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## The unmeasured burden: contribution of depression and psychological stress to patient-reported outcomes in atrial fibrillation

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### Abstract

**Introduction**—Patient-reported outcomes are routinely assessed in atrial fibrillation (AF) to evaluate efficacy of treatment and as clinical trial outcomes. The relation of depression to such measures has had limited study in AF.

**Methods**—In a cohort receiving treatment for AF, we assessed depression with the Patient Health Questionnaire-9 (PHQ; 0–4, normal range; 5–9, mild depression; 10 moderate depression). We related depression to disease-specific quality of life with the AF Effect on Quality of life (AFEQT, range 0–100) and the Global Perceived Stress Scale (GPPS, range 0–24) in multivariable-adjusted models.

**Results**—In 260 individuals (age 71.7±10.1, 44.6% women) with AF, 51 (26.1%) had PHQ scores 5 and 17 (6.5%) 10. AFEQT scores decreased progressively with depression severity (normal range PHQ, 81.4±14.1; mild depression, 65.8±17.1; moderate depression, 50.6±19.3). Individuals without depression had lower GPPS scores (3.0±2.6) than those with mild (4.9±2.5) or moderate (8.9±4.0) depression. In multivariable-adjusted models mild depression was associated with a 12.1-point (95% confidence interval [CI], –17.2 to –6.9) decrease in AFEQT and 1.9-point

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(95% CI, 1.1 to 2.7) increase in GPSS, while moderate depression a 27.7-point (95% CI, -35.5 to -19.8) decrease in AFEQT and 5.5-point (95% CI, 4.2 to 6.8) increase in GPSS, relative to normal range PHQ. Regression analyses confirmed significant correlations between depression and AFEQT and GPSS scores in multivariable-adjusted models.

**Conclusions**—We determined that depression is associated with a step-wise, progressively adverse change in patient-centered outcomes in individuals with AF. Our findings suggest the importance of assessing depression in the evaluation of AF.

### Keywords

health services; atrial fibrillation; risk factors; Atrial fibrillation; depression; quality of life; stress; patient-reported outcomes

## Introduction

Atrial fibrillation (AF) is a challenging and chronic condition for patients that is associated with depression.<sup>1</sup> The contribution of depression towards adverse clinical care and outcomes is recognized in multiple health conditions.<sup>2</sup> Individuals with cardiac and non-cardiac conditions and depression have increased health care utilization and mortality relative to those without.<sup>3-5</sup> There is further evidence that depression is associated with treatment adherence in cardiac and non-cardiac conditions.<sup>6,7</sup> The contributions of depression towards adverse clinical outcomes and poor self-care in cardiac disease are well summarized.<sup>8</sup>

In AF, the prevalence of depression in AF is estimated as ranging from 20% to 40% and similarly associated with deleterious care metrics and outcomes. Depression increases with the severity of AF,<sup>9-12</sup> and is correlated with health care utilization and mortality similar to other conditions.<sup>13,14</sup> Depression likewise affects the clinical management of AF; individuals with AF and depression are less likely to receive anticoagulation as well as have decreased adherence to such agents.<sup>15-18</sup>

Depression may also have an important effect on patients' subjective experience of AF. Individuals with depression have increased symptoms associated with AF, independent of the burden or severity of the arrhythmia,<sup>14,19</sup> compared to those without depression. AF has a deleterious effect on quality of life, and may further impact psychological stress.<sup>20,21</sup> Professional society guidelines have prioritized patient-reported outcomes as a central metric for the evaluation and management of AF.<sup>22</sup> Hence, examining the contribution of depression to patient-reported outcomes may inform patient-centered care and guide interdisciplinary treatment strategies that address depression rather than a predominant focus on the arrhythmia.

In this study we examined depression in relation to central patient-reported outcomes that are relevant to the patient experience of AF. First, we examined the relation of depression to disease-specific quality of life, in contrast to other investigations that have employed general quality of life instruments. Second, we examined the contribution of depression to psychological stress, given the association of stress to symptom burden in AF.<sup>23</sup> We

hypothesized that individuals with AF and depression would have worse disease-specific quality of life and increased psychological stress compared to those without depression.

## Methods

We enrolled individuals receiving care at ambulatory facilities affiliated with the University of Pittsburgh Medical Center in Pittsburgh, PA, a large, regional health care system. Individuals with prevalent, nonvalvular AF were identified by screening the electronic health record and direct contact during clinical visits, physician or provider referral, or self-referral. Eligibility criteria were age  $\geq 18$  years; history of non-valvular AF as documented by the electronic health record; CHA<sub>2</sub>DS<sub>2</sub>-VaSc<sup>24</sup> (congestive heart failure, hypertension, age, diabetes, stroke, vascular disease [history of MI, PVD, or aortic atherosclerotic disease], and sex category) score  $\geq 2$ ; having been prescribed oral anticoagulation for AF; and English-speaking at a level appropriate to provide informed consent and participate in this research protocol. Exclusion criteria were history of ischemic or hemorrhagic stroke, AF secondary to non-cardiac issues, AF within 30 days of any cardiothoracic surgery, or those not able to pass a three-item screening instrument prior to informed consent. From 2016 through 2018, our study team identified 1093 eligible individuals from the electronic health record. Of these we were able to approach the 486 who presented at scheduled clinic visits and were amenable to discussing participation in this study. Of these, we enrolled 339 for participation in this study, of which 260 had complete measures for inclusion in this analysis. By design, our study is cross-sectional, such that we obtained all data presented here at a single encounter with participants.

Baseline demographics including age, sex, and race were obtained by self-report. Clinical history pertinent to the CHA<sub>2</sub>DS<sub>2</sub>-VaSc and body mass index were extracted from the electronic health record. AF treatment, consisting in history of electrical or pharmacologic cardioversion, pulmonary vein isolation, and anticoagulant and antiarrhythmic medications (amiodarone, dofetilide, flecainide, lidocaine, propafenone and sotalol) were identified from the electronic record. Social factors obtained from participant self-report included annual household income, categorized as  $< \$19,000$ ;  $\$20,000$ - $\$49,999$ ;  $\$50,000$ - $\$99,999$ ;  $> \$100,000$ , and level of education (high school or vocational training; some part of college or an associate degree; bachelor's degree; or any graduate or professional school degree or enrollment). Health literacy was measured with the Short-Test Of Functional Health Literacy in Adults (S-TOFHLA).<sup>25</sup>

Depression was measured with the Patient Health Questionnaire (PHQ), a 9-item, validated instrument for quantification of depression severity over the previous 2 weeks that ranges from 0 to 27 with higher scores indicating more severe depression and a score of 0–4 defined as normal range, 5–9 suggesting mild depression, and  $\geq 10$  major depression.<sup>26</sup> Quality of life specific to AF was collected with the AF Effect on Quality of life instrument, a 20-item instrument scored from 0 to 100, where higher scores indicate greater quality of life over the prior 4 weeks.<sup>27</sup> The AFEQT includes a global score and 4 domain scores (symptoms, daily activities, treatment concerns, and treatment satisfaction). Global perceived psychological stress (GPPS) was measured with a validated instrument that measures 12-month stress on a 4-point scale (0 to 3) across 8 domains (caring for others,

employment, legal problems, medical problems, meeting basic needs, racism and discrimination, related to the neighborhood, and relationships) and ranging from 0–24.<sup>28,29</sup>

## Statistical analysis

We summarized continuous variables according to their means and standard deviation and categorical variables by their distributions. We evaluated PHQ results, our independent variable, according to prespecified categories (0–4, 5–9, and  $\geq 10$ ) and as a continuous variable.<sup>26</sup> We examined differences in the dependent variables (AFEQT and psychological stress score) by PHQ category using analysis of variance. We examined the associations of the PHQ and the AFEQT, AFEQT domains, and GPSS graphically using scatterplots and numerically with Pearson correlation coefficients. We employed multivariable-adjusted linear regression models to examine the relation of PHQ scores to AFEQT, AFEQT domains and psychological stress. Models adjusted for age, sex, race, body mass index, smoking history, heart failure, hypertension, diabetes, vascular disease, AF treatments, education and household income. All statistical analyses were conducted with SAS version 9.4 (Cary, North Carolina). Written informed consent was collected for each participant. The study was approved by the University of Pittsburgh institutional review board.

## Results

Of 339 individuals enrolled in the study, 79 entered the study prior to the study's adoption of the PHQ as its instrument for depression screening. As such, the 79 individuals recruited prior to the introduction of the PHQ lack an essential assessment and were consequently excluded from this analysis. In consequence, 260 participants were included in the present analysis (age  $71.7 \pm 10.1$  years, 116 [44.6%] women). The largest category of annual household income was in the \$20–\$49,999 range ( $n=74$ , 28.5%) and education for most participants was at the high school or vocational level ( $n=94$ , 36.2%). There were no significant differences in age, sex, race, level of education, or level of health literacy between participants by PHQ score category. Cohort characteristics for the cohort and are summarized by PHQ category in Table 1.

Table 2 presents the distribution of AF-specific quality of life, total and by AFEQT domain, and GPSS scores and their distributions by PHQ category. We noted a progressive reduction in mean AFEQT scores, both total and domain, with progressive increase in PHQ category of depression. Individuals with a normal range PHQ had a total AFEQT  $81.4 \pm 14.1$ , in contrast to a score of  $65.8 \pm 17.1$  for those with PHQ scores 5–9, and  $50.5 \pm 19.3$  for those with scores  $\geq 10$ . The largest contrast in AFEQT was seen in the domain of daily activities, where those with normal range PHQ scored  $76.5 \pm 21.8$  compared to  $36.9 \pm 20.0$  in those with PHQ  $\geq 10$ . Participants with PHQ scores  $\geq 10$  consistently scored lower across AFEQT domains than those with PHQ scores in the 5–9 range. Likewise, those with PHQ scores  $\geq 10$  had a nearly three-fold increased GPSS ( $8.9 \pm 4.0$ ) relative those with normal range PHQ scores ( $3.0 \pm 2.6$ ).

Table 3 summarizes the magnitude of difference by PHQ category in AFEQT and GPSS measurements in multivariable-adjusted linear regression models. The beta coefficients

present the difference in AFEQT score, total and by domain, and GPSS comparing each of the PHQ categories of mild depression (5–9) and major depression (≥ 10) those with normal range (0–4) PHQ scores. These data summarily demonstrate the magnitude of difference when comparing AFEQT and GPSS by PHQ category. For all measures, those with PHQ ≥ 10 had a significant decrease in AFEQT score and increase in GPSS. Of note, the estimate of the significant increase in GPSS between those with major depression ( $\beta = 5.5$ , 95% CI, 4.2 to 6.9) relative to normal range PHQ scores did not diminish with progressive multivariable adjustment.

Supplementary Table 1 summarizes the effect of just a single-point increase in PHQ in relation to AFEQT and GPSS measures. For every 1-point increase in PHQ, we observed consistent decreases in AFEQT total and domain scores, all meeting our threshold for statistical significance. A 1-point increase in PHQ was likewise associated with a 0.5 increase in GPSS. These associations did not attenuate and remained statistically significant with progressive multivariable adjustment. In Figure 1 we present the distributions of PHQ and total AFEQT measures, showing that patients with worse depressive symptoms tended to have lower AF-related quality of life (Pearson correlation =  $-0.52$ ,  $p < 0.01$ ). The Supplementary Figure provides a similar graphical presentation of the GPSS results, demonstrating a significant correlation between depression as determined by PHQ and psychological stress (Pearson correlation =  $0.53$ ,  $p < 0.01$ ).

## Discussion

In this moderate-sized cohort of individuals with prevalent AF, we identified significant and consistent associations between depression and both AF-specific quality of life and psychological stress. We identified step-wise associations between depression and these patient-reported outcomes. As such, both the AFEQT and GPSS scores were modified significantly across categories of normal range, mild and major depression. Those with major depression showed the poorest AFEQT scores in both total and the individual domains, and likewise significantly increased GPSS scores. Our results were not modified by multivariable adjustment for clinical or socioeconomic variables or by the treatment approach and regimen for AF. The persistent associations seen here between depression and AF-specific quality of life and psychological stress suggest that depression has critical relevance to how patients experience AF.

We noted critical difference in those with and without depression in our cohort. Individuals with less education and lower income were far more likely to experience depression than those with bachelor's or graduate education and higher income. Further, we identified differences in depression by AF treatment such that individuals who had undergone cardioversion or were prescribed antiarrhythmic medication had less likelihood of minor or major depression as identified by the PHQ. Conducting our study in a larger cohort would facilitate our performing a mediation analysis to identify how demographics, comorbid conditions, and social determinants may influence depression in AF.

## Clinical significance of these findings

Large amounts of health care resources are dedicated to procedures to treat symptomatic AF. Such treatment is highly specialized and includes catheter ablation and advanced pharmacologic therapies with the objective of managing and controlling patient-reported symptoms. A recent clinical trial evaluating the 12-month effect of catheter ablation versus pharmacologic management on disease-specific quality of life in AF reported a 5.3-point (95% CI, 3.7 to 6.9) difference in individuals receiving ablation.<sup>30</sup> In comparison our fully adjusted multivariable model identified a 12-point difference in AF-specific quality of life scores in those with mild depression and 28-point difference in those with major depression, relative to normal range PHQ. Changes in AFEQT scores of about 5 points, in either a positive or negative direction, have been considered clinically meaningful.<sup>31</sup> Our findings imply that treatment of depression – a highly prevalent comorbid condition in AF – may improve disease-specific quality of life and the psychological stress that may accompany this chronic arrhythmia. Furthermore, evaluation of depression is relevant to the model of integrated AF management articulated by current professional society guidelines.<sup>32</sup>

Recognizing and treating depression has been documented as crucial to improving outcomes and quality of life in cardiac diseases such as coronary artery disease and congestive heart failure.<sup>33–37</sup> In contrast, depression has not been well addressed by professional society guidelines for treatment of AF. An American Heart Association advisory statement on coronary heart disease has advocated routine screening for depression in individuals with coronary disease, given the significant contributions of depression towards adverse coronary disease prognosis.<sup>38</sup> Depression is recognized as one of the most common comorbid conditions in Medicare beneficiaries with AF. However, the guidelines for management of AF do not mention the relevance of screening and treating comorbid depression.<sup>22</sup>

AF and depression are both highly prevalent and the successful results of treatment of coronary disease and depression argues for enhanced strategies to address AF and comorbid depression. Potential avenues span screening individuals with symptomatic AF for depression and appropriate mental health referral; application of cognitive behavioral therapy as part of routine care as demonstrated in a limited-sized cohort<sup>39</sup>; and a collaborative care model similar to what has been successfully implemented and evaluated in heart failure and coronary disease.<sup>40–42</sup>

Our study further identified that individuals with mild and major depression experienced greater levels of psychological stress. AF is a challenging condition for patients with variable symptoms, complex treatments, and the necessity of long-term adherence for a chronic disease. Prior studies evaluating the association of psychological stress to incident AF have had variable results.<sup>43,44</sup> However, psychological stress has been related to symptoms associated with AF, regardless of the arrhythmia burden or ventricular rate during episodes of AF,<sup>23</sup> and similarly with increased risk of cardiovascular events and prognosis.<sup>45–47</sup> Our findings additionally support the importance of considering psychological stress as a component of patient evaluation and management in AF. Further studies to investigate how stress may contribute towards adverse clinical events associated with AF, patient-reported outcomes, or self-care behaviors such as medication adherence are essential.

## Strengths and limitations

Strengths of our study include its moderate size, use of a disease-specific quality of life instrument with domains pertinent to the patient experience of AF, and assessment of psychological stress with a validated measure as a complementary patient-reported outcome. We would note some important limitations of our work. First, we recruited a convenience cohort from a single, regional health center, and consequently recognize the inherent selection bias in establishing such a cohort. Selection for participation here required that individuals have access to health care and the social resources to present for an ambulatory appointment. We consider that a range of issues may limit access to care and adherence to visits, and as such express caution about the generalizability of our findings. However, we would qualify that albeit not representative, we consider our findings valid and expect that other settings will similarly demonstrate a strong association between depression and AF-specific quality of life and psychological stress. Second, our cohort had limited racial and ethnic diversity, which may further limit the generalizability of our findings. Third, we conducted a cross-sectional study, and are therefore not able to exclude reverse causality. It is possible that individuals with worse disease-specific quality of life may have greater general depressive symptoms, and the same may be true for those with greater psychological stress. We determined not to examine the reciprocal associations between either the AFEQT or the psychological stress measures employed here, as we sought to focus on depression as our independent variable. Fourth, we are not able to account for residual confounding, as multiple factors may influence depression, quality of life, and psychological stress. For example, our study does not account for the contributions of the social environment or lifestyle factors that may influence the associations examined here. Likewise, we did not include assessments of treatment or medication adherence. It is possible that individuals with depression had decreased adherence to treatments, thereby influencing their quality of life, specific to AF as measured by the AFEQT. Fifth, we did not include a history of treatment for depression or other mental health disorders. A more robust study of psychological health and mental health in individuals with AF would be informative to delineate how such factors affect the patient experience of this common, chronic arrhythmia.

## Conclusion

In conclusion, in a moderate-sized cohort of individuals with AF, we identified a significant association between depressive symptoms and disease-specific quality of life and psychological stress. Our findings suggest the relevance for consideration of depressive symptoms when evaluating patients with AF. Treatment of depression has shown benefit to individuals with other cardiovascular conditions, such as heart failure and coronary disease, and our findings indicate the necessity for further evaluation and treatment of depression as part of AF management.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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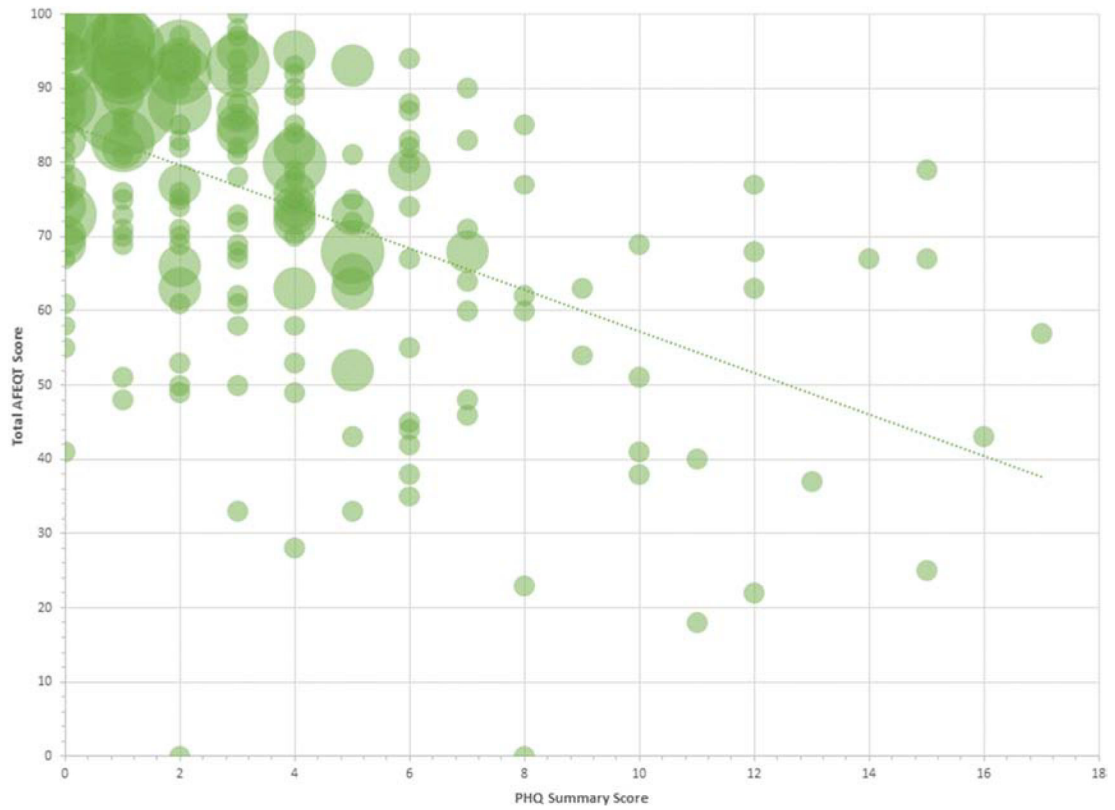
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### Highlights

- Depression is a frequent comorbid condition in individuals with atrial fibrillation (AF).
- Quality of life and psychological stress are relevant to patients' experience of AF.
- We identified strong associations between depression and these patient-reported outcomes.
- Addressing depression may improve patient-reported outcomes in AF.



**Figure 1.**

Plot showing correlation between depression, as measured by the Patient Health Questionnaire (PHQ), and quality of life specific to atrial fibrillation (AF), determined with the total Atrial Fibrillation Effect on QualiTy of life (AFEQT) score. The regression line indicates the significant negative correlation between depression and AF-specific quality of life (Pearson correlation  $-0.52$ ,  $P < 0.01$ ).

**Table 1.**

Characteristics of study cohort, total and according to Patient Health Questionnaire-9 (PHQ) category.

	All Participants	PHQ 0–4	PHQ 5–9	PHQ 10
<b>Characteristic</b>	<b>n = 260</b>	<b>n = 192</b>	<b>n = 51</b>	<b>n = 17</b>
Age	71.7 ± 10.1	71.9 ± 10.3	72.7 ± 9.3	67.4 ± 10.4
Female Sex	116 (44.6%)	83 (43.2%)	25 (49.0%)	8 (47.1%)
White Race	247 (95.0%)	183 (95.3%)	49 (96.1%)	15 (88.2%)
Body mass index (m/kg <sup>2</sup> )	31.4 ± 7.3	30.3 ± 6.4	35.3 ± 8.9	32.4 ± 8.2
Smoking History				
Never	126 (48.5%)	101 (52.6%)	19 (37.3%)	6 (35.3%)
Former	120 (46.2%)	86 (44.8%)	28 (54.9%)	6 (35.3%)
Current	14 (5.4%)	5 (2.6%)	4 (7.8%)	5 (29.4%)
Heart Failure	42 (16.2%)	25 (13.0%)	14 (27.5%)	3 (17.6%)
Preserved	22 (8.5%)	12 (6.3%)	8 (15.7%)	2 (11.8%)
Reduced	10 (3.8%)	6 (3.1%)	4 (7.8%)	0 (0.0%)
Not Specified	10 (3.8%)	7 (3.6%)	2 (3.9%)	1 (5.9%)
Hypertension	184 (70.8%)	130 (67.7%)	42 (82.4%)	12 (70.6%)
Diabetes	59 (22.7%)	39 (20.3%)	16 (31.4%)	4 (23.5%)
Vascular Disease	32 (12.3%)	24 (12.5%)	7 (13.7%)	1 (5.9%)
History of Cardioversion	68 (26.2%)	46 (24.0%)	18 (35.3%)	4 (23.5%)
History of ablation for AF	67 (25.8%)	56 (29.2%)	9 (17.6%)	2 (11.8%)
Prescribed antiarrhythmic medication	63 (24.2%)	45 (23.4%)	16 (31.4%)	2 (11.8%)
Education				
High school/Vocational	94 (36.2%)	61 (31.8%)	26 (51.0%)	7 (41.2%)
Some College	48 (18.5%)	38 (19.8%)	8 (15.7%)	2 (11.8%)
Bachelor's	60 (23.1%)	45 (23.4%)	11 (21.6%)	4 (23.5%)
Graduate	58 (22.3%)	48 (25.0%)	6 (11.8%)	4 (23.5%)
Income				
<\$19,999	33 (12.7%)	15 (7.8%)	11 (21.6%)	7 (41.2%)
\$20,000–49,999	74 (28.5%)	53 (27.6%)	15 (29.4%)	6 (35.3%)
\$50,000–99,999	71 (27.3%)	55 (28.6%)	14 (27.5%)	2 (11.8%)
>\$100,000	48 (18.5%)	45 (23.4%)	2 (3.9%)	1 (5.9%)
Refused/No Answer	34 (13.1%)	24 (12.5%)	9 (17.6%)	1 (5.9%)
S-TOFHLA	29.4 ± 5.1	29.8 ± 4.9	28.6 ± 5.9	28.1 ± 5.7

Continuous variables presented as mean±standard deviation and categorical by number (percentage). PHQ indicates Patient Health Questionnaire; TIA, transient ischemic attack; S-TOFHLA, Short-Test Of Functional Health Literacy in Adults.

**Table 2.**

Distribution of AF-specific quality of life and psychological stress score, according to presence of absent or mild depression as measured by the Patient Health Questionnaire.

	Patient Health Questionnaire			P-Value
	0-4	5-9	10	
<b>AFEQT</b>				
Total	81.4 ± 14.1	65.8 ± 17.1	50.6 ± 19.3	<0.001
Symptoms	87.8 ± 14.7	81.5 ± 19.1	66.9 ± 28.9	<0.001
Daily Activities	76.5 ± 21.8	53.0 ± 23.2	36.9 ± 20.0	<0.001
Treatment Concerns	83.5 ± 16.3	71.3 ± 21.1	52.5 ± 25.1	<0.001
Treatment Satisfaction	82.4 ± 21.4	71.1 ± 21.7	67.2 ± 23.3	<0.001
<b>Global Perceived Stress Score</b>	3.0 ± 2.6	4.9 ± 2.5	8.9 ± 4.0	<0.001

AFEQT indicates Atrial Fibrillation Effect on QualiTy of life measure.

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**Table 3.**

Association of Patient Health Questionnaire-9 (categorized as 0–4, 5–9, and 10) with AF-specific quality of life (AFEQT) and Global Psychological Stress Score.

AFEQT	Model 1			Model 2			Model 3		
	$\beta$	95% CI	p-value	$\beta$	95% CI	p-value	$\beta$	95% CI	p-value
<b>Total</b>									
PHQ 5–9 (vs. 0–4)	-15.4	(-20.0, -10.7)	<0.001	-13.0	(-18.1, -7.8)	<0.001	-12.1	(-17.2, -6.9)	<0.001
PHQ 10 (vs. 0–4)	-29.6	(-37.0, -22.1)	<0.001	-28.1	(-35.6, -20.5)	<0.001	-27.7	(-35.5, -19.8)	<0.001
<b>Symptom</b>									
PHQ 5–9 (vs. 0–4)	-6.2	(-11.2, -1.03)	0.019	-6.2	(-11.0, -0.5)	0.034	-5.2	(-10.9, 0.5)	0.073
PHQ 10 (vs. 0–4)	-19.3	(-27.5, -10.9)	<0.001	-19.3	(-27.8, -10.7)	<0.001	-18.8	(-27.6, -10.1)	<0.001
<b>Daily Activities</b>									
PHQ 5–9 (vs. 0–4)	-23.1	(-29.9, -16.2)	<0.001	-17.9	(-25.2, -10.5)	<0.001	-16.7	(-24.1, -9.3)	<0.001
PHQ 10 (vs. 0–4)	-39.2	(-50.2, -28.1)	<0.001	-35.7	(-46.6, -24.6)	<0.001	-35.3	(-46.6, -23.9)	<0.001
<b>Treatment concerns</b>									
PHQ 5–9 (vs. 0–4)	-12.1	(-17.4, -6.7)	<0.001	-11.4	(-17.1, -5.5)	<0.001	-10.7	(-16.6, -4.8)	<0.001
PHQ 10 (vs. 0–4)	-28.2	(-36.7, -19.6)	<0.001	-27.9	(-36.5, -19.2)	<0.001	-27.5	(-36.5, -18.6)	<0.001
<b>Treatment satisfaction</b>									
PHQ 5–9 (vs. 0–4)	-11.2	(-17.9, -4.4)	0.001	-9.4	(-16.7, -1.9)	0.014	-8.3	(-15.9, -0.8)	0.031
PHQ 10 (vs. 0–4)	-15.7	(-26.6, -4.8)	0.005	-15.3	(-26.4, -4.14)	0.008	-14.1	(-25.7, -2.6)	0.017
<b>GPSS</b>									
PHQ 5–9 (vs. 0–4)	1.9	(1.1, 2.7)	<0.001	1.8	(0.9, 2.7)	<0.001	1.9	(1.0, 2.7)	<0.001
PHQ 10 (vs. 0–4)	5.5	(4.2, 6.8)	<0.001	5.6	(4.3, 6.9)	<0.001	5.6	(4.2, 6.9)	<0.001

AFEQT indicates Atrial Fibrillation Effect on Quality of life measure; GPSS, Global Psychological Stress Score; CI, confidence interval. Estimates of difference in outcome measures (AFEQT/GPSS) by PHQ categorized in multivariable linear regression models. Each beta coefficient represents the estimated difference in each respective outcome for patients with PHQ 10 versus PHQ<10. For example, a patient with PHQ 10 has an estimated AFEQT total score 26.4 points (95% CI, -34.4, -18.4) lower than a patient with PHQ<10 after adjustment for age, sex, and race (Model 1).

Model 1 adjusted for age, sex, race.

Model 2 adjusted for age, sex, race, body mass index, smoking history, heart failure, hypertension, diabetes, and vascular disease.

Model 3 adjusted for Model 2 covariates and AF treatment (antiarrhythmics and pulmonary vein isolation), education, and estimated household income.