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High healthcare utilization near the onset of medically unexplained symptoms

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Objective: Patients with medically unexplained syndromes (MUS) often do not receive appropriate healthcare. A critical time for effective healthcare is the inception of MUS. The current study examined data from a prospective longitudinal study of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) veterans to understand the relationship of increasing physical symptom burden to healthcare utilization.

Methods: Data was examined from a prospective study of OEF/OIF veterans assessed before and one year after deployment ($n=335$). Physical symptom burden was measured with the Patient Health Questionnaire (PHQ-15). Analyses were conducted with polynomial regression and response surface analysis (RSA).

Results: Increases in physical symptom burden predicted greater healthcare utilization one year after deployment: primary care practitioner (slope = -0.26 , $F=4.07$, $p=0.04$), specialist (slope = -0.43 , $t=8.67$, $p=0.003$), allied health therapy (e.g., physical therapy) (slope = -0.41 , $t=5.71$, $p=0.02$) and mental health (slope = -0.32 , $F=4.04$, $p=0.05$). There were no significant difference in utilization between those with consistently high levels and those with increases in physical symptom burden.

Conclusion: This is the first prospective study to examine, and show, a relationship between onset of clinically significant physical symptoms and greater healthcare utilization. Our data

suggest that patients with increasing physical symptom burden have the same level of healthcare as patients with chronic physical symptom burden. Needed next steps are to better understand the quality of care at inception and determine how to intervene so that recommended approaches to care are provided from the onset.

Keywords: Medically unexplained symptoms; healthcare utilization; care seeking; veterans; deployment

An estimated 20% of primary care patients present with medically unexplained syndromes or chronic symptom disorders (e.g., fibromyalgia, chronic fatigue syndrome)(1-5). We use the term MUS as umbrella term to refer to conditions defined by multiple chronic physical symptoms not better defined by another disorder; for a discussion of terminology around MUS see (2, 6-9). Despite the name, MUS can be partially explained by a complex interaction of physiological and psychological factors (4). MUS causes disability that is as severe, or worse than, the disability of medically known conditions (e.g., cancer (10, 11)).

Further exacerbating the burden of MUS, patients with MUS often do not receive appropriate healthcare. They have up to double the annual healthcare costs and utilization as compared to patients without MUS (12). This healthcare is typically focused on trying to identify the cause of the symptoms (13-17) leading to extensive diagnostic testing, hospitalizations, inappropriate prescription of opioids (12-19) and care that is not patient-centered (20, 21). In contrast, recommended approaches to care for patients with MUS focus on patient-centered management of symptoms including: (1) a primary care provider evaluating the symptoms; (2) regular visits with the primary care provider to reduce emergency and unnecessary care; and (3) use of non-pharmaceutical, evidence-based treatments such as cognitive behavioral therapy as a first line approach (22-30).

Considering the vicious cycle of symptom occurrence, inactivity, deconditioning, and then worsening of symptoms and disability, a critical time for effective healthcare is at the inception of MUS (31, 32). Despite this, no study has followed patients at the development of

MUS to understand when healthcare utilization increases and what types of healthcare are received at the onset. One reason for this knowledge gap is that it is difficult to identify who will develop MUS (32). Combat exposure is, however, a known risk factor for developing MUS and an estimated 30% of combat veterans will develop chronic MUS (33-35). We used data from an existing study which assessed combat veterans prospectively from before to after deployment to help us understand the frequency and type of health care utilization that occurs early in the development of MUS.

While no study has prospectively looked at the relationship between onset of MUS and healthcare utilization, there are reasons to hypothesize that healthcare utilization increases immediately. Cross-sectional evidence finds a linear relationship between physical symptom burden and greater healthcare utilization (12). Studies of the development of MUS recruit patients using healthcare, suggesting that patients are seeking healthcare at the onset (14, 36, 37). *Thus, our primary hypothesis is that there will be an association between increases in physical symptom burden (from before to one year after deployment) and greater healthcare utilization one year after deployment.*

Increases in healthcare utilization may continue to increase over the duration of MUS. Two prospective studies of patients with long-standing MUS found healthcare utilization increased over time (38, 39). Further, a cross-sectional study of unexplained symptoms near the onset of symptoms, found a relationship between greater duration and increased healthcare utilization (40). *Thus, our second hypothesis is that healthcare utilization increases with duration of MUS. Specifically, veterans who report consistently high physical symptom burden (before and after deployment) will report more healthcare utilization one year after deployment as compared to veterans who reported an increase in physical symptom burden (new onset MUS).*

To test these hypotheses, we used data from a prospective study of Operation Enduring Freedom and Operation Iraqi Freedom soldiers assessed before and one year after deployment. Physical symptom burden was measured with the Patient Health Questionnaire

(PHQ-15), which has been used to screen for clinically significant levels of MUS [35]. Analyses were conducted with polynomial regression and response surface analysis (RSA) which allowed us to test the relationships in three dimensions and assess the influence of differing degrees of change in symptom burden on healthcare utilization.

Methods

Participants

The HEROES project recruited Army National Guard and/or Reserve soldiers prior to deployment to Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) from 2005-2008. Soldiers were approached during their standard preparation for deployment (for description see (35, 41-43)). Soldiers between 18 and 60 were invited to participate. Based on their influence on physical symptoms, exclusion criteria included (a) self-reported bipolar disorder, major depression, or schizophrenia, (b) high blood pressure, (c) certain medication, or (d) pregnancy. At the start of the study, 795 participants were eligible; 28 soldiers were excluded from analysis because they (a) ultimately were not deployed, (b) were officers, or (c) were killed in action.

Procedure

All study materials and procedures were reviewed by relevant institutional review boards and research development committees. Responses to questionnaires were collected across four phases: (1) before deployment, (2) immediately upon return from deployment, (3) three-months after deployment, and (4) one-year after deployment. Before deployment and immediately after deployment, questionnaires were administered in-person on base or through the mail. Questionnaires were administered and collected through mail for the other phases. The current data analysis was from the before deployment ($n=767$) and one year after deployment ($n=336$) time points.

Measures

Patient Health Questionnaire-15. Participants completed the PHQ-15 which asks how burdened they were by physical symptoms over the past fourteen days. Each item was measured on a scale from 0 = *not bothered at all* to 2 = *bothered a lot*. Burden was assessed using established threshold: above 15 was high, 10 to 14 was medium, 5 to 9 was low, and 0 to 4 was no/mild (44). We used the pre-determined physical symptom cut-offs as this allows interpretation between clinically significant (MUS; medium and high) and clinically non-significant (no-MUS; no/mild and low) levels of physical symptom burden and reduced the influence of outliers in our three dimensional graphs. The PHQ-15 is a screening instrument for MUS; the measure does not distinguish between medically explained and unexplained symptoms. The PHQ-15 had an internal consistency of $\alpha=.75$ before deployment and $\alpha=.69$ one year after deployment in our sample.

Healthcare Utilization. Healthcare utilization questions were adapted from the National Health Interview Survey (45, 46). Items asked about healthcare utilization in the past year including primary care practitioner, specialty care, allied health therapy (e.g., physical therapy, occupational therapy) and mental health. Before deployment, veterans were asked if they had seen any specialist. At one year after deployment, veterans were asked how many times they had seen a gastroenterologist, pulmonologist, rheumatologist, neurologist or other specialist; these items were added together for a total specialist score. Before deployment, the utilization questions asked if the patient had received each type of care (yes/no) and there was one question that asked how many medical appointments they had in the past year. At one year after deployment, veterans were asked if they had received each type of care and how many times they had received each type of care in the past year. To address the positive skew of the count items, after data collection these were transformed into a Likert scale consistent with the National Health Interview Survey (0, 1, 2-3, 4-9, 10 and above visits).

Analysis

Paired t-tests and McNemar Related-Samples Test were conducted to examine if physical symptoms and healthcare utilization increased from before to after deployment, a premise of our first hypothesis. A MANOVA was used to determine the cross-sectional relationship between level of physical symptom burden at one year after deployment and each of the four types of healthcare utilization.

Hypothesis 1: Increases in physical symptom burden (from before to one year after deployment) would be related to greater healthcare utilization one year after deployment.

Polynomial regression and response surface analysis (RSA) (47-49) were used to examine if changes in physical symptom burden were related to healthcare utilization at one year after deployment. The advantage of polynomial regression and RSA is that the relationships are represented in three dimensions as can be seen in Figure 1 (48-51). This allows us to tell the influence of *differing levels of change and different direction of change* in symptom burden on healthcare utilization, for different starting values of symptom burden. These nuances would not be possible if one were to test a difference-score between before and after deployment physical symptom burden as a single predictor or if one were to create artificial groups of veterans based on their change in symptom burden.

There are multiple steps to a polynomial regression analysis. In the first step, a linear polynomial model is created with centered independent variables (X =before deployment symptom burden and Y =after deployment symptom burden) that predict the outcome (Z =after deployment healthcare utilization). For the second step, a quadratic polynomial model is created. This model includes X^2 , XY , and Y^2 . The third step a polynomial model is constructed, including X^3 , XY^2 , X^2Y , Y^3 . When the cubic model (third step) is significant, a quartic model (fourth step) is tested. The interpreted step is the last step where the change in R^2 is statistically significant (see Table 4).

The polynomial and RSA analyses for this study controlled for frequency of receiving any healthcare before deployment. The three dimensional graph can only have three variables. To allow us to control for healthcare utilization before deployment, we regressed the control variable (healthcare utilization before deployment) on each dependent variable and saved the unstandardized residual. We then conducted the polynomial regression analysis using the each of these unstandardized residuals as the dependent variables. The regression coefficients of the final model were used to conduct the RSA analyses (48, 49, 51).

Figure 1 shows the RSA. The Z-axis (vertical) is the dependent variable, frequency of health care utilization, the X-axis is before deployment symptom burden and the Y-axis is after deployment symptom burden. A visual inspection of the graph shows the level of healthcare utilization at different combinations of before and after deployment symptom burden. To interpret the graph, it is useful to look at the surface along the line of congruence, which is when $X=Y$ or when before symptoms are the same as after symptoms (solid perpendicular line in Figure 1a); and the surface along the line of incongruence, which is when $X+Y=0$ or before and after deployment symptoms are different from each other (dashed perpendicular line in Figure 1a). The line of incongruence is conceptually the same as testing the difference score (after minus before deployment symptom burden) as a predictor of the outcome. Descriptions of polynomial regression and RSA can be found in (48-51).

For Hypothesis 1, we were interested in the slope of the surface along the line of incongruence. The slope of this line tells us: (a) if healthcare utilization was greater when symptom burden increased, (b) if healthcare utilization was greater when symptom burden decreased, or (c) if there was no relationship between change in symptom burden and healthcare utilization. We hypothesized a negative slope, which would indicate that healthcare utilization was greater when symptom burden increased from before to after deployment. We also examined if there was curvature (if quadratic) of the surface along the line of incongruence. This curvature would indicate that the relationship between change in symptoms and healthcare

utilization was not linear, meaning that the association between change in symptoms and healthcare utilization was different at the ends of the line of incongruence as compared to the center of the line of incongruence.

We next examined the slope of the surface along the line of congruence to understand if healthcare utilization was greater when before and after symptom burden were both high as compared to when both were low. Finally, we examined if there was curvature (if quadratic) of the surface along the line of congruence which would indicate that the relationship of consistently high or low symptom burden and healthcare utilization was not linear, meaning that the relationship between symptoms and healthcare utilization was different when symptoms were consistently high as compared to constantly low.

Hypothesis 2: Veterans who reported consistently high physical symptom burden both before and after deployment would report more healthcare utilization one year after deployment as compared to veterans who reported an increase in physical symptom burden.

This was first determined by visual examination of the three dimensional graph (See Figure 1a-1d). We next compared the healthcare utilization of veterans who had high levels of physical symptoms at before and after deployment (high/high; defined as medium to high physical symptom burden at both times) to veterans who had low physical symptoms at before and after deployment (low/low; defined as no/mild to low physical symptom burden at both times) to veterans who reported low symptoms (defined as no/mild to low physical symptom burden) at before deployment to high (defined as medium to high physical symptom burden) one year after deployment (low/high). A MANCOVA was conducted to determine if there were significant differences between the groups in each of the four types of healthcare utilization controlling for before deployment levels of healthcare utilization. Unlike the polynomial regression, Veterans were split into groups (high/high, low/low, low/high) for a direct comparison of the average levels of utilization between these groups. The ANCOVAs report the effect size

eta-squared which is the proportion of variance for which the dependent variable accounted and Pillai's Trace which is a test statistic.

Results

The majority of participants were male ($n=288$, 86%), white ($n=277$, 82.4%) with a mean age of 30.2 ($SD=9.1$). Participants who completed the one-year assessment post-deployment (compared to those who did not) were older and more likely to be male, and trend towards reporting more healthcare utilization at baseline (1.1 vs. .9; $p=.07$); there were no differences in physical symptom burden.

There was an average increase in physical symptom burden from before to one year after deployment (Table 1; $t=8.13$, $p<.001$). There was also an average increase in healthcare utilization (Table 2; All four of the McNemar Related-Samples Test, $p<.05$).

Consistent with previous research, preliminary analysis using MANOVA showed a cross-sectional relationship between greater physical symptom burden one year after deployment and greater healthcare utilization (primary care practitioner, specialist, therapy, mental health care) one year after deployment (Table 3; Pillai's Trace=.18, $F(12, 939)=5.12$, $p<.001$, Eta Squared=.06). The separate univariate ANOVAs showed a significant cross-sectional relationship between greater level of physical symptom burden and more frequent visits to a primary care ($F(3, 314)=15.6$, $p<.001$, Eta Squared=.13), specialist ($F(3, 314)=6.95$, $p<.001$, Eta Squared=.06), allied health therapist ($F(3, 314)=3.57$, $p<.01$, Eta Squared=.03) and mental health services ($F(3, 314)=12.57$, $p<.001$, Eta Squared=.11).

Hypothesis 1: Increases in physical symptom burden (from before to one year after deployment) would be related to greater healthcare utilization one year after deployment.

Primary Care Practitioner. The linear model was the final model of the polynomial regression analysis (R^2 change =0.05, $p<.001$; Figure 1a, Table 4) which is interpreted as

follows. In support of the hypothesis, there was greater utilization of a primary care practitioner when physical symptom burden increased (from before to after deployment) as compared to when physical symptom burden decreased; the slope of the surface along the line of incongruence was significant and negative (slope = -0.26, $F=4.07$, $p=0.04$). There was also greater utilization of a primary care practitioner when physical symptoms burden was consistently high as compared to when physical symptom burden was consistently low; the slope of the surface along the line of congruence (when physical symptoms were equal at before and after deployment) was positive and significantly greater than zero (slope = 0.25, $F=7.97$, $p<.01$).

Specialist Care. The cubic model was the final model (R^2 change=0.06, $p<.001$; Table 4) which is interpreted as follows. There was greater utilization of a specialist when physical symptom burden increased (from before to after deployment) compared to when physical symptom burden decreased; the slope of the surface along the line of incongruence was significant and negative (slope=-.43, $t=8.67$, $p=0.003$). Greater increases in physical symptom burden (towards the end of the line of incongruence) were associated with much greater utilization of specialist care; this is indicated by a significant curvature of the surface along the line of incongruence (curvature=0.71, $F=13.86$, $p<.001$). Similarly, when there were high levels of physical symptom burden at both before and after deployment (line of congruence) there was much greater utilization of specialist care; this is indicated by a positive and significant curvature of the surface along the line of congruence (curvature=0.32, $F=10.14$, $p=0.002$). The interpretation of the cubic component of the model is the same as described above, except that, as indicated in the Figure 1b, utilization was lowest in the middle of the surface (for closer-to-average levels of before and after symptom burden) than at the extremes.

Allied Health Therapy. The quadratic model was the final model of the polynomial regression analysis for allied health therapy utilization (R^2 change =0.024, $p=.04$; Figure 1c, Table 4) which is interpreted as follows. There was greater utilization of a therapist (e.g.,

physical therapist) when physical symptom burden increased (from before to after deployment) compared to when physical symptom burden decreased (see Figure 1c); the slope of the surface along the line of incongruence was significant and negative (slope=-.41, $t=5.71$, $p=0.02$). Greater increases in physical symptom burden was associated with much greater allied health utilization as compared to lower increases in physical symptom burden which were associated with lower allied health utilization; this is indicated by significant curvature of the surface along the line of incongruence (curvature=0.52, $F=5.40$, $p=0.021$). Finally, those with high levels of symptom burden at before and after deployment used therapy significantly more than those with low levels of symptom burden at before and after deployment; the slope of the surface along the line of congruence (when physical symptom burden before and after deployment were equal) was positive and significantly greater than zero (slope=0.26, $F=4.42$, $p=0.04$).

Mental Health. The polynomial regression analysis for mental health utilization showed the linear model was the final model (R^2 change =0.096, $p<.001$; Figure 1d, Table 4), which is interpreted as follows. There was greater utilization of mental health when physical symptom burden increased (from before to after deployment) as compared to when physical symptom burden decreased; the slope of the surface along the line of incongruence was significant and negative (slope=-.32, $F=4.04$, $p=0.05$). Those with high level of symptom burden at before and after deployment used mental health services significantly more than those with low level of symptom burden at before and after deployment; the slope of the surface along the line of congruence (when physical symptom burden before and after deployment were equal) was positive and significantly greater than zero (slope=0.49, $F=20.86$, $p<.001$).

Hypothesis 2: Veterans who report greater physical symptom burden both before and after deployment, will report more healthcare utilization one year after deployment compared to veterans who report an increase in physical symptom burden.

Visual inspection of the graphs of specialty care, allied health therapy and mental health (Figure 1a-d) suggest that for veterans with the highest levels of physical symptom burden, healthcare utilization may be higher for those with consistently high levels of physical symptom burden as compared to those who experience an increase in physical symptom burden. This is consistent with hypothesis two.

We conducted a MANCOVA to further test this hypothesis, which did not support hypothesis two (Table 5). As described below, while the overall model was significant, there were no main effects differences in healthcare utilization between veterans who had an increase in physical symptom burden as compared to veterans with consistently high physical symptom burden.

To conduct the MANCOVA, we split veterans into three groups, veterans who had consistently high levels of physical symptom burden (high/high) and veterans who increased their physical symptom burden (low/high) and veterans who had consistently low levels of physical symptom burden (low/low). The overall MANCOVA found the level of physical symptom burden change (low/low, low/high, high/high) was significantly related to healthcare utilization one year after deployment (Table 5 Pillai's Trace=.10, $F(8, 616)=3.91$, $p<.001$, Eta Squared=.05). There was an association between physical symptom burden change (low/low, low/high, high/high) and greater utilization for primary care practitioner ($F(2, 314)=4.09$, $p=.02$, Eta Squared=.03), specialty physician ($F(2, 314)=6.62$, $p<.01$, Eta Squared=.04), allied health therapy (e.g., physical therapy; $F(2, 314)=5.74$, $p<.01$, Eta Squared=.04) and mental health services ($F(2, 314)=10.49$, $p<.001$, Eta Squared=.06).

Comparing the main effects, there were no significant differences between veterans with low/high or high/high levels of physical symptoms burden, which was not supportive of hypothesis two. Veterans with low/low physical symptom burden had significantly less healthcare utilization as compared to veterans with low/high or high/high levels of physical symptom burden.

Discussion

The onset of medically unexplained physical syndromes (MUS) is a critical time for effective healthcare. Early intervention can lead to management approaches that improve disability and symptoms in the long-term. Despite this, no study has observed individuals from before to after the development of physical symptoms to understand early healthcare utilization. The current study examined data from a prospective longitudinal study of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) veterans to understand the relationship of increasing physical symptom burden to healthcare utilization.

A premise of our hypotheses was that veterans would have significant increases in physical symptom burden from before to after deployment; this was supported. Before deployment, 14% of veterans reported levels of physical symptoms burden that was likely clinically significant. After deployment, this number rose to 33%. This increase is consistent with previous studies which find approximately 30% of combat veterans report clinically significant MUS (33, 35, 52). This study captured MUS with the PHQ-15 where 'medium' to 'high' levels of MUS were considered clinically significant.

Increases in physical symptom burden predicted healthcare utilization one year after deployment. This was true for all four types of healthcare utilization: primary care, specialist, allied health therapy (e.g., physical therapy) and mental health. To our knowledge this is the first study to show a relationship between onset of physical symptom burden and greater utilization of multiple types of healthcare. Importantly, all these analyses controlled for frequency of healthcare utilization before deployment; controlling for baseline levels of utilization controlled for the variance accounted for by the individual tendency to seek healthcare. This suggests the results are not due to some veterans being simply more likely to seek healthcare.

Veterans with high levels of physical symptom burden after deployment show patterns of utilization that is both consistent and inconsistent with current recommendations. With the

Veterans Health Administration's (VHA's) move to primary care homes, primary care practitioners are more than ever expected to organize care in collaboration with a team of healthcare professionals (e.g., psychologists, physical therapists). In this setting, veterans with MUS would ideally receive more frequent care from their primary care, mental health and allied health providers, who deliver treatments with the strongest evidence (e.g., cognitive behavioral therapy). This study demonstrates guideline congruent increases in primary, mental health, and allied health care.

Clinical practice guidelines also suggest that specialist care be saved for exclusionary testing or second opinions. In this study, however, the slopes of incongruence (relationships between increasing physical symptoms and healthcare utilization) were strongest for specialty care and allied health therapy (.43 and .42 respectively) and lower for primary care practitioner and mental health care (.25 and .32 respectively). The graphs for specialty and allied health therapy also were more complex (i.e., curvature) as compared to primary care and mental health care (i.e., linear) which should be explored in future studies. The relationship between greater specialist care and increases in physical symptom burden suggests that veterans with high levels of physical symptom burden are receiving a significant portion of their care from specialists, which is inconsistent with recommendations. Further, while it is encouraging that veterans are using mental and allied health care, they made, on average, one visit a year which is not typically an effective dose of this care.

The hypothesis that veterans with consistent high levels of physical symptom burden would have greater utilization as compared to veterans who are first developing high levels of physical symptom burden was not supported with the MANCOVA. Patients with MUS receive up to double the levels of healthcare utilization and costs as compared to patients with known medical conditions (12, 18, 19). Our findings suggest that inappropriate healthcare could be occurring from the start. It is also possible that our comparison group of veterans with consistent

levels of high physical symptoms is not representative of patients with chronic MUS. Veterans who had high levels of physical symptoms before deployment may be healthier than civilians their age with MUS, as they were healthy enough to deploy and their healthcare utilization was not extremely high (Table 5). Alternatively, they may have been not healthier than civilians with chronic MUS, but deployed out of an obligation to their units.

While our MANCOVA results did not show significant difference between those with consistently high levels of physical symptoms (n=83) and those with increases in physical symptom burden (n=29), the graphs suggest that there may be non-significant differences for veterans with the most severe physical symptoms. As there were only 13 veterans with the highest levels of physical symptom burden after deployment we were not able to test this statistically. Future research with a larger population is needed to test this possibility.

A limitation of our study was not having a physician diagnosis of MUS. The PHQ-15 is a common screening measure of MUS. The PHQ-15 does not differentiate between medically explained and unexplained symptoms. This is consistent with current evidence that greater symptom burden is impairing regardless of the cause (2, 53) and has led to calls to change the term from MUS to physical symptom disorder or chronic multisymptom illness, among others (6, 8, 54). As there is not yet consensus on the best terminology, we used MUS to be consistent with the current literature. Other terms (6, 8, 54), better reflect the actual phenomena and what is captured by the PHQ-15, although are less frequently used in the literature. Regardless of terminology, physician diagnosis would help us understand if these symptoms were clinically relevant.

This study also did not capture the quality of care. It is unknown if veterans were receiving appropriate treatments (e.g., Cognitive-Behavioral Therapy) or less appropriate treatments (e.g., opioids). It is also unknown if veterans receive patient-centered care at the onset of MUS. Qualitative research finds some providers think treating MUS is difficult, which can lead to frustration with the patient (55).

The use of a military sample is a strength and limitation. Because combat deployment is a risk factor for developing MUS, observing soldiers before and after combat allowed us to prospectively observe participants as they developed significant physical symptom burden. Further, because MUS impacts 30% of combat veterans, this is an important population for whom to improve the management of MUS. We do not, however, know the generalizability of the results to a civilian population and the changes to mailing addresses and telephone numbers that occur from before to after deployment contributed to our high attrition rate.

In summary, this is the first prospective study to examine, and show, a relationship between onset of clinically significant physical symptoms (MUS) and greater healthcare utilization. Our data also suggest that patients with new onset physical symptom burden have the same levels of healthcare utilization as patients with chronic physical symptom burden. Effective healthcare can improve the management of MUS and in the long-term reduce disability and physical symptoms. Next steps are to better understand the quality of care at inception and determine how to intervene so that recommended approaches to care are provided from the start.

Table 1: Number of participants with each level of physical symptom burden (measured with the PHQ-15) before deployment and one year after deployment (n=336).

	No/mild sx	Low sx	Medium sx	High sx	Total Before
	1 Yr After Deploy	1 Yr After Deploy	1 Yr After Deploy	1 Yr After Deploy	Deployment
No/mild sx	88	45	24	14	171 (50.9%)
Before Deploy					
Low sx	26	47	35	10	118 (35.1%)
Before Deploy					
Medium sx	3	15	14	9	41 (12.2%)
Before Deploy					
High sx	0	0	2	4	6 (1.8%)
Before Deploy					
Total 1 Yr. After	117 (34.8%)	107 (31.8%)	75 (22.3%)	37 (11.0%)	
Deploy					

Deploy=Deployment, Sx=Symptoms, Yr=Year

Table 2: Number endorsing healthcare utilization before deployment and one year after deployment (n=318).

	Before Deployment	One Year After Deployment ^a
Primary Care	144 (44.0%)	217 (68.0%)
Specialist*	33 (10.1%)	100 (31.1%)
Allied Health	35 (10.6%)	82 (25.9%)
Mental Health	28 (8.5%)	113 (35.4%)

*Before deployment soldiers were asked if they had seen any specialist. At 1 year after deployment they were asked how many times they had seen a gastrologist, pulmonologist, rheumatologist, neurologist or other specialist, these items were added together for a total specialist score. ^aThere was an average increase in healthcare utilization; a McNemar Related-Samples Test for each type of healthcare utilization was significant, $p < .05$.

Table 3: Cross-sectional relationship of Physical Symptoms to Healthcare Utilization one year after deployment (% who self-reporting attending healthcare utilization; n=318).

	No/Mild Sx.	Low Sx.	Medium Sx.	High Sx.
Primary care	60.7%	72.7%	73.3%	65.6%
Specialist	18.8%	35.4%	30.7%	62.5%
Allied Health	10.8%	33.0%	29.3%	46.9%
Mental Health	21.4%	36.4%	42.7%	62.5%

Sx.=symptoms

Table 4: Polynomial regression analyses of differing degrees of change in physical symptoms (from before to one year after deployment) predicting healthcare utilization one year after deployment (n=315).^a

		Primary care Practitioner		Specialist		Mental Health		Allied Health Therapist	
		B (SE)	ΔR^2	B (SE)	ΔR^2	B (SE)	ΔR^2	B(SE)	ΔR^2
Step 1	Healthcare utilization (before)	.14 (.06)*	.02*	.09 (.61)	.01	.06 (.08)	.00	.11 (.07)	.01
Step 2	Healthcare utilization (before)	.13 (.06)*	.05*	.08 (.06)	.10*	.03 (.07)	.10*	.08 (.07)	.09*
	PHQ-15 (before)	-.00 (.09)		-.04 (.09)		.09 (.11)		.08 (.10)	
	PHQ-15 (after)	.26 (.07)*		.36 (.06)*		.41 (.08)*		.35 (.08)*	
Step 3	Healthcare utilization (before)		.01	.06 (.06)	.05*		.02	.07 (.07)	.02*
	PHQ-15 (before)			-.16 (.10)				-.07 (.12)	
	PHQ-15 (after)			.26 (.07)*				.33 (.09)*	
	PHQ-15 (before) ²			.38 (.11)*				.38 (.13)*	
	PHQ-15(before)			-.20 (.09)*				-.18 (.11)	
	PHQ-15(after)			.14(.07)				-.02 (.08)	
Step 4 [^]			.02		.05*		.01		.02

^aThe regression coefficients are not directly interpretable but are used to calculate the lines of congruence (when symptoms are the same at baseline and one year after deployment) and incongruence (when symptoms are different at baseline and one year after deployment). The slopes and curvatures of these calculated lines are in the results section, *p<.05, B=unstandardized regression weight, SE=standard error, ΔR^2 =change in R^2 for each step - the change is incremental and the total R^2 increases with each

step, before=before deployment, after=one year after deployment, PHQ-15=physical symptoms, ^Step 4 included step 1-3 variables, PHQ_15 (before)² interaction with PHQ_15(after), PHQ_15 (after)² interaction with PHQ_15 (after), PHQ_15 (before)³ and PHQ_15 (after)³. The beta weights of Step 4 are not directly interpretable and therefore not reported but are available upon request.

Table 5: Relationship of level of physical symptom change (from before to one year after deployment) to frequency* of healthcare utilization one year after deployment; mean* (standard error) (n=316).

	Low/Low	Low/High	High/High
Primary care Practitioner	1.17 (.08)	1.56 (.13) ^a	1.52 (.21) ^a
Specialist	.49 (.08)	.88 (.12) ^a	1.13 (.21) ^a
Allied Health Therapy	.50 (.09)	.99 (.14) ^a	1.05 (.24) ^a
Mental Health	.66 (.10)	1.43 (.15) ^a	1.36 (.26) ^a

*=likert scale of number of visits in the past year where 0=0 visits, 1=1 visit and 2=2-3 visits, 3=4-9 visits, and 4=10 or more visits, Low/Low= no/mild to low physical symptoms before deployment to no/mild to low physical symptoms one year after deployment; Low/High=no/mild to low physical symptoms before deployment to medium to high physical symptoms one year after deployment; High/High=Medium to high physical symptoms before deployment to medium to high physical symptoms one year after deployment. ^a= significant difference with low/low group.

1. Interian A, Allen LA, Gara MA, Escobar JI, Díaz-Martínez AM. Somatic complaints in primary care: further examining the validity of the Patient Health Questionnaire (PHQ-15). *Psychosomatics*. 2006;47(5):392-8.

2. Escobar JI, Cook B, Chen C-N, Gara MA, Alegría M, Interian A, et al. Whether medically unexplained or not, three or more concurrent somatic symptoms predict psychopathology and service use in community populations. *Journal of psychosomatic research*. 2010;69(1):1-8.
3. Escobar JI, Waitzkin H, Silver RC, Gara M, Holman A. Abridged somatization: a study in primary care. *Psychosomatic medicine*. 1998;60(4):466-72.
4. Burton C. Beyond somatisation: a review of the understanding and treatment of medically unexplained physical symptoms (MUPS). *The British journal of general practice : the journal of the Royal College of General Practitioners*. 2003;53(488):231-9.
5. Fink P, Sørensen L, Engberg M, Holm M, Munk-Jørgensen P. Somatization in primary care: prevalence, health care utilization, and general practitioner recognition. *Psychosomatics*. 1999;40(4):330-8.
6. Kroenke K. Physical symptom disorder: a simpler diagnostic category for somatization-spectrum conditions. *Journal of psychosomatic research*. 2006;60(4):335-9.
7. Greco M. The classification and nomenclature of 'medically unexplained symptoms': Conflict, performativity and critique. *Social science & medicine*. 2012;75(12):2362-9.
8. Eriksen TE, Kirkengen AL, Vetlesen AJ. The medically unexplained revisited. *Medicine, Health Care and Philosophy*. 2013;16(3):587-600.
9. Nimnuan C, Rabe-Hesketh S, Wessely S, Hotopf M. How many functional somatic syndromes? *J Psychosom Res*. 2001;51(4):549-57. Epub 2001/10/12. PubMed PMID: 11595242.
10. Hilderink PH, Collard R, Rosmalen JG, Oude Voshaar RC. How does ageing affect the impact of medically unexplained symptoms and medically explained symptoms on health-related quality of life? *International journal of geriatric psychiatry*. 2015;30(7):737-43.
11. Zonneveld LN, Sprangers MA, Kooiman CG, van't Spijker A, Busschbach JJ. Patients with unexplained physical symptoms have poorer quality of life and higher costs than other patient groups: a cross-sectional study on burden. *BMC health services research*. 2013;13(1):1.
12. Barsky AJ, Orav EJ, Bates DW. Somatization increases medical utilization and costs independent of psychiatric and medical comorbidity. *Archives of General Psychiatry*. 2005;62(8):903-10.
13. Smith GR, Monson RA, Ray DC. Patients with multiple unexplained symptoms: their characteristics, functional health, and health care utilization. *Archives of internal medicine*. 1986;146(1):69-72.
14. Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. *The American journal of medicine*. 1989;86(3):262-6.
15. Fink P. The use of hospitalizations by persistent somatizing patients. *Psychological medicine*. 1992;22(01):173-80.
16. Fink P. Surgery and medical treatment in persistent somatizing patients. *Journal of psychosomatic research*. 1992;36(5):439-47.
17. Fitzcharles M-A, Ste-Marie PA, Gamsa A, Ware MA, Shir Y. Opioid use, misuse, and abuse in patients labeled as fibromyalgia. *The American journal of medicine*. 2011;124(10):955-60.
18. Reid S, Crayford T, Patel A, Wessely S, Hotopf M. Frequent attenders in secondary care: a 3-year follow-up study of patients with medically unexplained symptoms. *Psychol Med*. 2003;33(3):519-24. Epub 2003/04/19. PubMed PMID: 12701672.
19. Stephenson D, Price J. Medically unexplained physical symptoms in emergency medicine. *Emergency Medicine Journal*. 2006;23(8):595-600.
20. Epstein RM, Shields CG, Meldrum SC, Fiscella K, Carroll J, Carney PA, et al. Physicians' responses to patients' medically unexplained symptoms. *Psychosomatic medicine*. 2006;68(2):269-76.
21. Stone L. Making sense of medically unexplained symptoms in general practice: a grounded theory study. *Mental health in family medicine*. 2013;10(2):101.

22. van der Feltz-Cornelis CM, Hoedeman R, Keuter EJW, Swinkels JA. Presentation of the Multidisciplinary Guideline Medically Unexplained Physical Symptoms (MUPS) and Somatoform Disorder in the Netherlands: disease management according to risk profiles. *Journal of psychosomatic research*. 2012;72(2):168-9.
23. Baker R, Shaw EJ. Guidelines: diagnosis and management of chronic fatigue syndrome or myalgic encephalomyelitis (or encephalopathy): summary of NICE guidance. *BMJ: British Medical Journal*. 2007;335(7617):446-8.
24. Whiting P, Bagnall A-M, Sowden AJ, Cornell JE, Mulrow CD, Ramírez G. Interventions for the treatment and management of chronic fatigue syndrome: a systematic review. *Jama*. 2001;286(11):1360-8.
25. Chambers D, Bagnall A-M, Hempel S, Forbes C. Interventions for the treatment, management and rehabilitation of patients with chronic fatigue syndrome/myalgic encephalomyelitis: an updated systematic review. *Journal of the Royal Society of Medicine*. 2006;99(10):506-20.
26. Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. *Jama*. 2004;292(19):2388-95.
27. Creed F, Henningsen P, Fink P. *Medically unexplained symptoms, somatisation and bodily distress: developing better clinical services*: Cambridge University Press; 2011.
28. Engel CC, Hyams KC, Scott K. Managing future Gulf War Syndromes: international lessons and new models of care. *Philosophical Transactions of the Royal Society B: Biological Sciences*. 2006;361(1468):707-20.
29. Bernstein CN, Fried M, Krabshuis J, Cohen H, Eliakim R, Fedail S, et al. World Gastroenterology Organization Practice Guidelines for the diagnosis and management of IBD in 2010. *Inflammatory bowel diseases*. 2010;16(1):112-24.
30. Smith RC, Lein C, Collins C, Lyles JS, Given B, Dwamena FC, et al. Treating patients with medically unexplained symptoms in primary care. *Journal of General Internal Medicine*. 2003;18(6):478-89.
31. Smeets RJ, Wittink H, Hidding A, Knottnerus JA. Do patients with chronic low back pain have a lower level of aerobic fitness than healthy controls?: are pain, disability, fear of injury, working status, or level of leisure time activity associated with the difference in aerobic fitness level? *Spine*. 2006;31(1):90-7.
32. Olde Hartman TC, Borghuis MS, Lucassen PL, van de Laar FA, Speckens AE, van Weel C. Medically unexplained symptoms, somatisation disorder and hypochondriasis: course and prognosis. A systematic review. *J Psychosom Res*. 2009;66. doi: 10.1016/j.jpsychores.2008.09.018.
33. Steele L. Prevalence and patterns of Gulf War illness in Kansas veterans: association of symptoms with characteristics of person, place, and time of military service. *American Journal of Epidemiology*. 2000;152(10):992-1002.
34. Blanchard MS, Eisen SA, Alpern R, Karlinsky J, Toomey R, Reda DJ, et al. Chronic multisymptom illness complex in Gulf War I veterans 10 years later. *Am J Epidemiol*. 2006;163(1):66-75. Epub 2005/11/19. doi: 10.1093/aje/kwj008. PubMed PMID: 16293719.
35. McAndrew LM, Helmer DA, Phillips LA, Ray K, Quigley K. Operation Enduring Freedom Operation Iraqi Freedom report symptoms consistent with Chronic Multi-Symptom Illness one year after deployment *Journal of Rehabilitation Research and Development*. In Press.
36. Nimnuan C, Hotopf M, Wessely S. Medically unexplained symptoms: an epidemiological study in seven specialities. *J Psychosom Res*. 2001;51(1):361-7. Epub 2001/07/13. PubMed PMID: 11448704.
37. Carson AJ, Ringbauer B, Stone J, McKenzie L, Warlow C, Sharpe M. Do medically unexplained symptoms matter? A prospective cohort study of 300 new referrals to neurology outpatient clinics. *Journal of Neurology, Neurosurgery & Psychiatry*. 2000;68(2):207-10. doi: 10.1136/jnnp.68.2.207.

38. Grabe HJ, Baumeister SE, John U, Freyberger HJ, Völzke H. Association of mental distress with health care utilization and costs: a 5-year observation in a general population. *Social Psychiatry and Psychiatric Epidemiology*. 2009;44(10):835-44. doi: 10.1007/s00127-009-0005-9.
39. den Boeft M, Twisk JW, Terluin B, Penninx BW, van Marwijk HW, Numans ME, et al. The association between medically unexplained physical symptoms and health care use over two years and the influence of depressive and anxiety disorders and personality traits: a longitudinal study. *BMC health services research*. 2016;16(1):1.
40. Speckens A, Van Hemert A, Bolk J, Rooijmans H, Hengeveld M. Unexplained physical symptoms: outcome, utilization of medical care and associated factors. *Psychological medicine*. 1996;26(04):745-52.
41. McAndrew LM, D'Andrea E, Lu SE, Abbi B, Yan GW, Engel C, et al. What pre-deployment and early post-deployment factors predict health function after combat deployment?: a prospective longitudinal study of Operation Enduring Freedom (OEF)/Operation Iraqi Freedom (OIF) soldiers. *Health Qual Life Outcomes*. 2013;11:73. Epub 2013/05/02. doi: 10.1186/1477-7525-11-73. PubMed PMID: 23631419; PubMed Central PMCID: PMC3704953.
42. Quigley KS, McAndrew LM, Almeida L, D'Andrea EA, Engel CC, Hamtil H, et al. Prevalence of environmental and other military exposure concerns in Operation Enduring Freedom and Operation Iraqi Freedom veterans. *Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine*. 2012;54(6):659-64. Epub 2012/05/17. doi: 10.1097/JOM.0b013e3182570506. PubMed PMID: 22588478.
43. Yan GW, McAndrew LM, D'Andrea EA, Lange G, Santos SL, Engel CC, et al. Self-reported stressors of National Guard women veterans before and after deployment: the relevance of interpersonal relationships. *J Gen Intern Med*. 2013;28 Suppl 2:S549-55. Epub 2013/07/03. doi: 10.1007/s11606-012-2247-6. PubMed PMID: 23807064; PubMed Central PMCID: PMC3695274.
44. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med*. 2002;64. doi: 10.1097/00006842-200203000-00008.
45. Pleis JR, Lethbridge-Çejku M. Summary health statistics for US adults: National Health Interview Survey, 2005. *Vital and health statistics Series 10, Data from the National Health Survey*. 2006(232):1-153.
46. Schiller JS, Adams PF, Nelson ZC. Summary health statistics for the US population: National Health Interview Survey, 2003. *Vital and health statistics Series 10, Data from the National Health Survey*. 2005(224):1-104.
47. Myers R, Montgomery, D., & Anderson-Cook, C. . *Response surface methodology: Process and product optimization using designed experiments*. . Hoboken, NJ: Wiley; 2009.
48. Edwards JR. Alternatives to difference scores: Polynomial regression and response surface methodology. *Advances in measurement and data analysis*. 2002:350-400.
49. Phillips LA. Congruence research in behavioral medicine: methodological review and demonstration of alternative methodology. *Journal of behavioral medicine*. 2013;36(1):61-74.
50. Edwards JR, Parry ME. On the use of polynomial regression equations as an alternative to difference scores in organizational research. *Academy of Management journal*. 1993;36(6):1577-613.
51. Shanock LR, Baran BE, Gentry WA, Pattison SC, Heggstad ED. Polynomial regression with response surface analysis: A powerful approach for examining moderation and overcoming limitations of difference scores. *Journal of Business and Psychology*. 2010;25(4):543-54.
52. Fukuda K, Nisenbaum R, Stewart G, Thompson WW, Robin L, Washko RM, et al. Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *Jama*. 1998;280(11):981-8. Epub 1998/09/28. PubMed PMID: 9749480.

53. Kisely S, Simon G. An international study comparing the effect of medically explained and unexplained somatic symptoms on psychosocial outcome. *J Psychosom Res.* 2006;60. doi: 10.1016/j.jpsychores.2005.06.064.
54. McAndrew L, Helmer D, Phillips L, Chandler H, Ray K, Quigley K. Iraq and Afghanistan Veterans report symptoms consistent with chronic multisymptom illness one year after deployment. *Journal of rehabilitation research and development.* 2016;53(1):59.
55. Czachowski S, Piszczek E, Sowińska A, olde Hartman TC. GPs' challenges in the management of patients with medically unexplained symptoms in Poland: a focus group-based study. *Family Practice.* 2011. doi: 10.1093/fampra/cmr065.
56. Yon K, Nettleton S, Walters K, Lamahewa K, Buszewicz M. Junior doctors' experiences of managing patients with medically unexplained symptoms: a qualitative study. *BMJ open.* 2015;5(12):e009593.