

Appendix 1: International Classification of Diseases, 9th Revision (ICD-9) Codes

Mental Health Condition	ICD-9 Codes
Anxiety Disorders	300.0x Anxiety disorders 300.1x Dissociative, conversion and factitious disorders 300.2x Phobic disorders 300.3x Obsessive-compulsive disorders
Bipolar Disorder	296.0x-296.1x 296.4x-296.9x
Major Depression	296.2x-296.3x 296.82 Atypical depressive disorder 300.4 Dysthymic disorder 311 Depressive disorder, not elsewhere classified
Post Traumatic Stress Disorder (PTSD)	309.81
Schizophrenia	295.x
Other Psychotic disorders	298.0 Depressive type psychosis 298.1 Excitatory type psychosis 298.4 Psychogenic paranoid psychosis 298.8 Other and unspecified reactive psychosis 298.9 Unspecified psychosis 297.1 Shared psychotic disorder 297.3 Delusional disorder

Appendix 2: Characteristics of patients with GAF scores and missing GAF scores, among experienced warfarin users with mental health conditions (N=28,216)

Variables	GAF Available N=13,628 %	GAF Missing N=14,588 %
% of patients with any outpatient MHC visit	99.4	93.7
Female Gender	3.5	2.7
Age Group		
20-54	16.1	8.2
55-59	23.9	14.2
60-64	17.8	14.1
65-69	8.7	10.8
70-74	10.2	13.9
75+	23.3	38.7
Race/Ethnicity		
Non-Hispanic White	81.7	85.9
Non-Hispanic Black	11.4	8.8
Others	6.9	5.3
Primary Indication for Warfarin*		
Atrial Fibrillation	52.2	59.6
Venous Thromboembolism	39.3	31.7
All Others Combined	8.5	8.7
Date of Warfarin Inception		
>= 6 months before study inception	68.2	72.1
6 months before study - First year of study	27.0	23.6
Second year of the study	4.9	4.3
Comorbid Conditions		
Cancer (newly diagnosed)	6.5	7.9
Chronic Kidney Disease	13.3	15.7
Chronic Liver Disease	2.1	1.3
Chronic Lung Disease	36.0	35.8
Diabetes	43.4	41.2
Epilepsy	5.3	4.0
Heart Failure	32.0	37.1
Dementia	9.8	8.7
Alcohol Abuse	22.7	11.8
Substance Abuse (non-Alcohol)	14.4	5.5

GAF: Global Assessment of Function

Appendix 3

Table 1: Distribution of mental health conditions

	% of those with MHCs	% of total population
Any MHC	---	27.2
Anxiety disorders	28.8	7.8
Bipolar	8.6	2.3
Depression	69.4	18.8
PTSD	26.8	7.3
Schizophrenia	3.9	1.1
Psychotic disorders	7.1	1.9

MHC: Mental Health Condition

PTSD: Post-Traumatic Stress Disorder

Table 2: Distribution of comorbid mental health diagnoses

	Bipolar (%*)	Depression (%)	PTSD (%)	Schizophrenia (%)	Other Psychotic disorders (%)
Anxiety disorders	628 (0.6)	4,340 (4.2)	1,628 (1.6)	206 (0.2)	353 (0.3)
Bipolar	---	1,312 (1.3)	679 (0.7)	200 (0.2)	163 (0.2)
Depression	---	---	4,285 (4.1)	429 (0.4)	807 (0.8)
PTSD	---	---	---	229 (0.2)	312 (0.3)
Schizophrenia	---	---	---	---	168 (0.2)

* Percentage of total study population

Table 3: Association between top dual psychiatric diagnoses, TTR and hemorrhage

	N (%)	Average % TTR	% with bleeds
Anxiety-Depression	4,340 (4.2)	55.8	5.9
Depression-PTSD	4,285 (4.1)	55.6	4.9
Anxiety-PTSD	1,628 (1.6)	56.6	5.7
Depression-Bipolar	1,312 (1.3)	52.0	5.4
Depression-Psychotic disorders	807 (0.8)	52.4	6.9
Anxiety-Bipolar	628 (0.6)	51.8	6.4

TTR: Percent Time in Therapeutic Range

Table 4: Association between the number of comorbid psychiatric diagnoses, TTR and hemorrhage

# of concurrent mental health conditions	N (% of total population)	Average % TTR	% with bleeds
1	18,406 (17.7)	58.1	5.6
2	7,485 (7.2)	56.0	5.4
3	1,973 (1.9)	54.0	5.4
4+	352 (0.3)	50.5	5.9

TTR: Percent Time in Therapeutic Range

Table 5: Effect of GAF method on average percentage time in therapeutic range (TTR) distribution

GAF Score	(Lowest GAF method)		(Average GAF method)	
	N	Average TTR	N	Average TTR
Missing	14,588	58.3%*	14,588	58.3%*
71-100	439	60.9%*	692	60.5%*
51-70 (reference)	6,759	57.3%	8,850	56.5%
31-50	6,067	54.3%*	3,979	54.0%*
0-30	363	49.0%*	107	50.5 %

*P<0.05 (ANOVA)

GAF: Global Assessment of Function

Appendix 4: Cox regression of major hemorrhagic incidences among all patients, including beta coefficients for covariates not shown in the manuscript

	All Patients		Only Patients with MHCs	
	Model 1:	Model 2:	Model 3: without imputation	Model 4: with imputation
Any mental health condition	1.19†			1.12
GAF >50			0.86	1.00
GAF missing			1.01	
Psychiatric hospitalization			1.10	1.12
Anxiety disorders		1.13*	1.12	1.10
Bipolar disorder		1.10	1.11	1.09
Depression		1.16†	1.14	1.12
PTSD		1.01	1.00	0.98
Schizophrenia		0.84	0.82	0.82
Other psychotic disorders		1.25*	1.24*	1.24*
Age <55	--	--	--	
Age 55-59	1.16	1.17	1.14	1.14
Age 60-64	1.33*	1.34*	1.35*	1.36*
Age 65-69	1.91†	1.91†	1.87†	1.87†
Age 70-74	2.55†	2.55†	2.32†	2.33†
Age ≥75	3.33†	3.33†	3.00†	3.04†
TTR 0-30	2.48†	2.47†	2.24†	2.24†
TTR 31-40	1.91†	1.91†	1.59†	1.59†
TTR 41-50	1.66†	1.65†	1.58†	1.58†
TTR 51-60	1.39†	1.39†	1.40†	1.39†
TTR 61-70	1.16†	1.16†	1.12	1.11
TTR >70	--	--	--	--
Hypertension	0.85†	0.85†	0.92	0.92
Stroke history	1.43†	1.43†	1.44†	1.44†
Chronic liver disease	1.74†	1.74†	2.20†	2.21†
Chronic kidney disease	1.95†	1.95†	1.72†	1.72†
Alcohol abuse	1.17*	1.17*	0.98	0.98
Non-alcohol substance abuse	1.22	1.20	1.15	1.15

MHC: Mental health condition; TTR: Percentage time in therapeutic range

*p < 0.05 and † p < 0.001

Appendix 5: Comparison of prevalence of mental health conditions between our database of 103,987 prevalent users of warfarin in VA, 2006-8, and the prevalence of similar conditions in the 1999 Veterans' Large Health Survey. Percentages of the total population are given.

	1999 Large Health Survey	Current Study
Anxiety	8.8	7.8
Bipolar Disorder	4.0	2.3
Depression	15.1	18.8
PTSD	6.8	7.3
Schizophrenia	4.6	1.1
Other Psychotic Disorders	Not assessed	1.9

Note – In the Large Health Survey, patients self-reported these conditions, in response to a question such as, “Has a doctor or medical professional ever told you that you have --?”. Statistical tests were not possible, as we did not possess the raw data from the 1999 Large Health Survey²⁰.

Appendix 6: Propensity score case-control match

Variables	Case (with MHCs) (%)	Control (without MHCs) (%)
Total	28,146	28,146
Female Gender	876 (3.1)	918 (3.3)
Age Group		
20-54	3,359 (11.9)	3,335 (11.8)
55-59	5,298 (18.8)	5,321 (18.9)
60-64	4,488 (15.9)	4,544 (16.1)
65-69	2,756 (9.8)	2,781 (9.9)
70-74	3,416 (12.1)	3,361 (11.9)
75+	8,829 (31.4)	8,804 (31.3)
Race/Ethnicity		
Non-Hispanic White	23,608 (83.9)	23,509 (83.5)
Non-Hispanic Black	2,816 (10)	2,995 (10.6)
Hispanic	979 (3.5)	972 (3.5)
Asian	94 (0.3)	87 (0.3)
Native American	139 (0.5)	84 (0.3)
Other/Unknown	510 (1.8)	499 (1.8)
Percent Poverty, Quintiles		
Wealthiest (0.0-5.9%)	5,302 (18.8)	5,255 (18.7)
Wealthy (5.9-9.0%)	5,631 (20)	5,523 (19.6)
Moderate (9.0-12.6%)	5,661 (20.1)	5,742 (20.4)
Poor (12.6-17.8%)	5,818 (20.7)	5,989 (21.3)
Poorest (17.8-100.0%)	5,734 (20.4)	5,637 (20.0)
Driving Distance to Nearest VA, Quintiles		
Nearest (3.1 miles or closer)	5,657 (20.1)	5,497 (19.5)
Near (3.1 – 6.0 mi.)	5,637 (20)	5,663 (20.1)
Moderate (6.0 – 10.5 mi.)	5,652 (20.1)	5,724 (20.3)
Far (10.5 – 20.3 mi.)	5,723 (20.3)	5,712 (20.3)
Farthest (20.3 mi. or farther)	5,477 (19.5)	5,550 (19.7)
Date of Warfarin Inception		
>= 6 months before study inception	19,778 (70.3)	19,944 (70.9)
6 months before study – First year of study	7,080 (25.2)	7,011 (24.9)
Second year of the study	1,288 (4.6)	1,191 (4.2)
Primary Indication for Warfarin‡		
Atrial Fibrillation	15,787 (56.1)	15,979 (56.8)
Venous Thromboembolism	9,941 (35.3)	9,729 (34.6)
All Others Combined	2,418 (8.6)	2,438 (8.7)
Physical Comorbid Conditions		
Cancer (newly diagnosed)	1,818 (6.5)	1,841 (6.5)
Chronic Kidney Disease	1,983 (7)	2,031 (7.2)
Chronic Liver Disease	314 (1.1)	362 (1.3)
Chronic Lung Disease	7,397 (26.3)	7,241 (25.7)

Coronary Artery Disease		
Diabetes	11,281 (40.1)	11,235 (39.9)
Epilepsy	909 (3.2)	925 (3.3)
Heart Failure	7,933 (28.2)	7,927 (28.2)
Hyperlipidemia	17,581 (62.5)	17,620 (62.6)
Hypertension	20,895 (74.2)	20,841 (74)
Pain Disorders	17,833 (63.4)	17,844 (63.4)
Peripheral Arterial Disease	4,039 (14.4)	4,198 (14.9)
Previous Stroke	6,129 (21.8)	6,358 (22.6)
Mental Comorbid Conditions		
Alcohol Abuse	1,998 (7.1)	1,927 (6.8)
Dementia	1,053 (3.7)	1,108 (3.9)
Substance Abuse (non-Alcohol)	713 (2.5)	669 (2.4)
Number of Non-Warfarin Medications		
0-7	6,371 (22.6)	6,324 (22.5)
8-11	9,144 (32.5)	9,184 (32.6)
12-15	7,238 (25.7)	7,232 (25.7)
16+	5,393 (19.2)	5,406 (19.2)
Number of Hospitalizations during Experienced Period		
None	17,851 (63.4)	17,782 (63.2)
1	4,695 (16.7)	4,695 (16.7)
2	2,371 (8.4)	2,457 (8.7)
3	1,267 (4.5)	1,223 (4.3)
4+	1,962 (7)	1,989 (7.1)
Average Time in Therapeutic Range (SD)	57.2 (22.5)	57.2 (22.8)

Appendix 7: Nested linear regression models of the association between mental health conditions and percent time in therapeutic range, a measure of anticoagulation control (all covariates included; N=103,897)

Variable	Model 1	Model 2	Model 3	Model 4
Intercept	63.06†	64.22†	66.35†	67.54†
Model R ²	0.0168	0.0306	0.0532	0.0756
Mental Health Conditions				
Anxiety disorders	-1.31†	-1.18†	-0.86†	0.18
Bipolar disorder	-5.50†	-4.55†	-3.74†	-2.63†
Depression	-5.06†	-4.41†	-3.54†	-2.26†
PTSD	-2.22†	-1.12†	-0.68*	-0.01
Schizophrenia	-4.40†	-2.22†	-1.43*	-0.36
Other psychotic disorders	-5.59†	-5.77†	-4.51†	-2.92†
Demographics				
Female Gender		-2.55†	-3.17†	-2.48†
Age Group				
20-54		-6.49†	-6.71†	-5.32†
55-59		-2.88†	-2.88†	-1.69†
60-64		-1.44†	-1.42†	-0.34
65-69		0.25	0.20	0.75†
70-74		0.58*	0.57*	0.87†
75+				
Race/Ethnicity				
Non-Hispanic White				
Non-Hispanic Black		-5.10†	-4.54†	-3.48†
Others		-1.17†	-1.20†	-0.83*
Physical Comorbid Conditions				
Cancer (newly diagnosed)			-5.22†	-3.79†
Chronic Kidney Disease			-5.29†	-3.98†
Chronic Liver Disease			-4.94†	-3.04†
Chronic Lung Disease			-2.69†	-0.58†
Diabetes			-1.60†	-0.63†
Epilepsy			-2.69†	-1.40*
Heart Failure			-2.44†	-0.66†
Hypertension			0.96†	2.00†
Prior Stroke			-0.53*	-0.67†
Mental Comorbid Conditions				
Alcohol Abuse			-8.22†	-7.64†
Dementia			-4.25†	-3.07†
Substance Abuse (non-Alcohol)			-4.25†	-3.08†
Date of Warfarin Inception				
>= 6 months before study inception				
6 months before study – First year of study				-3.52†
Second year of the study				-6.20†
Primary Indication for Warfarin‡				
Atrial Fibrillation				
Venous Thromboembolism				-1.11†
All Others Combined				-1.05†

Number of Non-Warfarin Medications				
0-7				
8-11				-2.12†
12-15				-3.70†
16+				-5.56†
Number of Hospitalizations during Experienced Period				
None				
1				-3.74†
2				-4.82†
3				-6.03†
4+				-8.45†