


# BMJ Open Acupuncture for atopic dermatitis: a systematic review and meta-analysis

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## ABSTRACT

**Objectives** Atopic dermatitis is a chronic, relapsing, inflammatory skin disease that impacts patients' quality of life and imposes substantial economic burdens on their families. Acupuncture holds promise as a viable treatment option for atopic dermatitis. This review aimed to evaluate the effect of acupuncture on atopic dermatitis.

**Design** Systematic review and meta-analysis.

**Data sources** PubMed, Embase, CENTRAL, the China National Knowledge Infrastructure, WanFang and VIP databases were searched through 17 September 2023, together with an updated search on 15 October 2024.

**Eligibility criteria for selecting studies** We included randomised controlled trials (RCTs) about acupuncture for atopic dermatitis. The primary outcome was the SCORing Atopic Dermatitis (SCORAD) score. The secondary outcomes were the eczema area and severity index (EASI) score, the visual analogue scale (VAS) score for pruritus, the dermatology life quality index (DLQI) score, serum IgE level and adverse events (AEs).

**Data extraction and synthesis** Two independent reviewers conducted separate searches of the databases, assessed eligible articles for inclusion and employed the Cochrane Collaboration's tool for assessing the risk of bias. The analyses were performed using RevMan 5.3 and Stata 13.0 software. The mean difference (MD) with 95% CI was employed to analyse continuous outcomes.

**Results** Eight studies with 463 participants were included. The meta-analysis indicated significant differences in the SCORAD score (MD=−10.61, 95% CI −17.77 to −3.45,  $p=0.004$ ), the VAS score for pruritus (MD=−14.71, 95% CI −18.20 to −11.22,  $p<0.00001$ ) and the DLQI score (MD=−2.37, 95% CI −3.57 to −1.18,  $p<0.0001$ ), but no significant differences in the EASI score (MD=−3.95, 95% CI −8.35 to 0.45,  $p=0.08$ ) and the IgE level (MD=−160.22 U/mL, 95% CI −334.13 to 13.68,  $p=0.07$ ) between treatment and control. The differences in the SCORAD score and the VAS score for pruritus reached minimal clinically important differences. No serious AEs were reported.

**Conclusions** Acupuncture might be an effective and safe treatment for atopic dermatitis. Due to the limited quantity and quality of the included studies, it is recommended to conduct multicentre, large-scale and high-quality RCTs to further confirm the findings.

**PROSPERO registration number** CRD42023470643.

## INTRODUCTION

Atopic dermatitis, also known as atopic eczema, is a chronic, relapsing, inflammatory

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The search strategy was robust and thorough, and the rigorous filtering criteria were implemented.
- ⇒ Subgroup analyses based on different interventions were conducted to strengthen the reliability of the conclusions.
- ⇒ The reliability and extrapolation of the overall findings were compromised due to the inclusion of a restricted number of randomised controlled trials and a small sample size.
- ⇒ The quality of the included studies was less than satisfactory.

skin disease characterised by recurrent eczema-like rash accompanied by significant xerosis and pruritus.<sup>1</sup> The global prevalence of atopic dermatitis was estimated to be 2.62%, with approximately 101.27 million affected adults and 102.78 million affected children worldwide, corresponding to rates of 1.95% and 3.96%, respectively.<sup>2</sup> The aetiology and pathogenesis of atopic dermatitis are highly complex and remain incompletely understood. Current research has demonstrated that the pathogenesis of atopic dermatitis is associated with genetic factors, immune abnormalities, environmental factors, impaired skin barrier function, disrupted skin microbiota and other contributing factors.<sup>3</sup> Depression and anxiety disorders are more common in patients with severe atopic dermatitis, and psychological stress can worsen the condition. The disease is characterised by a high risk of relapse, a protracted course and the potential to significantly impact patients' quality of life and impose substantial economic burdens on their families.<sup>4</sup> Therefore, addressing atopic dermatitis as a global issue necessitates the implementation of efficacious and standardised therapeutic interventions to alleviate symptoms and minimise recurrence.

The treatment of atopic dermatitis should focus on restoring the skin barrier, encompassing moisturisation and maintenance of the skin, prevention of scratching and

reduction of inflammation.<sup>5</sup> Emollients, bath oils and allergen avoidance are the basic therapies. Topical glucocorticosteroids, topical calcineurin inhibitors, UV therapy and wet wrap therapy are commonly used for topical treatment. If the disease cannot be controlled adequately with topical treatments, systemic immunosuppressive agents such as systemic glucocorticosteroids, cyclosporine A, methotrexate, mycophenolate mofetil and azathioprine should be used.<sup>6</sup> However, prolonged medication can lead to various adverse effects, such as skin atrophy, purpura, acneiform eruptions and adrenal suppression.<sup>6</sup>

Acupuncture, as an important part of complementary medicine, has been widely used for dermatologic diseases, such as chronic spontaneous urticaria,<sup>7</sup> herpes zoster<sup>8</sup> and neurodermatitis.<sup>9</sup> In recent years, several published articles have indicated that acupuncture holds promise as a viable treatment option for atopic dermatitis in terms of reducing itch intensity, ameliorating skin conditions and suppressing skin-prick reactions.<sup>10–11</sup> To date, three systematic reviews related to acupuncture for atopic dermatitis have been published.<sup>12–14</sup> The oldest study did not include any eligible randomised controlled trials (RCTs),<sup>12</sup> and the remaining two reviewed RCTs on acupuncture not only for atopic dermatitis but also for chronic eczema.<sup>13–14</sup> Following this period, several recent RCTs have emerged on acupuncture for atopic dermatitis.<sup>15–16</sup> Therefore, we conducted a systematic review and meta-analysis to investigate its effect, aiming to provide evidence-based recommendations for clinical application.

## METHODS

### Protocol and registration

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement checklist,<sup>17</sup> and was registered on the PROSPERO database (CRD42023470643).

### Search strategy

PubMed, Embase, CENTRAL, the China National Knowledge Infrastructure (CNKI), WanFang and VIP databases were searched for RCTs about acupuncture for atopic dermatitis from inception to 17 September 2023. An updated search was performed on 15 October 2024. The following terms were used in search strategies: (“acupuncture” OR “acupuncture therapy” OR “acupuncture point” OR “acupoint” OR “needl\*”) AND (“Dermatitis, Atopic” OR “Atopic Dermatitis” OR “Atopic Dermatitides” OR “Atopic Neurodermatitides” OR “Atopic Neurodermatitis” OR “Eczema, Atopic” OR “Atopic Eczema”). The detailed search strategies are shown in online supplemental table 1.

### Eligibility criteria

The inclusion criteria were as follows: (1) study design: RCTs published in journals. (2) Participants: patients diagnosed with atopic dermatitis. (3) Intervention: acupuncture alone or acupuncture plus conventional

medicine treatment, which was also applied in the control group. Acupuncture therapies using needles to insert into specific acupoints were included, such as manual acupuncture, electroacupuncture, warm acupuncture, fire acupuncture, press tack needle and so on. (4) Control: conventional medicine treatment, sham acupuncture or blank control. Blank control means no treatment at all (no medicine or no sham acupuncture used). (5) Outcomes: the primary outcome included the SCORing Atopic Dermatitis (SCORAD) score. The secondary outcomes included the eczema area and severity index (EASI) score, visual analogue scale (VAS) score for pruritus, dermatology life quality index (DLQI) score, serum IgE level and adverse events (AEs).

Exclusion criteria were as follows: (1) duplicate records, animal articles, crossover trials, reviews and case reports. (2) Studies of laser acupuncture, acupressure, massage, moxibustion and acupuncture point injection. (3) Studies with insufficient information or incomplete data.

### Study selection and data extraction

Two reviewers (SL and K-YH) conducted separate searches of the databases and assessed eligible articles for inclusion. Discrepancies were resolved through consultation with a third reviewer (N-GC). The reviewers (SL and K-YH) independently extracted the following details: authors' names, publication year, country, sample sizes, age range, details of treatment and control interventions and outcomes.

### Assessment of risk of bias

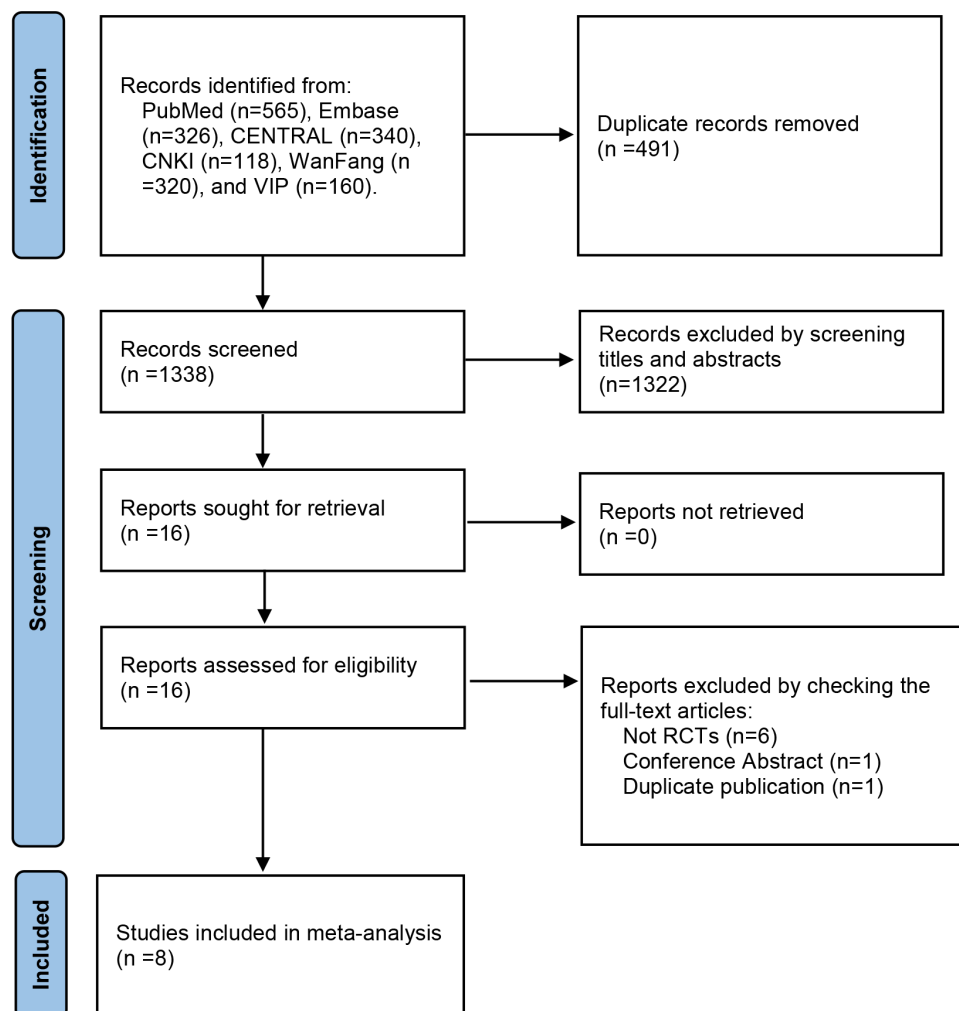
Two reviewers (SL and K-YH) individually employed the Cochrane Collaboration's tool for assessing the risk of bias.<sup>18</sup> The assessment of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias was categorised as ‘low risk’, ‘high risk’ or ‘unclear risk’. Discrepancies were resolved through consultation with a third reviewer.

### Statistical analysis

The analyses were performed using RevMan 5.3 and Stata 13.0 software. The mean difference (MD) with 95% CI was employed to analyse continuous outcomes. Heterogeneity was assessed by conducting the  $I^2$  test. Irrespective of the presence of heterogeneity, a random-effects model was used for conducting the meta-analysis.<sup>19</sup> Subgroup analyses were performed to explore potential factors contributing to the observed heterogeneity by considering different treatment and control interventions. If a minimum of 10 trials were included, the funnel plot was employed to evaluate potential publication bias. Egger's test was performed by Stata 13.0.  $p < 0.05$  was considered statistically significant.

### Patient and public involvement

No patient or public involvement.



**Figure 1** Flow diagram of the study selection process. CNKI, China National Knowledge Infrastructure; RCT, randomised controlled trial.

## RESULTS

### Study selection

A total of 1829 records were retrieved from various databases, including PubMed (n=565), Embase (n=326), CENTRAL (n=340), CNKI (n=118), WanFang (n=320) and VIP (n=160). After removing 491 duplicate records, the count was reduced to 1338. Then, 1322 records were excluded by screening titles and abstracts. The remaining 16 reports, which were potentially eligible, were sought for retrieval and assessed for eligibility. After checking the full-text articles, eight of them were excluded due to not being RCTs (n=6), being conference abstracts (n=1) and being duplicate publications (n=1). These eight reports, which were excluded after conducting a thorough examination of the full text, are listed in online supplemental table 2. Finally, eight studies were included.<sup>15 16 20–25</sup> A flow diagram of study selection is shown in figure 1.

### Study characteristics

A total of eight studies involving 463 participants were included, with 229 in the treatment groups and 234 in the control groups. These studies were conducted across three countries: two in Germany,<sup>15 21</sup> two in

Korea<sup>20 22</sup> and four in China.<sup>16 23–25</sup> Four studies were published in English,<sup>15 20–22</sup> and the remaining four were published in Chinese.<sup>16 23–25</sup> Six studies reported the SCORAD score,<sup>15 16 20–22 25</sup> four studies reported the EASI score,<sup>15 16 20 22</sup> three studies reported the VAS score for pruritus,<sup>15 20 21</sup> six studies reported the DLQI score,<sup>15 16 20 22 24 25</sup> three studies reported the IgE level<sup>16 23 24</sup> and five studies described AEs.<sup>15 16 20–22</sup> The characteristics of the included studies are listed in table 1.

### Acupuncture regimen and control interventions

Of the eight included studies, three studies adopted manual acupuncture,<sup>15 21 25</sup> three studies adopted fire acupuncture<sup>16 23 24</sup> and the remaining two adopted manual acupuncture+press tack needle.<sup>20 22</sup> The acupoints LI11 (*Quchi*), ST36 (*Zusanli*) and SP10 (*Xuehai*) were the most frequently used in four or more studies. The frequency of acupuncture varied from once a week to once every other day, with the total number of treatments ranging from 4 to 14. The course of acupuncture treatment ranged from 10 days to 5 weeks.

Two studies used blank controls,<sup>15 21</sup> two used sham acupuncture as a control<sup>20 22</sup> and the remaining four used

**Table 1** Characteristics of the included studies

Study	Country	Sample sizes (T/C)	Age (T/C)	Treatment group	Details of treatment group	Control group	Outcomes
Rotter 2022 <sup>15</sup>	Germany	78 (36/42)	31.4±10.9/31.1±10.8	Acupuncture	Manual acupuncture, eight treatments for 30 min, total 1–2 weeks (LI4, LI11, SP6, SP10)	Blank	SCORAD; EASI; VAS for pruritus; DLQI; AEs
Chen 2023 <sup>16</sup>	China	114 (57/57)	40±4/41±4	Acupuncture+medicine	Fire acupuncture, three times a week, total 2 weeks (ST15, BL67, Ashi points)	Medicine	SCORAD; EASI; DLQI; IgE level; AEs
Kang 2018 <sup>20</sup>	Korea	20 (10/10)	22.5±5.70/23.9±5.61	Acupuncture	Manual acupuncture+presstack needle. Three times a week for 15 min, total of 4 weeks (LI11, ST36, PC6); press tack needles were applied after removing the acupuncture needles (LI11, auricular Shenmen)	Sham acupuncture	SCORAD; EASI; VAS for pruritus; DLQI; AEs
Pfab 2011 <sup>21</sup>	Germany	10 (5/5)	31±7/26±3	Acupuncture	Manual acupuncture, two times per week for 20 min, total of 10 treatments (LI4, LI11, ST36, SP10)	Blank	SCORAD; VAS for pruritus; AEs
Park 2021 <sup>22</sup>	Korea	35 (18/17)	24.67±5.27/22.82±4.71	Acupuncture	Manual acupuncture+presstack needle. Two times per week for 15 min, total of 4 weeks (LI11, ST36, PC6); press tack needles were applied after removing the acupuncture needles (LI11, auricular Shenmen)	Sham acupuncture	SCORAD; EASI; DLQI; AEs
Deng 2021 <sup>23</sup>	China	80 (40/40)	35.82±4.32/34.56±5.11	Acupuncture	Fire acupuncture, once every other day, total of five treatments (BL13, LI11, SP10, ST36, Ashi points)	Medicine	IgE level
Wang 2022 <sup>24</sup>	China	60 (30/30)	34.95±3.67/35.21±3.72	Acupuncture+medicine	Fire acupuncture, once a week, total of 4 weeks (Ashi points)	Medicine	DLQI; IgE level
Liu 2021 <sup>25</sup>	China	66 (33/33)	34±10/33±9	Acupuncture+medicine	Manual acupuncture, once every other day for 30 min, total of 4 weeks (SP9, SP10, ST36, LI11)	Medicine	SCORAD; DLQI
AEs, adverse events; C, control group; DLQI, dermatology life quality index; EASI, eczema area and severity index; SCORAD, SCORing Atopic Dermatitis; T, treatment group; VAS, visual analogue scale.							



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chen 2023	+	?	-	?	+	?	+
Deng 2021	+	?	-	?	+	?	+
Kang 2018	+	+	+	+	+	+	+
Liu 2021	+	?	-	?	+	?	+
Park 2021	+	+	+	+	+	+	+
Pfab 2011	?	?	-	+	+	?	+
Rotter 2022	+	+	-	+	+	?	+
Wang 2022	+	?	-	?	+	?	+

**Figure 2** Risk of bias summary.

conventional medicine.<sup>16 23–25</sup> When sham acupuncture was used as a control, both studies used non-penetrating sham acupuncture at non-acupoints.<sup>20 22</sup> Four studies used conventional treatments, such as loratadine tablet+triamcinolone acetonide cream,<sup>23</sup> loratadine tablet+hydrocortisone butyrate cream,<sup>24</sup> loratadine tablet<sup>16</sup> and pimecrolimus cream.<sup>25</sup> Three studies employed a combined treatment of acupuncture and medicine, while the control groups received only medicine.<sup>16 24 25</sup> The medicine regimens in the treatment and control groups were identical.

### Risk of bias

The risk of bias assessment is shown in figure 2. Seven studies were deemed to have a low risk of selection bias

as comprehensive descriptions of their randomization methods.<sup>15 16 20 22–25</sup> However, one study had an unclear risk of selection bias, as it only briefly mentioned the use of randomization.<sup>21</sup> Allocation concealment was emphasised in three studies.<sup>15 20 22</sup> Two studies were categorised as having a low risk of bias due to the implementation of blinding techniques on participants and personnel.<sup>20 22</sup> The blinding of outcome assessments was clearly described in four studies.<sup>15 20–22</sup> The detailed reasons for case dropout or withdrawal were reported in all included studies. For selective reporting, two studies were conducted in accordance with protocols, thus categorising them as ‘low risk’,<sup>20 22</sup> and the remaining six studies had an ‘unclear risk’ assessment.<sup>15 16 21 23–25</sup>

### Effects on the SCORAD score

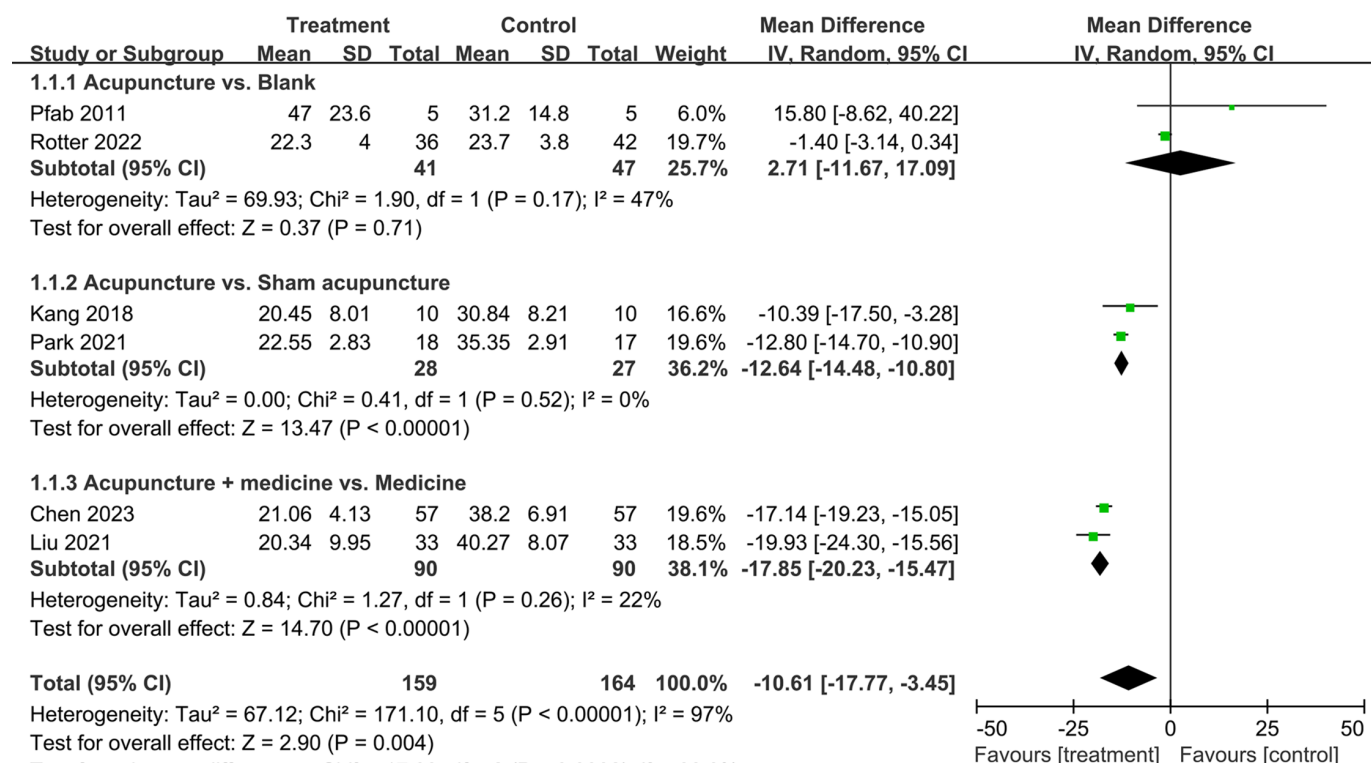
Six studies reported the SCORAD score.<sup>15 16 20–22 25</sup> The minimal clinically important difference (MCID) in the SCORAD score was defined as an 8.7 difference.<sup>26</sup> The meta-analysis showed a significant difference between the treatment and control groups ( $n=323$ ; MD=−10.61, 95% CI −17.77 to −3.45,  $p=0.004$ , figure 3) with high heterogeneity ( $I^2=97\%$ ,  $p<0.00001$ ) and the difference reached the MCID. Subgroup analysis based on different interventions was conducted. Two studies of acupuncture versus blank showed no significant difference (MD=2.71, 95% CI −11.67 to 17.09,  $p=0.71$ ) with moderate heterogeneity ( $I^2=47\%$ ,  $p=0.17$ ).<sup>15 21</sup> Two studies of acupuncture versus sham acupuncture showed a significant difference (MD=−12.64, 95% CI −14.48 to −10.80,  $p<0.00001$ ) with low heterogeneity ( $I^2=0\%$ ,  $p=0.52$ ) and the difference reached the MCID.<sup>20 22</sup> Two studies of acupuncture+medicine versus medicine also showed a significant difference (MD=−17.85, 95% CI −20.23 to −15.47,  $p<0.00001$ ) with low heterogeneity ( $I^2=22\%$ ,  $p=0.26$ ) and the difference reached the MCID.<sup>16 25</sup>

### Effects on the EASI score

Four studies reported the EASI score.<sup>15 16 20 22</sup> The MCID in the EASI score was defined as a 6.6 difference.<sup>26</sup> The meta-analysis showed no significant difference between the treatment and control groups ( $n=247$ ; MD=−3.95, 95% CI −8.35 to 0.45,  $p=0.08$ , figure 4) with high heterogeneity ( $I^2=99\%$ ,  $p<0.00001$ ). Subgroup analysis was also conducted. One study of acupuncture versus blank showed a significant difference (MD=−0.90, 95% CI −1.66 to −0.14,  $p=0.02$ ), while the reduction did not reach the MCID.<sup>15</sup> One study of acupuncture+medicine versus medicine also showed a significant difference (MD=−11.45, 95% CI −12.66 to −10.24,  $p<0.00001$ ) and the difference reached the MCID.<sup>16</sup> However, two studies of acupuncture vs sham acupuncture showed no significant difference (MD=−1.82, 95% CI −4.41 to 0.77,  $p=0.17$ ) with high heterogeneity ( $I^2=88\%$ ,  $p=0.004$ ).<sup>20 22</sup>

### Effects on the VAS score for pruritus

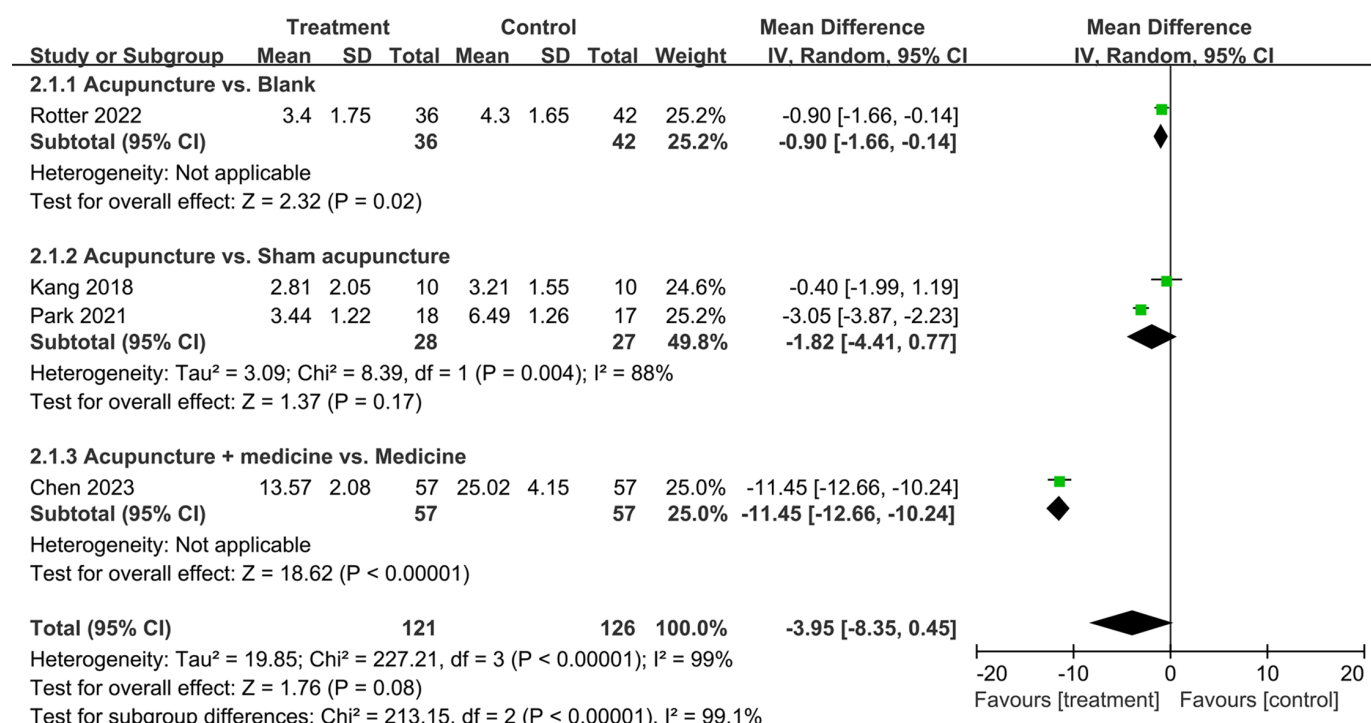
Three studies reported the VAS score for pruritus.<sup>15 20 21</sup> The MCID in the VAS score for pruritus was defined



**Figure 3** Forest plot of the SCORing Atopic Dermatitis score.

as a 13.4 difference.<sup>27</sup> The meta-analysis showed a significant difference between the treatment and control groups ( $n=108$ ;  $MD=-14.71$ , 95% CI  $-18.20$  to  $-11.22$ ,  $p<0.00001$ , online supplemental figure 1) with low heterogeneity ( $I^2=0\%$ ,  $p=0.62$ ) and the difference reached the MCID. Subgroup analysis was also conducted. Two studies of acupuncture versus blank

showed a significant difference ( $MD=-14.33$ , 95% CI  $-17.91$  to  $-10.75$ ,  $p<0.00001$ ) with low heterogeneity ( $I^2=0\%$ ,  $p=0.74$ ) and the difference reached the MCID.<sup>15 21</sup> One study of acupuncture versus sham acupuncture also showed a significant difference ( $MD=-21.85$ , 95% CI  $-37.38$  to  $-6.32$ ,  $p=0.006$ ) and the difference reached the MCID.<sup>20</sup>



**Figure 4** Forest plot of the eczema area and severity index score.

### Effects on the DLQI score

Six studies reported the DLQI score.<sup>15 16 20 22 24 25</sup> The MCID in the DLQI score was identified as 3.3.<sup>27</sup> The meta-analysis showed a significant difference between the treatment and control groups ( $n=373$ ; MD=-2.37, 95% CI -3.57 to -1.18,  $p<0.0001$ , online supplemental figure 2) with high heterogeneity ( $I^2=91\%$ ,  $p<0.00001$ ), while the difference did not reach the MCID. Subgroup analysis was also conducted. One study of acupuncture versus blank showed a significant difference (MD=-2.20, 95% CI -2.84 to -1.56,  $p<0.00001$ ), while the difference did not reach the MCID.<sup>15</sup> Two studies of acupuncture versus sham acupuncture showed no significant difference (MD=-1.12, 95% CI -2.67 to 0.43,  $p=0.16$ ) with moderate heterogeneity ( $I^2=38\%$ ,  $p=0.20$ ).<sup>20 22</sup> Three studies of acupuncture+medicine versus medicine showed a significant difference (MD=-2.99, 95% CI -4.60 to -1.39,  $p=0.0003$ ) with high heterogeneity ( $I^2=90\%$ ,  $p<0.0001$ ), while the difference did not reach the MCID.<sup>16 24 25</sup>

### Effects on the IgE level

Three studies reported the IgE level.<sup>16 23 24</sup> The meta-analysis showed no significant difference between the treatment and control groups ( $n=254$ ; MD=-160.22 U/mL, 95% CI -334.13 to 13.68,  $p=0.07$ , online supplemental figure 3) with high heterogeneity ( $I^2=100\%$ ,  $p<0.00001$ ). Subgroup analysis was also conducted. One study of acupuncture versus medicine showed a significant difference (MD=-217.89 U/mL, 95% CI -230.23 to -205.55,  $p<0.00001$ ).<sup>23</sup> Two studies of acupuncture+medicine versus medicine showed no significant difference (MD=-131.43 U/mL, 95% CI -371.34 to 108.48,  $p=0.28$ ) with high heterogeneity ( $I^2=100\%$ ,  $p<0.00001$ ).<sup>16 24</sup>

### Adverse events

Five studies described AEs.<sup>15 16 20-22</sup> No serious AEs were reported in any of the five studies. Four studies identified some mild AEs, such as contusion, numbness of the limbs, diarrhoea, dyspepsia and heartburn.<sup>15 16 20 22</sup> These symptoms were found to spontaneously resolve or abate within a few days.

### Publication bias

Due to the limited number of studies included (only eight), a funnel plot was not performed. Egger's test for the SCORAD score showed  $p=0.808$ , and Egger's test for the DLQI score showed  $p=0.887$ , indicating no significant publication bias in the meta-analysis of the SCORAD score and the DLQI score. Due to the limited number of studies included for other outcomes, Egger's test was not conducted.

## DISCUSSION

This was a further systematic review and meta-analysis that specifically focused on assessing the effect of acupuncture on atopic dermatitis. It included eight studies with 463 participants. The meta-analysis indicated significant

differences in the SCORAD score, the VAS score for pruritus and the DLQI score, but no significant differences in the EASI score and the IgE level between treatment and control. The differences in the SCORAD score and the VAS score for pruritus reached the MCID. The subgroup analysis revealed significant differences in changes in the SCORAD scores when acupuncture was compared with sham acupuncture and when acupuncture+medicine was compared with medicine. Significant differences in changes in the EASI score and the DLQI score were found when acupuncture was compared with blank and when acupuncture+medicine was compared with medicine. Acupuncture did have a significant effect on the VAS score for pruritus when compared with blank and sham acupuncture and on the IgE level when compared with medicine. The limited number and high risk of bias of included studies should be taken into account when interpreting these findings. Furthermore, uncertainties regarding the safety of acupuncture for atopic dermatitis persist due to the lack of studies reporting on AEs.

SCORAD and EASI are the commonly used scales for the measurement of atopic dermatitis severity. SCORAD integrates both objective assessments of disease extent and severity by physicians, as well as subjective evaluations from patients regarding itch and sleep disturbances, whereas EASI relies solely on objective physician estimates. Among all severity scales employed in atopic dermatitis, SCORAD stands out as the most extensively validated instrument for assessing disease severity.<sup>28</sup> In this meta-analysis, significant differences were observed between acupuncture and control groups for the SCORAD score, while no such differences were found for the EASI score. The limited number of included studies may be the main reason. Only six studies involving 323 participants reported the SCORAD score and four studies involving 247 participants reported the EASI score. Furthermore, the presence of heterogeneity could not be ignored. The heterogeneity in participant characteristics, acupuncture parameters, control interventions and the timing of outcome assessments across the included studies may significantly impact the results of the meta-analysis.

Significant heterogeneity was observed across the included studies, even after conducting subgroup analyses. Identifying the sources of the heterogeneity proved challenging due to the limited number and suboptimal quality of the studies reviewed. We hypothesised that various factors influencing acupuncture efficacy contributed to this variability. It is generally accepted that an acupuncture protocol comprises various factors, including the type of acupuncture needle, the acupoints selected, the treatment duration and the qualifications of the practitioner, all of which may affect the treatment outcome. Therefore, each of these factors served as a potential source of heterogeneity in the acupuncture meta-analysis. However, further subgroup analysis was not feasible given the scarcity of available RCTs.

We found that manual acupuncture and fire acupuncture were commonly used for atopic dermatitis, and LI11



(*Quchi*), ST36 (*Zusanli*) and SP10 (*Xuehai*) were the three acupoints most frequently used. LI11 (*Quchi*) is located near the elbow joint and can be used to treat dermatologic diseases and relieve itching. One animal study showed that acupuncture at LI11 (*Quchi*) had preventive and therapeutic effects on persistent itch and robust skin inflammation with epidermal thickening, possibly through the blockade of serotonin 5-HT<sub>2</sub> and 5-HT<sub>7</sub> receptors.<sup>29</sup> ST36 (*Zusanli*) is located on the anterolateral side of the calf and can suppress inflammation in allergic contact dermatitis by triggering local IL-10 production and inhibiting p38 MAPK activation.<sup>30</sup> SP10 (*Xuehai*) is located on the front of the thigh and the upper edge of the patella. A case report showed that acupoint autohe-motherapy at SP10 (*Xuehai*) and ST36 (*Zusanli*) triggered a local immune response, led to anti-inflammatory and immunomodulatory effects and successfully treated recalcitrant atopic eczema.<sup>31</sup>

Non-penetrating sham acupuncture at non-acupoints was the main method used to establish a control group for sham administration in this review. Setting sham control can help to assess the efficacy of true acupuncture after excluding placebo effects caused by expectancy and hope of recovery. Subgroup analyses demonstrated that acupuncture had a greater efficacy in reducing the SCORAD score and the VAS score for pruritus than sham acupuncture, which emphasised the specific effect of acupuncture on atopic dermatitis.

The potential mechanism of acupuncture for atopic dermatitis is a topic of great interest. Some studies have shown that acupuncture has a potential influence on various immunoregulatory substances, such as IL-4, IL-8, TNF- $\alpha$ , NF- $\kappa$ B, ERK1/2, JNK and p38, as some of them are known to activate basophils or reduce itch.<sup>32 33</sup> Acupuncture can significantly inhibit cutaneous hyperplasia and serum IgE levels and ameliorate skin inflammation by blocking the 5-HT receptor, which reduces histamine-induced acute itching.<sup>34</sup> In addition, acupuncture has been shown to attenuate comorbid anxiety and depressive-like behaviours in atopic dermatitis by modulating neuroadaptation in the brain reward circuit, thereby reducing the effects of emotional disorders on atopic dermatitis.<sup>35</sup>

In recent years, three systematic reviews have systematically reviewed the effect of acupuncture on atopic dermatitis.<sup>12–14</sup> The oldest one published in 2015, which did not include any eligible RCTs, failed to provide valid conclusions.<sup>12</sup> The systematic review, which was published in 2020, included eight RCTs, with seven specifically focusing on chronic eczema rather than atopic dermatitis and one exclusively looking at atopic dermatitis.<sup>13</sup> The systematic review published in 2022 explored the efficacy of acupuncture for atopic dermatitis and chronic eczema and included 11 RCTs about acupuncture for chronic eczema and only 3 RCTs about acupuncture for atopic dermatitis.<sup>14</sup> Limited by the insufficient number of included RCTs, these studies did not provide convincing conclusions. Compared with the previous three reviews,

this is the most current review that specifically focuses on acupuncture for atopic dermatitis. In our review, the search strategies were meticulously designed, and eight RCTs were included. We performed a meta-analysis on various outcomes, including the SCORAD score, the EASI score, the VAS score for pruritus, the DLQI score and the serum IgE level. Furthermore, we conducted subgroup analyses based on different interventions to explore potential factors contributing to the observed heterogeneity.

There are several strengths to this review. It is the newest systematic review to comprehensively and specifically investigate the effect of acupuncture on the SCORAD score, the EASI score, the VAS score for pruritus, the DLQI score and serum IgE level in patients with atopic dermatitis. The included studies were conducted in different countries, encompassing a more diverse sample, thereby potentially reducing selection bias and augmenting the generalizability of the findings. Subgroup analyses based on different interventions were conducted to strengthen the reliability of the conclusions. A standardised protocol was recorded in the PROSPERO database, and rigorous filtering criteria were implemented to effectively reduce potential reporting bias and bolster the credibility of this systematic review. To a certain extent, our study has provided supportive evidence for the clinical application of acupuncture in the treatment of atopic dermatitis.

The review, however, does have a few important limitations. First, the reliability and extrapolation of the overall findings were compromised due to the inclusion of a restricted number of RCTs and a small sample size. Second, the quality of the included studies was less than satisfactory. More than half of the included studies did not emphasise allocation concealment. Most of the studies did not perform blinding techniques on participants and personnel and were not conducted in accordance with protocols. Third, significant heterogeneity was observed when investigating the effect of acupuncture on the SCORAD score, the EASI score, the DLQI score and the IgE level. Fourth, due to insufficient RCTs for inclusion in this study, a funnel plot could not be performed to evaluate publication bias, and subgroup analyses based on different acupuncture therapies were not appropriate to be conducted. We assert that, given the extremely limited number of RCTs, the findings from subgroup analyses of different acupuncture therapies may lack convincing power and might not adequately reflect the actual circumstances.

Implications are described below. Because this systematic review suggests that acupuncture may be helpful for treating atopic dermatitis and that there is no indication of serious potential harm, we cautiously recommend acupuncture as an adjunctive therapy for atopic dermatitis treatment. To optimise the effect, acupuncturists may consider using LI11 (*Quchi*), ST36 (*Zusanli*) and SP10 (*Xuehai*) for manual acupuncture or fire acupuncture. As an individualised treatment method, acupuncture can be adjusted according to the specific conditions of atopic



dermatitis patients, so as to meet the treatment needs of different patients. It is simple to operate, with predictable therapeutic effects and no obvious AEs. Consequently, it holds significant potential for development in atopic dermatitis management. However, there are many clinical challenges in employing acupuncture for atopic dermatitis. The multifactorial aetiology of atopic dermatitis leads to variability in acupuncture efficacy among different patients. In actual clinical practice, variations in the efficacy of acupuncture may arise from disparities in practitioners' technical proficiency and operational experience. Therefore, in order to enhance the efficacy of acupuncture and the recovery process of patients, it is imperative to further standardise and regulate acupuncture practices. Further examination of the standardisation of acupuncture parameters would be helpful. Future studies should be conducted and reported in accordance with the CONSORT statement and the STRICTA guidelines to enhance the quality, transparency and reproducibility of acupuncture RCTs. Strict enforcement of allocation concealment, blinding of participants and personnel and preregistration of the trial protocol should be ensured. It is imperative to design and execute multicentre, large-scale and high-quality RCTs. Furthermore, in future systematic reviews, it is necessary to conduct subgroup analyses based on different acupuncture therapies when more relevant high-quality RCTs are published.

## Conclusions

Acupuncture might be an effective and safe treatment for atopic dermatitis, particularly in improving the SCORAD score and the VAS score for pruritus. The interpretation of the findings should be approached with caution due to the limited quantity and quality of the included studies. In the future, it is recommended to conduct multicentre, large-scale and high-quality RCTs to further confirm the findings.

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