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Background and Objective

- Since 2010 four non-vitamin K antagonist oral anticoagulants (NOACs), dabigatran, apixaban, rivaroxaban and edoxaban have been approved in the US.
- Indications include stroke prevention in patients with nonvalvular atrial fibrillation (NVAF), treatment and prophylaxis of deep vein thrombosis (DVT) and pulmonary embolism (PE) especially in patients undergoing hip or knee surgery.
- A recent study comparing NOACs have reported differential benefits and harms among those over age 65 years with atrial fibrillation (AF) ¹.
- However, little information is available on the benefit-harm profiles of NOAC use in those under age 65 years.
- **Objective:** To inform the feasibility of a comparative safety study in younger NOAC users we examined utilization and characteristics of NOAC initiators aged less than 65 years, along with indications for use, in the Sentinel Distributed Database.

Methods

NOAC cohorts	<ul style="list-style-type: none"> • Incident users of NOACs (rivaroxaban 10mg, 15mg and 20mg, apixaban 2.5 mg and 5mg and dabigatran 75mg and 150 mg) aged between 18 and 64 years from October 19, 2010 to September 30, 2015, were identified in SDD • The date of the first dispensing for a NOAC was defined as the index date
Exposure Assessment	<ul style="list-style-type: none"> • Incident use was indicated by no use of any NOAC or warfarin in the 183 days prior to the index dispensing (baseline period) • Exposure episodes were considered continuous if the gaps in therapy did not exceed 3 days
Descriptive Analysis	<ul style="list-style-type: none"> • Patients were categorized according to NOAC type and strength • To compare NOAC cohorts descriptive characteristics were examined : age, sex, health service utilization and potential indications for use, in the baseline period • Potential indications for use were identified by examining ICD 9-CM diagnosis codes for NVAF, PE, DVT, and surgery (hip, knee, spinal, & joint replacement) in the baseline period • Mean number of dispensings per user and days supplied per dispensing were also examined to estimate duration of use

Results

Overall	NOAC utilization	Most common indication -All NOACs	Most common indication- individual NOACs
<ul style="list-style-type: none"> • 128,954 NOAC initiators aged < 65 years identified • Mean age 54 years • 71.6% of users were aged between 51-64 years • 60.7% of NOAC initiators were male 	<ul style="list-style-type: none"> • Most common NOACs <ul style="list-style-type: none"> • Rivaroxaban 10mg (40,197 initiators) • Rivaroxaban 20mg (36,874 initiators) • Dabigatran 150mg (21,260 initiators) • Initiators of rivaroxaban 10mg, 15mg and apixaban 2.5mg used NOACs for shorter durations indicated by lower days supply per dispensing and mean number of dispensings per user 	<ul style="list-style-type: none"> • Atrial fibrillation (no DVT or PE) (40.9%) • DVT or PE no AF (19.6%) • Joint replacement (19.5%) • 38.5% had no history of AF, PE or DVT 	<ul style="list-style-type: none"> • Apixaban 2.5mg (70.7%) and rivaroxaban 10mg (94.7%) initiators typically had no history of AF, DVT or PE but had a history of surgery (Table 1) • Initiators of dabigatran 150mg (88.4%), dabigatran 75mg (78.6%), rivaroxaban 20mg (59.8%), and apixaban 5mg (78.2%) commonly had a history of AF and no history of DVT or PE (Table 1)

Table 1. Characteristics of individual NOAC initiators and potential indications for use, in SDD, from October 19, 2010 to September 30, 2015

	All NOACs	Apixaban 2.5 mg	Apixaban 5mg	Dabigatran 75 mg	Dabigatran 150 mg	Rivaroxaban 10 mg	Rivaroxaban 15 mg	Rivaroxaban 20 mg
Number of patients	128,954	1,372	13,183	683	21,260	40,197	21,238	36,874
Mean Age (SD)	54 (8.9)	55 (8.5)	56 (7.9)	57 (7.6)	56 (7.7)	55 (8.4)	50 (10.5)	54 (9.1)
	%	%	%	%	%	%	%	%
Age: 21-35 years	5.5	4.6	3.3	2.0	2.8	4.5	12.4	5.9
Age: 36-50 years	22.9	20.4	18.0	16.5	19.0	21.3	34.6	23.4
Age: 51-64	71.6	75.0	78.7	81.4	78.3	74.2	53.0	70.7
Gender (Male)	60.7	46.7	69.7	69.1	76.0	45.9	56.4	67.8
Potential indications								
Atrial fibrillation (AF)	41.9	21.4	79.7	79.8	89.4	2.8	6.9	61.3
AF with no PE or DVT	40.9	20.0	78.2	78.6	88.4	2.7	4.4	59.8
DVT or PE with no AF	19.6	7.9	12.2	4.4	2.6	2.6	76.6	25.0
Neither AF nor PE nor DVT	38.5	70.7	8.1	15.8	8.0	94.7	16.5	13.7
Hip surgery	6.3	13.2	0.3	0.3	0.2	19.0	0.5	0.4
Knee surgery	11.6	23.1	0.5	0	0.3	35.0	1.1	0.7
Spinal surgery	0.7	0.7	0.5	0.1	0.2	1.1	1.1	0.6
Joint replacement	19.5	38.6	2.2	1.6	1.7	56.3	2.9	2.5

Discussion and Conclusions

- A substantial number of NOAC initiators aged less than 65 years were identified in SDD between October 2010 and September 2015.
- Rivaroxaban was the most commonly dispensed NOAC followed by dabigatran.
- Rivaroxaban 10mg, as well as apixaban 2.5mg, tended to be used in prophylaxis of DVT or PE for surgical indications rather than AF, whereas rivaroxaban 15mg tended to be used for treatment of PE or DVT which is in-line with current treatment guidelines.
- Rivaroxaban 10mg, 15mg and apixaban 2.5mg were used for shorter periods than other NOACs indicated by days supplied per dispensing and mean number of dispensings which would be expected if used mostly for surgical prophylaxis of DVT or treatment of DVT or PE.
- Those with a history of NVAF were more likely to initiate Rivaroxaban 20mg, Apixaban 5mg or dabigatran any strength and tended to have longer durations of use.