Internalizing psychopathology and all-cause mortality: a comparison of transdiagnostic vs. diagnosis-based risk prediction

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Previous studies have documented the utility of a transdiagnostic internalizing factor in predicting important future outcomes (e.g., subsequent mental disorder diagnoses). To date, however, no study has investigated whether an internalizing factor predicts mortality risk. Also, while previous studies of mortality risk have emphasized its associations with particular internalizing disorders, no study has assessed how the transdiagnostic internalizing factor vs. disorder-specific variance differently predict that risk. The primary aims of this study were to explore: a) whether the internalizing factor predicts mortality risk, b) whether particular internalizing psychopathologies uniquely predict mortality risk over and beyond the transdiagnostic internalizing factor, and c) whether there is a significant interaction of internalizing with self-reported health in the prediction of mortality risk. We utilized a large national sample of American adults from the Midlife in the United States (MIDUS), a longitudinal study that examined midlife development of individuals across multiple waves between 1995 and 2015. Data were analyzed for the 6,329 participants who completed the phone interview and self-administered questionnaire in MIDUS 1 (1995-1996) and were then followed up until October 31, 2015 or until death. To investigate the association between internalizing and mortality risk, we used the semi-parametric proportional hazards Cox model, where survival time was regressed on a latent internalizing factor. Overall findings indicate that a transdiagnostic internalizing factor significantly predicts mortality risk over a 20-year period (hazard ratio, HR=1.12, 95% CI: 1.05-1.16, p<0.01) and that internalizing outperforms disorder-specific variance (e.g., depression-specific variance) in the prediction of that risk. Further, there was a significant interaction between transdiagnostic internalizing and self-reported health, whereby internalizing psychopathology had a specific association with early death for individuals with excellent self-reported health condition (HR=1.50, 95% CI: 1.17-1.84, p<0.05). This highlights the clinical utility of using the transdiagnostic internalizing factor for prediction of an important future outcome, and supports the argument that internalizing psychopathology can be a meaningful liability to explore in public health practice.

Key words: Internalizing factor, mortality, transdiagnostic prediction, diagnosis-based prediction, major depressive disorder, generalized anxiety disorder, panic disorder, neuroticism

Numerous studies have reported that individuals with depressive or anxiety symptoms are at higher risk of experiencing various negative physical health conditions subsequently, compared with individuals without those symptoms. For example, depressive symptoms are associated with greater decline in physical performance in the later stages of life[1], increased risk of developing various forms of cardiovascular disease[2,3], and excessive risk of developing some forms of cancer[4]. Furthermore, childhood separation anxiety symptoms predict poor physical health in later stages of development[5]; generalized anxiety disorder (GAD) symptoms are associated with risk for coronary heart disease[6]; and GAD and post-traumatic stress disorder symptoms longitudinally predict shorter leukocyte telomere length (a biomarker for age-related diseases)[7].

Not surprisingly, a number of studies have reported the association of depression and/or anxiety with a higher risk of mortality[8-10]. For example, using survival analysis, a study investigated mortality rate in a large Danish population-based cohort (N=5,103,699), reporting that individuals with unipolar depression had a higher risk of early death[11]. Several studies also found that individuals with anxiety symptoms were exposed to a higher risk of premature death[12,13]. Additionally, some studies have indicated that individuals with a higher level of neuroticism, a personality trait with a close relation to mood and anxiety disorders[14], also have a higher mortality risk[15,16].

Although informative, a major limitation of prior research is that it mainly focused on how particular categorical diagnostic constructs were associated with mortality risk, while there has been growing evidence supporting the value of a dimensional conceptualization of psychopathology[17-21]. According to this latter approach, each mental disorder can be conceptualized as a manifestation of relatively few underlying transdiagnostic dimensions, which account for the co-occurrence among various disorders (i.e., comorbidity). For example, major depressive disorder (MDD) and GAD tend to co-occur more frequently than it is expected by chance[22]. This may indicate that they are highly correlated through the transdiagnostic internalizing factor. Indeed, numerous studies have reported that the internalizing factor accounts for the commonalities among various mood and anxiety disorders[22-25].

This framework provides the opportunity to investigate how the transdiagnostic internalizing factor, compared to particular forms of internalizing pathology (e.g., diagnostic categories), is associated with mortality risk[26]. A few prior studies have suggested a possible association of the common variance among various internalizing disorders with that risk[15,27,28]. For example, Mirza et al[27] reported that the relationship between anxiety symptoms and mortality risk was no longer significant after adjusting for comorbid depressive symptoms. This finding seems to suggest that it is the common variance that anxiety shares with depression which leads to higher mortality, and that the anxiety

disorder-specific variance may not predict mortality risk meaningfully once comorbid depression is controlled for.

There are several advantages of using the transdiagnostic internalizing factor as a predictor. Previous research has shown notable structural invariance of internalizing across different samples[29], high long-term stability of internalizing over time[30], and notable predictive validity for important future outcomes (e.g., subsequent mental disorder diagnoses)[30-32]. Given these findings, transdiagnostic internalizing could be a reliable and strong predictor of mortality risk.

It is also probable that the anticipated relationship between transdiagnostic internalizing and mortality risk is moderated by other factors. A possible moderator is one's self-reported health, given some prior studies suggesting that the association of depression and neuroticism with mortality risk varied depending on one's self-reported health condition[11,15].

Taking all the research discussed above into consideration, major limitations of the prior literature are that: a) no study has investigated whether or not a transdiagnostic internalizing dimension meaningfully predicts mortality risk, and b) previous studies have focused on the associations of individual diagnostic constructs with that risk, leaving it unclear whether these constructs have a general or a specific and unique association with early mortality[8,9,11,28,33]. This underscores the necessity to compare the prediction of mortality risk from various internalizing disorders' shared variance (i.e., transdiagnostic internalizing) versus the specific (unique) variance of each disorder, to ascertain which is a more robust predictor.

The primary aims of the current study were: a) to investigate whether the transdiagnostic internalizing factor predicts mortality risk in a longitudinal probability sample of American adults, b) to compare the utility of the transdiagnostic internalizing factor versus disorder-specific variance in the prediction of that risk, and c) to examine whether self-rated physical health moderates the association between internalizing and early mortality.

METHODS

Participants

This study utilized a large national sample of American adults from the Midlife in the United States (MIDUS)[34], which is a longitudinal study examining midlife development of individuals across multiple waves. Our study initially utilized information on the 7,108 participants who were recruited in the initial survey at MIDUS 1 (1995-1996). In order to be included in the final sample, participants needed to complete the MIDUS 1 phone interview and self-administered questionnaire, which yielded the final analytic sample of 6,329 individuals (mean age: 46.77±12.92 years; 52.64% females; 88.04% White, 4.90% African American).

These individuals were followed up until October 31, 2015 or until death. A total of 1,234 people were deceased during the study period (i.e., from 1995 to 2015). The mean survival time for all participants was 19.23±4.16 years. The mean survival time for decedents was 11.50±5.28 years.

Measures

To model a transdiagnostic internalizing factor, we included continuous symptom scores for MDD, GAD, panic disorder and neuroticism. Past 12-month MDD, GAD and panic disorder symptoms were measured using the Composite International Diagnostic Interview - Short Form (CIDI-SF) version 10, whose good diagnostic reliability and validity have been reported by numerous studies[35-37]. Neuroticism was assessed using the relevant subscale of the Midlife Development Inventory Personality Scales, whose internal consistency has been found to be good (Cronbach's alpha = .74)[38].

We chose six covariates based on the following criteria: a) whether a given covariate had been previously identified to likely influence mortality risk, and b) whether there was a large enough response rate for a given covariate (more than 6,000 responses). Based on these criteria, the six covariates chosen were: age (a standardized variable), age squared, sex (a binary variable), education level (ranged from 1 to 12, with larger numbers indicating higher educational levels), experienced severe health condition (a continuous variable ranged from 0 to 3, where higher scores indicate more severe physical health condition), and heart disease family risk (a binary variable).

Analyses

To investigate the association between the transdiagnostic internalizing factor and mortality risk, we used the semi-parametric proportional hazards Cox model. This model makes fewer assumptions about the distribution of survival time than do parametric models (e.g., Weibull, exponential models), enabling one to estimate regression coefficients and hazard ratios (HRs) even though the baseline hazard is not specified. This advantage makes it a practical and reasonable choice.

To model the transdiagnostic internalizing factor, we used confirmatory factor analysis (CFA), including four indicators (MDD, GAD, panic disorder, and neuroticism) assessed at MIDUS 1. This internalizing model (estimated from these same data and indicator variables) was previously identified as invariant across the different age cohorts and stable over time[39]. After modeling internalizing, we saved the factor scores to include them in the main Cox regression model.

The factor score approach may raise an issue of factor indeterminacy. In order to mitigate this concern, we further checked the factor determinacy index, which was calculated by the correlation between the estimated and true factor scores (ranging from 0 to 1; the higher the better representation of the true factor scores).

We performed survival analyses using maximum likelihood estimation with robust standard errors (MLR), with the latent internalizing variable standardized to have a variance of 1 and a mean of 0. All analyses were performed in Mplus version 8.0.

In order to compare the predictive validity of internalizing versus disorder-unique variance, we parameterized an explicit residual variance factor for each of the three internalizing disorders and neuroticism (i.e., the unique variance remaining in

each indicator after the common variance is accounted for by the latent internalizing variable). We then saved the factor scores from transdiagnostic internalizing and the four construct residual factors, and regressed survival time on both internalizing and the residual factor scores simultaneously.

RESULTS

The key assumption that Cox regression poses is that each predictor's multiplicative effect on the hazards function remains constant over time (proportional hazards assumption)[40,41]. We tested this assumption by assessing time-by-covariates interaction, which has been proven to be powerful for detecting non-proportionality[42]. This method involved creating the interaction term of internalizing x survival function time, including it in a Cox model with internalizing, and testing the significance of the interaction term. The result showed that the interaction term was not significant (HR=1.01, 95% CI: 0.99-1.01), indicating that the proportional hazards assumption was met.

We first examined how each of the four indicators assessed at MIDUS 1 (MDD, GAD, panic disorder, and neuroticism) was associated with mortality risk by use of hierarchical regression. A set of four two-stage hierarchical regression models were conducted where all covariates were entered at stage 1 and each of the indicators was entered one at a time at stage 2. Results showed that MDD, GAD and neuroticism significantly predicted mortality risk in this framework, while panic disorder did not (see Table 1).

We then explored whether the transdiagnostic internalizing factor predicted mortality risk. Our CFA model of internalizing showed an excellent fit to the data: root mean square error of approximation (RMSEA) = .008; comparative fit index (CFI) = .999; Tucker-Lewis index (TLI) = .998. The factor determinacy index for our CFA model was .78, which mirrored the recommended threshold of 0.80 to indicate that a model is "adequate for most scientific purposes"[43]. The Cox regression analysis showed that internalizing significantly and positively predicted mortality risk (HR=1.12, 95% CI: 1.05-1.16, p<0.01), after adjusting for age, age squared, sex, education level, experienced severe health condition, and heart disease family risk (see Table 2).

In order to compare the prediction of mortality risk from internalizing disorders' shared variance (i.e., transdiagnostic internalizing) and disorder-specific variance, we regressed mortality on internalizing and the residual variance of MDD, GAD, panic disorder and neuroticism simultaneously in the Cox regression framework (see Figure 1). The results showed that internalizing significantly predicted mortality risk across all analyses (HR ranged from 1.11 to 1.14), while MDD (HR=1.02, 95% CI: 0.98-1.06), GAD (HR=1.01, 95% CI: 0.94-1.09), panic (HR=0.94, 95% CI: 0.88-1.00), and neuroticism (HR=1.02, 95% CI: 0.92-1.12) residuals did not (see Table 3).

We then examined how the initial associations of MDD, GAD and neuroticism with mortality risk (panic disorder did not significantly predict that risk) were attenuated when adjusting for internalizing. Compared with the hierarchical regression analysis results, the comparative predictive validity analysis showed that the degrees to which MDD, GAD and neuroticism predicted mortality risk were attenuated, respectively, by 67.2%, 86.9% and 87.1%, when their shared variance captured in internalizing was accounted for.

To explore whether the association between internalizing and mortality risk was moderated by individuals' self-reported health condition, we created an interaction term and included it in our Cox regression model following the method use by Gale et al[15]. We then compared the models with and without the interaction term. Results showed that the Bayesian information criterion (BIC) was lower for the model with the interaction term included (BIC=10622.6) than for the model without the interaction term (BIC=10635.3). BIC differences of 10 between two models indicate 150:1 posterior odds in favor of the model with superior (lower) BIC.

Given the statistical significance of the interaction term, we further analyzed the association of internalizing with mortal-

Table 1 Hierarchical regression analysis of individual internalizing pathologies predicting mortality risk (regression coefficients with 95% CI)

	Stage 1	Stage 2			
		MDD	GAD	PAN	NEURO
Age	8.39 (8.19-8.59)***	8.69 (8.49-8.89)***	8.52 (8.32-8.73)***	8.47 (8.27-8.67)***	8.66 (8.45-8.86)***
Age squared	0.94 (0.66-1.21)	0.94 (0.66-1.21)	0.94 (0.66-1.21)	0.94 (0.66-1.21)	0.94 (0.66-1.20)
Sex	0.75 (0.63-0.88)***	0.74 (0.62-0.86)***	0.75 (0.63-0.87)***	0.75 (0.63-0.87)***	0.75 (0.63-0.87)***
Education level	0.82 (0.76-0.88)***	0.82 (0.76-0.88)***	0.82 (0.76-0.88)***	0.82 (0.76-0.88)***	0.82 (0.76-0.88)***
Experienced physical illness	1.52 (1.45-1.60)***	1.51 (1.43-1.58)***	1.52 (1.44-1.59)***	1.52 (1.44-1.59)***	1.50 (1.43-1.58)***
Heart disease family risk	1.23 (1.12-1.35)**	1.23 (1.12-1.35)**	1.23 (1.12-1.35)**	1.23 (1.12-1.35)**	1.23 (1.12-1.35)**
MDD		1.06 (1.02-1.09)**			
GAD			1.08 (1.02-1.15)*		
PAN				1.03 (0.96-1.09)	
NEURO					1.12 (1.02-1.21)*

MDD – major depressive disorder, GAD – generalized anxiety disorder, PAN – panic disorder, NEURO – neuroticism
*p<0.05, **p<0.01, ***p<0.001

Table 2 Results for Cox regression models of the effect of change in internalizing on mortality risk

Predictor	Hazard ratio (95% CI)
Age	5.50 (5.29-5.71)***
Age squared	0.95 (0.75-1.16)
Sex	1.28 (1.18-1.37)***
Education level	0.86 (0.81-0.91)***
Experienced physical illness	1.37 (1.31-1.44)***
Heart disease family risk	1.18 (1.09-1.28)***
Internalizing	1.12 (1.05-1.16)**
AIC	10588.07
BIC	10635.26

AIC – Akaike information criterion, BIC – Bayesian information criterion
**p<0.01, ***p<0.001

ity risk stratified by self-rated physical health level (5-point scale ranged from poor to excellent, with 5 being excellent). Results showed that internalizing significantly predicted mortality risk specifically among individuals whose self-reported physical health was excellent (HR=1.50, 95% CI: 1.17-1.84, p<0.05), but not in individuals with poorer self-rated physical health (see Table 4).

DISCUSSION

Internalizing and mortality risk

The primary aim of our study was to investigate the association between a transdiagnostic internalizing factor and mortality risk. Our findings show that higher levels of internalizing pathology are associated with a significantly increased mortality risk, even after adjusting for covariates known to affect that risk (e.g., age, sex, education level, heart disease family risk, experienced severe health condition). There was a 12.3% increase in mortality rate for every 1-standard deviation unit increment in the internalizing factor level. These findings are consistent with the previously reported close link between individual internalizing disorders and high mortality rates[8-11,28,33,44], but our study is the first to demonstrate that it is a transdiagnostic internalizing factor that predicts mortality risk, rather than the variance that is unique to MDD, GAD, panic, or neuroticism.

There are several possible explanations for why mortality rates are greater in individuals with higher levels of internalizing. One pathway is via maladaptive coping. Given that individuals with high internalizing experience frequent negative affect, they may attempt to manage their negative emotions via unhealthy coping, such as heavy drinking or drug abuse. Indeed, an internalizing pathway model has been proposed[45], in which early and persistent internalizing symptoms lead individuals to use substances as a means of coping. Issues with substance and alcohol abuse tend to emerge after trauma exposure[46], which also has additive negative effects on mental and physical health.

It is also possible that internalizing predicts mortality risk through physical inactivity. People with internalizing psychopathology tend to be physically inactive[47,48], which can lead to adverse physical health outcomes, eventually resulting in high mortality rates. Indeed, a number of prior studies indicated that physical inactivity is one of the main risk factors for cardiovascular disease[49-51], and that engaging in regular activity can meaningfully reduce the risk of premature death[52,53].

In addition, people with high levels of internalizing are more likely to experience various adverse life outcomes, such as unemployment[54], marital discord[55,56], poor social functioning[57,58], and poor quality of life[57,59], which may play a role as mediating factors in the relationship between internalizing and high mortality risk.

The superior predictive validity of the transdiagnostic internalizing factor

Contrary to the underlying assumption of traditional diagnostic systems that each mental disorder is a discrete entity, many internalizing disorders co-occur more frequently than expected
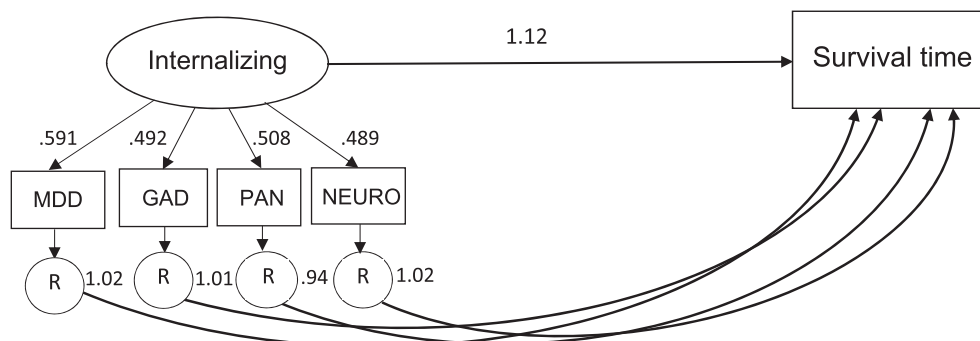

Figure 1 Comparative predictive validity analysis. Arrows flowing from the latent internalizing factor to its indicators represent factor loadings, which were all statistically significant at p<0.001. The arrow leading from internalizing to survival time represents the hazard ratio of the Cox regression model, which was significant at p<0.01. Arrows leading from each of the residual variance to survival time represent the hazard ratios of each Cox regression model, which were all non-significant. MDD – major depressive disorder, GAD – generalized anxiety disorder, PAN – panic disorder, NEURO – neuroticism, R = residual variance.

Table 3 Results of the comparative predictive validity analysis (hazard ratios with 95% CI)

	Models			
	Internalizing vs. MDD	**Internalizing vs. GAD**	**Internalizing vs. PAN**	**Internalizing vs. NEURO**
Age	5.48 (5.28-5.69)***	5.49 (5.28-5.71)***	5.47 (5.26-5.69)***	5.50 (5.29-5.72)***
Age squared	0.95 (0.74-1.17)	0.95 (0.75-1.17)	0.95 (0.74-1.17)	0.95 (0.75-1.17)
Sex	1.27 (1.18-1.37)***	1.27 (1.18-1.37)***	1.27 (1.17-1.37)***	1.28 (1.18-1.38)***
Education level	0.86 (0.81-0.92)***	0.86 (0.81-0.92)***	0.86 (0.81-0.92)***	0.86 (0.81-0.92)***
Experienced physical illness	1.37 (1.31-1.44)***	1.38 (1.31-1.44)***	1.37 (1.31-1.43)***	1.37 (1.31-1.43)***
Heart disease family risk	1.18 (1.09-1.28)***	1.18 (1.09-1.28)***	1.18 (1.09-1.28)***	1.18 (1.09-1.28)***
Internalizing	1.11 (1.03-1.18)**	1.12 (1.04-1.20)**	1.14 (1.07-1.22)***	1.12 (1.05-1.20)**
MDD residual	1.02 (0.98-1.06)			
GAD residual		1.01 (0.94-1.09)		
PAN residual			0.94 (0.88-1.00)	
NEURO residual				1.02 (0.92-1.12)

MDD – major depressive disorder, GAD – generalized anxiety disorder, PAN – panic disorder, NEURO – neuroticism
**p<0.01, ***p<0.001

by chance. A significant relationship between a particular internalizing disorder and high mortality risk can be attributed to that disorder's unique variance or to the common variance that the disorder shares with other internalizing disorders (i.e., the transdiagnostic internalizing factor). To our knowledge, our study is the first to explore which of these two sources more significantly predicts mortality risk. Our findings show that, once the commonalities among the individual diagnostic constructs are accounted for by the internalizing factor, the unique variance that is specific to each construct no longer predicts mortality risk meaningfully. The significant associations between particular internalizing pathologies and mortality risk reported in prior studies may be therefore largely attributed to an underlying internalizing factor.

Of note, internalizing accounted for 34.93% of the variance in MDD (i.e., 65.07% of the variance was MDD-specific), 24.21% in GAD (i.e., 75.79% of the variance was GAD-specific), 25.81% in panic disorder (i.e., 74.19% of the variance was panic disorder-

specific), and 23.91% in neuroticism (i.e., 76.09% of the variance was neuroticism-specific). Nevertheless, none of those disorder-specific variances significantly predicted mortality risk.

It is worth further speculating about why mortality risk was mainly predicted by the commonalities among the internalizing pathologies rather than by the residual variance of each internalizing construct. Previous studies that looked at the stability of various diagnostic constructs reported a long-term instability of mood and anxiety disorders[60-62]. Given the transitory nature of these pathologies, one's particular internalizing disorder symptoms may not be a strong predictor of long-term outcomes. By contrast, a transdiagnostic internalizing dimension has high temporal stability and structural invariance over time[29,30], thus being a more reliable prospective predictor of long-term outcomes such as death.

It was especially notable to find the insignificant association between neuroticism residual variance and mortality risk, after the common variance was saturated by the internalizing fac-

Table 4 Results for Cox regression models of the effect of change in internalizing on mortality risk stratified by self-rated physical health (hazard ratios with 95% CI)

	Excellent health (N=1,217)	Very good health (N=2,506)	Good health (N=2,386)	Fair health (N=796)	Poor health (N=192)
Age	7.86 (7.21-8.51)***	2.59 (2.36-2.83)***	2.69 (2.50-2.87)***	2.28 (2.04-2.53)***	1.86 (1.57-2.15)***
Age squared	1.16 (0.54-1.78)	0.98 (0.72-1.23)	1.09 (0.87-1.32)	0.91 (0.63-1.20)	0.77 (0.43-1.12)
Sex	1.11 (0.81-1.4)	1.14 (1.04-1.24)**	1.14 (1.05-1.22)**	1.22 (1.10-1.34)**	1.07 (0.88-1.26)
Education level	0.88 (0.75-1.02)	0.92 (0.82-1.02)	0.86 (0.77-0.95)**	0.97 (0.85-1.09)	1.02 (0.84-1.19)
Experienced physical illness	1.54 (1.33-1.75)***	1.06 (1.00-1.13)*	1.19 (1.11-1.26)***	1.19 (1.07-1.31)**	1.23 (1.03-1.44)*
Heart disease family risk	1.54 (1.26-1.82)**	1.03 (0.93-1.13)	1.12 (1.03-1.20)**	1.05 (0.94-1.16)	1.01 (0.83-1.18)
Internalizing	1.50 (1.17-1.84)*	1.04 (0.93-1.14)	1.04 (0.93-1.16)	1.04 (0.89-1.19)	0.82 (0.59-1.06)

*p<0.05, **p<0.01, ***p<0.001

tor. While a number of prior studies have reported a significant connection between neuroticism and mortality risk[15,16,28], our findings indicate that such significant effects may be largely accounted for by the common variance that neuroticism shares with other internalizing pathologies, and that neuroticism itself may not be a consistent predictor of mortality risk[63].

The significant interaction between internalizing and self-rated health condition

Of note, the meaningful association between internalizing and mortality risk was moderated by one's self-reported health condition. That is, internalizing predicted mortality risk in individuals whose self-reported physical health was excellent, but not in individuals with poorer self-reported health. Individuals with excellent self-rated physical health are exposed to a 50.2% increase in the risk of premature death for every 1-standard deviation unit increment in the internalizing level, after adjusting for other covariates.

This significant interaction between internalizing and self-reported health indicates that internalizing psychopathology may not confer additional risk of early death to those with poor physical health. However, if individuals are currently physically healthy, then internalizing psychopathology is more likely to have an effect on mortality risk. This is in line with prior findings that the association between individual internalizing pathologies and mortality risk was moderated by one's self-reported health condition[11,15]. It is likely that self-reported health is a strong predictor of mortality, closely covarying with internalizing in our study.

Limitations

The current study was not without limitations. First, we included only four internalizing indicators (MDD, GAD, panic disorder, and neuroticism), since they were the only internalizing pathologies assessed in MIDUS 1. Future research needs to replicate our findings by including other internalizing disorder indicators. Second, the study was unable to test the association of a transdiagnostic externalizing factor with mortality risk, given that sufficient indicators were not available to model an externalizing factor in MIDUS. Third, although our final Cox regression model adjusted for many covariates, we were unable to control for some other covariates also known to influence mortality risk (e.g., body mass index, smoking status), due to large missing values for those variables. Fourth, given that the information regarding causes of death was not available in MIDUS, the current study was unable to further investigate the degree to which internalizing predicts mortality risk differently depending on the various causes of death. Last, our study included a binary sex variable as one of the covariates: future research could further explore how the association of internalizing with mortality risk differs in non-binary individuals.

CONCLUSIONS

Our study is the first to identify the role of the transdiagnostic internalizing factor in predicting the risk of early death. Results show that one's level of internalizing meaningfully predicts mortality risk over a 20-year period, and that internalizing outperforms disorder-specific variance in the prediction of that risk. Moreover, the significant interaction between internalizing and physical health indicates that the former dimension is more likely to have an effect on early death for currently physically healthy individuals.

These findings highlight the clinical utility of using the transdiagnostic internalizing factor for prediction of an important future outcome, and support the argument that internalizing psychopathology can be a meaningful liability to incorporate into intervention and prevention research, and to explore in public health practice.

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