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Efficacy of integrated online mindfulness and self-compassion training for adults with atopic dermatitis: A randomized controlled trial

Sanae Kishimoto, MHS, MPH[1], Norio Watanabe, MD[2], PhD, Yosuke Yamamoto, MD, PhD[3,4], Takumi Imai, PhD[5], Rei Aida, MHS[5], Christopher Germer, PhD[6], Risa Tamagawa-Mineoka, MD, PhD[7], Ryosuke Shimizu, MD[8], Steven Hickman, PsyD[9,10], Yujiro Nakayama, MD, MPH[11], Takafumi Etoh, MD[12], Ethan Sahker, PhD,[1,13], Martha B Carnie, AS[14], Toshi A. Furukawa, MD, PhD[1]

Affiliations

1. Department of Health Promotion and Human Behavior, Kyoto University Graduate School of Medicine/School of Public Health, Kyoto, Japan
2. Department of Psychiatry, Soseikai General Hospital, Kyoto, Japan
3. Department of Dermatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan
4. Department of Healthcare Epidemiology, Graduate School of Medicine/School of Public Health, Kyoto University, Kyoto, Japan
5. Department of Medical Statistics, Graduate School of Medicine, Osaka Metropolitan University, Osaka, Japan
6. Department of Psychiatry, Harvard Medical School/Cambridge Health Alliance, Cambridge, Massachusetts, United States
7. Department of Dermatology, Kyoto Prefectural University of Medicine, Kyoto, Japan
8. Shimizu Dermatology Clinic, Kobe, Hyogo, Japan

9. University of California at San Diego, Center for Mindfulness, San Diego, California, United States
10. Global Compassion Coalition, San Rafael, California, United States
11. Faculty of Medical Sciences, Shonan University of Medical Sciences, Yokohama, Kanagawa, Japan
12. Atago Dermatology Clinic, Tokyo, Japan
13. Population Health & Policy Research Unit, Medical Education Center, Kyoto University, Kyoto, Japan
14. Center for Patients and Families, Brigham and Women's Hospital, Boston, Massachusetts, United States

Corresponding author:

Sanae Kishimoto, MHS, MPH

Department of Health Promotion and Human Behavior, Kyoto University Graduate School of Medicine/School of Public Health, Yoshida Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan

Phone: +81-75-753-9491

Fax: +81-75-753-4641

Email: sanae.kishimoto@post.harvard.edu

Key points

Question:

Is online group mindfulness and self-compassion training efficacious in improving the quality of life (QOL) of adults with atopic dermatitis (AD)?

Findings:

In this randomized controlled trial of 107 adults with AD, mindfulness and self-compassion training in addition to usual care showed significantly greater improvements in patient-reported skin-disease-specific QOL, AD symptoms, and adherence to dermatological treatment, compared to a waitlist control at 13-week assessment. There were few dropouts, and the effect size was large.

Meaning:

Online group mindfulness and self-compassion training improves QOL and AD symptoms in synergy with dermatological treatments.

Abstract

Importance:

Quality of life (QOL) of patients with atopic dermatitis (AD) is reported to be the lowest among skin diseases. Mindfulness and self-compassion training (M&SC) has not been evaluated for adults with AD.

Objective:

To evaluate the efficacy of M&SC for adults with AD.

Design:

A randomized controlled trial conducted from March 2019 through October 2022. Participants were randomized to the intervention or waitlist group, in addition to usual

care.

Setting:

Participants were recruited from multiple outpatient institutes in Japan and through the study's social media outlets and website.

Participants:

Adults with AD, whose Dermatology Life Quality Index (DLQI) score, a skin-disease-specific QOL measure, was greater than 6 (corresponding with moderate or greater impairment).

Interventions:

Eight 1.5-hour weekly group sessions of online M&SC. Both groups were allowed to receive any dermatological treatment except for dupilumab.

Main Outcomes and Measures:

The primary outcome was the change in the DLQI score from baseline to week 13.

Results:

We randomized 107 adults to the intervention group (n=56) or the waitlist (n=51). Participant mean [SD] age was 36.3 [10.5], 85 [79%] were women, and the mean AD duration was 26.6 [11.7] years. Fifty-five (98.2%) participants from the intervention group attended six or more of the eight sessions. One hundred and five (98.1%) completed the assessment at 13 weeks. The intervention group demonstrated greater improvement in the DLQI at 13 weeks (group difference estimate -6.34, 95%CI: -8.27 to -4.41, P<0.0001). The standardized effect size at 13 weeks was d=-1.06 (95% CI: -1.39 to -0.74). All other secondary outcomes including patient-reported eczema severity (group difference estimate -6.28, 95%CI: -8.54 to -4.01, P<0.0001, d=-0.95 (95%CI: -

1.30 to -0.61), participants' adherence to dermatologist-advised treatments, and psychological symptoms, showed greater improvements in the intervention group than in the waitlist group.

Conclusions and Relevance:

For adults with AD, integrated online M&SC training, in addition to usual care, resulted in greater improvement in the skin-disease-specific QOL and other patient-reported outcomes, including eczema severity. These findings suggest that M&SC training is an effective treatment option for adults with AD.

Trial Registration:

UMIN Clinical Trials Registry: UMIN000036277

Introduction

Atopic dermatitis (AD) is a chronic relapsing inflammatory, multifactorial skin disease associated with intense itching[1,2]. The prevalence of AD is estimated to be 15 to 30% in children and 2 to 10% in adults, with the incidence increasing in industrialized countries[1,3,4]. Sleep difficulties, anxiety, and depression are reported to be common comorbidities of AD. Symptoms of AD significantly impact patients' quality of life (QOL)[5,6]. AD is associated with significant effects on patients' QOL[7]. Given its prevalence and impact, AD has the highest disease burden among skin diseases, as measured by disability-adjusted life-years (DALYs)[8]. Treatment options include medications, skincare, and lifestyle changes. There are new biologic medications that show effectiveness, but they may not be widely available due to high costs, and they need to be investigated for their long-term safety. While previous studies have highlighted the importance of psychological interventions[9,10], they are mostly conducted in pediatric populations[11], often limited in sample size, delivered in individual formats, combined with specific physical treatments, and studies have not examined the impact on QOL[12-15]. A recent review reported that patients with AD would benefit from cognitive behavioral therapy plus dermatological treatment compared to only receiving the standard-of-care treatment. [16]

Mindfulness-Based Stress Reduction (MBSR) was introduced in the 1970s for coping with chronic pain[17,18], and has been increasingly applied to various clinical disorders[19-26]. Self-compassion is a key factor in mindfulness-based interventions[27,28]. Mindful Self-Compassion (MSC) was developed in 2010[29] and has been applied to general and clinical populations[30]. While MBSR focuses on building a non-judgmental relationship with stress, MSC emphasizes a compassionate relationship with oneself during a time of suffering. Standard MBSR and MSC courses require eight weekly interactive sessions, each lasting 150-180 minutes, a full or half-day silent retreat, and at least 30-40 minutes

of daily home practice.

One study showed that MBSR resolves symptoms four times faster than phototherapy treatments alone among patients with moderate to severe psoriasis[31]. No studies to date have examined the efficacy of MBSR or MSC in patients with AD. Thus, clinically relevant programs for AD are needed. We developed an integrated program that adapted and combined elements of MBSR and MSC. We hypothesized that the intervention would improve the skin-disease-specific quality of life and reduce the patient-reported AD severity and other symptoms. To the best of our knowledge, this is the first study to examine the efficacy of an online group mindfulness and self-compassion integrated intervention (M&SC) for adults diagnosed with AD.

Methods

Trial design:

The self-compassion and mindfulness integrated online program for people living with eczema (SMiLE) study is a randomized controlled trial (UMIN000036277). The study was approved by the Ethics Committee of Kyoto University Graduate School of Medicine. The study followed the consolidated Standards of Reporting Trials (CONSORT) guideline (Supplement 1).

Participants:

Participants were recruited at multiple outpatient academic medical centers and private practices in Japan, via social media posts and through the study website from July 2019 and June 2022.

Participants were assessed for eligibility and were included in the study if they (1) were 18–64 years old, (2) reported a dermatologist-confirmed AD diagnosis; (3) met self-reported criteria of itchy skin and bilateral symmetric eczema with continuing symptoms

for over six months; (4) scored greater than six points on the Dermatology Life Quality Index (DLQI)[32,33], indicating moderate to extremely large skin-disease-specific QOL impacts; (5) could access the internet for the online program; and (6) could attend all sessions and complete home practice. Patients were excluded if they were (1) administered dupilumab treatment, the only newly marketed drug at study commencement; (2) diagnosed with psychosis, personality disorders, post-traumatic stress disorder, or acute stress disorder; (3) receiving psychotherapy during the study; (4) attended other mindfulness/compassion programs; (5) unable to understand Japanese; (6) relatives of study researchers; or (7) deemed ineligible to participate by study researchers.

All applicants were first requested to confirm these criteria on the Research Electronic Data Capture (REDCap) website[34]. Additional screening interviews and an explanation of the trial took place in an individual one-hour online meeting. All participants provided electronically signed informed consent.

Randomization/Blinding:

After completing screening and creating a cohort, we randomized participants 1:1 to the M&SC or waitlist group, using block randomization with a block size of four, stratified by sex, age (<30 or ≥30), and baseline DLQI score (<11 or ≥11 on a 0–30 scale). An independent statistician received the participant list and conducted the randomization remotely. Participant group allocation was concealed until they were placed in their respective group.

Participants and the therapist/investigator were not blinded to the treatment allocation because of the nature of the interventions. All outcome assessments were completed electronically by the participants. The therapist and the statistician remained blind to

the outcome data until the RCT was completed and analyzed.

Interventions:

The online group-based M&SC was a psychological/behavioral training integrating elements of MBSR and MSC. This involved weekly 90-minute interactive online sessions over eight weeks, an optional silent five-and-a-half-hour meditation retreat, and an optional 120-minute videoconferencing booster session (Zoom Video Communications Inc., 2016). All eight sessions were conducted entirely online weekly on the same day and time of the week. Participants chose between an offline or online format for the optional silent meditation retreat. After the COVID-19 outbreak, this optional retreat was only conducted online.

The first three sessions incorporated key elements of MBSR. Sessions four to eight contained key elements of MSC (Table1). Each session included meditation, informal psychoeducation, inquiry, and a short lecture. Just as MBSR or MSC, this hybrid program intentionally was not limited to disease-specific topics, but mainly focused on living as a person with AD and taking care of oneself wisely and kindly. Participants were not advised on any particular treatment plan, and the therapist respected their dermatological treatment decisions. Participants were given home practice regimens. Participant instructions were available on the education technology platform, PowerSchool Learning (PowerSchool Group LLC., 1997). Participants could watch videos to deepen their understanding. All sessions were video recorded for monitoring facilitation quality and protocol adherence.

Interventions were led by a masters-level Japanese licensed clinical psychologist (SK), with formal MBSR and MSC training, and teaching experience as a Japanese certified instructor. The intervention manual was developed by SK. CG, co-developer of MSC, affirmed the quality of the program and manual. The control was a waitlist group. Both

groups were allowed to receive usual care as determined by individual patients and their physicians. We instructed participants not to begin dupilumab, psychotherapy, or other mindfulness interventions during the trial in order for the researchers to accurately evaluate the efficacy of the intervention.

Outcomes:

Primary outcome

We administered the skin-disease-specific DLQI, at baseline, mid-intervention (week 4), post-intervention (week 9), and at four weeks post-intervention follow-up (week 13). The primary outcome was the change on the DLQI from baseline to week 13. The eAppendix provides detailed explanations of the study scales.

Secondary outcomes

We assessed secondary outcomes at baseline, week 9, and week 13. Secondary outcomes included the Patient−Oriented Eczema Measure (POEM), itchiness-related numeric rating scales (intensity of itchiness before sleep, bothered by itchiness, intensity of scratching), Freiburg Mindfulness Inventory (FMI), Self-Compassion Scale (SCS), Hospital Anxiety and Depression Scale (HADS), Internalized Shame Scale (ISS; consisting of shame and self-esteem), and dermatological treatment adherence to self-care measuring patient willingness to follow physician advice. Additionally, participants rated their home practice time and frequency, and provided descriptive experiential feedback.

Data collection:

Study data were collected using REDCap electronic data capture tools[34], hosted at the Department of Medical Biostatics, Graduate School of Medicine, Osaka Metropolitan University.

Sample size:

In our single-arm feasibility and acceptability study (UMIN000036277), participants with a baseline DLQI score of 6 or higher showed a DLQI reduction of -3.7 (SD 6.7). Because our target population was adults with long-lasting AD, and we expected minimal change while they were on the waitlist, we set the difference to be detected at 3.7 (SD 6.7) with two-sided α at $p<0.05$ and β at 0.20. The required sample size was 105, and assuming a dropout rate of 10%, the target number of participants was set at 58 in each group, for a total of 116 participants.

During the study execution, it was found that the dropout rate was less than 2%. As dropout was negligible, recruitment was halted at N=107 without considering the 10% dropout anticipated in the protocol.

Statistical methods:

We conducted the analyses in accordance with the predefined statistical analysis plan on an intention-to-treat basis. For the primary outcome of baseline DLQI change, we used the mixed-effects models for repeated measures (MMRM) including treatment, time, and time-by-treatment interaction adjusted for age, sex, and baseline DLQI score. We estimated the least squares means and their 95% confidence intervals at each time point for within-group DLQI change scores and differences between groups. Treatment efficacy was judged by the group difference in the primary outcome with the two-sided alpha-level of $p<0.05$. We applied the same model to the secondary outcomes to explore the intervention effects. We did not adjust for multiple comparisons for secondary outcomes as they were exploratory in nature.

For the DLQI, we performed three additional prespecified analyses. First, percentages of patients with more than four-point improvements were estimated for each group and time point with 95% confidence intervals by the Clopper-Pearson method. The minimal

clinically important difference of the DLQI is four points[35]. Second, heterogeneity in treatment efficacy was assessed for the following predefined subgroups: sex, age (divided by the median values at baseline) and baseline DLQI (divided by the median values at baseline). Third, group differences were evaluated on the per-protocol basis. All statistical analyses of MMRM used the restricted maximum likelihood methods of SAS 9.4 MIXED procedure with Kenward–Roger correction and unstructured variance-covariance matrix[36].

Patient and family involvement:

Patient and family involvement was highly valued in this trial and a pragmatic framework was used for authentic patient-researcher partnership in clinical research[37,38]. A Patient-Family Advisory Council was formed for this trial by selecting members from the pilot study. The Council collaborated with the researchers from the protocol phase to the interpretation of the results. For example, elements of self-compassion were increased, and outcomes were finalized based on patient input. This approach helped assure that participants felt safe and comfortable and would stay in the trial.

Results

Participants:

Figure 1 displays the CONSORT flowchart of the trial. Of 1053 participants assessed for eligibility, 107 were ultimately included and randomized. Recruitment took place between July 2019 and June 2022, and assessment were conducted until October 2022. Of the 107 randomized, two (1.9%) dropped out from the primary outcome assessment at week 13. Of the 56 allocated to the intervention group, one (1.8%) participant attended only four and another attended only six out of the eight sessions. All participants were included in the primary intention-to-treat analysis by MMRM. Several new drugs were introduced to the market after the study began, but only two participant

from the M&SC group used topical delgocitinib, and one participant from the waitlist used baricitinib.

Table 2 summarizes the participant characteristics at baseline. Three participants lived outside Japan: in Belgium, Singapore, and Spain. The participants were mainly in their 30s and 40s, predominantly female (85 of 107, 79%), and most had higher education. They suffered from AD for over two decades and three-quarters were attending outpatient dermatology clinics.

Primary outcome and sensitivity analysis:

The primary outcome intention-to-treat analysis at 13 weeks showed that the intervention group demonstrated significantly greater improvement on the DLQI than the control group (between-group difference estimate -6.34, 95%CI: -8.27 to -4.41, *P<0.0001*). QOL of the intervention group continued to improve through the intervention and afterwards up to week 13 (Figure 2). The standardized effect size at week 13 was -1.06 (95% CI: -1.39 to -0.74, Table 3).

The percentage of participants showing minimal clinically important difference (MCID) on the DLQI at 13 weeks was 81.5% (95% CI, 68.6% to 90.7%) in the M&SC group and 33.3% (95% CI, 20.8% to 47.9%) in the waitlist group at week 13 (eTable1).

No treatment effect heterogeneity among subgroups was confirmed (eTable2a, eTable2b). The group differences in the per-protocol population were consistent with those of the full analysis set (eTable3).

Secondary outcomes:

Intention-to-treat analysis showed that all secondary outcomes including AD symptoms,

itch and scratching related visual analog scales, self-compassion and all its subscales (eTable4), mindfulness, internalized shame, anxiety, and depression, showed significant improvement with large effect sizes in the M&SC group compared to the waitlist at all time points (Table 3, eFigure1).

Dermatological treatment adherence showed that those in the M&SC group were more likely to follow medical treatment plans by dermatologists from baseline to week 13, including moisturizer use and topical steroid use (eFigure2, eFigure3, eTable5). Comments from participants suggested that their feeling of resistance/worry about use of medications decreased, and they applied them early, mindfully, and compassionately rather than automatically.

The majority of participants in the M&SC group reported they completed home practice either every day or every other day. The average home practice minutes (SD) per day at week 4, week 9, and week 13 was 43.5 (17.1), 41.7 (22.2), and 32.9 (17.9) respectively (eTable6, eTable7).

Serious adverse events:

One serious adverse event was identified. One participant had been diagnosed with uterine fibroids and had undergone surgery prior to her enrollment. Her results came back after starting the program and early-stage endometrial cancer was diagnosed. Subsequently she underwent surgery and recovered well. We judged this event to be unrelated to the intervention. With approval from the Ethics Committee at Kyoto University she continued to participate in the study.

Discussion

The present study demonstrated the efficacy of integrated online M&SC for adults with

moderate to severe AD. We found that skin-disease-specific QOL improved over time with a large effect size. The dropout rate was very low.

The present study is the first to show that group format M&SC enhances QOL for adults with AD. A previous systematic review reported MBSR had moderate effect on QOL for a range of target populations but recommended further research to ensure quality of evidence.[39] People with AD suffer from chronic symptoms and integrating self-compassion may have contributed to the observed large effect of the intervention. Improved QOL in the present study may also have been due to improved physical wellbeing.

The study confirmed the M&SC reduced patient-reported AD symptoms. The M&SC intervention combined with the usual care enabled physiological symptoms to improve. Importantly, participants in the M&SC group enhanced their dermatological treatment adherence. This likely contributed to improved physiological responses. Additionally, multiple psychological and biological factors appeared interconnected. For example, the present findings support previous work demonstrating mindfulness meditation leads to improved immunological response[40], and self-soothing touch reduces cortisol levels[41].

Prior studies reported the effectiveness of habit training in improving the itch-scratch cycle[42-45]. Patients are often in pain, managing difficult symptoms, and experiencing unnecessary distress due to self-judgment and self-criticism. When an itch arises, M&SC teaches patients to see there is a choice to respond mindfully, either scratch, apply soothing touch or simply let go. When one scratches, self-compassion teaches that there is no need for self-blame. There is instead a choice to direct compassion, understanding, and self-care to their skin and themselves. These skills seemed to help break the negative cycle. However, teaching these skills does require extensive training.

The program in the present study was developed and taught by an experienced female compassionate psychologist who also has a history of AD. The present findings support existing effect sizes in self-compassion, depression, and anxiety with MSC[29]. Based on participant comments, session seven's topic, shame, was the highlight as self-compassion is an antidote to shame. An example of a common participant comment included: *"I thought me without AD should be the real me, but it's ok to have AD, ok to be imperfect like all humans. Now I have begun to like myself."*

Strengths and Limitations:

One of this trial's strengths is its high internal validity, including independent random sequence generation, allocation concealment, low dropouts, statistician blinding, and full reports of the pre-planned analyses. In particular, the dropout from intervention and assessment was very low. In general trials of psychotherapy with adults 19.7% dropout is reported[46]. Completion rates of online mindfulness courses vary depending on the population and completion criteria[47]. In a recent online MBSR study, only 67.6% completed at least six of eight classes[48]. Online compassion-focused self-help therapy for psoriasis reported a dropout rate of 29%[49]. The integrated M&SC program was appealingly presented for people with AD. Finally, the online format is highly scalable and accessible, including for those who were hesitant to go outside due to AD symptoms.

There are some limitations of note. First, external validity may not be high. Only highly motivated/committed Japanese participants applied to this study. However, this may speak to the urgency surrounding AD treatment as nearly all included participants were highly motivated to find something that could ease their pain. It is not clear what the results would look like with less motivated participants, populations in other countries, or different clinical settings. It is possible that the Japanese population are just well-suited for mindfulness-based approaches, or that care delivery for AD in Japan could be associated with greater acceptability of behavioral health approaches. Further research

with other populations and clinical settings is necessary to increase generalizability and transportability of the current findings. Also, participants were on conventional treatment rather than newly introduced drugs, as the intention was to accurately evaluate the efficacy of M&SC. In addition, although it was not statistically significant, male patients demonstrated less response than females with differences in the point estimates nearly the magnitude of the DLQI minimally important difference. Heterogeneity between the sexes needs further investigation to clarify. Second, using the waitlist as a control group may have led to a larger effect size than using the other control condition such as no treatment or placebo psychotherapy[50]. Third, there was only one therapist due to the lack of resources in Japan. To assure generalizability and scalability, and to establish effectiveness, therapists need to be trained adequately and ascertain their effectiveness. Trials using multiple therapists will allow for process research with therapist factors such as treatment fidelity and the therapeutic alliance. Fourth, M&SC required a time amount of 12 hours total for 8-week online live group interactive sessions. Further utilizing information and communication technologies could make the intervention more efficient, as in internet CBT by Hedman-Lagerlöf et al[51]. Fifth, no objective outcomes were evaluated. In this trial, the focus was on patient-reported outcomes. While combining clinician-reported outcomes will be needed in future studies, patients who did not see dermatologists but had dermatological needs were able to participate in this trial. Sixth, in this study, the intention-to-treat principle was adhered to and examined the effect of assigning participants to the interventions rather than the effect of adhering to the treatments. We understand the importance of detailed path analysis for the intervention effect, and this will be within the scope of the next studies.

Conclusion

Online mindfulness and self-compassion in addition to usual care work in synergy with demagogical standard care and improve the patient QOL, AD symptoms, and

psychological well-being.

Author's contributions

SK had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: SK, NW, YY, TI, RA, CG, RS, MC, and TAF.

Acquisition, analysis, or interpretation of data: SK, NW, YY, TI, RA,CG, RM, RS, SH, YN, TE, ES, MC, and TAF.

Drafting of the manuscript: SK.

Critical revision of the manuscript for important intellectual concept: All authors.

Statistical analysis: TI.

Obtaining funding: SK.

Administrative, technical, or material support: RA.

Supervision: NW, YY, ES and TAF.

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Conflict of interest disclosures

TAF reports personal fees from Boehringer-Ingelheim, DT Axis, Kyoto University Original, Shionogi and SONY, and a grant from Shionogi, outside the submitted work; In addition, TAF has patents 2020-548587 and 2022-082495 pending, and intellectual properties for Kokoro-app licensed to Mitsubishi-Tanabe. YY reports personal fees from Sun Pharma, Asahi Kasei Pharma, Nippon Shinyaku, and Ono, outside the submitted work. TI reports personal fees from JCR Pharmaceuticals and Kyowa Kirin, outside the submitted work. TE reports personal fees from Maruho, Kyowa Kirin, AbbVie, LEO Pharma, and Eli Lilly, outside the submitted work. No other disclosures were reported.

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Role of Funder/Sponsor

These funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement

If the data sharing was requested from other researchers, we would obtain permission from the Ethics Committee to share.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki on the ethical principles established for research involving human subjects and the ethical guidelines for clinical studies published by the Japanese Ministry of Health, Labor, and Welfare. The study was approved by the Ethics Committee of Kyoto University Graduate School of Medicine (protocol code C1431 and March 2019). Compensation of online gift card was made $8 for 4-week and 9-week assessment and $16 for 13-week assessment for both groups.

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Table1. Outline of program sessions

Module	Adaptation from	Main Theme	Length of time (min)
0		Orientation	120
1	MBSR	Introduction to mindfulness, Awareness of body	90
2	MBSR	Awareness of body and breath	90
3	MBSR	Reactivity and responding to stress	90
4	MSC	Introduction to self-compassion	90
5	MSC	Loving-kindness for oneself, inner compassionate voice for self-motivation	90
6	MSC	Meeting with difficult emotions	90
7	MBSR/MSC	One-day silent meditation retreat	330
8	MSC	Being with shame kindly	90
9	MSC	Self-appreciation integration for continued practice	90
10		Booster session	120

Grey: Optional sessions
Abbreviations: MBSR, Mindfulness Based Stress Reduction; MSC, Mindful Self-Compassion.

Table 2. Baseline characteristics of participants by group

Characteristics	M&SC[a] Group (N=56)	Waitlist (N=51)
Age (years), mean (SD)	37.21 (10.44)	35.22 (10.55)
Sex (female), No. (%)	46 (82)	39 (76)
Education (years), mean (SD)		
<High school	8 (14)	3 (6)
Some college or vocational school	9 (16)	6 (12)
College graduate	35 (62)	28 (55)
Graduate school	4 (7)	14 (27)
Marital status, No. (%)		
Single, never married	31 (55)	27 (53)
Divorced, separated, or widowed	0 (0)	1 (2)
Married	25 (45)	23 (45)
Living situation, No. (%)		
By oneself	12 (21)	10 (20)
With someone	44 (79)	41 (80)
Work situation, No. (%) [b]		
Full-time worker	26 (51)	26 (58)
Part-time worker	15 (29)	7 (16)
Medical leave	0 (0)	6 (13)
Homemaker	0 (0)	0 (0)

Students	5 (10)	6 (13)
Unemployed	5 (10)	0 (0)
Disease duration in years, mean (SD)	27.64 (11.98)	25.53 (11.32)
Outpatient clinic visit (yes), No. (%)	41 (73)	39 (76)
Frequency of out-patient visit, No. (%)		
Monthly or more	9 (22)	12 (31)
Up to once in three months	21 (51)	21 (54)
Up to once in six months	4 (10)	4 (10)
Less than once in six months	2 (5)	2 (5)
Infrequent	5 (12)	0 (0)
Dermatological treatment: multi-selection, No. (%)		
Moisturize	43(77)	39 (76)
Topical steroid	36 (64)	31 (61)
Tacrolimus ointment	19 (34)	13 (25)
Anti-allergic oral medication (anti-itch medication)	31 (55)	27 (53)
Cyclosporine (immunosuppressant)	3 (5)	2 (4)
Steroid intake	2 (4)	4 (8)
Phototherapy	1 (2)	2 (4)

a. M&SC, Mindfulness and Self-compassion
b. Only work situation question item, there were missing data on waitlist

Table 3. Primary and secondary outcomes

	LS Mean estimates (95% CI)				Differences in LS Mean changes	P value	Standardized effect size (Cohen's d)
Week	n	M&SC	n	Waitlist	(95% CI)		(95% CI)
Primary outcome							
DLQI (Skin specific QOL)							
Baseline	56	14.75 (13.24 to 16.26)	51	12.75 (11.16 to 14.33)			
4-week	55	10.02 (8.51 to 11.52)	51	12.51 (10.93 to 14.09)	-3.61 (-5.43 to -1.80)	<.001	-0.70 (-1.05 to -0.35)
9-week	54	7.24 (5.91 to 8.57)	51	11.10 (9.71 to 12.49)	-4.98 (-6.66 to -3.30)	<.001	-0.95 (-1.27 to -0.63)
13-week	54	5.89 (4.46 to 7.31)	51	11.10 (9.62 to 12.58)	-6.34 (-8.27 to -4.41)	<.001	-1.06 (-1.39 to -0.74)
Secondary outcomes							
POEM (AD severity)							
Baseline	56	18.14 (16.65 to 19.64)	51	17.51 (15.94 to 19.08)			
9-week	54	11.58 (9.95 to 13.20)	51	16.37 (14.68 to 18.06)	-5.33 (-7.44 to -3.22)	<.001	-0.86 (-1.20 to -0.52)
13-week	54	10.64 (8.94 to 12.35)	51	16.39 (14.63 to 18.16)	-6.28 (-8.54 to -4.01)	<.001	-0.95 (-1.30 to -0.61)
Intensity of itching before sleep							
Baseline	56	5.27 (4.62 to 5.92)	51	5.54 (4.85 to 6.22)			
9-week	54	3.02 (2.35 to 3.68)	51	4.62 (3.93 to 5.31)	-1.49 (-2.34 to -0.64)	<.001	-0.60 (-0.94 to -0.26)
13-week	54	2.47(1.83to 3.12)	51	4.72 (4.06 to 5.38)	-2.12 (-2.99 to -1.26)	<.001	-0.80 (-1.13 to -0.48)
Intensity of scratching							
Baseline	56	5.71 (5.10 to 6.31)	51	5.93 (5.30 to 6.57)			
9-week	54	3.21 (2.60 to 3.82)	51	5.34 (4.71 to 5.98)	-2.01 (-2.76 to -1.25)	<.001	-0.92 (-1.27 to -0.58)
13-week	54	3.14 (2.48 to 3.79)	51	5.11 (4.43 to 5.78)	-1.84 (-2.70 to -0.98)	<.001	-0.73 (-1.07 to -0.39)
Itch bothersomeness							

Baseline	56	5.11 (4.48 to 5.74)	51	5.04 (4.38 to 5.69)			
9-week	54	2.50 (1.90 to 3.10)	51	4.48 (3.85 to 5.10)	-2.06 (-2.82 to -1.30)	<.001	-0.86 (-1.18 to -0.54)
13-week	54	2.41 (1.77 to 3.06)	51	4.49 (3.83 to 5.15)	-2.16 (-3.04 to -1.28)	<.001	-0.79 (-1.12 to -0.47)
SCS (Self-compassion)							
Baseline	56	2.55 (2.38 to 2.72)	51	2.52 (2.34 to 2.70)			
9-week	54	3.62 (3.46 to 3.78)	51	2.70 (2.54 to 2.87)	0.91 (0.71 to 1.10)	<.001	1.58 (1.24 to1.91)
13-week	54	3.70 (3.53 to 3.86)	51	2.68 (2.55 to 2.85)	1.00 (0.79 to 1.21)	<.001	1.52 (1.20 to 1.85)
FMI (Mindfulness)							
Baseline	56	29.64 (27.75 to 31.54)	51	30.96 (28.97 to 32.95)			
9-week	54	38.98 (37.10 to 40.85)	51	31.00 (29.05 to 32.95)	8.91 (6.72 to 11.10)	<.001	1.41 (1.06 to 1.75)
13-week	54	39.06 (37.18 to 40.94)	51	31.55 (29.60 to 33.49)	8.42 (6.08 to 10.76)	<.001	1.22 (0.88 to 1.56)

Abbreviations: CI, Confidence interval; M&SC, Mindfulness and Self-Compassion; DLQI, Dermatology Life Quality Index; POEM, Patient-Oriented Eczema Measure; AD, Atopic dermatitis; SCS, Self-Compassion Scale; FMI, Freiburg Mindfulness Inventory; HADS, Hospital Anxiety and Depression Scale; ISS, Internalized Shame Scale.

Table 3. *Continued*

	LS Mean estimates (95% CI)				Differences in LS Mean changes	P value	Standardized effect size (Cohen d)
Week	n	M&SC	n	Waitlist	(95% CI)		(95% CI)
Secondary outcome							
HADS Anxiety							
Baseline	56	8.30 (7.19 to 9.41)	51	8.12 (6.96 to 9.28)			
9-week	54	5.76 (4.80 to 6.72)	51	8.78 (7.79 to 9.78)	-3.08 (-4.34 to -1.83)	<.001	-0.76 (-1.06 to -0.45)
13-week	54	4.61 (3.55 to 5.66)	51	8.16 (7.07 to 9.24)	-3.62 (-5.00 to -2.24)	<.001	-0.86 (-1.19 to -0.53)
HADS Depression							
Baseline	56	8.29 (7.33 to 9.24)	51	8.31 (7.32 to 9.31)			
9-week	54	4.91 (3.99 to 5.84)	51	7.92 (6.96 to 8.88)	-2.98 (-4.12 to -1.84)	<.001	-0.85 (-1.18 to -0.53)
13-week	54	4.69 (3.68 to 5.70)	51	7.69 (6.65 to 8.72)	-2.97 (-4.26 to -1.68)	<.001	-0.78 (-1.12 to -0.44)
ISS Shame							
Baseline	56	47.89 (43.59 to 52.20)	51	51.29 (46.78 to 55.81)			
9-week	54	33.29 (29.16 to 37.42)	51	49.65 (45.34 to 53.96)	-13.76(-18.03 to-9.48)	<.001	-1.12 (-1.47 to -0.77)
13-week	54	31.27 (27.01 to 35.54)	51	49.22 (44.79to 53.64)	-15.33(-20.07 to 10.60)	<.001	-1.13 (-1.47 to -0.78)
ISS Self-esteem							
Baseline	56	12.16 (11.01 to 13.31)	51	11.53 (10.32 to 12.74)			
9-week	54	14.66 (13.50 to 15.82)	51	11.73 (10.52 to 12.93)	2.46 (1.48 to 3.44)	<.001	0.93 (0.56 to 1.30)
13-week	54	15.47 (14.26 to 16.69)	51	11.88 (10.62 to 13.15)	3.12 (1.96 to 4.27)	<.001	1.02 (0.65 to 1.40)

Abbreviations: CI, Confidence interval; M&SC, Mindfulness and Self-Compassion; DLQI, Dermatology Life Quality Index; POEM, Patient-Oriented Eczema Measure; AD, Atopic dermatitis; SCS, Self-Compassion Scale; FMI, Freiburg Mindfulness Inventory; HADS, Hospital Anxiety and Depression Scale; ISS, Internalized Shame Scale.