The Mediating Role of Insomnia in the Relationship Between Disease Severity and Mental Health, Quality of Life and Productivity in Atopic Dermatitis

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Introduction

- Atopic dermatitis (AD) is a chronic inflammatory skin condition that impairs physical health, psychological well-being and socio-economic productivity. [1,2]
- Sleep disturbances may play a key mediating role in the development of mental health issues. [3,4]

Objective

To explore the mediating role of sleep disturbances in the relationship between AD severity and mental health, quality of life (QoL), work productivity, and daily activities.

Methods

Study design: post-hoc analysis of an observational, cross-sectional study conducted in Greece during January-September 2023. [5]

Participants: adult members of the patients' association 'EPIDERMIA', diagnosed with AD, who provided signed informed consent.

Data collection

Participants were invited to complete a structured questionnaire which included

- demographics & medical history
- the Patient Oriented Eczema Measure (POEM): AD severity,
- the Athens Insomnia Scale (AIS-8): severity of insomnia symptoms,
- Patient Health Questionnaire-9 (PHQ-9): severity of depressive symptoms,
- Generalized Anxiety Disorder-7 (GAD-7): anxiety levels,
- Work Productivity and Activity Impairment (WPAI) questionnaire: impact of AD on work and daily activities,
- Dermatology Life Quality Index (DLQI): impact of dermatological conditions on participants' QoL. [6-11]

Mediation analysis

Mediation analysis was conducted to explore alternative pathways through which AD severity influences psychological and socio-economic outcomes via the mediator of insomnia.

- The approach followed the procedures described by Imai et al. and implemented in STATA by Hicks and Tingley. [12,13]

Two sets of covariates were used for adjustment in all models:

1) Age, sex, BMI, (Model A)
2) Age, sex, BMI, education, work status, work-related exposure (Model B).

To address the possibility of unmeasured confounding between mediator and outcomes, sensitivity analyses were performed, as proposed by Imai et al., to evaluate the robustness of findings under violations of the sequential ignorability assumption.

Statistical analysis

For each outcome, two regression models were constructed:

*(1) **Mediator model:*** AIS-8 score as dependent variable; POEM score and covariates as predictors.

*(2) **Outcome model:*** outcome (PHQ-9, GAD-7, work impairment, activity impairment, DLQI) as dependent variable; POEM score, AIS-8 score, and covariates as predictors.

Mediation analysis estimated:

- Average Causal Mediation Effects (ACME)
- Average Direct Effects (ADE)
- % of total effect mediated by insomnia

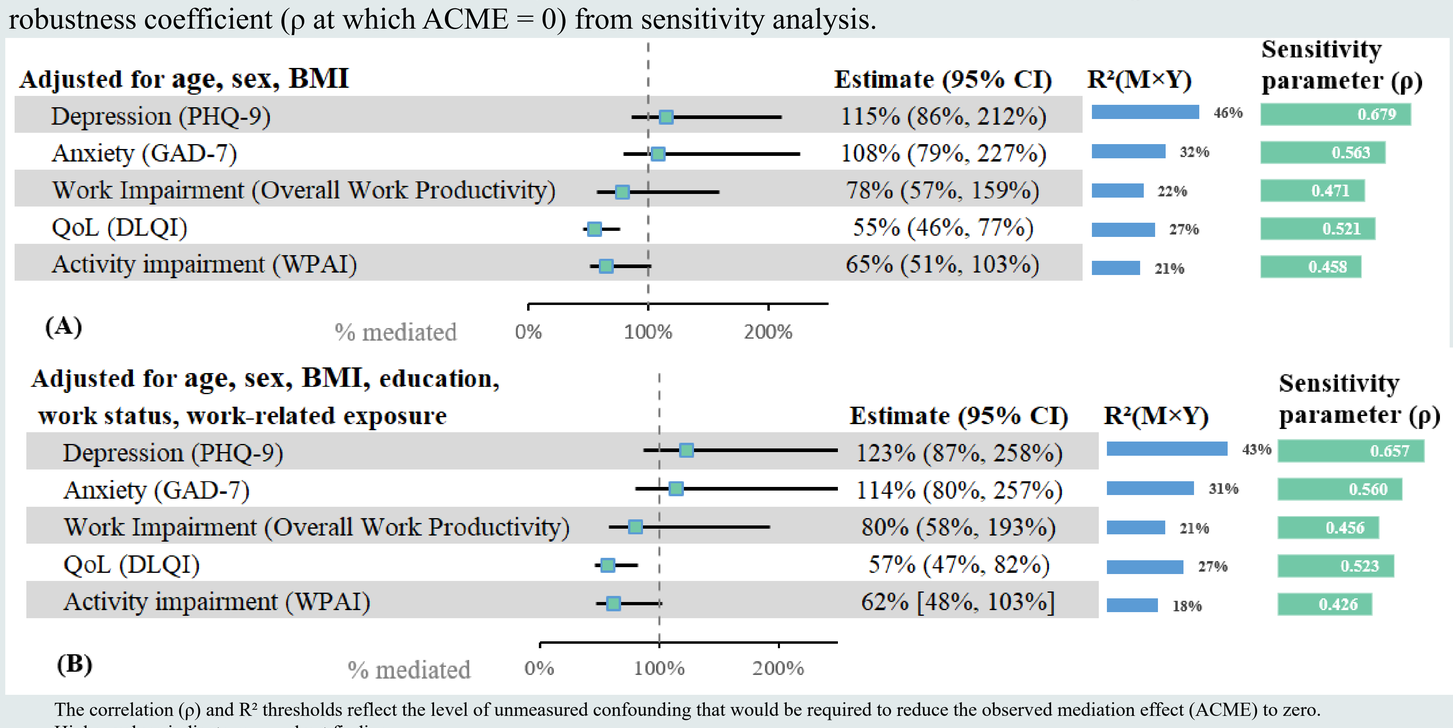
Estimates are reported as means with 95% confidence intervals (CI), based on 150 quasi-Bayesian Monte Carlo simulations.

- **Sensitivity analyses** estimated the correlation (ρ) and the *joint proportion of variance* explained in the mediator and outcome models (R^2) that would be required to reduce the ACME to zero.

Results

- 150 participants with AD, 55% female, with median (Q1 – Q3) age of 37 (28 – 43) years, and mean (SD) BMI of 26 (4.7) kg/m^2.
- Insomnia significantly mediated the relationship between AD severity and all outcomes examined.
- Mediation analysis revealed that insomnia significantly mediated the association between AD severity and all five outcomes. The proportion of the total effect mediated ranged from 54.8% to 114.8% in Model A and from 57.1% to 122.9% in Model B, with the highest effects observed for depression and anxiety.
- Substantial mediation was also found for work impairment (78%–80%), activity impairment (62–65%), and QoL (55%–57%).
- Sensitivity analyses showed that the average causal mediation effect (ACME) would be reduced to zero only if an unmeasured confounder induced a residual correlation (ρ) ranging from 0.426 to 0.679 or explained 18% to 46% of the residual variance across the two models. These findings suggest moderate to strong robustness of the mediation effects, particularly for depression and anxiety.

Figure 1. Forest plots showing the **percentage of the total effect of AD severity on outcomes mediated by insomnia**, with 95% CI. Results are presented for models adjusted for (A) age, sex, BMI, and (B) age, sex, BMI, education, work status, and work-related exposure. Blue bars indicate the R^2 thresholds, and green bars the robustness coefficient (ρ at which ACME = 0) from sensitivity analysis.



The correlation (ρ) and R^2 thresholds reflect the level of unmeasured confounding that would be required to reduce the observed mediation effect (ACME) to zero. Higher values indicate more robust findings.

Conclusions

- Insomnia was identified as a **key mediator** in the pathway from AD severity to depression, anxiety, quality of life, work productivity, and activity impairment.
- The mediating effect was particularly strong for **mental health outcomes** (depression, anxiety >100%) and substantial for **work impairment and daily functioning** (65–79%).
- These results highlight the **clinical importance of targeting sleep disturbances** in AD management to indirectly improve psychological well-being, quality of life, and socio-economic outcomes.
- Due to the **cross-sectional design**, causal pathways cannot be definitively established. Longitudinal studies are needed to confirm causal directionality.

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