The Relationship Between Psychiatric Illnesses and Skin Disease

A Longitudinal Analysis of Young Australian Women

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Objective: To examine longitudinally the relationship between skin disease and psychological morbidity in young women, testing the hypothesis that psychological morbidity (depression, anxiety, and stress) is a factor in the causation of skin disease.

Design: The Australian Longitudinal Study on Women's Health was designed to investigate multiple factors affecting the health and well-being of women over a 20-year period. Data from 3 surveys (conducted in 2000, 2003, and 2006) were analyzed. Multivariate longitudinal generalized estimating equation models, with and without time lag, were used to determine significant factors associated with skin disease (including anxiety, depressive symptoms, and stress).

Setting: An Australian community-based study.

Participants: Women, aged 22 to 27 years at the time of the first survey, were randomly selected from the Australian National Medicare database. Participant numbers for the surveys from the years 2000, 2003, and 2006 were 9688, 9081, and 8910, respectively.

Main Outcome Measures: Outcome measures were the scores from the Center for Epidemiologic Studies Depression Scale, the Perceived Stress Questionnaire for Young Women, and an item to elicit reporting of anxiety symptoms.

Results: Of 6630 women providing data on skin diseases on all 3 surveys, 8.0% (n=523) reported having skin problems on all 3 occasions; 12.1% (n=803) on 2 occasions; and 23.9% (n=1582) on 1 occasion. On the 2000, 2003, and 2006 surveys, prevalence of skin problems was 24.2%, 23.9%, and 24.3%, respectively. In the generalized estimating equation models, depression symptoms and stress (but not anxiety) were significantly associated with skin problems (P < .005).

Conclusion: The findings of this relationship of depression and stress to skin disease may have considerable clinical implications, including implications for adjunctive psychological interventions in the management of patients with skin disease.

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Other studies have been broadly population-based or school-based studies. Furthermore, all of these studies are cross-sectional in design, and so no conclusions can be drawn regarding direction of causality in the relationship of skin disease with psychological morbidity. Longitudinal studies would provide evidence of direction of causality, but thus far, while studies have demonstrated improvement in psychological morbidity with disease treatment (including correlation with improvements in disease severity), longitudinal studies are largely lacking.

We report herein the results of a community-based longitudinal cohort study of Australian women in which participants self-reported the presence of skin disease and anxiety symptoms and completed validated measures of depression symptoms and stress. Using our longitudinal data to examine causality in the relationship, we have approached the skin disease–psychological morbidity relationship with the hypothesis that psychological factors have a causative role in precipitating or exacerbating skin disease.

METHODS

SAMPLE

This research was conducted as part of the Australian Longitudinal Study on Women’s Health (widely known as “Women’s Health Australia”), which was designed to investigate multiple factors affecting the health and well-being of women over a 20-year period. In 1996, women in 3 age groups (younger, 18–23 years; middle aged, 45–50 years; and older, 70–75 years) were randomly selected from the Australian National Medicare database, with overrepresentation of women living in rural and remote areas. The focus of the present study is women from the younger cohort. The baseline survey, survey 1 (n=14,779), was conducted in 1996, and the respondents were shown to be broadly representative of the national population of women in the target age groups. Survey 2 (n=9,068) was conducted in 2000; survey 3 was conducted in 2003 (n=9,081); and survey 4 was conducted in 2006 (n=8910). Questions relating to depression and anxiety were not asked in survey 1, so we will only consider surveys 2 through 4.

SKIN PROBLEMS

Women were asked how often they had experienced skin problems in the previous 12 months. Women who responded sometimes or often were defined as having skin problems, while women who responded never or rarely were defined as not having skin problems.

MEASURES OF PSYCHOLOGICAL SYMPTOMS

The 3 measures of psychological symptoms include measures of depression, anxiety, and stress. The 10-item Center for Epidemiologic Studies Depression Scale (CESD-10), one of the most commonly used instruments to estimate and monitor the prevalence of depression, was used to measure depressive symptoms. The possible score ranges from 0 to 30, higher scores indicating more depressive symptoms.

Women were asked if they had experienced episodes of intense anxiety (eg, panic attacks) in the previous 12 months. Only those women who indicated that they often experienced episodes of intense anxiety were considered to have experienced intense anxiety. Women who indicated never, rarely, or sometimes were not. Perceived stress was measured using a validated instrument.

Participants were asked to rate how stressed they were in the previous 12 months as a result of the following potential stressors: their own health, health of family members, work, living arrangements, study, money, and relationships (including partner, parents, other family, and friends). Responses (and coding) were graded on a 5-point scale ranging from 0 (not applicable or not at all stressed) to 4 (extremely stressed). Mean stress scores were calculated as the average of the nonmissing stress items, creating a range of 0 to 4.

CONFounding VARIABLES

The confounding variables included measures of demographic characteristics and health status. Date of birth was used to determine the women’s age at each survey. The postal code of residence at the time of each survey was used to classify the area of residence as urban or nonurban. Women were asked about their current marital status and the highest educational qualification they had completed.

The question “in general, would you say that your health is excellent, very good, good, fair, or poor?” was used to determine a general level of health. Women were asked whether a physician had ever told them that they had any of the following 6 chronic medical conditions: diabetes, heart disease, hypertension, anemia or iron deficiency, asthma, and/or cancer.

Questions about history of smoking (categorized as [1] current smoker or [2] ex-smoker/never smoked) and alcohol use (categorized as [1] risky/high-risk drinker or [2] not in that category) were also included. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, was calculated using self-reported weight and height. Women were asked if they were currently using an oral contraceptive pill or taking prescription medications for depression or nerves and sleep. They were also asked if in the last 3 years (ie, the time between the current and previous surveys) they had been diagnosed or treated for postnatal depression.

The degree of social support was measured using a modified version of the MOS (Medical Outcomes Study) Social Support Index. The index measures functional support (eg, emotional support, informational support, tangible support, positive social interaction, appraisal support, and affectionate support). The final score is the sum of 6 items, with a possible range of 6 to 30; higher scores indicating stronger social support.

Women were asked if they had experienced any of 35 major life events in the past 12 months (eg, death of a family member, divorce or separation, loss of job, or natural disaster). The proportion of these life events was calculated for each woman. Optimism was measured using the 6-item Revised Life Orientation Test.

Response options strongly disagree, disagree, neutral, agree, and strongly agree were coded from 0 to 4 for the 3 positively phrased items and in reverse order for the negatively phrased items. The summed optimism score had a range from 0 to 24, higher scores indicating higher optimism.

statistical analysis

The skin problem and psychiatric illness measures were compared using χ2 tests for categorical variables and t tests for continuous variables. In response to the large sample size and multiple comparisons, P < .005 was adopted for statistical significance.

For the purpose of graphically displaying the relationship between skin problems and the various psychiatric illnesses, we classified the women as having prevalent, intermittent, or incident
effect.21 In both models, the dependent variable was skin problems, and the independent variables were psychological symptom variables over time.

Generalized estimating equation models are an extension of generalized linear models, so for this study the GEE models can be thought of as being an extension of logistic regression models. While logistic regression models can only analyze data cross-sectionally, the extension component of the GEE model allows for the analysis of the data longitudinally, thus reflecting the relationship between the longitudinal development of skin problems and the longitudinal development of the psychological symptom variables over time.

One indication of whether a relationship between 2 variables is causal is the temporal sequence of the relationship, i.e., when the predictor variable (in this case, the psychological symptom) precedes the outcome variable (skin problems). With a small change to the standard GEE model, the GEE time lag model can be used to evaluate whether the risk factors repeatedly studied were related to the skin problems reported 1 survey later, thus taking into account the temporal sequence of cause and effect.21 In both models, the dependent variable was skin problems, and the independent variables were the psychological symptom variables and all of the confounding variables. All analyses were conducted using SAS statistical software, version 8.2 (SAS Institute Inc, Cary, NC).

Table 1. Measures of Mental Health in Women With and Without Skin Problems

<table>
<thead>
<tr>
<th>Mental Health Measure</th>
<th>Skin Problems</th>
<th>2000</th>
<th>2003</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=2336)</td>
<td>No (n=7352)</td>
<td>Yes (n=2165)</td>
<td>No (n=6916)</td>
</tr>
<tr>
<td>Intense anxiety symptoms, %a,b</td>
<td>No</td>
<td>97</td>
<td>98</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>3</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Depression CESD-10 score, mean (SD)c</td>
<td>8.7 (5.9)</td>
<td>7.2 (5.3)</td>
<td>8.1 (5.7)</td>
<td>6.6 (5.1)</td>
</tr>
<tr>
<td>Perceived stress score, mean (SD)c</td>
<td>1.09 (0.63)</td>
<td>0.89 (0.56)</td>
<td>1.04 (0.58)</td>
<td>0.86 (0.51)</td>
</tr>
</tbody>
</table>

Abbreviation: CESD-10, 10-item Center for Epidemiologic Studies Depression Scale.17

a Significant association (P < .05) in the 2003 survey.
b Significant association (P < .05) in the 2006 survey.
c Significant association (P < .05) in the 2000 survey.

RESULTS

In 2000, when the women were aged 22 to 27 years, 24.2% indicated that they had skin problems (n = 2336). Three years later, when the women were aged 25 to 30 years, 23.9% indicated that they had skin problems (n = 2165). Three years later again, when the women were aged 28 to 33 years, 24.3% indicated that they had skin problems (n = 2139).

There were 6630 women who answered the question on skin problems for all 3 surveys, 8.0% of whom reported having skin problems on all 3 occasions (n = 523), 12.1% on 2 occasions (n = 803), and 23.9% on 1 occasion (n = 1582).

Table 1 summarizes the psychological instrument scores of women with and without skin problems for all 3 surveys. These unadjusted (cross-sectional) prevalence estimates show that a greater percentage of women with skin problems reported more intense anxiety symptoms (P < .005) in the 2000 and 2006 surveys than women without skin problems. In the 2003 and 2006 surveys, a greater percentage of women with skin problems reported higher levels of depression symptoms (P < .005) and perceived stress (P < .005) than women without skin problems.

Figure 1 presents graphically the depression scores at each of the 3 survey times for women with each category of skin disease (prevalent, incident, intermittent, and never reported). It demonstrates that the women with prevalent skin problems had the highest levels of depression symptoms at all 3 survey periods, while women with intermittent skin problems had the second highest levels of depression at all 3 survey periods. Women with incident skin problems had the same levels of depression symptoms as women who never reported skin problems at the 2000 survey, but then moved to levels similar to those reported by women with prevalent and intermittent skin problems at the 2003 survey. They continued to have similar levels of depression symptoms as women who reported intermittent skin problems at the 2006 survey.

Figure 2 shows the association of skin problems with stress (mean stress score) across the 3 surveys. The women
who never reported having skin problems clearly and consistently had the lowest stress. Women who had prevalent skin problems had the highest stress for the 2003 and 2006 surveys but had similar stress levels to those of women with intermittent and incident skin problems in the 2006 survey. Women with intermittent and incident skin problems had similar levels of stress for all 3 surveys.

Figure 3 shows that the women who never reported skin problems had the lowest proportion of reported intense anxiety at all 3 surveys. The women with intermittent skin problems had the second lowest proportion of reported intense anxiety at the 2000 survey, increasing to a proportion similar to that of women with incident skin problems, then declining to a proportion slightly higher than that of never cases by 2006. Women with prevalent and incident skin problems had similar (highest) proportions of intense anxiety at the 2000 and 2006 surveys but not in 2003.

A multivariate longitudinal GEE model was used to determine the mental health factors significantly associated with skin problems (Table 2). The model included all confounding variables. Of the 3 measures of psychological symptoms, only depression symptoms and stress were significantly associated with skin problems. Specifically, the odds of having skin problems increased by a factor of 1.427 (95% confidence interval [CI], 1.326-1.535) for every 1 unit increase in the mean stress score and a factor of 1.016 (95% CI, 1.008-1.024) for every 1 unit increase in the CESD-10 (depression) score. In terms of intense anxiety, the odds of having skin problems were 1.079 (95% CI, 0.891-1.306) times greater for those with intense anxiety than for those without.

A time lag GEE model was also used to determine the factors significantly associated with skin problems, accounting for the temporal sequence of cause and effect (Table 3). The model included all confounding variables. There was little difference in the findings between the GEE model with (Table 3) and without (Table 2) a time lag. Specifically, the odds of having skin problems increased by a factor of 1.371 (95% CI, 1.246-1.509) for every 1 unit increase in the mean stress score and a factor of 1.019 (95% CI, 1.009-1.030) for every 1 unit increase in the CESD-10 (depression) score. The odds of having skin problems was 1.005 (95% CI, 0.781-1.295) times greater for those with intense anxiety than for those without.

The univariate results of significant associations of stress, intense anxiety, and depression symptoms with skin disease at most time points in our study is broadly consistent with previous cross-sectional and unadjusted literature in this area. The relationship is further supported by the findings of regression analyses with skin disease as the dependent variable (Figures 1, 2, and 3), showing consistent trends for patients with a current or intermittent skin disease having greater levels of depression symptoms, stress, and intense anxiety than those who never had skin disease.

Although the use of a longitudinal study design does not allow us to make certain conclusions on cau-
sality, a comparison of the GEE models with and without a time lag and adjustment for confounding variables does provide us with more insight into the effect of psychiatric illnesses on skin problems. The results from both models clearly point in the same direction, thus providing strong evidence for depression symptoms and stress (but not intense anxiety) as being causative of skin disease. Note that while the odds ratios of the 2 GEE models were quite similar, this can be explained by the relative stability of the psychiatric illness measures over the follow-up periods. While effect sizes are small, these significant findings are of considerable clinical interest.

Most previous attention in this area has focused on the propensity of skin disease to cause psychological morbidity. It is equally biologically plausible that psychological distress might precipitate or exacerbate skin disease.22,23 A number of studies have concluded that stress does indeed precipitate skin disease.24-26 The defining feature of these studies, however, is their cross-sectional or case-control design, with levels of stress assessed by retrospective recall. As has been commented on,25 much of the literature in this area has methodologic limitations, being anecdotal, uncontrolled, unadjusted for confounders, or retrospective in design.

An exception is a study that used a diary technique to prospectively assess the skin disease symptoms, depressive symptoms, and interpersonal stress of 50 subjects with established atopic eczema.27 The authors concluded that atopic eczema causes depression and not vice versa. This study also found scores on interpersonal stress to be predictive of scores on eczema symptoms the following day (and vice versa). The clinical implications of this short-term finding, however, are limited (and it should be noted that the duration of the study was only 2 weeks—a time frame at odds with the accepted disease pathogenesis and natural history of clinical depression syndromes).28,29 In a further study, Chiu et al30 found a significant correlation between examination stress and students’ acne severity in a small prospective study in which possible confounders might not have been adequately controlled for.

The present study, as well as being prospective, examined changes in skin disease and psychological status over an extended period, measured a great many potential confounding variables, included these variables in the multivariate analyses, and was adequately powered to conduct these analyses. To our knowledge, Huerta et al31 published the only comparable report, a nested case-control study within a cohort of British general practice patients examining 3994 cases of psoriasis and 10,000 controls. While in that study, stress was not found to be a risk factor for psoriasis, their methods differed substantially from those of the present study. First, Huerta et al studied only psoriasis rather than skin disease in general. Second, they evaluated the narrower relationship of incident cases of psoriasis to diagnosed stress disorders. Our use of a validated instrument of perceived stress rather than general practitioners’ recorded diagnoses of stress disorder is likely to be more sensitive in detecting a relationship. Finally, the finding of Huerta et al of no relationship between the use of antidepressant medications and incident psoriasis should not be directly compared with our findings using a validated instrument for depressive symptoms.

Our negative finding regarding intense anxiety as a precipitant of skin disease is subject to some caveats. Anxiety was assessed via a single question regarding episodes of intense anxiety (e.g., panic attacks) rather than a validated instrument, as was used for depression symptoms and interpersonal stress. Also, this question reflects a rather limited symptom spectrum, and its sensitivity in eliciting other types of anxiety is limited.

The clinical implications of our study are considerable. Given the prevalence of skin diseases and the burden of suffering associated with them, a remediable factor in cause or exacerbation is of some importance. Stress reduction techniques and psychological interventions have been proposed as adjunctive treatments in skin disease, but evidence for their efficacy is unconvincing. The results of the present study suggest that the rationale for these interventions is sound, and trials of efficacy are indicated.

There are a number of limitations of our study. It includes only women, and there is evidence of sex differences in the skin-psyche relationship.32,33 The use of self-report of skin disease rather than clinician diagno-

<table>
<thead>
<tr>
<th>Mental Health Factor</th>
<th>OR (95% CI)</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Depression, CESD-10</td>
<td>1.016 (1.008-1.024)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Stress, mean stress score</td>
<td>1.427 (1.326-1.535)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Anxiety No</td>
<td>1 [Reference]</td>
<td>NA</td>
</tr>
<tr>
<td>Anxiety Yes</td>
<td>1.079 (0.891-1.306)</td>
<td>.44</td>
</tr>
</tbody>
</table>

Abbreviations: CESD-10, 10-item Center for Epidemiologic Studies Depression Scale; CI, confidence interval; NA, not applicable; OR, odds ratio.

a Derived from a longitudinal analysis using a generalized estimating equation model that included measures of psychological symptoms and confounding variables.
sis is a further limitation. Self-report of skin disease has been used, however, in a number of large cross-sectional community-based studies of psychological and quality of life associations of skin disease, and there is evidence for the validity of self-reported presence of skin disease and of self-reported skin symptoms as measures of objective disease presence. A further limitation of the study is in its analysis at the level of skin diseases as a whole—a heterogeneous grouping—rather than defining individual skin diseases for separate analysis. But this is a common approach in the psychodermatologic literature, and such an approach would tend to bias results to the null rather than the opposite. Furthermore, previous studies have failed to find a difference in psychological morbidity associated with different skin diseases or have yielded contradictory results. A consideration of the limitations of this and other studies in this area suggests that the inclusion of clinical assessments of skin disease as well as psychological measures in large population-based cohort studies is required. The enrollment of subjects in these studies should be at an early age, prior to the usual ages of development of skin diseases.

In conclusion, the causes of skin disease are complex and multifactorial, but our findings provide evidence for a role of stress and depression symptoms in the etiology. This may have clinical and therapeutic implications, but further longitudinal examination of the relationship is required.

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Author Contributions: Dr Sibbritt had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Magin and Sibbritt. Analysis and interpretation of data: Magin, Sibbritt, and Bailey. Drafting of the manuscript: Magin, Sibbritt, and Bailey. Critical revision of the manuscript for important intellectual content: Sibbritt and Bailey. Statistical analysis: Sibbritt. Administrative, technical, and material support: Sibbritt and Bailey.

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Additional Contributions: We are grateful to the women who provided the survey data.

REFERENCES


Archives Web Quiz Winner

Congratulations to the winner of our May quiz, Nahayat Dashgir, MD. The correct answer to our May challenge was Churg-Strauss syndrome (allergic granulomatosis). For a complete discussion of this case, see the Off-Center Fold section in the June Archives (Farley-Loftus R, Anandasabapathy N, Bossenbroek N, Rosenman K, Pomeranz MK. An unusual pruritic eruption of the feet. Arch Dermatol. 2009;145(6):715-720).

Be sure to visit the Archives of Dermatology Web site (http://www.archdermatol.com) to try your hand at the interactive quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the Archives. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of The Art of JAMA II.