Self-Reported Mental Health Predicts Acute Respiratory Infection

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ABSTRACT

Background: Poor mental health conditions, including stress and depression, have been recognized as a risk factor for the development of acute respiratory infection. Very few studies have considered the role of general mental health in acute respiratory infection occurrence. The aim of this analysis is to determine if overall mental health, as assessed by the mental component of the Short Form 12 Health Survey, predicts incidence, duration, or severity of acute respiratory infection.

Methods: Data utilized for this analysis came from the National Institute of Health-funded Meditation or Exercise for Preventing Acute Respiratory Infection (MEPARI) and MEPARI-2 randomized controlled trials examining the effects of meditation or exercise on acute respiratory infection among adults aged >30 years in Madison, Wisconsin. A Kendall tau rank correlation compared the Short Form 12 mental component, completed by participants at baseline, with acute respiratory infection incidence, duration, and area-under-the-curve (global) severity, as assessed by the Wisconsin Upper Respiratory Symptom Survey.

Results: Participants were recruited from Madison, Wis, using advertisements in local media. Short Form 12 mental health scores significantly predicted incidence ($P=0.037$) of acute respiratory infection, but not duration ($P=0.077$) or severity ($P=0.073$). The Positive and Negative Affect Schedule (PANAS) negative emotion measure significantly predicted global severity ($P=0.036$), but not incidence ($P=0.081$) or duration ($P=0.125$). Mindful Attention Awareness Scale scores significantly predicted incidence of acute respiratory infection ($P=0.040$), but not duration ($P=0.053$) or severity ($P=0.70$). The PHQ-9, PSS-10, and PANAS positive measures did not show significant predictive associations with any of the acute respiratory infection outcomes.

Conclusion: Self-reported overall mental health, as measured by the mental component of Short Form 12, predicts acute respiratory infection incidence.

INTRODUCTION

Acute respiratory infection (ARI), including influenza, is one of the most common categories of illness in the United States and worldwide.[1] Influenza and noninfluenza ARI yield an inordinate economic burden.[2] The United States bears estimated annual costs of $40 billion for noninfluenza ARI.[2] At a time when health care is seeking to rein in excessive spending, public health efforts could profit from identifying and targeting factors that increase susceptibility to ARI.

Poor mental health has been implicated as a risk factor for developing ARI.[3] Cohen and colleagues identified an association between increased stress and respiratory infection vulnerability. This was demonstrated by an increased likelihood of developing ARI upon viral challenge for people with higher mental or social life challenges.[4] A more recent population-based retrospective cross-sectional study revealed that individuals with any diagnosed Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) mental disorder had a 44% greater risk of having developed a cold in the previous 12 months.[3] However, such research is in its infancy, and mental health's impact on ARI susceptibility is still uncertain.[3] Despite evidence implicating specific mental conditions such as stress and DSM-IV disorders in the development of ARI, no prospective cohort research has yet looked at whether general mental health influences ARI occurrence.

The Short Form 12 Health Survey (SF-12), a validated instrument measuring generic health-related quality of life, is a reliable measure of overall physical and mental health status.[5] Like the Short Form 36 Health Survey (SF-36) from which it was derived, the SF-12 can be divided into 2 summary measures: the Physical Component Summary and the Mental Component Summary (MCS-12).[5] The primary aim of this study was to determine if general mental health, as assessed by the mental component of

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the SF-12, is correlated with incidence, duration, or severity of ARI illness. We also looked at the relationships of a variety of other self-report psychosocial measures to ARI illness.

METHODS

Design

Data utilized for this paper came from 2 National Institutes of Health-funded randomized controlled trials: the Meditation or Exercise for Preventing Acute Respiratory Infection (MEPARI) study as well as the first 2 cohorts of the follow-up MEPARI-2 study. The primary aim of the MEPARI and MEPARI-2 trials was to determine if training in mindfulness meditation or exercise might be effective in decreasing ARI illness burden when compared to the control group.[6] The pilot MEPARI trial found positive results, especially for meditation.[6,7] The MEPARI-2 trial is in progress. Detailed methods can be found at www.clinicaltrials.gov (National Library of Medicine Identifier: NCT01654289). The following serves to briefly describe the methods pertinent to this analysis.

The MEPARI and MEPARI-2 trials enrolled adults >50 and 30-69 years of age, respectively. Participants were recruited from Madison, Wisconsin by means of advertising in local media. Prospective participants were screened by telephone using a scripted protocol. Following telephone screening, eligible adults were enrolled in a 2-week run-in trial to assess ability to adhere to the study protocol. Eligibility criteria included healthy adults who reported having either >2 colds in the last 12 months or >1 cold per year on average. Exclusion criteria included moderate exercise >2 times per week, vigorous exercise >1 time per week, regular practice or previous training in meditation, autoimmune, immunodeficiency, or malignant disorder, a score of >14 on the Patient Health Questionnaire (PHQ-9) Depression Screen, current or anticipated use of antibiotic or antiviral medications, pregnancy or plans of becoming pregnant, and previous allergic reaction to eggs or the seasonal influenza vaccine.[6] Upon successful completion of the run-in trial, participants were eligible for consent and enrollment in the main trial. Participants were randomized to 1 of 3 parallel groups: meditation, exercise, or observational control. Those randomized to the meditation and exercise arms underwent 8 weeks of training in their respective behavioral intervention. All participants were monitored for ARI occurrence until study exit, with regular contact with study staff and daily reporting on the Wisconsin Upper Respiratory Symptom Survey (WURSS-24) during ARI illness episodes. Participants in cohort 1 and cohort 2 of the MEPARI trial were enrolled for 9 and 5 months, respectively. MEPARI-2 cohorts were enrolled for 9 months each.

Measures

Psychosocial Measures

The following psychosocial measures were completed at baseline. The mental component of the SF-12 version 2 (MCS-12) includes 5 of the 12 SF-12 items, and is calculated using an item-weighted algorithm.[8] Three items were derived from the 5-item Mental Health Inventory assessing common diagnostic symptoms of depression and anxiety disorders, while the other items in the MCS-12 pertain to the level of functional impairment attributable to poor mental health.[5] The Positive and Negative Affect Schedule (PANAS) is a valid measure of positive and negative emotion consisting of two 10-item scales.[9] PANAS has been used more for research than clinical applications. The PHQ-9 is a self-administered measure used to assess and monitor depression severity.[10] Individuals with scores >14 (moderately severe depression) were excluded from the MEPARI and MEPARI-2 trials. The Perceived Stress Scale (PSS-10) is an instrument assessing psychological stress that has been used widely in clinical and epidemiological research.[11] The Mindful Attention Awareness Scale (MAAS) is a well-developed and validated 15-item measure of trait mindfulness.[12]

Measures of ARI Illness

Incidence

All participants were monitored for ARI from study onset until study exit, using either biweekly telephone check-in (MEPARI) or weekly electronic surveys (MEPARI-2) and at-home daily self-reports during ARI episodes. ARI incidence was determined by study personnel using the Jackson Scale. The Jackson Scale is a sum of symptom scores for the following health outcomes: sneezing, headache, malaise, chilliness, nasal discharge, nasal obstruction, sore throat, and cough.[13] Each symptom is rated as absent (0), mild (1), moderate (2), or severe (3). An ARI illness episode was defined by a score of >2 on the Jackson scale, with at least 1 of the following cold symptoms: nasal discharge, nasal obstruction, sneezing, or sore throat. Participants had to answer "yes" to "Do you think you have a cold?" or "Do you think you are coming down with a cold?"

Duration

Total duration of an ARI illness episode was assessed as time from first reported ARI symptom to the last time the person reported being ill. The end of the episode was confirmed by a person marking themselves as "not sick" for 2 days in a row. Self-report times were recorded in hours and minutes and converted to decimalized days.

Global Severity

The WURSS-24 is a validated illness-specific questionnaire assessing symptom severity and quality of life impact.[14] The WURSS-24 was used to assess daily symptom severity during each ARI illness episode. Items are rated on a 7-point Likert-style severity scale. For each participant, a daily global severity score was calculated by summing WURSS-24 items 2 to 23.[6] Total illness burden was represented by a WURSS-AUC (area-under-curve) global severity score, calculated using trapezoidal approxi-

Table 1. Demographic Information for MEPARI and MEPARI-2 Trials

	MEPARI 1	MEPARI-2[a]	MEPARI 1 and 2
N	149	204	353
Number of ARIs[a]	93	193	286
Percent female	82%	75%	78%
Race, white	94%	90%	92%
Ethnicity, non-Hispanic	99%	93%	96%
Mean age (SD)	59.3 (6.6)	50.5 (11.2)	54.2 (10.4)
Education, college grad or higher	65.8%	75.5%	71.4%
Income > $50,000	56.4%	61.0%	59.1%

[a]Data reflects the first 2 cohorts of the ongoing 4-cohort MEPARI-2 trial.
Abbreviations = MEPARI, Meditation or Exercise for Preventing Acute Respiratory Infection; ARI, acute respiratory infection

mation across all days of each illness episode (with duration on the X-axis and WURSS-24 severity on the Y-axis).[6]

Statistical Analysis

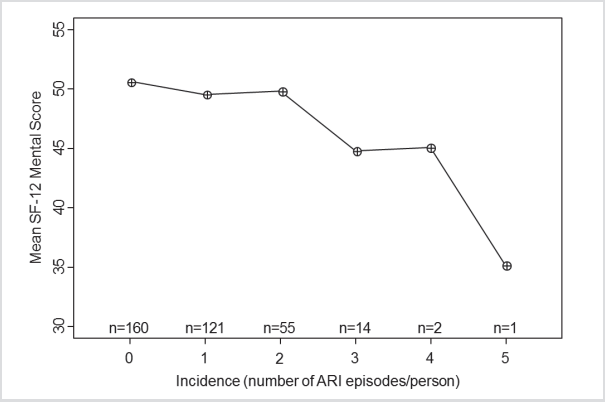
Data were analyzed using the R package Version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria). Predictive associations between baseline psychosocial measures and subsequent ARI outcomes were assessed using Kendall's tau rank correlation. Kendall tau rank correlations are unconditional assessments examining the number of concordant and discordant pairs after ordering the values based on ranking each of the quantities.[15] Kendall tau rank correlation was chosen because of the skewed distributional nature of the dependent variables, duration and global severity, and the binomial nature of incidence.

RESULTS

Eight hundred eighty-three adults were screened for the MEPARI study; 204 of those screened were entered into the run-in trial, 154 were randomized into the main trial, and 149 were followed through the monitoring period. For the MEPARI-2 studies, 503 adults were screened; of those, 250 were entered into the run-in trial, 204 were randomized into the main trial, and 191 were followed through the monitoring period. MEPARI participants underwent assigned 8-week interventions (meditation or exercise) beginning in September 2009 for cohort 1 and January 2010 for cohort 2. MEPARI-2 interventions began in September 2012 for cohort 1 and September 2013 for cohort 2. Both MEPARI and MEPARI-2 participants were monitored through May of the years in which they participated. A more detailed description of results from the MEPARI trial can be found elsewhere.[6] Furthermore, as the MEPARI-2 trial is ongoing, the described results pertain only to the first 2 cohorts of this 4-cohort study. Demographic information is presented in Table 1.

Baseline SF-12 scores in the MEPARI and MEPARI-2 trials ranged from 18.6 to 66.8 with a mean (SD) of 49.8 (8.89). Possible SF-12 mental scores can be as low as 0 and as high as 100, with greater scores representing better mental health-related quality of life. SF-12 mental scores are calculated by an item-weighted algorithm, normed to a mean of 50.0 and a standard deviation of 10.0.[16] In 2001, mean scores (by age group) in the United States were 48.9 (25-34), 48.8 (35-44), 49.9 (45-54), 50.8 (55-64), 51.6 (65-74) and 48.9 (75+).[16]

Figure. SF-12 Mental Score in Relation to Coincidence.



ARI outcomes from the MEPARI and MEPARI-2 studies were as follows. There were 282 ARI illness episodes, with a minimum incidence of 0 and a maximum incidence of 5. The mean (SD) incidence per person was 0.81 (0.91) illnesses. Duration ranged from 0 to 85+ days of ARI illness, with a mean (SD) duration of 7.8 (11.3) days. WURSS-AUC global severity scores ranged from 0 to 8724 with a mean (SD) of 298 (656).

The Figure depicts the relationship between SF-12 mental scores at baseline and the number of subsequent ARI episodes. While the sample size for those with 3 or more illness episodes is limited (n = 17), the trends are consistent and rather striking.

Table 2 depicts Kendall tau rank correlation coefficients for each psychosocial measure with regards to ARI outcomes (incidence, duration, and severity). SF-12 mental scores significantly predicted incidence ($P = 0.037$) but not duration ($P = 0.077$) or severity ($P = 0.073$) of ARI. Though not statistically significant, the relationships between duration and severity with SF-12 mental scores trended in the predicted (negative) direction. The PANAS negative measure significantly correlated with global severity ($P = 0.036$) but not incidence ($P = 0.081$) or duration ($P = 0.125$) of ARI. MAAS scores were significantly associated with incidence ($P = 0.040$) but not duration ($P = 0.053$) or severity ($P = 0.070$) of ARI. The PANAS positive, PSS-10 and PHQ-9 measures did not show significant predictive relationships with any of the ARI outcomes.

DISCUSSION

This paper provides additional support to the previously reported relationship between poor mental health status and ARI outcomes. Of the 6 psychosocial measures analyzed, baseline scores for the SF-12 mental, PANAS negative, and MAAS significantly predicted ARI outcomes in the expected directions. Aside from

the PHQ-9 and the PANAS positive emotion measure, which showed no discernible trends, the correlation coefficients for the 6 psychosocial measures with all 3 ARI outcome measures were in predicted directions. That is, psychosocial measures reflecting better mental health pointed towards fewer, shorter and less severe ARIs, while psychosocial measures reflecting poor mental health were correlated with or trended towards predicting more frequent, longer and more severe ARIs (Table 2).

The relationship between the SF-12 mental health score and ARI incidence depicted in the Figure is especially provocative. Understanding of these associations could be further strengthened with a larger population that included more individuals with 3 or more colds.

Table 2. Predictive Correlations of Mental Health Scores with Acute Respiratory Infection (ARI) Outcomes Using Kendall Tau Rank Correlations

Instrument	Mean (SD)	Incidence: # of ARI illnesses tau (SE)	Duration: # of ARI illness days tau (SE)	Severity: total WURSS global severity score tau (SE)
SF-12 Mental	49.87 (8.83)	**-0.09 (0.04)[a]** **P=0.037**	**-0.07 (0.04)** **P=0.077**	**-0.07 (0.04)** **P=0.073**
PANAS +	35.60 (6.67)	0.00 (0.04) P=0.942	**-0.01 (0.04)** **P=0.802**	0.00 (0.04) 0.989
PANAS -	16.87 (5.84)	**0.07 (0.04)** **P=0.081**	**0.06 (0.04)** **P=0.125**	**0.08 (0.04)[a]** **P=0.037**
PHQ-9	2.82 (2.55)	-0.05 (0.04) P=0.276	-0.01 (0.04) P=0.716	**0.01 (0.04)** **P=0.803**
PSS-10	12.22 (5.63)	**0.01 (0.04)** **P=0.723**	**0.01 (0.04)** **P=0.778)**	**0.03 (0.04** **P=0.392**
MAAS	4.38 (0.78)	**-0.09 (0.04)[a]** **P=0.036**	**-0.08 (0.04)** **P=0.053**	**-0.07 (0.04)** **P=0.070**

Kendall tau rank scores are analogous to correlation coefficients.
[a]Significant association, *P*-value < 0.05
BOLD = expected direction of relationship (positive or negative)
Abbreviations = SF-12, Short Form 12 Health Survey; PANAS, Positive and Negative Affect Schedule; PHQ-9, Patient Health Questionnaire; PSS-10, Perceived Stress Scale; MAAS, Mindful Attention Awareness Scale

Several potential explanations exist regarding the relationship between poor mental health and increased ARI occurrence and severity. To begin, a common risk factor such as negative emotion may increase an individual's susceptibility to both ARI and poor mental health. Previous studies have demonstrated that in individuals vulnerable to depression, increased negative emotion activates dysfunctional thinking and attitudes,[17] which in turn could negatively influence the experience and functional impact of ARI symptoms. Likewise, negative emotion has been shown to interfere with the release of secretory immunoglobulin-A (s-IgA), a primary antibody in the defense against the common cold.[17] Therefore, negative emotion may be a causative or mediating agent in the development of both poor mental health and ARI illness.

It is also quite possible that poor mental health may influence ARI outcomes through health-related behaviors. It is documented that rates of smoking[18] and excessive alcohol consumption[19] are greater among individuals with mental illness. Prior research has shown that such behaviors increase an individual's susceptibility to respiratory infection by subduing the host immune response.[20] Thus, poor mental health may heighten ARI vulnerability by means of health-related behaviors, such as smoking, excessive alcohol consumption, or other mediators that impact immunity or susceptibility to infection.

A third consideration is that individuals with poor mental health may merely report more symptoms. In a previous study, for example, it was noted that individuals with a greater negative emotional style reported more unfounded cold symptoms.[21] The intensive ARI-monitoring and laboratory verification measures in the MEPARI studies (multiplex polymerase chain reaction viral identification, not shown here) argues against this as a sole explanation for the associations observed, but self-report tendencies and potential biases should not be discounted.

Finally, a complex interplay of the above factors, or as yet unknown causal or mediating pathways, might better explain the observed relations between poor mental health and ARI occurrence.

Our data and analyses have both strengths and limitations. Although past research has investigated the impact of specific mental disorders on ARI outcomes, this paper expands current research by examining nonspecific, overall mental health, using validated measures with a prospective cohort study design. Noteworthy was the use of stringent criteria to define and monitor ARI illness episodes. One of the best previous studies was retrospective and relied on 12-month recall of ARI incidence.[3] Also distinct in our work was the daily assessment of ARI severity; research by Cohen and colleagues assessed cold symptoms for up to 9 consecutive days regardless of cold duration,[22] whereas subjects enrolled in the MEPARI and MEPARI-2 trials assessed symptom severity daily from illness onset until 2 days of no reported symptoms, regardless of the actual duration of illness.

An important limitation is the fact that the MEPARI-2 trial is yet ongoing; consequently, this manuscript lacks data pertaining to the final 2 cohorts of the study, an estimated 200 participants. We expect that incorporation of these final 2 cohorts will strengthen our conclusions, as the increased sample size will provide greater statistical power. Furthermore, due to the current nature of the study with group status blinded to investigators, we were unable to analyze the 3 groups (meditation, exercise, and control) separately and, therefore, our data does not take into account potential confounding effects of meditation and exercise.

Having analyzed only baseline mental health indicators, controlling for interventions should not have altered the self-reported mental health scores included in this manuscript, yet the ARI outcomes reported in this paper may have been alleviated by meditation or exercise. As these interventions were assigned randomly and not in relation to mental health, and as any ARI-prevention efforts would reduce the number of illness episodes that mental health indicators could be related to, we do not believe this would invalidate our results.

In addition, the population in this analysis may not be representative of the general adult population. A larger proportion of our study cohort was white (92%), non-Hispanic (96%) and college educated (71.4%) (Table 1) than the general adult population in the United States.[23,24] Thus, it is unclear how these conclusions would translate to other populations.

Finally, despite the significant *P*-values, the Kendall tau rank correlation coefficients were small; the extent to which ARI variability is explained by self-reported mental health scores appears to be limited.

CONCLUSION

In conclusion, using high quality prospective cohort data, we found evidence to support the hypothesis that mental health may influence the occurrence and impact of acute respiratory infection. This is consistent with previous findings, and may have important implications for clinical practice, population health, and public policy. Future studies will be needed to confirm and extend these findings, and to discover ways to reduce impacts of both mental health and respiratory infection.

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