The general relationship between internalizing psychopathology and chronic physical health conditions: a population-based study

Iris van de Pavert, Matthew Sunderland, Maartje Luijten, Tim Slade, Maree Teesson

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Abstract Studies have consistently demonstrated a reciprocal relationship between internalizing disorders and several chronic physical health conditions. Yet, much of the extant literature fails to take into account the role of comorbidity among internalizing disorders when examining the relationship with poor physical health. The current study applied latent variable modelling to investigate the shared and specific relationships between internalizing (fear and distress factors) and a range of physical health conditions. Data comprised 8841 respondents aged 16–85 years who took part in the 2007 Australian National Survey of Mental Health and Wellbeing. Multiple indicator, multiple causes models were used to parse the shared and specific relationships between internalizing disorders and variables associated with poor physical health. The study found that several physical conditions were significantly related to mean levels of fear and distress. The results were broadly similar but minor differences emerged depending on whether lifetime or past 12 months indicators of mental disorders and physical conditions were utilized in the model. Finally, the results demonstrated that the association between individual mental disorders and physical health conditions are better accounted for by indirect relationships with broad transdiagnostic dimensions rather than including additional disorder-specific relationships. The results indicate that researchers should focus on common mechanisms across multiple internalizing disorders and poor physical health when developing prevention and treatment initiatives.

Keywords Internalizing · Comorbidity · Physical health · Obesity · Tobacco use · Latent variable models

Introduction Studies have consistently demonstrated the reciprocal relationship between mood and anxiety disorders and a number indicators of poor physical health such as the presence of chronic health conditions. Indeed, Teesson and colleagues [1] demonstrated that people with chronic physical conditions (e.g., cancer, cardio-vascular disease, etc.) had a significantly higher chance of having mood (OR = 1.5) or anxiety disorders (OR = 1.8) than people without chronic physical conditions [1]. The experience of a mood or anxiety disorder in isolation is related to a significant degree of disability and premature mortality [2]. When complicated with factors associated with poor physical health, such as chronic physical conditions, the degree of disability is significantly amplified, the disorders become more complex to treat, and are associated with poorer treatment outcomes [3, 4]. As such, it is integral that researchers, clinicians, and health policy makers gain a greater understanding of the complex relationship between mood and anxiety disorders and factors associated with poor physical health. A greater understanding of this complex and reciprocal relationship may ultimately reduce the high rates of associated disability and mortality through combined efforts to prevent and treat poor physical and mental health.
Much of the extant literature has focused on examining the role that poor physical health conditions have on putatively distinct psychiatric disorders [e.g., major depressive disorders, generalized anxiety disorder (GAD), panic disorder, etc.]. The measurement of these disorders relies on several assumptions outlined in the extant psychiatric nosologies, for example the DSM-5 and ICD-10, which specify disorders as distinct categorical conditions that can be demarcated using standardised criteria and diagnostic cut-points. The assumptions placed on diagnostic categories imply that disorders are independent of each other and correlate only at chance levels. Yet these studies often fail to consider the significant correlations observed within mood and anxiety disorders. In a study conducted by Lahey, Zald, Hakes, Krueger, and Rathouz [5], using two waves of the National Epidemiologic Study of Alcohol and Related Conditions (NESARC), mental disorders were found to be robustly related to each other beyond chance levels suggesting that mental disorders are not fixed and independent constructs. Instead, the finding of high rates of comorbidity within and between broad disorder groupings have led some researchers to postulate that certain disorders are linked by a series of common non-specific latent variables that form an overarching meta-structure [6–8]. Several mood and anxiety disorders are thought to share one or two broad underlying dimensional factors, namely the ‘internalizing’ dimension that is sometimes split into “fear” and “distress” sub-factors [9]. Numerous studies using latent variable modelling techniques as well as genetic twin modelling have subsequently confirmed that depression and anxiety can be represented by a single dimension representing liability to experience internalizing disorders in the general population [10–15]. These findings have led to calls for a new approach to psychiatric classification that takes into account commonalities across multiple levels in a broader hierarchy (HiTOP [16]).

There are notable advantages associated with the use of latent variables when modelling psychopathological data to examine the relationship with other clinical relevant and meaningful factors (such as indicators of poor physical health). First, these models better account for the high rates of comorbidity observed within mental disorders by assuming that disorders can be accounted for by a series of common latent variables. Modelling disorders in this manner can help determine if an association between a disorder (e.g., depression) and a covariate of interest (e.g., diabetes) could be attributed to the common variance (e.g., factors that are shared across multiple mental health conditions) associated with the latent variable rather than any unique variance specific to the disorder (e.g., factors specific to depression that separates it from GAD). Indeed, a multiple indicator, multiple cause (MIMIC) model provides the modelling framework to investigate indirect associations between mental disorders and covariates of interest via the common latent variables and furthermore examine the additional role of specific direct relationships in the full model. Figure 1 graphically outlines an example MIMIC model in relation to mental and physical health with direct relationships modelled between diabetes and obsessive compulsive disorder (OCD) as well as asthma and MDE. Such investigations can lead to improvements in the treatment and prevention of these problems (for example more tailored or combined treatment programs of physical health and internalizing) as well as our understanding of biological and psychosocial causes of comorbid physical conditions and internalizing psychopathology.

Second, latent variable models specifically acknowledge the dimensional and hierarchical nature of psychopathology (i.e., disorders are markers of severity of a broader trait). This allows for the relationship between mental and physical health to be modelled across the full range of broad disorder psychopathology rather than limiting conclusions to only those who score above or below a subjective threshold on putatively distinct categories.

To the best of our knowledge, only two published studies have applied latent variable models to investigate the relationship between internalizing and indicators of poor physical health. Slade [17] applied latent variable models to cross-sectional data from the Australian general population with the aim of examining the physical health profiles of people who score highly on the underlying dimensions of distress [major depression, dysthymia, general anxiety disorder, and post-traumatic stress disorder (PTSD)] and fear (social phobia, panic disorder, agoraphobia and OCD). The results indicated that people suffering from any physical illness scored higher on distress ($\beta = 0.22$) and fear ($\beta = 0.15$) in comparison to those without any physical illness. Specifically, digestive conditions were significantly and strongly related to distress ($\beta = 0.60$) and respiratory conditions were significantly related to both dimensions ($\beta = 0.14$ for both). In a similar study, Eaton and colleagues [18] investigated the relationship between latent factors of internalizing and a limited number of physical health conditions, namely past-year angina pectoris or chest pain and past-year stomach ulcer. They used data from two waves of the National Epidemiologic Study on Alcohol and Related Conditions (NESARC) and demonstrated that distress and fear significantly accounted for future angina and ulcer (accounting for 6.5 and 6% of angina and ulcer variance, respectively). More importantly, overall fear and distress liability dimensions better accounted for these important physical health outcomes relative to any single disorder-specific relationship.
The current study expands on the scant literature regarding internalizing psychopathology and factors associated with poor physical health in several important ways. First, a large scale general population survey will be utilised to model sub-factors of internalizing as a means of taking into account the complex relationship between putatively distinct diagnoses of mood and anxiety disorders. Second, the relationship between these latent variables and six chronic physical health conditions and obesity (measured using self-reported body mass index) will be empirically modelled simultaneously. Third, the significance of the disorder-specific relationships between mental disorders and each indicator of poor physical health use will be assessed over and above the relationship with the broad latent variables to determine if there remains any unique relationship associated with specific disorders. Fourth, the relationships will be examined using mental disorders and chronic physical health conditions experienced across the lifespan and within the past 12 months to maximize the likelihood of examining overlapping conditions. Given the dominance of the fear-distress dimensional factors to explain the relationship between multiple mental disorders in previous studies, it is hypothesized that the majority of relationships between mood and anxiety disorders and indicators of poor physical health can be explained via mean differences in these latent variables rather than any remaining disorder-specific effects.

**Methods**

**Sample**

Data for the current study were from the 2007 Australia National Survey of Mental Health and Wellbeing (NSMHWB). This survey consisted of 8841 participants from the Australian population, aged between 16 and 85 ($M = 46.35$, $SD = 18.99$). One respondent was randomly chosen from each selected household out of a possible 14,805 households, resulting in a response rate of 60%. To assess the reliability of the data, extensive non-response analyses were conducted including comparisons to other data sources. Further details can be found in the surveys user’s guide [19]. To make sure the sample was representative, the survey oversampled young and older adults given that these age bands are often under-represented in population-based epidemiological surveys.

**Assessment**

**Mental disorders**

For the measurement of lifetime and past 12 months disorders, DSM-IV diagnostic criteria were applied using the World Mental Health version of the Composite International Diagnostic Interview, version 3.0 (WMH-CIDI 3.0).
were measured using self-report. Participants were scored on BMI, which is calculated by dividing the weight of a person by their length squared. Both weight and height of participants was calculated by dividing the weight of a person by their length squared. The BMI measurement of obesity, namely: ‘Body Mass Index’. The BMI was used to assess obesity, with a score of 30 or higher indicating obesity. Given that obesity was treated as an independent variable in the analysis, participants with missing values for BMI were excluded in models that included the physical health covariates resulting in an analysed sample size of 8661.

**Physical health issues**

The lifetime and past 12 months presence of six chronic physical conditions were assessed by asking whether the respondent had ever been told by a doctor or a nurse that they had (1) asthma, (2) any type of cancer, (3) a stroke, (4) any heart or circulatory condition such as heart attack, angina, or high blood pressure, (5) gout, rheumatism, or arthritis, and (6) diabetes or high sugar levels in blood or urine. Additional questions were then asked to determine whether the respondent had or received treatment for each of the six conditions in the past 12 months. An example for the lifetime physical health conditions is: ‘Where you ever told you have asthma?’ The answer options were either ‘Yes’ (scored as present), ‘No’ (scored as absent), ‘Not applicable’ (scored as absent), ‘Not known’ (scored as missing) or ‘Refusal’ (scored as missing). An example for the past 12 months physical health issues is: ‘Did you have asthma or received treatment for asthma in the last 12 months?’ The answer options were the same.

**Covariates**

Additional variables were identified and included as control in the analysis given their previously determined significant relationship between mental disorders, the physical conditions, or both. The MIMIC models controlled for age and sex given previously identified differences in the prevalence of mental and physical disorder depending on age and sex. Similarly, tobacco use and obesity have been extensively linked to overall poor health as well as the mental disorders and physical conditions under investigation in the current study [21–24]. Daily tobacco use was measured based on a single question included in the survey, namely: “Do you currently smoke every day, weekly, or not at all?” Participants who indicated that they currently smoked everyday were coded as current daily smokers. Additional tobacco use and obesity were measured using self-report. Participants were scored as obese if they scored a BMI of 30 or higher. There were 180 participants who did not provide height or weight information and, therefore, their BMI could not be calculated. Given that obesity was treated as an independent variable in the analysis, participants with missing values for BMI were excluded in models that included the physical health covariates.

**Analyses**

The analysis was broken down into two related stages: the first stage involved testing the measurement model and constructing the broad transdiagnostic latent dimensions using confirmatory factor analysis (CFA); the second stage then involved building a MIMIC model to examine the direct and indirect effects of chronic conditions separately on mean levels of lifetime and past 12 months psychopathology. All the analyses were conducted using Mplus version 7.3 [25]. These data were weighted to account for the unequal probability of selection and the sociodemographic characteristics of the Australian population according to the most recent census [19].

**Confirmatory Factor Analysis**

Based on previous studies [12, 14, 26], two separate CFA models were tested and compared. The first model was a one-factor model, where all the eight mental disorders were assigned to a single latent factor, labelled internalizing. The second model was a two-factor model, where MDE, dysthymia, GAD and PTSD were coupled together on one latent factor (labelled distress), and social phobia, panic disorder, agoraphobia, and OCD on the other latent factor (labelled fear). The CFA models were estimated using tetrachoric correlation matrices and a weighted least squares mean and variance adjusted (WLSMV) estimator suitable for categorical data [25].

A range of different indices were used to measure model fit. The first index was the root mean square error of approximation (RMSEA). This assesses the approximate fit of the model, where values close to 0.06 or below indicate good fit [27]. The second index was the comparative fit index (CFI), which uses a hypothetical baseline model with unrelated observed variables to compare the model. Values close to 0.95 or higher indicate good fit [27]. The last index measure used was the Bayesian information criterion (BIC). To generate this fit index required re-estimating the model using a full-information robust maximum likelihood estimator suitable for categorical data. BIC is useful when comparing models estimated in large samples and between models that use more parameters [28]. The lower the BIC score the better the fit. When comparing models, a
difference of up to six between two BIC scores is considered strong and a difference of 10 or more is considered very strong [29]. Additionally, loadings and factor correlations were inspected to ensure that each disorder represented a salient indicator of the factor ($\lambda > 0.4$).

**MIMIC Modelling**

The MIMIC model can be broken down into two components: indirect and direct effects (see Fig. 1). The indirect effects explain the relationship or the effect of the six chronic conditions on the individual indicators of internalizing as completely mediated through mean differences in the latent dimension. Direct effects, on the other hand, account for any additional specific relationship between chronic physical conditions and each disorder in a model that already contains the indirect effects. The modelling steps included first fitting a MIMIC model with the best fitting CFA as the measurement component. The structural component included the six physical health issues entered simultaneously as independent variables and controlling for sex, age, daily tobacco use, and obesity in the regression with the latent variables treated as continuous dependent variables. These regression effects are labelled indirect effects given the relationship between the latent variable indicators and the predictor variables are mediated by the latent dimensions. The significance of the direct effects between the indicators of the latent variables and the independent variables were then examined using modification indices. These indices provide an indication about whether the overall model fit would significantly improve if the direct effects between the latent variable indicators and independent variables were estimated at a time in a model that already contains the indirect effects. Modification indices for each of the direct effects were considered significant if they were larger than 3.84 (representing a $p$ value of $<0.05$ for a log-likelihood difference test with 1 degree of freedom). Separate models using lifetime and past 12 month indicators were estimated.

**Results**

**Prevalence rates**

Table 1 provides the lifetime and past 12 months prevalence for mental disorders and physical health issues. The highest prevalence was observed for MDE across both lifetime and past 12 months followed closely by PTSD and social phobia. In terms of physical illness, a sizeable proportion reported heart conditions followed by arthritis, asthma, and diabetes.

**Confirmatory factor analysis**

Both models evidenced good fit for lifetime mental disorders, but the two-factor model evidenced slightly better fit, based on the RMSEA (one factor model = 0.03 vs. two factor model = 0.02), the CFI (one factor model = 0.97 vs. two factor model = 0.99) and the BIC (one factor model = 27442 vs. two factor model = 27291). Similarly, both models fit the data well when using the indicators of past 12 months mental disorders. However, the two-factor model fit evidenced slightly better, the RMSEA was similar (one factor model = 0.02 vs. two factor model = 0.02), the CFI value was slightly larger (one factor model = 0.98 vs. two factor model = 0.99) and the BIC was smaller by a margin of more than 10 (one factor model = 16718 vs. two factor model = 16628). Based on these results, the remainder of the analyses focused on the two-factor fear-distress model. Inspection of the factor loadings for the two-factor model in both lifetime and past 12 months models indicated that all disorders generated significant and salient loadings ($\lambda > 0.4$) with respect to the distress and fear dimensions.

**MIMIC modelling**

**Indirect effects**

**Distress** Of the lifetime physical conditions, controlling for age, sex, current daily tobacco use, obesity, and the other variables in the model, asthma, stroke, gout/rheumatism/arthritis and heart condition were significantly related to distress. As can be seen in Table 2, the significant variables had a positive relationship with distress, indicating that the presence of these physical conditions was associated with increased mean levels of latent distress. Of the physical conditions present in the past 12 months, controlling for age, sex, current daily tobacco use, obesity, and the other variables in the model, only asthma and gout/rheumatism/arthritis remained significantly related to distress. The direction of the relationship remained the same.

**Fear** Controlling for age, sex, current daily tobacco use, obesity and the other variables in the model, asthma, stroke, and gout/rheumatism/arthritis were significant in lifetime model. The significant variables, as seen in Table 4, had a positive relationship, indicating that the presence of these physical conditions was associated with increased mean levels of latent fear. Of the conditions that have been presented in the past 12 months, asthma and gout/rheumatism/arthritis remained significant, however, there was no evidence to suggest stroke was significantly related to fear whereas the presence of cancer was now
significantly related to fear. Again, the direction of the relationship remained positive indicating the higher rates of mean latent fear associated with the presence of the physical conditions in the past 12 months.

Direct effects

Inspection of the modification indices for the lifetime and past 12 months MIMIC models with indirect effects revealed no direct effects associated with a modification index greater than 3.84 (associated a \( p \) value <0.05 with 1 degree of freedom). This indicates that inclusion of additional direct relationships between indicators of the latent variables and the physical health conditions would not significantly improve the overall model fit after taking into account the indirect relationship between mental and physical disorder via the latent fear and distress factors.

Discussion

The current study sought to examine the relationship between broad latent levels of internalizing psychopathology, namely fear and distress dimensions, and various
factors associated with poor physical health, including six physical health conditions, obesity, and daily tobacco use. Of specific interest was whether the relationship between mental disorders and physical ill health could be parsimoniously explained via the mediating relationship of these broad factors of whether multiple unique relationships exist between specific mental disorders and physical conditions. Briefly, the study found that the presence of several physical conditions were significantly related to mean levels of fear and distress, with higher mean levels found to be associated with an increased likelihood of having received a diagnosis of chronic physical conditions. The results pertaining to asthma and gout/rheumatism/arthritis were similar depending on whether lifetime or past 12 months indicators of mental disorders and physical conditions were utilised in the models. Finally, the results demonstrated that the significant association between individual mental disorder and physical health conditions can be parsimoniously described using broad transdiagnostic dimensions with the addition of direct disorder-specific relationships contributing little to the model.

The results of the current study confirm and extend those found previously. Similar to results reported by Slade [17] using an earlier survey of the Australian population, the current study demonstrated significant relationships between past 12 months fear and distress factors with respiratory conditions (e.g., asthma) and gout/rheumatism/arthritis. These results were replicated when examining disorders and conditions measured across the lifespan with the addition of significant relationships identified between stroke, heart conditions, and distress as well as stroke and fear. Importantly, these relationships also held in multivariate models adjusting for sex, age, tobacco use, obesity, and other physical health conditions, which demonstrates the independent relationship of these conditions on the fear and distress factors.

Multiple possible mechanisms exist to explain the overall broad association between mental disorder and various physical health conditions, including shared genetic and/or environmental risk factors (e.g., childhood adversity, socioeconomic factors), the compounding bidirectional effects of chronic stress and rumination shared by both physical and mental health, or direct causal pathways between physical conditions impacting shared risk factors associated with common mental disorders (increased disability, hopelessness, medication use, etc.). One possible explanation that may contribute to the significant broad relationships between internalizing and asthma, gout/rheumatism/arthritis, heart conditions, and stroke, which has received increasing attention in the literature could be the shared association with inflammation. Recently, studies have shown that inflammatory responses have an important role in the pathophysiology of depression, stress, anxiety, bipolar and psychosis [30–32]. Indeed, inflammation is a core component across multiple medical illnesses, including respiratory illness, arthritis, heart conditions, and stroke. This inflammatory response may also be triggered by the effects of stress, rumination, and heightened fear responses on the sympathetic and parasympathetic nervous systems [33], all of which are considered as broad transdiagnostic effects of internalizing psychopathology [34, 35]. Despite the multiple possible mechanisms responsible for comorbid mental and physical health, the current study further highlights the general role of internalizing liability (e.g., broad underlying or associated factors accounting for multiple mental disorders representing fear and distress) on chronic physical illness. These broad relationships warrant further investigative efforts.

In contrast to the above findings, the current study did not find evidence to suggest a significant independent association between distress and fear with diabetes and found only significant associations between past 12 months fear and cancer and lifetime distress and heart conditions. The previous literature has provided mixed support regarding the association between diabetes and individual mental disorders, particularly depression, in samples of the general population [36–38]. The mixed results have been attributed to differences in assessment, sampling, differences in the definition of mental disorders, not distinguishing between type 1 and type 2 diabetes, and the influence of other confounding factors. Moreover, the use of a population-based sample in comparison to a clinical sample results in smaller subsamples with comorbid conditions and differences between studies and weak evidence of association found in the current results may possibly emerge from the greater influence of sampling and/or measurement errors. Prior evidence has also indicated the confounding role of functional impairment, sociodemographics, personality, service utilization, and other medical conditions not assessed in the current study that warrant further investigation [37].

The results of the current study supported the original hypothesis. The relationship between specific mood and anxiety disorders and factors associated physical ill health can be explained via the use of broad latent variables (e.g., indirect relationships). This hypothesis links directly to the empirical question of whether separate diagnoses for comorbid mood and anxiety disorders are beneficial for our understanding of poor mental health and its correlates rather than alternative conceptualizations. The current findings support Eaton et al. [18], who also noted that the direct relationships between specific indicators of internalizing and future onset of angina and ulcer represented less than 3.5% of the variance and, therefore, provided little clinical meaning over the relationship between latent internalizing and physical health. These findings again
support the call for mood and anxiety disorders to be represented as dimensional factors in a hierarchical meta-structure rather than represented as putatively distinct categorical constructs [8]. Moreover, the findings further highlight the validity and utility of the alternative and recently proposed hierarchical taxonomy of psychopathology at the broader fear and distress level in relation to physical health [16]. The knowledge of what specific mood or anxiety disorders are present provides little additional information to the association with physical health once a person’s liability to broad fear and distress is considered. More importantly, if internalizing disorders predict physical health outcomes then the findings suggest that new transdiagnostic treatment modalities for internalizing disorders may alleviate additional complications associated with physical ill health. Inversely, if poor physical health predicts internalizing disorder outcomes then healthy lifestyle prevention efforts and interventions to reduce chronic conditions may have a follow-on effect of reducing incidence of multiple mood and anxiety disorders rather than any one specific condition [39, 40]. In any case, the results of the current study suggest that treatment efforts that combine programs associated with internalizing disorders and healthy lifestyles are warranted and require more attention.

There are some limitations to the current study that warrant further discussion. First, the relationships identified in this study cannot be considered causal given the cross-sectional nature of the survey. Second, there could be some degree of recall bias that influences the results particularly with respect to the lifetime indicators. However, the conditions asked about tend to reflect substantial life events and, therefore, more likely to be salient in a respondent’s mind, so it would be expected most people would remember broad details about the presence or absence of various mood and anxiety disorders and physical conditions. Moreover, the questionnaire used various memory probes to aid recall and the results using past 12 months disorders, which are less likely to be impacted by recall bias, were similar to those found using lifetime indicators. Third, the survey relied on the use of self-report data, which could introduce bias associated with social desirability. Nonetheless, the survey was anonymous with multiple mechanisms in place to ensure confidentiality, which lowers the chance of socially desirable answers. Fourth, the current study analysed indicators of internalizing psychopathology at the disorder or diagnostic level only rather than investigating symptom level data. Additional and perhaps more detailed results might emerge if these relationships were to be examined at the symptom level. Finally, tobacco use and obesity were included in the current study as background control variables in the models given the previously demonstrated association between these variables and physical health and mental health. However, it is possible that smoking and obesity might act as a mediator in the relationship between physical health conditions and factors of internalizing. The mediating role of smoking and obesity in the mental—physical health relationship is beyond the scope of the current study but future research may provide further evidence regarding this issue.

To conclude, the current study demonstrates significant relationships between internalizing psychopathology and various physical health conditions, obesity and daily tobacco use. Moreover, these relationships are better accounted for using broad dimensional constructs that represent liability to fear and distress rather than any direct connections with disorder-specific indicators. These results indicate that researchers should focus on common mechanisms associated with a broad range of mental and physical health when developing prevention and treatment programs.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

References


