Perceived stigma mediates the relationship between health-related quality of life and depression in people with atopic dermatitis

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Positionality statement

Mindful that our identities can influence our approach to science (Roberts, et al. 2020), the authors

wish to provide the reader with information about our backgrounds. With respect to gender, when

the manuscript was drafted, two authors self-identified as women and one author as a man. With

respect to race, all three authors self-identified as white.

Ethics approval

Approval was obtained from the ethics committee of the University of Hull. The procedures used in

this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Competing Interests

Author CN, Author SvB, and Author HH declare that they have no conflict of interest.

Abstract

Atopic dermatitis significantly impacts an individual's life. Prior research has found positive correlations between the disease's impact on daily quality of life, depression, and perceived stigmatization. However, the interaction of these variables in predicting depression levels in people with atopic dermatitis is currently not well understood. The present study aimed to address this knowledge gap by investigating whether the relationship between health-related quality of life and depression is mediated by perceived stigmatization. Using an online survey, a sample of people with atopic dermatitis (N=334) completed the Dermatology Life Quality Index (DLQI) to assess disease impact, the Patient Health Questionnaire (PHQ-8) to assess mood impairment, and a 6-item Stigmatization Scale (6-SS) to measure perceived stigmatization. Results indicated that the relationship between disease impact and depression was partially mediated by stigma. Since stigma can partially explain the link between disease impact and depression, psychosocial support interventions should aim to target stigma to alleviate depressive symptoms as a common co-morbidity of atopic dermatitis.

Keywords

Clinical impact statement

We know that people with visible skin diseases are more likely to develop depression. One example of such a visible skin disease is atopic dermatitis, the most common form of eczema. Our study indicates that one important variable that determines whether or not someone with atopic dermatitis will develop a depression is perceived stigmatization which is the degree to which they expect to be negatively judged and treated by others because of their skin disease. In our study we found that the link between health-related quality of life and depression is less strong once

perceived stigmatization is taken into account. Psychosocial support for atopic dermatitis should

therefore target stigmatization to reduce the risk of depression in people with atopic dermatitis.

Introduction

Atopic dermatitis (AD), a chronic skin disorder currently without a cure, is characterized by symptoms such as itchy, red, dry and inflamed skin. It ranks among the most prevalent skin diseases and poses a significant health concern, affecting up to 20% of children and 3% of adults worldwide (Williams & Flohr, 2006). Over the last 30 years, the prevalence of AD in developed countries has increased two-to threefold (Grillo et al., 2006). In the UK, AD accounts for 10-20% of all dermatologist referrals and 30% of dermatology consultations (Charman et al., 2003).

AD affects not only a person's skin, but also has significant negative effects on sleep, a person's personal, social and work life as well as their intimate relationships (Kage et al., 2020; van Beugen et al., 2022; Zeiser et al., 2021). However, the visible extent of the disease does not correlate well with the extent to which patients are experiencing this psychosocial impact of AD (Chren, 2012). The negative impact of AD on health-related quality of life (HRQoL) is better captured with psychometric instruments such as the Dermatology Life Quality Index (DLQI, Finlay & Khan, 1994) or the Skindex-16 (Chren, 2012). Rather than being a clinician-assessed measurement of disease severity, these HRQoL instruments arguably measure what really matters to patients, i.e. the degree to which the disease negatively affects their daily life (Chren, 2012).

Compared to healthy controls, people with AD report a lower overall quality of life, with domains such as mental health and social functioning most affected (for review, see Birdi et al., 2020). There is evidence suggesting that AD is associated with the largest reduction in HRQoL among common skin diseases (Balieva et al., 2017) and the degree of HRQoL impairment is correlated with levels of depression (Ferrucci et al., 2021; Lugović-Mihić et al., 2021; Wittkowski et al., 2004). A recent meta-analysis reported an increased risk of suicidal ideation in people with AD (Pompili et al., 2021). These findings underline the double burden of the disease: In AD, there are not only skin symptoms that require treatment, but also significant psychological concerns. The currently un-met psychosocial

support needs of people with AD have been identified before (Topp et al., 2019; Wittkowski et al., 2004), but such interventions are difficult to implement in a resource-limited public health system.

To develop targeted interventions for people with AD, a better understanding of factors mediating the relationship between HRQoL and depression is required. Since AD has complex effects on both personal and interpersonal levels, interventions should target those vulnerability factors that are most strongly linked with the risk of a person with AD developing a depressive co-morbidity. One factor that may causally contribute to establishing a link between disease impact and depression could be the degree to which people with AD are experiencing *perceived stigmatization*, i.e. the experience or anticipation that others devalue, negatively judge and exclude them because of their skin condition. For example, in the context of AD, there are still widespread misconceptions that the disease may be contagious or due to lack of self-hygiene (Gochnauer et al., 2017; McNiven & Ryan, 2022). Many patients report experiences of rejection, humiliation and ridicule (Germain et al., 2021) because of these misconceptions. Such repeated experiences of public stigmatization can result in the person affected to come to anticipate and expect negative evaluations of others (Bos et al., 2013).

There is already some evidence consistent with the idea that perceived stigma may mediate the relationship between disease HRQoL and depression in people with AD. Quite a few studies have reported bivariate correlations between these 3 variables and found small to moderately sized correlations. As has already been reported above, HRQoL is correlated with levels of depression (Ferrucci et al., 2021; Lugović-Mihić et al., 2021; Wittkowski et al., 2004). Additionally, stigma is correlated with both HRQoL (Lu et al., 2003; Wittkowski et al., 2004) as well as depression (Wittkowski et al., 2004) in people with AD.

However, bivariate correlations cannot determine which factors act as unique predictors and considerably fewer studies have analysed the effect of stigma in multivariate models. One such study was carried out by Wittkowski et al. (2004). Using a multiple regression approach, they

observed that disease severity, experience of stigmatization and depression are all independent predictors of the HRQoL in people with AD. However, the Wittkowski study did not include a formal test for mediation. Vasiliou et al. (2023) investigated whether psychological flexibility, conceptualized as a set of trainable coping mechanisms, moderates the relationship between stigma and QoL. No evidence for such a moderation effect was observed which may have been due to the relatively small sample size. Furthermore, only 15% of participants were affected by eczema, with the remaining participants affected by other visible skin diseases. Dixon and colleagues (2019) tested whether the relationship between levels of anxiety and HRQoL is mediated by anxiety sensitivity (i.e. fear about the consequences of experiencing anxiety). In a sample of people with dermatology conditions, they observed a full mediation, with the relationship between anxiety and HRQoL no longer significant once the mediating effect of anxiety sensitivity was accounted for. However, it is unknown how many participants in the Dixon study were affected by AD. In summary, while there is some evidence that stigma makes significant and unique contributions towards predicting the psychosocial impact of living with a skin disease, a formal test of whether stigma mediates the relationship between HRQoL and depression in people with AD is still outstanding.

The present study aims to fill this gap in current knowledge, by testing how the relationship between HQQoL and depression can be explained. We considered HRQoL as a predictor variable since impairment in QoL caused by AD may be considered as a precursor to depression (i.e. depression was used as outcome variable). We formally tested whether this relationship between HRQoL and depression can be explained by perceived stigma by including stigma as a mediator variable. The study measured levels of depression (PHQ-8), HRQoL (DLQI) and perceived stigma (6 item stigmatization scale, 6-SS) in a sample of 354 adults with AD. A bootstrapped mediation analysis was conducted on the data using HRQoL as the predictor variable, perceived stigma as the mediator and levels of depression as the outcome variable. We predicted a significant indirect effect, in that the relationship between HRQoL and depression would be significantly reduced once the mediating effect of stigma is accounted for.

Methods

Participants

The study protocol was approved by the Ethics Committee of the Faculty of Health Sciences at the University of Hull. Following an advertisement by the National Eczema Society on their Facebook, Twitter and Instagram accounts, a total of 354 participants took part in the study. Inclusion criteria were a diagnosis of AD as well as being over 18 years of age. A total of 17 participants were excluded from the analysis because of missing responses, and a further 3 were excluded because they were under the age of 18. This left a total of 334 participants for the statistical analysis (299 female, 32 male, 2 non-binary, 1 undisclosed gender, mean age 36.4 years, range 18 – 70 years). Data was collected over the course of 2 weeks in February 2023. Participants did not receive any compensation for taking part. A post-hoc power calculation indicated that a mediation analysis as in the current study (3 continuous variables, N = 334) has a power of 91% to detect an indirect effect, should it exist in the population (Qin, 2023).

Materials

DLQI

The Dermatology Life Quality Index (DLQI, Finlay & Khan, 1994), a 10-item questionnaire commonly used in dermatology services, was administered to measure the impact of AD on quality of life. The range of the DLQI is 0-30, with higher scores indicating a stronger negative impact on quality of life (0-1 = no effect at all on patient's life, 2-5 = small effect on patient's life, 6-10 = moderate effect on patient's life, 11-20 = very large effect on patient's life, 21-30 = extremely large effect on patient's life). In the present study, Cronbach's α of the DLQI was 0.90.

PHQ-8

The Patient Health Questionnaire 8 (PHQ-8) is a diagnostic and severity measure for depressive disorders that is commonly used in both clinical as well as population-based studies (Kroenke et al.,

2009). It consists of 8 items with a score range of 0 – 24. A total score of 0 to 4 represents no significant depressive symptoms. A total score of 5 to 9 indicates mild depressive symptoms; 10 to 14, moderate; 15 to 19, moderately severe; and 20 to 24, severe. A PHQ-8 score of ≥10 has an 88% sensitivity and 88% specificity for major depression and typically represents clinically significant depression (Kroenke et al., 2009). In the present study, Cronbach's α of the PHQ-8 scale was 0.89.

ISDL 6-item stigmatization scale (6-SS)

The final questionnaire administered was the 6-item stigmatization subscale (6-SS) from the instrument 'Impact of Chronic Skin Disease on Daily Life' (ISDL, Evers et al., 2008). This scale assesses to what extent the patient feels stigmatized as a result of the skin condition (i.e., perceived stigmatization). Example items are 'other people think that my skin disease is contagious' and 'other people avoid contact with me because of my skin disease'. Participants are presented with six statements and asked to rank how much they identify with that statement on a scale. The global score can range from 6 points, interpreted as a lack of stigmatization, to 24 points, which corresponds to maximum stigmatization. In the present study, Cronbach's α of the 6-SS was 0.84.

Design

The present study used a cross-sectional design to investigate the relationship between disease impact on quality of life, depression and stigmatization in people with AD. A mediation analysis was conducted on the data, using dermatological quality of life (as measured by the DLQI) as the predictor variable, depressive symptoms (measured by the PHQ-8) as the outcome variable and perceived stigmatization (measured by the 6-SS) as the mediator variable.

Procedure

Participants were informed that the study would be investigating experiences of mood and stigma in those with AD. The questionnaire was distributed and completed online using Jisc online surveys (https://www.onlinesurveys.ac.uk/). Before starting the questionnaire, the participants were required to read an information sheet about the study and complete a participant consent form.

They were also provided with researcher contact details if they had follow-up questions. Then participants completed three questionnaires: the DLQI, the PHQ-8, and the 6-SS, which typically took no more than 10 minutes in total. Once the questionnaires were completed the full aims of the study were revealed in the debrief. The debrief also included contact information for the Samaritans UK and Mind UK, in case any distress had been caused.

Data analysis

Data were analysed using R version 4.2.0 (RRID:SCR_001905, R Core Team, 2022). DLQI, PHQ-8 and 6-SS questionnaires were scored according to the published manuals. The mediation analysis was conducted by fitting a structural equation model to the data using the lavaan package (Rosseel, 2012). This approach uses bootstrapping, which involves repeatedly sampling from the data with replacement (10,000 bootstrap resamples) to create an approximation of the sampling distribution of the indirect effect and to generate confidence intervals for these effects. The indirect effect is deemed significant if the confidence interval does not include zero.

Data availability statement

The raw data and all analysis scripts are available at

https://osf.io/ndjxt/?view_only=e4b4bda93d814b9eb219816c92f13857 .

Results

Descriptive results and intercorrelations

On average, participants reported a considerable effect of their AD on their quality of life (mean DLQI score: 15.12, *SD* = 7.56), with 59 participants (17.6%) reporting a moderate, 119 (35.6%) a very large and 72 (21.5%) an extremely large impact of AD on their quality of life (see Figure 1). The average score on the depression questionnaire was 11.20 (*SD* = 6.28), with more than half of the participants (189 out of 334, 56.6%) showing a PHQ-8 score at or above the clinical-cut off (>= 10). The average stigmatization score across all respondents was 13.62 (*SD* = 3.89). All 3 variables were

positively correlated with each other (all $p < 0.001$), with the strongest correlation observed between HRQoL and depression ($r(332) = 0.689$ [0.741, 0.628]) and somewhat weaker correlations between HRQoL and perceived stigma ($r(332) = 0.449$ [0.359, 0.530]) and depression and perceived stigma ($r(332) = 0.450$ [0.360, 0.532].

PLEASE INSERT FIGURE 1 ABOUT HERE

Result of mediation analysis

A mediation analysis was conducted using HRQoL as predictor variable, perceived stigma as mediator and depression as outcome variable (see Figure 2). Key assumptions were tested for and not found to be violated. A non-significant Shapiro-Wilk test ($W = 0.996$, $p = 0.677$) indicated that residuals were normally distributed and a non-significant Durban-Watson test ($DW = 1.95$, $p = 0.702$) suggested that the assumption of independence of residuals was also not violated. Multicollinearity was also not an issue in this dataset (all VIFs <= 1.25).

The bootstrapped mediation analysis indicated that all conditions of mediation were met (Baron & Kenny, 1986). First, the predictor variable HRQoL significantly affected the mediator variable perceived stigma (i.e., path a was significant), $b_a = 0.231$, 95% CI [0.174, 0.280], $p < 0.001$. Second, the predictor variable HRQoL significantly affected the outcome variable depression when these 2 variables were looked at in isolation (i.e. the total effect was significant), $b_{c+(a*b)} = 0.572$, 95% CI [0.513, 0.626], $p < 0.001$. Third, the mediator variable perceived stigma significantly affected the outcome variable depression when controlling for the influence of the predictor HRQoL (i.e. path b was significant, $b_b = 0.284$, 95% CI [0.125, 0.436], $p < 0.001$).

This pattern means that there is evidence of partial (but not full) mediation. The effect of HRQoL on depression is reduced when considering the mediating influence of perceived stigma (i.e. the direct effect c is smaller than the total effect c+(a*b)). The magnitude of mediation is captured by the significant indirect effect ($b_a*b_b = 0.066$, 95% CI [0.0270, 0.106], $p < 0.001$).

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Discussion

The aim of the present study was to test whether the relationship between HRQoL and depression is mediated by perceived stigma in people with AD. We observed a significant indirect effect. However, the relationship between HRQoL and depression was still significant once the indirect effect was taken into account suggesting a partial instead of a full mediation.

Before discussing the results of the mediation analysis, the descriptive and correlational results merit attention. The sample of the present study showed considerable levels of depression. More than half of participants in the present study scored above the clinical cut-off for depression and the severity of mood impairment was strongly correlated with disease impact. This is in line with earlier studies (Ferrucci et al., 2021; Lugović-Mihić et al., 2021; Wittkowski et al., 2004) and underlines the significant burden that living with AD places on a person's mental health. Stigmatization showed a moderate correlation with both disease impact and depression, again replicating earlier findings (Lu et al., 2003; Wittkowski et al., 2004).

Our study advances existing knowledge in that it does not just report a bivariate correlation between HRQoL and depression as previous studies have done, but also provides insights into why this relationship exists. Our results suggest that the relationship between HRQoL and depression can be explained, at least partially, as a function of the degree to which a patient has experienced perceived stigmatization. Since perceived stigma has this important mediating function, it follows that psychosocial support interventions for patients with AD should consider the role of stigma, as explained below.

Perceived stigma may act as a vulnerability factor that may establish, maintain and exacerbate depression in people with AD. Both stigma and depression share the aspect of social avoidance. Since misconceptions and negative stereotypes about AD are unfortunately still prevalent in the wider public (Gochnauer et al., 2017; McNiven & Ryan, 2022), many people with AD have

experienced stigmatization and negative evaluation in social contexts. As a consequence, fear of social rejection and humiliation are frequent (Germain et al., 2021). Every time a person with atopic dermatitis experiences a negative social reaction from others, this fear of social rejection is further reinforced and can lead to further social withdrawal.

Since stigma was identified as an important mediator variable, and the substantial psychosocial impact of perceived stigmatization in itself, it is vital to advance development and implementation of interventions focused on destigmatization. Previous research suggests that on an individual level, cognitive behavioral treatment can effectively reduce the impact of perceived stigmatization by improving coping skills, restructuring negative thoughts and beliefs resulting in shame or self-blame, and preparing patients for future interactions (Topp et al., 2019; Traxler et al., 2024; Wittkowski & Richards, 2007). Furthermore, emerging evidence suggests that acceptance and commitment therapy and mindfulness-based approaches may also be beneficial as they foster psychological flexibility, self-compassion, non-judgmental awareness, which helps individuals detach from shame and societal judgment (Traxler et al., 2024; Zucchelli et al., 2018). Ultimately, addressing stigma effectively requires a multi-level approach, as stigma manifests across individual, interpersonal, community, and societal levels; therefore, intervention strategies must be designed to target these interconnected levels to alleviate the psychosocial impact of stigmatization and its contribution to depression in chronic skin conditions (Rao et al., 2019).

Cognitive Behavioral Therapy (CBT) is the most evidence-based approach to reduce skin-related stigma (Traxler et al., 2024). The result of the present study suggests that perceived stigma may explain why HRQoL in AD is correlated with levels of depression. Once the effect of stigma was accounted for, the correlation between disease impact and depression was less strong. For interventions, targeting stigma might be critical to help break the link between HRQoL and depression. This idea is consistent with findings from an intervention study, where

repeated sessions of CBT led to decreased stigmatization beliefs and reduced levels of depression, whilst improving HRQoL (Wittkowski & Richards, 2007). CBT techniques in this study targeted self-stigma by identifying maladaptive beliefs, promoting insight and practicing more adaptive coping strategies (Wittkowski & Richards, 2007).

The results of the present study demonstrate that the relationship between disease impact and depression in people with AD is partially mediated by perceived stigma. Since a partial and not a full mediation was observed, this raises the question which other variables could act as additional mediators. One candidate that warrants further attention is sleep. Sleep is negatively affected in AD, with patients often being kept awake at night due to intense itch (Silverberg et al., 2021). The degree of sleep disturbance may mediate the relationship between disease impact and depression. Another interesting factor to consider in future research is not just perceived stigmatization, but also the degree to which patients with AD fear to be stigmatized in social situations. A similar mediation effect was observed in skin patients in the context of anxiety (Dixon et al., 2019) and may generalize to depression.

The abovementioned results should be interpreted in light of the following limitations. First, in this online study there was no independent verification of the diagnosis of atopic dermatitis. Second, we only obtained basic demographic data from our participants (age and gender), but did not assess other characteristics such as disease severity, ethnicity or level of education. Third, we did not assess anxiety or fear of stigmatization (in addition to stigmatization itself). These are important variables that future studies should consider (Ferrucci et al., 2021). Finally, the cross-sectional nature creates temporal ambiguity, as we cannot make strong conclusions about whether the predictor HRQoL preceded the outcome depression or vice versa. Both possible directions have been considered in previous research (for review, see Adesanya et al., 2023), albeit only in cross-sectional designs. Future longitudinal studies could shed more light on this issue.

In conclusion, the present study advances existing knowledge about the psychosocial burden of AD by demonstrating that the relationship between disease impact and depression is mediated by perceived stigma. Since stigma can partially explain the link between disease impact and depression, psychosocial support interventions should aim to target stigma to alleviate depressive symptoms as a common co-morbidity of atopic dermatitis.

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Figure captions

Figure 1   Violin plots showing distribution of the three main variables, the Dermatology Life

Quality Index (DLQI), the Patient Health Questionnaire 8 (PHQ-8) and the 6 item stigmatization scale

(6-SS). For the DLQI and PHQ-8, the horizontal lines show the clinical cut-off scores, for the 6-SS, the

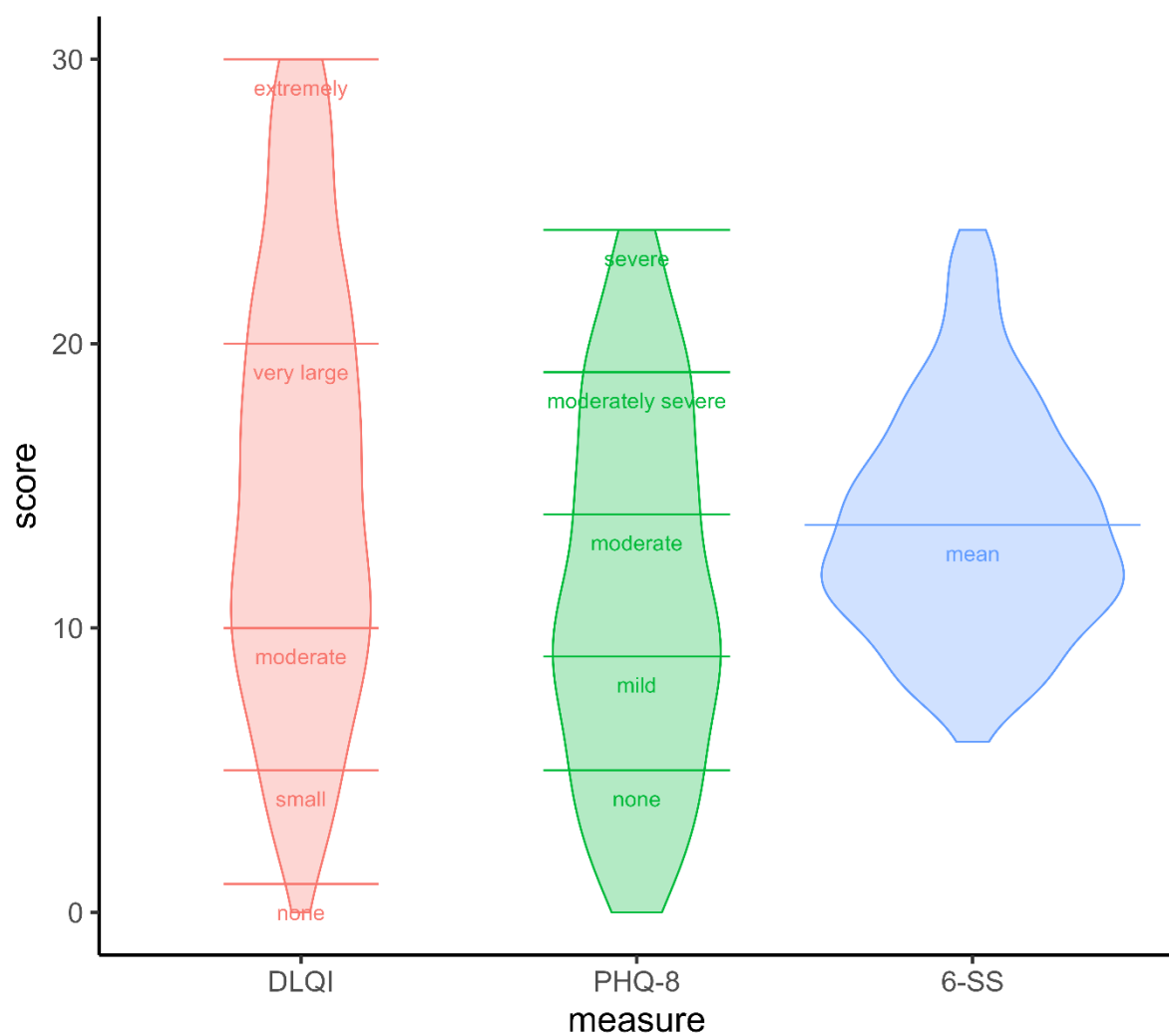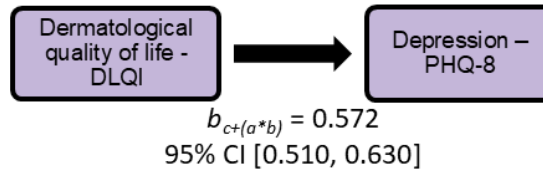horizontal line shows the mean.

Figure 2   Result of mediation analysis, showing the simple (top) as well as the mediated

relationship (bottom). Estimates for path coefficients include the 95% CI. Coefficients are significant

when the confidence interval does not include 0. All coefficients shown are significant (all p < 0.001)

Simple relationship:

```
┌─────────────────┐              ┌─────────────────┐
│ Dermatological  │              │  Depression –   │
│ quality of life-│  ━━━━━━━▶    │     PHQ-8       │
│     DLQI        │              │                 │
└─────────────────┘              └─────────────────┘
```

$b_{c+(a*b)}$ = 0.572
95% CI [0.510, 0.630]

Mediated relationship:

Indirect effect = b_a * b_b = 0.231 * 0.284 = 0.066, 95% CI [0.030 0.106]

```
                    ┌─────────────────┐
                    │   Perceived     │
                    │  Stigma – 6-SS  │
                    └─────────────────┘
                    ▲                 ╲
                   ╱                   ▼
```

b_a = 0.231 b_b = 0.284
95% CI [0.179, 0.282]   95% CI [0.135, 0.440]

```
┌─────────────────┐              ┌─────────────────┐
│ Dermatological  │              │  Depression –   │
│ quality of life-│  ━━━━━━━▶    │     PHQ-8       │
│     DLQI        │              │                 │
└─────────────────┘              └─────────────────┘
```

b_c = 0.506
95% CI [0.430, 0.578]