaria                               | 62 (9.2)                   | 171 (25.4)                  | 440 (65.4)                |         | 33 (6.3)                      | 97 (18.4)                   | 398 (75.4)                |         |
| Psoriasis                               | 14 (12.5)                  | 36 (32.1)                   | 62 (55.4)                 |         | 12 (5.6)                      | 39 (18.1)                   | 165 (76.4)                |         |
| Tinea                                   | 38 (13.6)                  | 92 (32.9)                   | 150 (53.6)                |         | 69 (9.5)                      | 129 (17.7)                  | 529 (72.8)                |         |
| Frequency of hospital visits            |                            |                             |                           |         |                               |                             |                           |         |
| At least once per half year             | 181 (9.9)                  | 431 (23.7)                  | 1210 (66.4)               | 0.022   | 178 (7.2)                     | 445 (18.0)                  | 1846 (74.8)               | 0.031   |
| Less than once per half year or unknown | 7 (4.3)                    | 49 (30.3)                   | 106 (65.4)                |         | 12 (4.1)                      | 43 (14.6)                   | 239 (81.3)                |         |
| Main healthcare institution             |                            |                             |                           |         |                               |                             |                           |         |
| University hospital                     | 13 (13.7)                  | 27 (28.4)                   | 55 (57.9)                 | 0.383   | 8 (6.6)                       | 17 (13.9)                   | 97 (79.5)                 | 0.336   |
| Municipal hospital                      | 34 (10.0)                  | 81 (23.9)                   | 224 (66.1)                |         | 36 (7.3)                      | 101 (20.4)                  | 358 (72.3)                |         |
| Private clinic or other                 | 138 (9.0)                  | 369 (24.0)                  | 1031 (67.0)               |         | 145 (6.8)                     | 365 (17.1)                  | 1620 (76.1)               |         |
| Experience of drug effectiveness        |                            |                             |                           |         |                               |                             |                           |         |
| Yes                                     | 168 (10.3)                 | 416 (25.5)                  | 1050 (64.3)               | < 0.001 | 175 (7.4)                     | 423 (17.9)                  | 1767 (74.7)               | 0.016   |
| No                                      | 20 (5.7)                   | 64 (18.3)                   | 266 (76.0)                |         | 15 (3.8)                      | 65 (16.3)                   | 318 (79.9)                |         |
| Experience of adverse events            |                            |                             |                           |         |                               |                             |                           |         |
| Yes                                     | 28 (8.0)                   | 87 (24.9)                   | 234 (67.1)                | 0.585   | 24 (6.3)                      | 65 (17.0)                   | 293 (76.7)                | 0.810   |
| No                                      | 160 (9.8)                  | 393 (24.0)                  | 1082 (66.2)               |         | 166 (7.0)                     | 423 (17.8)                  | 1792 (75.3)               |         |
| Overall satisfaction with treatment     |                            |                             |                           |         |                               |                             |                           |         |
| Satisfied                               | 115 (9.9)                  | 310 (26.6)                  | 740 (63.5)                | 0.005   | 126 (7.9)                     | 291 (18.2)                  | 1180 (73.9)               | 0.023   |
| Unsatisfied                             | 73 (8.9)                   | 170 (20.8)                  | 576 (70.3)                |         | 64 (5.5)                      | 197 (16.9)                  | 905 (77.6)                |         |

Values are n (% of row total) unless stated otherwise. <sup>a</sup>6 million yen is about £34 000 (at the time of writing).

to elucidate the disease-specific sociomedical factors that are associated with it.

## Acknowledgments

We deeply thank Professor Akihito Hagihara for his extensive revision of this manuscript.

<sup>1</sup>Department of Dermatology and

<sup>2</sup>Department of Health Services Management and Policy, Kyushu University, Maidashi 3-1-1, Higashiku, Fukuoka 812-8582, Japan

<sup>3</sup>Department of Dermatology, Federation of National Public Service Personnel Mutual Aid Associations, Hamanomachi Hospital, Fukuoka, Japan

<sup>4</sup>Department of Dermatology, Graduate School of Medicine, Osaka University, Osaka, Japan

<sup>5</sup>Department of Dermatology, Faculty of Medicine, University of Tokyo, Tokyo, Japan

<sup>6</sup>Department of Dermatology, Kyoto Prefectural University of Medicine, Kyoto, Japan

<sup>7</sup>Department of Dermatology, Integrated Health Sciences, Institute of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan

<sup>8</sup>Department of Dermatology, Shimane University Faculty of Medicine, Shimane, Japan

<sup>9</sup>Department of Dermatology, Nippon Medical School, Tokyo, Japan

<sup>10</sup>Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

<sup>11</sup>Department of Dermatology, Tokyo Women's Medical University, Tokyo, Japan

<sup>12</sup>Department of Dermatology, Kanazawa Medical University, Ishikawa, Japan

<sup>13</sup>Department of Dermatology, University of Occupational and Environmental Health, Kitakyushu, Japan

<sup>14</sup>Department of Dermatology, Showa University School of Medicine, Tokyo, Japan

<sup>15</sup>Department of Dermatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

<sup>16</sup>Department of Dermatology, Faculty of Medicine, Fukuoka University, Fukuoka, Japan

<sup>17</sup>Sapporo Skin Clinic, Sapporo, Japan

<sup>18</sup>Department of Environmental Immunodermatology, Yokohama City University

M. FURUE<sup>1</sup>

D. ONOZUKA<sup>2</sup>

S. TAKEUCHI<sup>3</sup>

H. MUROTA<sup>4</sup>

M. SUGAYA<sup>5</sup>

K. MASUDA<sup>6</sup>

T. HIRAGUN<sup>7</sup>

S. KANEKO<sup>8</sup>

H. SAEKI<sup>9</sup>

Y. SHINTANI<sup>10</sup>

Y. TSUNEMI<sup>11</sup>

S. ABE<sup>12</sup>

M. KOBAYASHI<sup>13</sup>

Y. KITAMI<sup>14</sup>

M. TANIOKA<sup>15</sup>

S. IMAFUKU<sup>16</sup>

M. ABE<sup>17</sup>

N. INOMATA<sup>18</sup>

D.E. MORISKY<sup>19</sup>

N. KATOH<sup>6</sup>

Graduate School of Medicine, Kanagawa,

Japan

<sup>19</sup>UCLA Fielding School of Public Health,

Department of Community Health Sciences,

Los Angeles, CA, U.S.A.

Correspondence: Masutaka Furue

E-mail: furue@dermatol.med.kyushu-u.ac.jp

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## Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

**Table S1.** Adherence studies using the Morisky Medication Adherence Scale-8.

Funding sources: The web questionnaire was supported by Mitsubishi Tanabe Pharma Corporation and MPR KK.

Conflicts of interest: none declared.