Running Head: PHYSICAL SYMPTOMS AND HEALTH FUNCTION

Longitudinal relationship between onset of physical symptoms and functional impairment

Lisa M. McAndrew, Ph.D.

War Related Illness and Injury Study Center, Veterans Affairs, New Jersey Health Care System

Department of Educational and Counseling Psychology, University at Albany

Drew A. Helmer, M.D., M.S.

War Related Illness and Injury Study Center, Veterans Affairs, New Jersey Health Care System

New Jersey Medical School, Rutgers University

Shou-En Lu, Ph.D.

Environmental Epidemiology and Statistics, School of Public Health, Rutgers University

War Related Illness and Injury Study Center, Veterans Affairs, New Jersey Health Care System

Helena K. Chandler, Ph.D.

War Related Illness and Injury Study Center, Veterans Affairs, New Jersey Health Care System

Sarah Slotkin, M.A.

Department of Educational and Counseling Psychology, University at Albany

Karen S. Quigley, Ph.D.

Interdisciplinary Affective Science Laboratory, Northeastern University,

Department of Veterans Affairs, Bedford Memorial Hospital

Author Note

Lisa M McAndrew, War Related Illness and Injury Study Center, Veterans Affairs, New Jersey Health Care System, Department of Educational and Counseling Psychology, University at Albany

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Lisa M. McAndrew 385 Tremont Ave, East Orange, NJ 07081; lisa.mcandrew@va.gov.

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Abstract

Patients with chronic physical symptoms (e.g., chronic pain) often have significant functional impairment (i.e., disability). The fear avoidance model is the dominant theoretical model of how the relationship between chronic physical symptoms and functional impairment develops and proposes a cyclical/bidirectional relationship. There has never been a definitive test of the proposed bi-directional relationship. The current study followed 767 Operation Enduring Freedom/Operation Iraqi Freedom soldiers from pre-deployment, when they were relatively healthy, to one year after deployment, when it was anticipated that symptoms would increase or develop. Over the four assessment time points, physical symptom severity consistently predicted worse functional impairment at the subsequent time point. Functional impairment did not show a consistent relationship with worsening of physical symptom severity. These findings suggest that changes to functional impairment do not have a short-term impact on physical symptom severity.

Keyword: disability, health function, chronic pain, medically unexplained symptoms, Iraq, Veteran, fear avoidance model, health status, fatigue

Longitudinal relationship between physical symptom severity and functional impairment

Patients with chronic physical symptoms (e.g., chronic pain) often have significant functional impairment (i.e., disability or limitations in the ability to perform daily and social activities). Cross-sectional studies find that physical symptoms and functional impairment have a strong association. For example, a cross-sectional study of physical symptoms and functional impairment found each accounted for 35% of the variance in the other (Kroenke et al., 1994). This relationship is significant when controlling for mental health variables (e.g., depression, PTSD; (Helmer et al., 2009; Jackson et al., 2006; Tomenson et al., 2013)) and among patients with medically unexplained symptoms/illnesses (Hoffman & Dukes, 2008) and medically explained symptoms/illnesses (Sogutlu, Levenson, McClish, Rosef, & Smith, 2011) leading some to conclude that chronic physical symptoms and functional impairment are inextricably linked.

The fear avoidance model, a cognitive behavioral model, is the dominant theoretical model of the relationship between chronic physical symptoms and functional impairment and has guided our understanding of this relationship for the past three decades (Lethem, Slade, Troup, & Bentley, 1983). The fear avoidance model proposes a cyclical/bidirectional relationship between physical symptoms and functional impairment (Crombez, Eccleston, Van Damme, Vlaeyen, & Karoly, 2012; Wideman et al., 2013). Specifically, according to the model, acute physical symptoms are hypothesized to trigger pain catastrophizing (a cognitive error in which there is exaggeration of the consequences of an event) which causes fear and avoidance of activity. Avoidance of activity leads to physical deconditioning and functional impairment. Functional impairment (and associated physical deconditioning) then increases the severity of the physical symptoms. The fear avoidance model is also the basis for the dominant behavioral treatment for chronic physical symptoms, cognitive behavioral therapy (Wideman et al., 2013). In cognitive behavioral therapy, patients are encouraged to challenge catastrophizing beliefs and to slowly increase activity to reduce physical symptoms and functional impairment (Brown, 2004; Castell, Kazantzis, & Moss-Morris, 2011).

Recently, however, there have been questions about the directionality and cyclical nature of the fear avoidance model (Wideman et al., 2013). Studies on the direction of the relationships between variables within the fear avoidance model suggest that common assumptions may be incorrect (Sullivan et al., 2009; Wideman & Sullivan, 2011). For example, two recent prospective studies failed to find that pain catastrophizing precedes fear of activity (Bergbom, Boersma, & Linton, 2012; Wideman, Adams, & Sullivan, 2009). The cyclical relationship between physical symptoms and functional impairment is a foundational assumption of the fear avoidance model, yet there has not been a study that examines this *bidirectional* relationship.

There studies that examine one direction of this relationship. These studies find longitudinal evidence that physical symptoms lead to increases in the severity of functional impairment (Momsen, Jensen, Nielsen, & Jensen, 2014; Tomenson et al., 2013). There is conflicting evidence, however, that functional impairment leads to increases in the severity of physical symptoms. Two prospective studies found that functional impairment was associated with greater physical symptoms over time (Bergbom et al., 2012; Bergman, Jacobsson, Herrström, & Petersson, 2004) while two reviews found limited evidence that physical deconditioning increases physical symptoms (Smeets et al., 2006; Verbunt et al., 2003). In the fear avoidance model physical deconditioning is proposed to explain the relationship between functional impairment and physical symptoms.

The goal of the current study is to examine the prospective bidirectional (cross-lagged) relationship between physical symptoms and functional impairment. We examined this relationship among Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) military personnel who were first assessed before deployment at a time when we expected to see relatively few physical symptoms and minimal functional impairment, and then assessed again immediately after deployment, 3 months after deployment and one year after deployment. Combat deployment leads to chronic physical symptoms for approximately 30% of Veterans (McAndrew et al., 2016). By examining the cross-lagged relationships between physical symptoms and functional impairment among deploying military personnel, we can better understand these relationships as physical symptoms and functional impairment are developing.

Methods

Participants

Participants were recruited as part of the HEROES Project, a prospective longitudinal study of Army National Guard and Army Reserve enlisted soldiers deploying to Operation Iraqi/Enduring Freedom. Details on the HEROES project including response bias and drop out can be found in our prior published work using this sample (L. McAndrew et al., 2016; Lisa M. McAndrew et al., 2013; Lisa M McAndrew, Markowitz, et al., 2017; Lisa M McAndrew, Phillips, et al., 2017; Yan et al., 2013). Military personnel between the ages of 18 and 60 were eligible. Exclusion criteria included (a) high blood pressure, (b) medications that produced cardiovascular or autonomic effects, (c) self-reported depression, schizophrenia, or bipolar disorder, or (d) pregnancy. These were specified because they are known to impact physical symptoms and the physiological measures obtained in the study (the latter are not reported here).

Procedures

The HEROES study was a longitudinal study of military personnel from before to one year after deployment. Soldiers were asked to complete questionnaires at four time points: (a) at before deployment while at the Army installation (Time 1; n=767), (b) immediately upon or within a few days of return from deployment at the Army installation or through the mail if they did not return to the base from which they deployed (Time 2; n=422), (c) three-months after deployment through mail (Time 3; n=286), and (d) one-year after deployment through mail (Time 4; n=335). Physical symptom severity at baseline was not related to the likelihood of being lost to follow-up at one year post-deployment (X^2 = 0.80, p=0.85).

Soldiers were recruited during their deployment readiness medical processing. Study personnel emphasized the voluntary nature of participation and provided study information. At the start of the study 795 enrolled soldiers were eligible; 28 were excluded from analysis because they did not deploy, were officers, or were killed in action. At all-time points, soldiers with significant physical or psychological health concerns were offered referrals to appropriate care providers. Participants were not able to be compensated for their participation while on active duty (Time 1 and 2), but those not on active duty at Time 3 and 4 were reimbursed for their time and effort. All study protocols were approved by multiple Institutional Review Boards and other relevant research committees.

Measures

Physical Symptoms. Physical symptom severity was measured using the Patient Health Questionnaire-15 (PHQ-15), a widely used self-report questionnaire that measures the presence of common physical health symptoms and their severity (Kroenke, Spitzer, & Williams, 2002). Participants were asked the extent to which they were bothered by each of 15 symptoms listed (e.g., stomach pain; back pain; pain in arms, legs, or joints; menstrual cramps; headaches; chest pain) during the past seven days. Response options were 0 (*not bothered at all*), 1 (*bothered a little*), and 2 (*bothered a lot*) and responses were added to create a summary score. Participants responded to the PHQ-15 at all four time points.

Functional impairment. Functional impairment was measured using the mental health composite score (MCS) and physical health composite score (PCS) from the Veterans Rand-36 (VR-36; (Kazis et al., 2004), which was derived from the widely used MOS Short-Form 36 (Ware, 1992). For the purposes of this paper, we will refer to the measure as the SF-36. The mental health functional impairment (i.e., MCS) captured the degree to which participants experienced problems in social roles and activities because of emotional problems over the past four weeks. The physical health functional impairment (i.e., PCS) captured the impact of participant's physical health problems on their daily roles and activities. The composite scores were calculated using a standard algorithm. Scores were reported as T-scores (M = 50, SD = 10), with lower scores indicating more functional impairment. According to the norms, a 2 to 3 point difference is considered clinically meaningful. Use of the SF-36 as a measure of functional impairment has been demonstrated to have construct validity through comparisons with conceptually similar measures (McHorney, Ware, Lu, & Sherbourne, 1994).

Analyses

Descriptive statistics of the sample and Pearson's correlation coefficients for the relationships between physical symptom severity, physical health functional impairment, and mental health functional impairment at all four time points were calculated. We did not impute missing data for the descriptive statistics.

Cross-lagged analyses using a series of linear regression models was used to allow for multiple imputation to handle missing data (Raghunathan, Solenberger, & Van Hoewyk, 2002;

Schafer, 1999). We controlled for age and gender due to previous research indicating that they are significant factors related to symptom reporting (Tomenson et al., 2013). All variables included in the cross-lagged analyses were standardized to a mean of 0 and variance of 1 so that results of the regressions could be reported as standardized coefficient estimates.

For example, the following is a description of the cross-lagged analysis equation in which physical symptoms severity (PHQ-15) is being predicted: Y_t is the physical symptoms severity at Time t, Z_t is physical health functional impairment (SF-36 PCS) score at Time t, for t = 1,2,3,4, and ε_Y and ε_Z represent random errors. For Time t = 2,3,4, we fitted linear regression models:

$$Y_t = \beta_0+\beta_{t-1}\, Y_{t-1}+\gamma_{t-1}\, Z_{t-1}+ \varepsilon_Y \text{ +effects of covariates (age, gender)}$$

$$\text{and } Z_t = \alpha_0+ \alpha_{t-1}\, Z_{t-1}+\lambda_{t-1}\, Z_{t-1}+ \varepsilon_z \text{ +effects of covariates (age, gender).}$$

These equations provided the associations of present physical symptom severity with previous physical symptom severity (β_{t-1}) and physical health functional impairment (γ_{t-1}). They also provided the associations of present physical health functional impairment with previous physical symptom severity (α_{t-1}) and physical health functional impairment (λ_{t-1}). Cross-sectional correlations of physical symptom severity and physical health functional impairment at the same time point were calculated using the Pearson's correlation coefficients (r) between the residuals from previously described models of Y_t's and Z_t's. At Time 1, physical symptom severity and physical health functional impairment correlation was calculated by the Pearson's correlation coefficient between residuals from linear regression models that separately fitted Y_1 and Z_1 as a linear function controlled for age and gender.

We used multiple imputation to handle missing data and created 40 imputed datasets using IVEware (Raghunathan et al., 2002). We then conducted the above described cross-lagged analyses on each imputed dataset, and then combined results using the SAS MIANALYSE procedure (SASv9.4). Sensitivity analysis was conducted using cross-lagged structural equation modeling in SPSS with the subset of the data with complete data. Results were similar (data not shown). We also conducted sensitivity analysis with the subset of participants with greater physical symptom severity and the subset with greater functional impairment and found that the correlations between physical symptom severity and functional impairment were the same as compared to using the complete data.

Results

Demographics

Our sample was primarily male (89.7%), Caucasian (77.2%; 9.0% African American, 12.4% Hispanic) and Army National Guard (72.2%; 26.6% Army Reserve or 1.4% Active/Other). On average, participants reported 12.7 (1.6 SD) years of education, or some college education. The average age was 28.0 years (8.38 SD).

Descriptive analyses

The bivariate correlations revealed a strong cross-sectional correlation between physical symptom severity, physical health functional impairment and mental health functional impairment at all time points (Table 2).

Cross-lagged analyses

The cross-lagged analyses allowed us to examine the cross-sectional and longitudinal relationships between the variables in each model (Figure 1 is physical health functional impairment and physical symptoms and Figure 2 is mental health functional impairment and physical symptoms). We found a moderate cross-sectional relationship between physical symptom severity and physical health functional impairment at all time points (before deployment: $r = -.35$, immediately after deployment $r = -.28$, 3 months after deployment $r = -.32$, and 1 year after deployment r = -.26; Figure 1). There was a strong cross-sectional relationship between physical symptom severity and mental health functional impairment (before deployment: r=-.53, immediately after deployment r = -.40, 3 months after deployment r =-.52, and 1 year after deployment r = -.47; Figure 2).

There was a strong longitudinal relationship between physical symptom severity at each time point to the subsequent time point. This was true for the model with physical health functional impairment (before deployment to immediately after deployment β=.44, immediately after deployment to 3 months after deployment β=.50, three months after deployment to one year after deployment β=.63; Figure 1) and the model with mental health functional impairment (before deployment to immediately after deployment β=.47, immediately after deployment to 3 months after deployment β=.47, three months after deployment to one year after deployment β=.63; Figure 2).

The data revealed a moderate to strong longitudinal relationship between physical health functional impairment at one time point and at the subsequent time point (from before deployment to immediately after deployment λ=.28, from immediately after deployment to 3 months after deployment λ=.47 and from 3 months after deployment to one year after deployment λ=.44; see Figure 1). The data revealed a significant longitudinal relationship between mental health functional impairment at one time point and those at the subsequent time point (from before deployment to immediately after deployment λ=.31, from immediately after deployment to 3 months after deployment λ=.53 and from 3 months after deployment to one year after deployment λ=.56; see Figure 2).

Physical symptom severity at each time point showed a consistent small association with worse physical health functional impairment at the subsequent time point (controlling for prior physical symptom severity and physical health functional impairment). Physical symptom severity captured before deployment was related to physical health functional impairment (λ_1=-.12) and mental health functional impairment (λ_1=-.15) after deployment, physical symptom severity immediately after deployment predicted physical health functional impairment (λ_1=-.14) and mental health functional impairment (λ_1=-.14) 3 months after deployment and physical symptoms 3 months after deployment predicted physical health functional impairment (λ_1=-.21) and mental health functional impairment (λ_1=-.17) (Figures 1 & 2).

The cross-lagged result did not show a consistent relationship between either physical or mental health functional impairment to later physical symptom severity (after controlling for physical symptom severity or functional impairment). Neither physical nor mental health functional impairment before deployment was related to physical symptom severity immediately after deployment. Physical health functional impairment ($\hat{\gamma}_2$ =-.13, p=.059) and mental health functional impairment ($\hat{\gamma}_2$ =-.17) immediately after deployment showed a small relationship with physical symptom severity 3 months after deployment (Figures 1& 2). Neither physical nor mental health functional impairment 3 months after deployment was related to physical symptom severity 1 year after deployment.

Discussion

The goal of this study was to examine the bidirectional relationship between physical symptoms and functional impairment proposed by the fear avoidance model. We examined this relationship in a sample of OEF/OIF Veterans who were assessed from before to one year after deployment. This allowed us to examine the relationships among a relatively healthy sample as they were developing new or worsening chronic symptoms.

As expected, greater physical symptom severity was prospectively associated with worsening mental and physical health functional impairment. This is consistent with the extant literature which has shown a relationship between having chronic physical symptoms and physical health functional impairment (Kroenke et al., 1994; Tomenson et al., 2013). The current study adds to the literature by examining this relationship using a prospective longitudinal design and by assessing this relationship as physical symptoms are developing. Previous studies mostly examine this relationship among patients with established chronic symptoms.

There was not a consistent relationship between greater physical or mental health functional impairment and increasing physical symptom severity. This is consistent with a review that found no relationship between physical deconditioning and increases in physical symptoms (Verbunt et al., 2003). Our data suggest that in the short-term, functional impairment likely does not significantly contribute to acute physical symptoms becoming chronic, as is proposed by the fear avoidance model (Leeuw et al., 2007; Wideman et al., 2013).

This study examined the prospective relationship of functional impairment to subsequent physical symptoms over the course of two years. The findings do not preclude the possibility that functional impairment may cause increases in physical symptoms over a longer time period. Functional impairment is a predictor of mortality and major morbidity (Afilalo et al., 2012; Idler & Kasl, 1991) and is thought to contribute to obesity, diabetes and heart disease (Bortz II, 1984; Kaplan et al., 1996). Obesity, diabetes, and heart disease are all linked to increases in pain and physical symptoms over the course of a lifetime (Calcutt, 2002; Fernandez et al., 2016; Shiri, Karppinen, Leino-Arjas, Solovieva, & Viikari-Juntura, 2009).

Our sample consisted of a relatively healthy population of soldiers and most had average or better health function one year after deployment; soldiers with certain, more serious medical conditions were excluded. It is possible that there is a relationship between functional impairment and subsequent physical symptoms among individuals with more severe functional impairment. We explored this possibility, and did not find different results when examining a subset of those with the worst functional impairment or a subset of those with the greatest physical health symptoms as compared to the full sample (data available upon request). This should be explored further in future studies among populations with more medical conditions. Another consideration is our use of a self-report measure of functional impairment. It will be important to examine these relationships using other measures, particularly objective measures, such as the 6 minute walk.

The use of a military sample was a strength and a limitation. Deployment is a known predictor of increases in functional impairment and physical symptoms. Thus, studying military personnel allowed us to examine the relationship between these variables while they are developing. Further, Veterans are disproportionately burdened by functional impairment and chronic symptoms, therefore understanding the relationship between these variables in a military sample is particularly important. A limitation is that we do not know how generalizable these findings are to other populations. Further, the difficulty following military personnel as they returned from deployment contributed to our high attrition.

The findings of the current study suggest that there is not a bi-directional relationship between physical symptoms and functional impairment while they are developing, rather physical symptoms are associated with decrements in functional impairment and not vice versa. These findings suggest the need to rethink the cyclical nature of the fear avoidance model and to better explore the mechanisms through which acute symptoms become chronic. Cognitive behavioral treatments for disorders characterized by physical symptoms (chronic pain, fibromyalgia) have smaller effect sizes as compared to treatments for other disorders, such as depression (Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012). A better understanding of the pathways by which acute symptoms become chronic and relate to functional impairment may lead to better treatments and improvements in patient outcomes.

Table 1: The Mean (Standard Deviation) of Physical Symptoms, Physical Health Functional Impairment and Mental Health Functional Impairment across the Deployment Spectrum

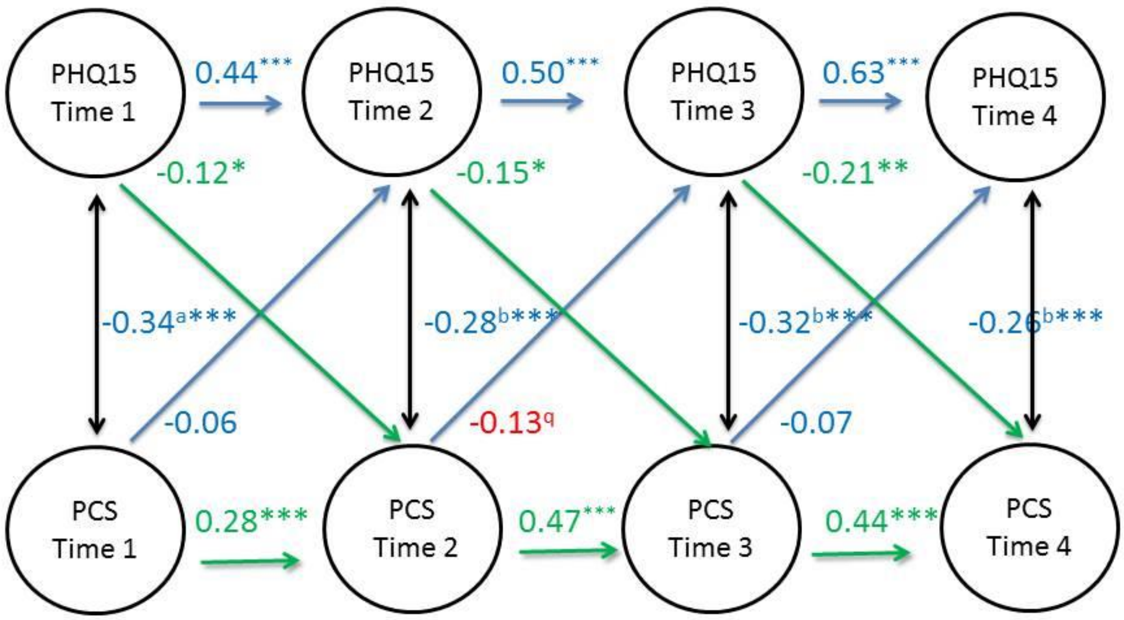
	Before deployment (Time 1)	Immediately After Deployment (Time 2)	3 Months After Deployment (Time 3)	One Year After Deployment (Time 4)
Physical Symptom Severity	5.25 (3.93)	7.94 (4.86)	7.67 (5.11)	7.71 (5.35)
Physical Health Functional Impairment	55.50 (5.21)	53.68 (6.93)	52.84 (7.59)	51.49 (8.75)
Mental Health Functional Impairment	47.98 (9.11)	45.71 (10.71)	44.96 (11.49)	44.90 (12.36)

Table 2: Bivariate Correlations between physical symptom severity, mental and physical health functional impairment across the deployment spectrum.

	2	3	4	5	6	7	8	9	10	11	12
1. Phy. Sx. Before	-.33*	-.48*	.49*	-.22*	-.32*	.46*	-.15*	-.27*	.40*	-.16*	-.23*
2. Phy. health func. Before	1	-.15*	-.19*	.34*	-.02	-.23*	.30*	.07	-.17*	.29*	.02
3. Mental health func. Before	-.15*	1	-.22*	.12	.42*	-.24*	-.00	.41*	-.14*	-.06	.34*
4. Physical Sx Immediately After	-.19*	-.22*	1	-.35*	-.45*	.60*	-.38*	-.41	.58*	-.26*	-.40
5. Phy. health func. Immediately After	.34*	.01	-.35*	1	-.20*	-.29*	.56*	.06	-.35*	.50*	.10
6. Mental health func. Immediately After	-.02	.42*	-.45*	-.20	1	-.40*	-.02	.56*	-.28*	-.02	.55*
7. Phy. Sx. 3 Months After	-.23*	-.24*	.60*	-.29*	-.40*	1	-.46*	-.59*	.73*	-.44*	-.51*
8. Phy. health func. 3 Months After	-.30*	-.00	-.38*	.56*	-.02	-.46*	1	.06	-.37*	.59*	.19*
9. Mental health func. 3 Months After	.07	.41*	-.41*	.06	.59*	-.59*	.06	1	-.43*	.09	.66*
10. Phy. Sx. 1 Year After	-.17*	-.14*	.58*	-.35*	-.28*	.73*	-.37*	-.43*	1	-.46*	-.57
11. Phy. health func. 1 Year After	.29*	-.06	-.26*	.50*	-.02	-.44*	.59*	.09	-.46*	1	-.00
12. Mental health func. 1 Year After	.02	.34*	-.40*	.10	.55*	-.51*	.19*	.66*	-.57*	-.00	1

Phy. Sx.= Physical Symptom Severity, Phy. health func=physical health functional impairment, Mental health func.=Mental health functional impairment, Before=Before Deployment, After=After Deployment, *= correlations significant at $p<.01$

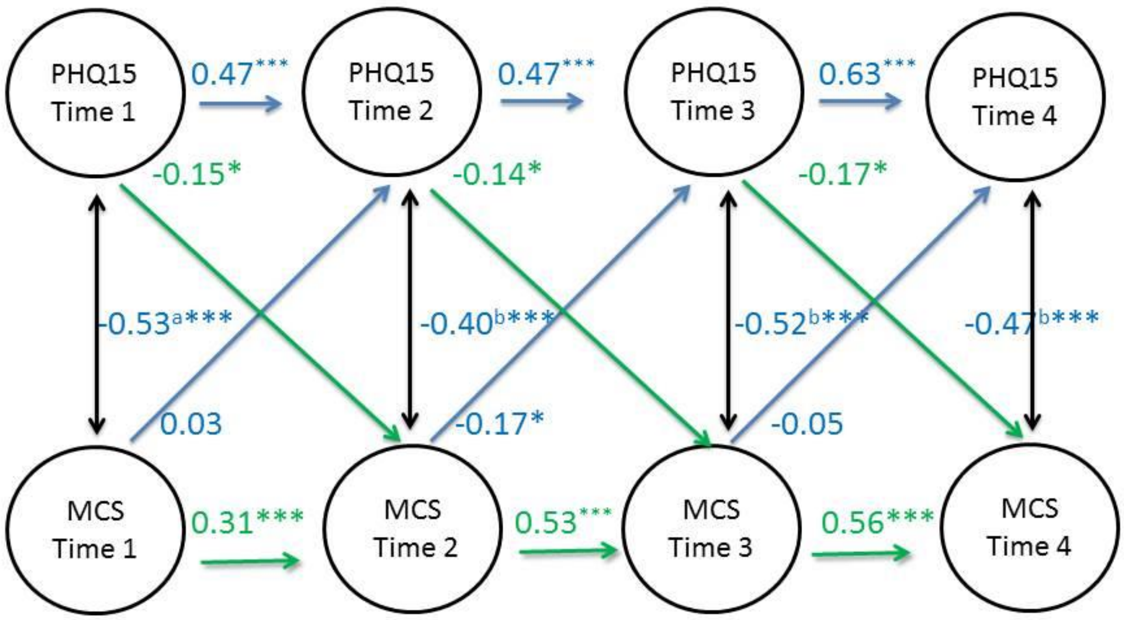
Figure 1: Cross-lagged Relationship between Physical Symptom Severity (PHQ15) and Physical Health Functional Impairment (PCS)



q: p=0.059 *: p<0.05; ** p<0.01; ***p<0.0001; cross-lagged analysis was conducted using series of linear regression models adjusting for age and gender. Multiple imputation (40 datasets) was used to handle missing data (IVEware) with results compiled using Proc MIANALYZE in SAS v9.4.

a: Pearson correlation coefficient; b: correlation between residuals of regression analyses

Figure 2: Cross-lagged Relationship between Physical Symptom Severity (PHQ15) and Mental Health Functional Impairment (MCS)



*p<0.05; **p<0.01; ***p<0.0001; cross-lagged analysis was conducted using series of linear regression models adjusting for age and gender. Multiple imputation (40 datasets) was used to handle missing data (IVEware) with results compiled using Proc MIANALYZE in SAS v9.4.
a: Pearson correlation coefficient; b: correlation between residuals of regression analyses.

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