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Health-Related Quality of Life Associated with Warfarin and Direct Oral Anticoagulants in Venous Thromboembolism

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Supplemental Material for Appendix (See separate Appendix file)

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Abstract

Introduction—Venous thromboembolism (VTE) is commonly treated with oral anticoagulants, including warfarin or direct oral anticoagulants (DOACs). Although DOACs are associated with favorable treatment satisfaction, few studies have assessed whether quality of life differs between DOAC and warfarin users.

Materials and Methods—We invited adults enrolled in two California-based integrated health care delivery systems and with a history of VTE between January 1, 2015 and June 30, 2018 to complete a survey on their experience with anticoagulants. Health-related quality of life (QOL) was assessed using the RAND 36-item Short Form Health Survey (SF-36), which measures QOL in 2 general component scores (physical and mental). We used multivariable linear regression to compare mean QOL component scores between DOAC-users and warfarin-users, adjusting for patient and clinical characteristics.

Results—Overall, 2,230 patients (43.1% women and 31.8% >75 years of age) taking anticoagulants answered at least 1 question on the SF-36, 975 taking DOACs and 1255 taking warfarin. After adjustment for patient-level factors, there were no significant differences in either physical component scores (39.2 v 38.3, p=0.24) or mental component scores (48.5 v 49.0, p=0.42) between DOAC and warfarin users.

Conclusions—Health-related QOL did not significantly differ between DOAC and warfarin users with a history of VTE.

Keywords

Thrombosis; Quality of life; Venous thromboembolism (VTE); Pulmonary embolism (PE); Deep vein thrombosis (DVT); Anticoagulation

Background

Venous thromboembolism (VTE) is a common cardiovascular condition, affecting ~100 per 100,000 people annually in the United States, and in some circumstances leads to chronic symptoms and the need for extended treatment.[1] Anticoagulant medications are the primary treatment for acute VTE and are also used to prevent recurrence of events.[2] The two categories of oral anticoagulants used for VTE treatment and prevention are vitamin K antagonists (e.g., warfarin sodium) and the direct oral anticoagulants (DOACs), which include dabigatran, rivaroxaban, apixaban, and edoxaban. DOACs are administered in fixed doses, do not require routine drug monitoring, and are associated with fewer drug-drug and dietary interactions compared with warfarin. DOACs are also associated with greater satisfaction with treatment, although the magnitude of the difference is small.[3] Relatively few studies have explored whether there are also differences in health-related quality

of life (QOL) with DOAC use as compared to warfarin.[4–7] Health-related QOL reflects patients' perspectives on how they are affected by a disease or treatment and is essential to understanding the net impact therapeutics have on people.[8] Our study's objective was to compare the health-related QOL between DOAC-users and warfarin-users in a large community-based population of adults taking anticoagulants for VTE.

Methods

Participants and setting

This study included adults (aged ≥18 years) enrolled in Kaiser Permanente Northern California (KPNC) or Kaiser Permanente Southern California (KPSC), integrated healthcare delivery systems that provide care to >9 million people and are representative of the racially and ethnically diverse population of California.[9,10]

We identified and invited a set of eligible patients to participate in a survey on their experience with anticoagulants. Eligible patients were all non-deceased adults who completed an initial 3-month treatment course of oral anticoagulants after an incident diagnosis of acute VTE that occurred between January 1, 2015 and June 30, 2018; were actively enrolled in the health plan; had a valid mailing address and/or telephone number at the time of the survey; and whose primary language was English, Spanish, or Chinese. We excluded patients with a previous diagnosis of VTE or who were dispensed an oral anticoagulant in 4 years before the VTE diagnosis. We also excluded patients with missing age or gender information or with less than 12 months of continuous enrollment and pharmacy benefits prior to the VTE index date.

From diagnosis codes, we categorized the index VTE events as pulmonary embolism (PE) with or without other thrombosis, lower extremity deep venous thrombosis (DVT), upper extremity DVT, and other VTE (e.g., mesenteric thrombosis). Data on subject demographics (age, self-reported gender and race, and Hispanic ethnicity) were obtained from health plan administrative databases. All warfarin and DOAC prescriptions were identified from the health plan pharmacy dispensing databases. Patients were defined as "DOAC-users" or "warfarin users" based on the anticoagulant dispensed most proximal to the survey completion date.

As previously described, surveys were delivered by ANA Research, Inc., a market research company, and occurred in two waves, the first during Summer 2018 and the second in Spring 2019.[3] Subjects were mailed a survey invitation and, when possible, sent an email invitation as well. Surveys were available in English, Spanish, or Chinese and could be completed on a paper form, by telephone, or online via secure web link. Follow-up phone calls were issued to non-respondents. Subjects were offered an honorarium of US $25 upon survey completion.

The survey included questions about marital status, educational attainment, household income, history of bleeding complications from anticoagulants, and whether the subject had a history of switching from one anticoagulant to another. For this analysis, we only

included responses from patients who indicated they were actively taking anticoagulants in the 4 weeks before completing the survey.

Health-related QOL was measured using the RAND 36-Item Health Survey Version 1.0 (SF-36), a general measure of health-related QOL and the most widely used and validated patient-reported measure.[11] The SF-36 assesses 8 health subscales: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perception. Each item on the SF-36 is scored from 0 to 100 such that a high score correlates to a more favorable health state. Items in the same scale are then averaged to create the 8 subscales as well as 2 general component scores (a physical component score and a mental component score). As per developer recommendations, missing responses were not taken into account when calculating a subscale.

Statistical Analysis

The goal of the study was to determine whether there were differences in health-related QOL between DOAC-users and warfarin-users. The primary outcomes were the Physical Component Summary Score (PCS) and the Mental Component Summary Score (MCS). For the general component scores, the raw summary score was transformed into a norm-based T score such that a score and standard deviation of 50 (±10) reflects the mean of the general US population. For comparison, a difference of between 10 to 12.5 on the SF-36 subscales and component scores has been considered a minimal clinically important difference in chronic lung disease and heart disease.[12] As secondary outcomes, we also compared whether there were differences between DOAC and warfarin users in terms of the individual subscales.

We then created separate general multivariable linear regression models, modeling as the outcomes the PCS and MCS, and with the primary independent variable of anticoagulant category (warfarin versus DOAC). Models were adjusted for clinical and demographic characteristics that were plausibly related to the choice of anticoagulant treatment and QOL; these variables included a history of prior anticoagulant-related bleeding and a history of switching from one anticoagulant to another. Differences in the mean PCS and MCS were computed as the Least Squares mean, adjusted for the means of the other covariates. Aside from including a “missing/not-reported” category for race and ethnicity, the other variables had minimal missing data, so we developed the models using only complete data. There were no missing data for the primary independent variable, anticoagulant category.

Because subjects were not randomly allocated to one treatment type or another, we attempted to control for the possibility that some patients were more likely to be prescribed DOACs or warfarin by including in the models a high-dimensional propensity score (hdPS) that represented the likelihood a patient was prescribed a DOAC. hdPS are developed through automated or data-driven algorithms that take advantage of the availability of large administrative data sources and may approximate point estimates of risk more accurately than standard propensity scores.[13] The hdPS for this study was developed using 5 dimensions (principal inpatient/emergency department [ED] diagnoses

only, secondary inpatient/ED diagnoses, outpatient/ED diagnoses, procedures from any setting, and outpatient drug claims) and used a look-back period of 4 years. Within each dimension, the 300 most common codes were ranked by frequency, and then the final hdPS was developed by regressing the exposure variable (anticoagulation type) on the covariates. The hdPS was then included as an adjustment variable in the multivariable models.

Finally, because patients who change anticoagulant types may have done so due to dissatisfaction with a given treatment, we repeated the analyses restricting to patients who did not report a history of switching anticoagulants.

This study was approved by the institutional review boards of the participating sites. The authors had full access to all the data in the study and take responsibility for its integrity and the data analysis.

Results

There were 12,737 people with a history of VTE who met initial eligibility criteria and were invited to participate in the survey of anticoagulation experience, out of whom 5,017 (39.3%) answered at least one survey question. A total of 2,244 subjects reported they were actively taking anticoagulants and of these, 2,230 answered at least one question on the SF-36. Among the latter, 975 were DOAC-users and 1255 were warfarin-users.

Compared with warfarin users, patients taking DOACs were on average younger and had higher educational attainment and household income (Table 1). More DOAC users had PE than DVT as their index VTE event compared with warfarin users (Table 1). Given the known increased uptake of DOACs over time, DOAC users had been diagnosed with VTE more recently than patients taking warfarin (Table 1). In addition, more DOAC than warfarin users reported switching from one anticoagulant to another (43.1% v. 9.6%, $p<0.001$).

In unadjusted analyses, the overall QOL of the DOAC and warfarin groups did not significantly differ, with similar mean PCS scores (40.7 v 39.1, $p=0.147$, Table 2) and MCS scores (49.7 v 49.5, $p=0.471$). Within individual subscales, DOAC-users on average reported better physical functioning (63.9 v 59.0, $p=0.002$), social functioning (74.5 v 71.7, $p=0.029$), and bodily pain (64.9 v 62.2, $p=0.024$) than warfarin-users. Physical role limitations, emotional health limitations, mental health, and vitality did not significantly differ between DOAC- and warfarin-users (Table 2). On average, DOAC-users had better general health perception than warfarin-users (56.8 v 54.5, $p=0.018$).

After multivariable adjustment, there remained no significant difference in overall QOL between DOAC- and warfarin-users, with comparable mean PCS scores (39.2 v 38.3, $p=0.239$, Table 3) and MCS scores (48.5 v 49.0, $p=0.420$, Table 4). Multivariable models were adjusted for age, gender, race, Hispanic ethnicity, household income, educational attainment, marital status, patient-reported history of bleeding, VTE type, year of diagnosis, whether the patient reported switching anticoagulants, and the hdPS. Several other factors were associated with differences in PCS and MCS scores. In particular, female gender, older age, and a history of bleeding were all associated with lower PCS scores (Table 3). Female

gender and history of bleeding were also associated with lower MCS scores, while older age was associated with higher MCS scores (Table 4).

Results were similar in a subgroup analysis restricted to patients who did not report a history of switching anticoagulants: on average, patients taking DOACs and warfarin without a switch did not have significant differences in PCS or MCS scores (Appendix Tables A and B).

Discussion

In this study of 2,230 people taking anticoagulants for VTE, general health-related QOL was not significantly different between DOAC and warfarin users. Although DOAC users reported better QOL on subscales for physical functioning, social functioning and bodily pain, these differences were small.

To place these findings in context, we found that people taking anticoagulants for VTE had lower PCS scores than those with other chronic conditions but similar MCS scores. For example, adults with chronic lung disease, congestive heart failure and ischemic heart disease have mean PCS scores ranging between 47.5 and 48.6 and MCS scores between 49.6 to 49.7.[14] Furthermore, we found that PCS scores were lower among those who had lived the longest with VTE, while MCS scores were not affected, consistent with prior studies that have demonstrated a decline in physical but not mental health over time.[15]

Our findings expand on the limited existing data on differences in QOL between patients taking DOACs and warfarin. A cross-sectional study of 100 patients with VTE showed no difference in general QOL between those taking DOACs versus warfarin.[4] Similarly, in another cross-sectional study of 208 patients, there was no difference in QOL between the 52.4% receiving warfarin and 47.6% receiving DOAC.[5] Both of these studies are limited by their lack of adjustment for potential confounders. In a sub-analysis of the RE-LY trial that randomized adults with atrial fibrillation (AF) to dabigatran or warfarin for stroke prevention, there was no difference in QOL between those receiving dabigatran or warfarin.[7] The GAInN study, which randomized patients with AF on warfarin to switching to DOAC or remaining on warfarin, also demonstrated no difference in health-related QOL between those who switched to DOAC versus those who remained on warfarin.[6] Notably, in the GAInN study, mean scores on the SF-36 were higher than in our study: in GAInN, PCS was 47 for DOACs and 51 for warfarin and MCS was 55 for DOAC and 55 for warfarin versus PCS 39.2 for DOACs and 38.3 for warfarin, and MCS 48.5 for DOACs and 49.0 for warfarin in our study. This may reflect the careful selection and close monitoring of patients enrolled in clinical trials, or the different clinical indication for anticoagulation. Our study was conducted in a diverse population in the United States, of which there have been few assessments, and specifically addressed patients with VTE, offering insights into real-world practice.

Although not the primary objective of our study, we found significant differences in QOL on anticoagulants in certain subgroups. Women and those with a history of bleeding had lower

scores for both mental and physical function on either DOACs or warfarin. Older patients had lower physical function scores but higher mental function scores.

QOL is a patient-reported outcome and should be prioritized as highly as clinical outcomes such as thrombotic and bleeding events.[8] Thus, incorporating QOL information, in addition to efficacy and safety, is key to aligning anticoagulant decision-making with patient-centered goals and values. Although warfarin is considerably less convenient than DOACs, it is interesting that prior studies have not found being on warfarin (as opposed to fixed dose therapies such as aspirin and DOACs) to substantially impact QOL.[16] In contrast, treatment satisfaction, a related but distinct patient-reported outcome, appears higher with DOACs, although the differences were clinically small.[3] Measurement of different facets of patient experience, including both QOL and treatment satisfaction, is key to incorporating patients' voices in optimizing care.

The limitations of our study are related to its observational design. In addition to multivariable modeling, we incorporated a high dimensional propensity score to mitigate confounding by indication. However, unmeasured factors leading to a patient or clinician to choose a specific anticoagulant may have residual influence on QOL. In addition, although this was a large survey with more than 2000 responders, those who chose to respond may differ from those who declined to respond such that the results of this study do not apply to the overall population. Finally, although our study sampled patients at different phases of treatment after the initial 3-month period, longitudinal QOL measurement would add additional information on the impact of these chronic therapies.

In this large, community-based survey of patients with VTE taking anticoagulants, we found no differences in overall QOL between patients taking DOACs versus warfarin, although DOACs were associated with small improvements in physical functioning, social functioning and bodily pain. This serves as preliminary evidence that the choice between DOAC versus warfarin may not substantially impact patients' QOL. Future studies should incorporate treatment- or condition-specific patient-reported measures, as these may provide more detailed QOL information not captured by generic measures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Survey of 2230 Patients Taking Anticoagulants for Venous Thromboembolism Who Answered at Least One Question on the SF-36, Comparing Characteristics of DOAC and Warfarin Users

Characteristic	DOAC users (n=975)	Warfarin users (n=1,255)	p-value
Age at time of survey			0.02
≤ 54 yrs	158 (16.2%)	227 (18.1%)	
55–64 yrs	211 (21.6%)	255 (20.3%)	
65–74 yrs	318 (32.6%)	352 (28%)	
75–84 yrs	223 (22.9%)	297 (23.7%)	
≥85 yrs	65 (6.7%)	124 (9.9%)	
Women	407 (41.7%)	555 (44.2%)	0.24
Self-reported Race			0.18
White	741 (76%)	900 (71.7%)	
Black or African-American	89 (9.1%)	131 (10.4%)	
Asian or Pacific Islander	26 (2.7%)	32 (2.5%)	
Multiple race or Other race	88 (9%)	138 (11%)	
Missing	31 (3.2%)	54 (4.3%)	
Self-reported Ethnicity			0.43
Hispanic	95 (9.7%)	143 (11.4%)	
Non-Hispanic	853 (87.5%)	1075 (85.7%)	
Missing	27 (2.8%)	37 (2.9%)	
Educational attainment			<0.0001
Less than HS Graduate	35 (3.6%)	43 (3.4%)	
12th grade, HS graduate or GED, Some college or technical school	461 (47.2%)	714 (56.9%)	
Completed Bachelor degree	230 (23.6%)	252 (20.1%)	
Completed Graduate degree	212 (21.7%)	197 (15.7%)	
Unknown/Missing	37 (3.8%)	49 (3.9%)	
Household income			0.005
Income ≤ $25,000	92 (9.4%)	142 (11.3%)	
Income $25,001 to $50,000	125 (12.8%)	222 (17.7%)	
Income $50,001 to $100,000	270 (27.7%)	363 (28.9%)	
Income ≥$100,001	273 (28%)	271 (21.6%)	
Income: Prefer not to answer	215 (22.1%)	257 (20.5%)	
Marital status			0.55
Married or in a committed relationship	639 (65.5%)	797 (63.5%)	
Widowed; Single, Divorced, or separated	302 (31.0%)	416 (33.2%)	
History of switching anticoagulant			<0.001
Yes	420 (43.1%)	120 (9.6%)	
No	516 (52.9%)	1075 (85.7%)	
Self-reported History of Bleeding			0.045
Yes	100 (10.3%)	162 (12.9%)	
No	864 (88.6%)	1069 (85.2%)	

Characteristic	DOAC users (n=975)	Warfarin users (n=1,255)	p-value
Index VTE type			0.01
PE	566 (58.1%)	652 (52.0%)	
Lower Extremity DVT	354 (36.3%)	501 (39.9%)	
Other VTE	27 (2.8%)	60 (4.8%)	
Upper Extremity DVT	28 (2.9%)	42 (3.4%)	
Year of Index VTE			<0.001
2015	157 (16.1%)	464 (37.0%)	
2016	319 (32.7%)	486 (38.7%)	
2017	323 (33.1%)	233 (18.6%)	
2018	176 (18.1%)	72 (5.7%)	

Abbreviations: DOAC (direct oral anticoagulant); yrs (years); HS (high school); GED (general educational development); VTE (venous thromboembolism); DVT (deep venous thrombosis); PE (pulmonary embolism)

Table 2.

Unadjusted SF-36 Subscales and the Physical Component Summary and Mental Component Summary of Patients Taking Anticoagulants for Venous Thromboembolism. SD: standard deviation.

	DOAC users (n=975)		Warfarin users (n=1,255)		
	N	**Mean (SD)**	**N**	**Mean (SD)**	**p-value**
Physical functioning	971	63.9 (31.36)	1252	59.0 (33.49)	0.002
Social functioning	968	74.5 (27.82)	1246	71.7 (29.08)	0.03
Physical role limitations	969	54.7 (43.98)	1242	51.3 (43.65)	0.08
Emotional health limitations	967	70.1 (39.33)	1239	67.2 (40.85)	0.11
Mental health	960	74.5 (18.76)	1237	73.9 (19.25)	0.50
Vitality	960	50.8 (22.82)	1237	49.0 (23.51)	0.06
Bodily pain	964	64.9 (26.90)	1246	62.2 (27.53)	0.02
General health perception	975	56.8 (22.23)	1255	54.5 (22.52)	0.02
Physical Component Summary	954	40.7 (12.17)	1226	39.1 (12.72)	0.15
Mental Component Summary	954	49.7 (10.80)	1226	49.5 (11.04)	0.47

*Denominator varies due to subjects not answering all items on the SF-36

Table 3.

Quality of Life Among 2,180 Patients with Venous Thromboembolism: Adjusted Least Mean Physical Component Summary with 95% Confidence Intervals (CI), and P-values for the Difference in Means from Multivariable General Linear Model.*

Variable	Adjusted Mean SF-36 Physical Component Scale (95% CI)	p value
Anticoagulant type		
DOAC	39.16 (37.30–41.02)	0.24
Warfarin	38.29 (36.40–40.18)	ref
Age		
age <=54	43.70 (41.73–45.67)	ref
age 55–64	40.65 (38.67–42.62)	0.0003
age 65–74	38.75 (36.81–40.67)	<.0001
age 75–84	36.83 (34.84–38.83)	<.0001
age >=85	33.70 (31.19–36.21)	<.0001
Gender		
Women	37.00 (35.20–38.81)	<.0001
Men	40.45 (41.73–45.67)	ref
Self-reported race		
Asian or Pacific Islander	39.59 (36.09–43.09)	0.46
Black or African American	39.67 (37.39–41.96)	0.15
Multiple, Other Race, or Unknown	37.27 (35.27–39.27)	0.24
White	38.37 (36.71–40.03)	ref
Self-reported Hispanic ethnicity		
Yes	38.88 (36.60–41.17)	0.76
No	38.57 (36.88–40.26)	
Educational attainment		
Less than HS Graduate	37.10 (33.79–40.41)	ref
12th grade, HS graduate or GED, Some college or technical school	37.21 (35.46–38.96)	0.95
Completed Bachelor degree	41.01 (39.06–42.95)	0.02
Completed Graduate degree	39.59 (37.57–41.60)	0.15
Household income		
Income ≤ $25,000	35.05 (32.85–37.25)	ref
Income $25,001 to $50,000	37.65 (35.59–39.71)	0.01
Income $50,001 to $100,000	40.49 (38.57–42.42)	<.0001
Income ≥ $100,001	41.87 (39.78–43.96)	<.0001
Income: Prefer not to answer	38.57 (36.42–40.72)	0.0015
Marital status		
Married or in a committed relationship	39.09 (37.17–41.01)	0.25
Widowed; Single, Divorced, or separated	38.36 (36.60–40.12)	ref
History of switching anticoagulant		
Yes	38.33 (36.40–40.27)	<.0001
No	39.12 (37.35–40.88)	ref

Variable	Adjusted Mean SF-36 Physical Component Scale (95% CI)	p value
Self-reported History of Bleeding		
Yes	36.73 (34.59–38.87)	<.0001
No	40.72 (39.06–42.38)	ref
Index VTE type		
PE	37.24 (35.64–38.85)	ref
Lower Extremity DVT	38.48 (36.83–40.14)	0.03
Other VTE	40.14 (37.20–43.09)	0.04
Upper Extremity DVT	39.04 (35.86–42.21)	0.23
Year of Index VTE		
2015	37.54 (35.62–39.46)	ref
2016	38.94 (37.09–40.79)	0.036
2017	38.11 (36.16–40.06)	0.46
2018	40.32 (38.05–42.60)	0.005
hdPS	NA	0.58

Abbreviations: DOAC (direct oral anticoagulant); yrs (years); HS (high school); GED (general educational development); VTE (venous thromboembolism); DVT (deep venous thrombosis); PE (pulmonary embolism); hdPS (high dimensional propensity score)

Table 4.

Quality of Life Among 2,180 Patients with Venous Thromboembolism: Adjusted Least Mean Mental Component Summary with 95% Confidence Intervals (CI), and P-values for the Difference in Means from Multivariable General Linear Model.*

Variable	Adjusted Mean SF-36 Mental Component Scale (95% CI)	p value
Anticoagulant type		
DOAC	48.48 (46.78–50.18)	0.42
Warfarin	49.03 (47.29–50.76)	Ref
Age		
age ≤54	45.24 (43.45–47.04)	Ref
age 55–64	47.69 (45.89–49.50)	0.002
age 65–74	49.26 (47.49–51.03)	<.0001
age 75–84	50.21 (48.39–52.03)	<.0001
age ≥85	51.36 (49.07–53.66)	<.0001
Gender		
Women	47.97 (46.32–49.61)	0.002
Men	49.54 (47.87–51.21)	Ref
Self-reported race		
Asian or Pacific Islander	50.09 (46.89–53.29)	0.60
Black or African American	49.69 (47.60–51.78)	0.64
Multiple, Other Race, or Unknown	45.94 (44.11–47.76)	<.0001
White	49.30 (47.77–50.82)	Ref
Self-reported Hispanic ethnicity		
Yes	49.50 (47.41–51.59)	0.12
No	48.01 (46.46–49.55)	
Educational attainment		
Less than HS Graduate	47.70 (44.67–50.73)	Ref
12th grade, HS graduate or GED, Some college or technical school	48.25 (46.65–49.85)	0.71
Completed Bachelor degree	49.94 (48.16–51.71)	0.15
Completed Graduate degree	49.13 (47.28–50.97)	0.37
Household income		
Income ≤ $25,000	46.17 (44.16–48.18)	Ref
Income $25,001 to $50,000	48.44 (46.56–50.32)	0.02
Income $50,001 to $100,000	48.80 (47.04–50.55)	0.004
Income ≥$100,001	50.72 (48.81–52.63)	<.0001
Income: Prefer not to answer	49.64 (47.67–51.61)	0.0006
Marital status		
Married or in a committed relationship	48.37 (46.62–50.12)	0.19
Widowed; Single, Divorced, or separated	49.14 (47.53–50.74)	Ref
History of switching anticoagulant		
Yes	48.57 (46.81–50.34)	0.55
No	48.93 (47.32–50.55)	Ref

Variable	Adjusted Mean SF-36 Mental Component Scale (95% CI)	p value
Self-reported History of Bleeding		
Yes	47.14 (45.19–49.09)	<.0001
No	50.37 (48.85–51.88)	Ref
Index VTE type		
PE	47.98 (46.51–49.44)	Ref
Lower Extremity DVT	48.42 (46.91–49.93)	0.38
Other VTE	48.36 (45.67–51.05)	0.76
Upper Extremity DVT	50.26 (47.35–53.17)	0.10
Year of Index VTE		
2015	50.29 (48.54–52.05)	Ref
2016	48.24 (46.55–49.93)	0.0008
2017	48.32 (46.54–50.10)	0.005
2018	48.16 (46.08–50.24)	0.02
hdPS	NA	0.10

Abbreviations: DOAC (direct oral anticoagulant); yrs (years); HS (high school); GED (general educational development); VTE (venous thromboembolism); DVT (deep venous thrombosis); PE (pulmonary embolism); hdPS (high dimensional propensity score)