


The Relationship Between COVID-19 Related Stress and Medication Adherence Among High-Risk Adults During the Acceleration Phase of the US Outbreak

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Purpose: To assess the relationship between stress regarding COVID-19 and medication adherence.

Patients and Methods: Older adults with ≥ 1 chronic condition(s) were recruited from 4 active, federally funded studies in Chicago to participate in a longitudinal telephone survey. Participants self-reported stress regarding COVID-19 in the last week. Adherence was measured via the ASK-12 survey.

Results: Most participants reported feeling stressed “some of the time” (54.0%), while 18.2% felt stressed “most” or “all of the time” and 27.8% “never” felt stressed. In bivariate analyses, participants who reported being stressed “most” or “all of the time” had worse medication adherence than participants who reported being stressed “some of the time” or “never” ($p < 0.001$). In multivariable analyses, participants who reported feeling stressed “most” or “all of the time” had worse adherence than those who “never” felt stressed (Adjusted Least Square Mean (Standard Error): 21.3 (0.6) vs 19.7 (0.6), $p=0.01$).

Conclusion: Stress due to COVID-19 has significantly impacted medication adherence, which has negative implications for the course of both COVID-19 and comorbid conditions. Healthcare providers should be aware of the potential impact of COVID-19 on patients’ mental and physical well-being and consider ways to routinely assess patient experiences.

Keywords: COVID-19, stress, medication adherence, comorbidity

Introduction

Coronavirus-19 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in December 2019 and has rapidly evolved into a worldwide pandemic.¹ The United States alone has amassed over 28 million cases and more than 500,000 deaths to date—a scope of infection not seen in nearly a century.^{2,3} The population most at risk for severe disease or death from COVID-19 is older adults with underlying comorbidities such as hypertension, diabetes, or kidney disease.^{4,5} Early evidence and clinical guidelines suggest that effective chronic disease self-management in this population is key to reducing COVID-19 related morbidity and mortality.

Medication adherence is often a cornerstone of chronic disease self-management. In the midst of COVID-19, supporting safe and consistent medication use among patients with chronic conditions has therefore become paramount. Yet,

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COVID-19 has disrupted adults' daily lives, introducing barriers to medication access and use and inducing stress and anxiety.⁶ Studies conducted prior to the pandemic have shown that stress and other strong emotional responses—such as anger, anxiety, or depression—have a negative influence on adherence to prescribed medications; those who are more stressed have a higher likelihood of being non-adherent to their medication regimens than those who have lower or no stress.^{7,8} However, little is known about patients' experiences with stress due to the COVID-19 outbreak and how this may impact medication use.

We took advantage of a unique opportunity to examine this relationship among a cohort of high-risk patients enrolled in the Chicago COVID-19 Comorbidities (C3) Survey. The purpose of this analysis is to explore the relationship between feelings of stress and nervousness regarding COVID-19 and adherence to prescribed medications among a cohort of adults living with chronic disease.

Methods

Parent Study Participants and Data Collection Procedures

The Chicago COVID-19 Comorbidities (C3) Survey is an on-going, telephone-based cohort study among predominantly older adults with at least one chronic condition in Chicago, IL.⁹ To date, it has consisted of five waves of surveys conducted at different stages of the pandemic. Primary objectives of the C3 Survey are to longitudinally assess pandemic-related knowledge, beliefs and behaviors among a diverse higher risk population.

The participants in the C3 Survey were active enrollees in four ongoing, federally funded studies; details of these clinical trials and cohort studies have previously been described.^{10–13} Participants were recruited to these parent studies after obtaining care from one of five academic practices or two community health centers in Chicago, IL.

Specific eligibility criteria differed between the participants' parent studies; however, study populations generally consisted of middle-aged or older patients with at least one chronic condition. One trial included adults who were Spanish-speakers, while the rest only enrolled English-speaking patients.¹² In order to participate in the C3 survey, participants had to have completed an interview for one of the parent studies between 2018 and 2020. They also had to have previously consented to being approached for future research studies. All participants who completed

a Wave 1 interview were eligible to participate in subsequent waves.

The process of data collection was standardized across the existing five waves of the C3 Survey. Participants were called by research staff and invited to participate in a 30-minute survey related to COVID-19. All participant responses were recorded by trained research staff using REDCap software.¹⁴ Participants were given a \$15 gift certificate for participation. The Northwestern University Institutional Review Board (IRB) approved all study procedures in accordance with the Declaration of Helsinki.

Sub-Study Participants and Data Collection

For this sub-study, we utilized data from Wave 3 of the C3 Survey. Wave 3 was conducted May 1–May 20, 2020 and included a total of 565 adult participants out of the 630 who were eligible. Of those who did not participate, 47 could not be reached for the follow-up interview and 18 declined to participate, for an overall cooperation rate of 89.7%. Our aim was to examine levels of patient stress and nervousness from COVID-19 and its relationship to self-reported barriers to appropriate medication use in May 2020, a period of time during which COVID-19 cases in Chicago reached over 47,000 and deaths exceeded 2200.⁹

Measures

As part of the NIH-funded parent studies, participants completed a number of standardized assessments measuring personal and health-related characteristics. This included sociodemographic information (eg, age, sex, race/ethnicity, educational attainment, income) and health status (chronic conditions, overall self-reported health). Health literacy was assessed via The Newest Vital Sign (NVS), a commonly used, validated measure that asks participants to interpret information found on a nutrition label.¹⁵ Summed scores of 0–1 reflect a high likelihood of limited literacy, while scores of 2–3 reflect a possibility of limited literacy; scores of 4–6 nearly always represent adequate literacy. Patient activation, or the degree to which an individual is actively engaged in their personal health, was measured with the Consumer Health Activation Index (CHAI).¹⁶ The CHAI is a validated measure that can be utilized among diverse individuals, including those who have low health literacy; furthermore, it can be administered across varying research and healthcare settings.

During Wave 3, stress and nervousness due to COVID-19 was measured by asking participants to self-report how often they felt stressed or nervous due to COVID-19 during the past week. Response options included: all of the time, most of the time, some of the time, or never. Unlike other measures of stress, this measure was specific to COVID-19. To measure medication adherence, the Adherence Starts with Knowledge (ASK-12) questionnaire was utilized. ASK-12 is a shortened, validated version of the 20-item ASK-20. For the ASK-12, participants rate their level of agreement (strongly agree, agree, neutral, disagree, strongly disagree) with twelve statements pertaining to medication adherence. Domains include adherence behavior, health beliefs, and inconvenience/forgetfulness. Scores range from 12 to 60, with higher scores signifying greater barriers to adherence.¹⁷

Analyses

Descriptive statistics, such as means and percentage frequencies, were calculated for the overall sample. Associations between stress and patient characteristics were assessed using χ^2 tests. Bivariate analyses were used to determine differences between adherence, patient-level characteristics, and stress levels using t-tests or analysis of covariance, as appropriate. A multivariate general linear regression model was used to further examine the association of ASK-12 adherence and stress. The final model included stress levels as a primary covariate, as well as other socio-demographics variables (gender, race, age, poverty, insurance type), health-related outcomes (number of chronic diseases, self-reported health status), and parent study. We also included patient health activation and health literacy as control variables, as previous studies have demonstrated associations between these factors and medication adherence.¹⁸ We reported least-square means (LSM) and standard errors of covariates. Statistical analyses were performed using SAS, version 9.4.

Results

Table 1 displays the study sample characteristics. Participants were racially diverse; most were female (61.4%) and the average age of respondents was 62.3 years old. Almost half of the sample (46.6%) had a “high likelihood of limited literacy” or “possibility of limited literacy” according to the NVS (hereafter referred to as “low” or “marginal” health literacy, respectively), and 59.3% had three or more chronic conditions.

When asked if they had felt stressed or nervous because of COVID in the last week, 27.8% of participants answered “never.” More than half (54.0%) reported feeling stressed “some of the time” and 18.2% said they felt stressed “most” or “all of the time” (Table 1). Women were significantly more likely to be stressed than men ($p=0.02$), with 20.8% of women reporting that they felt stressed “most” or “all of the time” compared to 14.2% of men (Table 1). Additionally, participants differed in their level of stress by race; participants identifying as Hispanic, Black, or Other reported feeling stressed “most” or “all of the time” more than participants identifying as White ($p=0.005$) (Table 1). The mean ASK-12 medication adherence score for our sample was 20.2 (standard deviation (SD) 5.2). Participants who were female, non-white, living below the poverty line, and those with limited English proficiency, multiple chronic conditions, poor overall health, and low patient health activation were more likely to have worse medication adherence (Table 2).

In bivariate analyses, participants who reported being stressed “most” or “all of the time” were more likely to report more barriers to medication adherence than those who were “never” stressed or who were stressed only “some of the time” (ASK-12 score (SD): 19.3 (5.3) vs 20.1 (5.0), respectively, $p < 0.001$; Table 2). There was also a significant relationship between stress and adherence in multivariable analyses, adjusting for relevant covariates ($p=0.04$; Table 3). In particular, participants who reported feeling stressed “most” or “all of the time” had significantly poorer adherence than those who reported “never” feeling stressed (Adjusted LSM (SE): 21.3 (0.6) vs 19.7 (0.6), $p=0.01$). In adjusted analyses, participants with marginal health literacy, those who were older and those with private insurance were also independently less likely to report barriers to adherence, while those with low health activation and who reported poor health had worse adherence (Table 3).

Discussion

Within our sample of primarily older adults with one or more comorbid medical conditions surveyed during the acceleration stage of the COVID-19 crisis in the US, rates of self-reported stress were high. Nearly three-quarters of participants endorsed experiencing at least some degree of stress due to the pandemic, with almost 20% reporting feeling stressed “most” or “all of the time.” In particular, women reported feeling more stressed than men, as did participants who identified as non-white

Table I Patient Characteristics and Reported Stress and Nervousness Due to COVID-19 (n = 565)

		Never	Some of the Time	Most/ All of the Time	
	Overall	27.8	54.0	18.2	P
Variable					
Age group, %					0.13
<60 y	35.3	24.4	55.1	20.5	
60–69 y	37.0	25.4	55.9	18.7	
≥70 y	26.7	35.7	49.7	14.6	
Sex, %					0.02
Females	61.4	23.9	55.3	20.8	
Males	38.6	33.9	51.8	14.2	
Race†, %					0.005
Hispanic	21.9	18.8	57.4	23.8	
White	45.1	28.3	57.0	14.7	
Black	29.8	34.9	47.0	18.1	
Other	3.2	11.1	50.0	38.9	
English proficiency, %					0.52
Limited	11.3	21.9	59.4	18.7	
Adequate	88.7	28.5	53.3	18.2	
Living below poverty level, %					0.48
Yes	29.2	24.4	56.7	18.9	
No	70.8	29.4	52.8	17.8	
Marital Status‡, %					0.16
Married	39.3	26.6	59.4	14.0	
Single	60.1	28.5	51.9	19.6	
Health insurance, %					0.06
Medicare	16.1	35.2	46.1	18.7	
Medicaid	12.8	15.3	56.9	27.8	
Private	25	24.1	56.7	19.2	
Medicare and private	29.6	29.3	53.9	16.8	
Medicare and Medicaid	16.5	33.3	54.9	11.8	
Care setting, %					0.27
Academic	68.7	29.6	53.4	17.0	
Federally qualified health center	31.3	23.7	55.4	20.9	

(Continued)

Table I (Continued).

		Never	Some of the Time	Most/ All of the Time	
	Overall	27.8	54.0	18.2	P
Employment status, %					0.82
Working for pay	27.3	27.3	55.8	16.9	
Not working	72.7	28.0	53.2	18.8	
Health literacy, %					0.94
Low	23.4	29.5	50.8	19.7	
Marginal	23.2	28.2	54.2	17.6	
Adequate	53.4	26.8	55.3	17.9	
Health activation, %					0.33
Low	47.6	25.6	53.9	20.5	
High/ Moderate	52.4	29.7	54.1	16.2	
Number of chronic conditions, %					0.51
1	24.2	23.4	54.0	22.6	
2	16.5	28.0	54.8	17.2	
≥3	59.3	29.6	53.7	16.7	
Self-reported overall health, %					0.43
Excellent	9.0	43.1	43.1	13.8	
Very good	29.9	27.2	53.9	18.9	
Good	39.7	27.2	54.9	17.9	
Fair	17.9	21.8	58.4	19.8	
Poor	3.5	30.0	50.0	20.0	

compared to those who identified as white. These disparities by gender and race are consistent with other population-based surveys examining COVID-related stress.^{19,20} This is likely due to the disproportionate burden these groups have faced in regard to the economic and caregiving consequences of the pandemic.

Our results also suggest that increased stress and nervousness due to COVID-19 may have a negative impact on patient adherence to prescribed medications, although it should be noted that the magnitude of these differences

Table 2 ASK-12 Adherence Across Patient Characteristics (n = 565)

	ASK-12 Adherence Mean (SD)	P
Variable	20.2 (5.2)	
Over the past week, how often have you felt nervous or “stressed” because of the coronavirus?		<0.001
Never	19.3 (5.3)	
Some of the time	20.1 (5.0)	
Most/All of the time	21.1 (5.2)	
Age group		0.85
<60 y	20.3 (5.5)	
60–69 y	20.2 (4.9)	
≥70 y	20.0 (5.2)	
Sex		<0.001
Females	20.8 (5.3)	
Males	19.2 (4.8)	
Race†		0.008
Hispanic	21.3 (5.6)	
White	19.5 (4.9)	
Black	20.5 (5.1)	
Other	20.3 (4.5)	
English proficiency		<0.001
Limited	22.5 (5.0)	
Adequate	19.9 (5.2)	
Living below poverty level‡		0.02
Yes	21.0 (5.2)	
No	19.9 (5.2)	
Marital Status§		0.12
Married	19.8 (5.2)	
Single	20.5 (5.2)	
Health insurance		0.01
Medicare	21.1 (5.1)	
Medicaid	21.2 (5.2)	
Private	19.2 (4.8)	
Medicare and private	19.8 (5.3)	
Medicare and Medicaid	20.8 (5.5)	
Care setting		<0.001
Academic	19.3 (4.9)	
Federally qualified health center	22.0 (5.3)	
Employment status		0.39
Working for pay	19.9 (5.2)	
Not working	20.3 (5.2)	

(Continued)

Table 2 (Continued).

	ASK-12 Adherence Mean (SD)	P
Health literacy		0.07
Low	20.9 (5.4)	
Marginal	19.5 (4.6)	
Adequate	20.2 (5.3)	
Health activation		<0.001
Low	21.8 (5.3)	
High/Moderate	18.7 (4.6)	
Number of chronic conditions		0.003
1	21.5 (5.2)	
2	20.1 (5.4)	
≥3	19.7 (5.1)	
Self-reported overall health		<0.001
Excellent	18.8 (5.7)	
Very good	18.8 (4.5)	
Good	20.4 (4.9)	
Fair	22.2 (5.5)	
Poor	22.5 (7.0)	

Notes: †Missing data for 20 participants. §Missing data for 46 participants.

was relatively small, making the clinical significance of this finding unclear. Specifically, when participants reported feeling stressed “most” or “all of the time” they tended to have more barriers to adherence than participants who reported feeling stressed “some of the time” or “never.” Furthermore, while participants who reported feeling stressed “some of the time” did have better adherence than participants who reported feeling stressed “most” or “all of the time,” they still had worse adherence than participants reporting “never” feeling stressed with regard to COVID-19. This indicates a possible gradient effect of related stress on adherence, with increasing levels of stress due to the virus leading to more barriers.

Medication adherence is a complex behavior influenced by multi-level factors.²¹ Before the COVID-19 pandemic, medication adherence was often noted as being negatively impacted by factors such as polypharmacy, interference with the patient’s daily schedule, poor physician-patient communication, access to care, or costs.^{22,23} However, researchers had also previously assessed the negative relationship between perceived stress and medication adherence across chronic disease contexts.^{6,24–28} Our results contribute to this broader

Table 3 Multivariate Models Examining Patient Characteristics, Stress Levels and Adherence (n = 546) *

Variable	ASK-12 Adherence	
	LS Means (SE)	P
Over the past week, how often have you felt nervous or “stressed” because of the coronavirus?		0.04
Never	19.7 (0.6)	Ref
Some of the time	20.1 (0.5)	0.39
Most/All of the time	21.3 (0.6)	0.01
Health Literacy		
Adequate	20.9 (0.5)	Ref
Marginal	19.6 (0.6)	0.02
Low	20.7 (0.6)	0.78
Sex		0.10
Males	20.0 (0.5)	Ref
Females	20.8 (0.5)	0.10
Race		0.14
White	19.4 (0.5)	Ref
Hispanic	20.5 (0.6)	0.10
Black	20.4 (0.5)	0.07
Other	21.3 (1.2)	0.12
Age group		0.06
<60 y	21.3 (0.5)	Ref
60–69 y	20.1 (0.5)	0.03
≥70 y	19.7 (0.7)	0.03
Poverty		0.46
Above Poverty level	20.6 (0.5)	Ref
Below Poverty level	20.2 (0.6)	0.46
Insurance		0.02
Medicare	21.7 (0.7)	Ref
Medicaid	19.7 (0.7)	0.03
Medicare and Medicaid	20.0 (0.7)	0.03
Medicare and Private	21.0 (0.6)	0.28
Private	19.5 (0.7)	0.003
Health activation		<0.001
High/Moderate	19.0 (0.5)	Ref
Low	21.7 (0.5)	<0.001
Number of Chronic Conditions		0.65
1	20.5 (0.6)	Ref
2	20.1 (0.7)	0.50
3 or more	20.6 (0.5)	0.85

(Continued)

Table 3 (Continued).

Variable	ASK-12 Adherence	
	LS Means (SE)	P
Self-reported overall health		0.003
Good	20.2 (0.5)	Ref
Excellent	20.1 (0.8)	0.91
Very Good	18.9 (0.5)	0.06
Fair	21.3 (0.6)	0.34
Poor	21.3 (1.2)	0.01

Note: *Model is adjusted for parent studies.

literature by investigating how an intense stressor, such as COVID-19, further exacerbates poor medication adherence.

The Multidimensional Coping Inventory (MCI) offers insight into the potential mechanisms through which stress affects medication adherence. According to the MCI, there are three primary types of strategies for coping with stress: task-oriented coping, emotion-oriented and avoidance-oriented coping.²⁹ Emotion-oriented coping was found to be one of the most significant predictors of poor medication adherence in a study conducted among older adults living with chronic disease; the more that participants focused on their emotions during stressful situations, the less likely they were to be adherent to their medications.²⁶ Similarly, the stress and coping model of medication adherence and viral load²⁴ suggests that negative mood (conceptualized as anger, depression and anxiety) leads to avoidant coping strategies that, in turn, result in poor medication adherence. With deaths in the United States topping 500,000, the COVID-19 pandemic is both stressful and emotional.⁶ While we did not assess coping specifically, other research has suggested that lockdown policies have diminished the supportive systems and positive coping strategies on which many older adults living with chronic conditions rely.³⁰

Results from this analysis raise concerns about the less visible impact that COVID-19 has had, and may continue to have, on the management of other non-communicable diseases that require ongoing adherence to prescribed medications. Based on our analysis, this impact may disproportionately affect older patients, as well as those with low health literacy or those without private insurance. This is in line with data

from previous studies examining medication adherence prior to the pandemic, which have shown lower medication adherence in patients who are older, those who have lower education levels, as well as those who grapple with high treatment costs.^{23,31}

As COVID-19 cases in the United States continue, stress may persist, or perhaps increase, and continue to affect patient adherence to medication. As a result, other pre-existing conditions may worsen, which subsequently can possibly increase risk for COVID-19 morbidity and mortality.^{32,33} In light of this, physicians should be made aware of these new barriers their patients may be facing in taking their medications. Many patients may not share their feelings of stress with their provider, or feel open to discussing suboptimal medication use due to feelings of shame, embarrassment, or social desirability.³⁴ Thus, it is vital for physicians to ask their patients at each visit about stressors they may be experiencing and the degree to which those stressors may be affecting their ability to take their medications as prescribed. Furthermore, it is important for providers to remain non-judgmental and be understanding of any obstacles that arise regarding their patient's medication use during the pandemic.

This study has limitations. Participants were generally older, had at least one chronic condition, and all participants resided in the greater Chicago metropolitan area. Because of this, the study's conclusions may not be generalizable to other populations. Furthermore, because of the self-report nature of this survey, social desirability bias may have affected how participants reported their adherence to medication, possibly resulting in overestimation of adherence. The relatively high rates of adherence reported by our sample, all of whom had at least one chronic medical condition, support this possibility. There was also no baseline measure of adherence measured before COVID-19 to which current ASK-12 scores can be compared. Finally, a single item was used to measure for stress and nervousness due to COVID-19; however brief, validated measures of stress specific to the pandemic were not widely available at the time this study was conducted.

Conclusion

Our assessment of the C3 Survey data pertaining to stress and medication adherence revealed that participants who have experienced more stress due to COVID-19 report more adherence barriers to their prescribed medications. These results raise concerns regarding the progression of non-communicable diseases, which have been shown to increase risk for COVID-19 morbidity and mortality, especially when uncontrolled, during this unprecedented time. Physicians

should continue to emphasize the importance of medication adherence to their patients, but also make sure to work with them to understand their barriers and stressors so as to help them better engage in appropriate mental and physical self-care.

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