Physical health and mental health functional status during and following hospitalization for an acute respiratory illness

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A B S T R A C T

Background: Influenza is a serious respiratory illness causing thousands of hospitalizations annually. This study used the Short Form 12 (SF-12) to evaluate physical and mental health status during and post hospitalization for an acute respiratory illness (ARI).

Methods: Adults ≥18 years of age enrolled in the Hospitalized Adult Influenza Vaccine Effectiveness Network study – Pittsburgh site in the 2017–2018 and 2018–2019 influenza seasons with an ARI with cough of ≤10 days’ duration were eligible. Enrollees were included regardless of respiratory pathogen identified by respiratory viral panel testing of nasopharyngeal specimens. Respondents completed the SF-12 at enrollment and 3–14 weeks later. Respondents were grouped using discriminant cluster analysis based on SF-12 individual scores and age. Linear regression was used to predict convalescent physical and mental health composite scores.

Results: Of 72 enrollees who completed both surveys, 35 were grouped as the high functioning group (HFG), 12 as the low functioning group (LFG) and 25 as the medium functioning group (MFG). At enrollment, the LFG more frequently reported body aches and confusion, lower pre-illness physical activity levels and other measures of physical function than the HFG (P < 0.016). At approximately 5 weeks post enrollment, the HFG reported significant decrements in most SF-12 individual scores and overall physical health (−4.26 ± 8.1; P = 0.017) and mental health (−5.98 ± 10.5; P = 0.011) composite scores. Changes in mental but not physical composite scores from enrollment to convalescence differed significantly (P = 0.016) between HFG and LFG.

Conclusions: Although their enrollment and convalescent SF-12 scores were higher, HFG reported larger losses in mental function during an ARI hospitalization than groups with lower enrollment SF-12 scores.

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1. Introduction

Over the eight influenza seasons spanning 2010–2011 through 2017–2018, an estimated 140,000 to 960,000 influenza-related hospitalizations and 4.3 million to 23 million influenza-related medical visits occurred annually (Centers for Disease Control and Prevention). While most cases of influenza are self-limited and recovery takes place within 1–2 weeks, previous research has shown that older patients, hospitalized patients, and those with high-risk conditions are typically the most compromised following influenza (Fiore et al., 2013). Moreover, those with acute respiratory distress syndrome requiring intensive care unit (ICU) admission and/or use of extracorporeal membrane oxygenation (ECMO) have residual reduction in function and reduced health-related quality of life (Hodgson et al., 2012).

Measuring functional status following hospitalization or respiratory infection especially in the elderly is not new and resultant declines in functional status have been well documented (Barker et al., 1998). These studies are less common among non-frail, younger adults. A study of working age adults performed in Spain using the European Quality of Life-5 Dimensions (EQ-5D) as a measure of health-related quality of life reported that influenza was associated with a significant reduction in the EQ-5D scores (Pradas et al., 2009). Following the 2009 A/H1N1 pandemic, another study from Spain reported health-related quality of life measured with the EQ-5D pre-, during and post influenza illness among inpatients and outpatients ≥8 years old. EQ-5D scores decreased significantly during illness, but rebounded to pre-illness levels for all groups but outpatient males over age 50 (Hollmann et al., 2013). A more recent, large, case-control analysis from the UK found an increased risk of

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developing depression following an influenza infection (Bornand et al., 2016).

Much of the research on influenza’s impact on health-related quality of life has had an economic focus, measuring quality-adjusted life years or quality-adjusted life days lost, with some studies also reporting the personal cost of influenza in terms of physical and mental health functional status (Van Hoek et al., 2011; Yang et al., 2017; Bilke et al., 2014). Few of these studies have differentiated among the various domains of health-related quality of life. Thus, more information about the short term, residual effects of hospitalization for an acute respiratory illness (ARI) may provide a clearer picture of these relationships.

This study examined physical health and mental health functional status measured with the Short Form 12 (SF-12) among adult inpatients with an ARI, during their hospitalization and 3–14 weeks post hospitalization. The SF-12 is a rapid measure of self-reported physical and mental functioning for a period of up to 4 weeks prior to completion of the survey. Outcomes were compared across a range of pre-illness functional status levels.

2. Materials and methods

This study was conducted with the approval of the University of Pittsburgh Human Research Protection Office on a convenience sample of participants of the Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN) – Pittsburgh site. Methods for the HAIVEN study have been previously published (Balasubramani et al., 2019). Briefly, adults ≥18 years of age who had been hospitalized for <72 h and who had a new onset (≤10 days) ARI or newly worsening cough were eligible for enrollment and provided informed consent. Patients who had received antiviral medication in the 7 days prior to enrollment, were younger than 6 months old, had enrolled in the study during the previous 14 days, or had received influenza vaccine within 14 days of enrollment were not eligible.

Viral infections were confirmed by clinical respiratory viral panels using the Genmark Luminex test from a nasopharyngeal swab collected within 72 h of admission or by real-time reverse transcription polymerase chain reaction tests for influenza and RSV from combined nasal and pharyngeal swabs, using Centers for Disease Control and Prevention standardized protocols, collected ≤10 days from onset of symptoms.

Data on demographics, symptoms and other measures of current health and well-being, general health status, and self-report of influenza vaccination were collected during patient enrollment interviews. High-risk conditions identified by International Classification of Diseases code (Versions 9 and 10 [ICD-9/10]) assigned to a medical encounter during the year prior to enrollment were used to determine the presence of underlying health conditions associated with an increased risk of severe influenza (Jackson et al., 2017; Grohskopf et al., 2015). ICD codes were derived from electronic medical records (EMR). Enrollees who consented at enrollment to providing a stored plasma sample (2017–18) or a blood draw (2018–19) were administered the SF-12 at enrollment and at approximately 3–14 weeks post illness onset, either in person or by mail. The survey specifically asks respondents to think about the past 4 weeks when considering their responses.

2.1. Statistical analyses

SF-12 surveys were scored according to the developer’s instructions, and individual scale scores, as well as physical and mental health composite scores were recorded. The K-means clustering method was used to separate enrollees into groups whose members were as similar as possible based on enrollment SF-12 responses. The variables used in the analysis were first standardized to the same scale with an overall sample mean of zero and a standard deviation of 1 because cluster solutions should not be driven by variables measured on larger scales. Pseudo-random centroids were used because of the small number of observations available to form cluster groupings (n = 72). The number of clusters was determined using three methods: 1) pseudo T-square; 2) pseudo F; and 3) cubic clustering criterion. The values from those methods were plotted and the final cluster decision was based on the elbow curve of the plotted values. To aid in visual interpretation of cluster differences, canonical discriminant analysis was used. The multiple dimensions of the observed data were reduced into two dimensional, scored canonical variables and plotted.

The baseline measures of the three clusters were compared using Chi-square or Wilcoxon tests for discrete measures and one-way ANOVA for continuous measures. Paired t-tests were used to test paired differences for SF-12 individual scores within each cluster; the means of the paired differences across the clusters were tested using analysis of one-way classification (ANOVA) and variance ratio tests (F-tests) for significance. For statistically significant findings of bivariate analyses, post-hoc tests with Bonferroni adjustments for multiple comparisons for pairwise tests were set at P < 0.017. To identify the factors independently associated with the change in physical and mental health composite scores, separate multivariable linear regression models were fitted. A type I error or a P value < 0.05 was used as the threshold for statistical significance.

Data analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

During the 2017–2018 and 2018–2019 influenza seasons, 90 HAIVEN enrollees who completed an enrollment SF-12 were asked to complete a convalescent SF-12. Of those, 72 participants (80%) completed the SF-12 survey at an average of approximately 5 weeks post illness onset (38–44 days). Discriminant analysis based on age and enrollment SF-12 individual scores resulted in three clusters, named the high functioning group (HFG) n = 25, medium functioning group (MFG) n = 35, and low functioning group (LFG) n = 12, as shown in Fig. 1.

Table 1 shows the demographic and health characteristics of participants at enrollment as well as functional status scores at enrollment and convalescence. Post hoc analyses were conducted only on the variables for which significant differences across clusters were identified. Patients in the LFG more often were privately insured, received assistance at home, and reported body aches, confusion, shortness of breath and wheezing at enrollment than the HFG (all P < 0.013). As expected, individual functional status scores differed significantly across groups, as they were the basis for the cluster groupings, with the HFG having overall higher individual and composite scores than the MFG and LFG. Although there were no differences across groups in the proportions of influenza cases and RSV cases, the proportion of influenza/RSV negative patients was significantly greater in the LFG (P = 0.029).

During convalescence, the groups differed significantly on most of the individual functional status scores and on the physical health and mental health composite scores. These differences primarily were observed between the HFG and the LFG. During convalescence, the HFG’s scores were higher than those of the LFG. Notably, there was no difference across groups for the number of days between completion of the enrollment and convalescent SF-12 surveys.

Table 2 shows the differences in individual and composite scores from enrollment to convalescence for the three groups. The HFG had significant decreases in six of the eight individual scores as well as the physical health and mental health composite scores. Whereas, the MFG had significantly higher vitality score (P < 0.01) and significantly lower role-emotional score (P < 0.01) at convalescence and the LFG had a significant increase in vitality (P < 0.05), with no other significant changes over time. Thus, the HFG was experiencing lower physical and mental health functional status a month after enrollment than immediately before their illness and hospitalization, while the MFG and LFG reported little to no change during that time.

In regression analyses shown in Table 3, using change in physical composite score as the outcome variable, none of the predictor variables was significantly related to functional status group. However, change in the mental composite score was significantly, negatively related to being
in the HFG compared with the LFG. That is, a patient hospitalized for an ARI with lowest mental health composite score was likely to experience no change in mental health functional status from enrollment to convalescence while a patient in the group with the highest functional status was more likely to experience a decrease in mental health functional status over the course of illness and recovery. When influenza was removed from the model, being in the HFG was still associated with a decrease in mental health composite score ($P < 0.001$; data not shown).

### 4. Discussion

In a study of adults hospitalized for an acute respiratory illness, discriminant cluster analysis based on individual component scores was used to separate enrollees into three groups classified as high, medium and low functioning, with significantly different mean scores. We found physical health composite scores and mental health composite scores to be below the age and sex adjusted mean for adults (QualityMetric, 2017).

Older, previous research has reported declines in functional status among adults ≥65 years following hospitalization (Fried et al., 1997) or influenza-like illness (Barker et al., 1998). These studies typically measure functional status using activities of daily living or instrumental activities of daily living scales as opposed to more subtle changes in functional status that can be measured among non-dependent individuals. More recent studies among populations of various ages have used the EQ-5D questionnaire (Pradas et al., 2009; Hollmann et al., 2013; Van Hock et al., 2011; Yang et al., 2017; Blicke et al., 2014), which results in responses for self-care, mobility, usual activities, pain/discomfort and anxiety/depression. These studies have used the composite score for comparisons between time points and reported the percent of participants reporting no/some/severe problems for each dimension. The SF-12 scores eight domains – four physical and four mental – and produces both physical health and mental health composite scores. It measures overall and individual factors related to physical and mental health and functional status well before an individual would be unable to live independently, thus making it applicable to younger age groups.

In this study, the highest functioning individuals at enrollment who were hospitalized with an acute respiratory illness retained significantly higher physical health and mental health composite scores at convalescence than either the medium or low functioning groups. However, neither the medium functioning nor lowest functioning group reported a significant change in those composite scores over the course of their illness whereas, the highest functioning group’s scores were significantly lower during convalescence than at enrollment. Similarly, a population-based study from the UK reported increased risk of depression following influenza infection (OR = 1.57, 95% CI = 1.36–1.81) in a population that was >80% working-age adults (Bornand et al., 2016). In contrast, in a study of working-age adults in Spain, participants reported losses in dimensions of health-related quality of life including, ability to perform daily activities or personal care, mobility, pain/discomfort, and anxiety or depression while sick with influenza (Pradas et al., 2009). The largest decrease was observed for ability to perform daily activity (~88%) and the smallest decrease was observed for anxiety or depression (~24%).

As the cause of tens of thousands of hospitalizations and deaths in the U.S. annually, the seriousness of influenza is undeniable. Yet, with a vaccination rate among working age adults of 37% in 2017–18, millions are not vaccinated against influenza (Centers for Disease Control and Prevention, 2018). A frequent reason given for not being vaccinated is not believing that influenza is in fact a serious disease, that is, vaccines are not necessary, influenza can be treated naturally (Nowalk et al., 2019) and perceived risk is low (Wooten et al., 2012; Hofmann et al., 2006). These data show that even high functioning adults who are hospitalized with an ARI experience a loss in mental health functional status that is apparent long after most symptoms would have resolved, over a month after their illness onset. Thus, a hospitalization for influenza or another respiratory infection may have lingering serious consequences. Furthermore, it emphasizes the importance of vaccination to prevent influenza, a primary cause of ARI.

#### 4.1. Strengths and limitations

One of the limitations of using the K-means clustering method is that it is typically not recommended for samples with fewer than 100 observations. To overcome this limitation, we replaced the initial centroid selection with pseudo random centroids, by randomly selecting the mean of a variable for the observations in the cluster. A second limitation was...
Table 1
Demographic and health characteristics of all participants with acute respiratory infection at enrollment (N = 72).

| Variable | High functioning N = 35 | Medium functioning N = 25 | Low functioning N = 12 | P value Overall | P values for cluster comparisons |
|----------|-------------------------|---------------------------|------------------------|-----------------|-------------------------------|
| Age, years, mean (SD) | 55.1 (16.5) | 60.7 (14.1) | 50.3 (7.3) | 0.309 | - - - - |
| Female sex, ref. = male, n (%) | 20 (57.1) | 18 (78.3) | 9 (75.0) | 0.201 | - - - - |
| Non-white race, ref. = white, n (%) | 15 (42.9) | 8 (32.0) | 8 (66.7) | 0.137 | - - - - |
| Private insurance, ref. = public, n (%) | 14 (41.2) | 13 (52.0) | 10 (83.3) | 0.043 | 0.410 0.066 0.012 |
| Vaccinated against influenza, ref. = not vaccinated, n (%) | 25 (71.4) | 20 (80.0) | 7 (58.3) | 0.383 | - - - - |
| Able to live independently, n (%) | 10 (28.6) | 9 (36.0) | 6 (50.0) | 0.399 | - - - - |
| Receives assistance at home, n (%) | 2 (6.1) | 5 (21.7) | 5 (41.7) | 0.018 | 0.081 0.216 0.004 |

Symptoms at enrollment

| Bodily pain | 70.7 (30.6) | 50.0 (33.9) | 35.4 (32.8) | 0.002 | 0.013 0.001 0.000 |
| Bodily pain | 85.4 (12.3) | 59.5 (23.7) | 41.7 (27.9) | 0.008 | 0.074 0.121 0.002 |
| Role-emotional | 94.6 (11.9) | 84.5 (20.8) | 37.5 (32.0) | 0.008 | 0.074 0.121 0.002 |
| Social functioning | 75.0 (27.8) | 58.0 (29.5) | 35.4 (32.0) | 0.008 | 0.074 0.121 0.002 |
| Physical functioning | 74.3 (30.4) | 48.0 (40.8) | 16.7 (22.2) | 0.000 | 0.009 0.005 0.001 |
| Role-physical | 79.6 (19.7) | 40.5 (27.1) | 18.8 (28.9) | 0.000 | 0.001 0.003 0.000 |
| Bodily pain | 90.7 (17.2) | 48.0 (33.8) | 20.8 (20.9) | 0.000 | 0.001 0.001 0.001 |
| General health | 55.4 (26.8) | 49.8 (27.6) | 14.6 (12.9) | 0.000 | 0.043 0.001 0.001 |
| Vitality | 56.4 (16.4) | 12.0 (17.9) | 10.4 (16.7) | 0.000 | 0.001 0.001 0.001 |
| Social functioning | 88.6 (16.4) | 56.0 (34.1) | 16.7 (16.3) | 0.000 | 0.001 0.001 0.001 |
| Role-emotional | 94.6 (11.9) | 84.5 (20.8) | 37.5 (32.0) | 0.000 | 0.035 0.001 0.001 |
| Mental health | 85.4 (12.3) | 59.5 (23.7) | 41.7 (27.9) | 0.000 | 0.001 0.001 0.001 |
| Physical health composite | 47.7 (7.5) | 37.1 (11.5) | 29.4 (5.9) | 0.000 | 0.001 0.001 0.001 |
| Mental health composite | 56.3 (5.1) | 46.6 (9.9) | 34.6 (9.6) | 0.000 | 0.001 0.001 0.001 |

Table 2
Differences in SF-12 scores from Enrollment to Convalescence (N = 72).

| Variable | High functioning N = 35 | Medium functioning N = 25 | Low functioning N = 12 | P value Overall | P values for cluster comparisons |
|----------|-------------------------|---------------------------|------------------------|-----------------|-------------------------------|
| Physical functioning | -16.4 (6.1)* | -15.0 (8.7) | 10.4 (13.2) | 0.126 | - - - - |
| Role-physical | -21.1 (5.0)** | 0 (7.5) | 8.3 (9.4) | 0.010 | 0.019 0.516 0.006 |
| Bodily pain | -20.0 (4.6)** | 2.0 (7.1) | 14.6 (10.0) | 0.002 | 0.008 0.313 0.001 |
| General health | 0.6 (3.7) | -9.2 (5.5) | 12.9 (6.7) | 0.037 | 0.134 0.022 0.108 |
| Vitality | -10.7 (5.5) | 22 (6.7)** | 20.8 (9.1)** | 0.001 | 0.001 0.020 0.010 |
| Social functioning | -13.6 (5.4)** | 2.0 (6.9) | 18.8 (9.8) | 0.013 | 0.076 0.174 0.004 |
| Role-emotional | -20.0 (4.6)** | -29.0 (8.1)** | -2.1 (13.0) | 0.335 | - - - - |
| Mental health | -13.6 (3.7)** | 4.7 (5.2) | 13.5 (10.1) | 0.003 | 0.005 0.393 0.025 |
| Physical health | -4.0 (1.2)** | -0.6 (2.3) | 4.3 (2.6) | 0.024 | 0.198 0.191 0.003 |
| Mental health composite | -6.2 (1.9)** | -1.1 (2.2) | 4.7 (4.6) | 0.024 | 0.090 0.207 0.013 |
the small sample size and limited duration. Thirdly, the persistence of this reported diminution of mental status beyond 3–14 weeks post illness onset is not known. More data are needed with a larger sample of inpatients, diverse locations, and repeated assessments to determine at what point the scores return to enrollment levels. Future studies could also include outpatients to determine if similar changes in SF-12 scores are observed in those with less severe illness. Finally, the mechanism for the observed changes in mental status among these ARI patients is unknown.

5. Conclusions

Subtle losses in mental health status may occur as a result of hospitalization for acute respiratory illnesses including influenza, even among high functioning individuals. In addition to the economic cost of lost productivity and direct medical care, losses of health-related quality of life may increase the burden of influenza.

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