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Cost of Hospital Admissions in Medicare Patients With Atrial Fibrillation Taking Warfarin, Dabigatran, or Rivaroxaban

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Clinical trial data suggest that direct oral anticoagulants (DOACs) are effective at preventing stroke in patients with nonvalvular atrial fibrillation (AF) but increase gastrointestinal (GI) bleeding risk relative to that of warfarin. The relative costs of DOACs and warfarin in real-world patients are unknown. Therefore, we examined the impact of anticoagulant choice on inpatient costs in patients with AF.

We identified Medicare beneficiaries with AF newly diagnosed (1) from November 2011 through October 2013, who had begun dabigatran, 150 mg, rivaroxaban, 20 mg, or warfarin therapy within 90 days of diagnosis. Patients were excluded if they were <66 years of age; were enrolled in Medicare managed care; had received oral anticoagulant therapy prior to AF diagnosis; underwent open heart surgery within 30 days prior to diagnosis; experienced joint replacement surgery, pulmonary embolism, or deep vein thrombosis within 6 weeks prior to anticoagulant use (to ensure that anticoagulants were intended for long-term use); and had a mechanical heart valve or were of dialysis status. The final samples included 21,979, 23,177, and 101,715 patients who began dabigatran, rivaroxaban, and warfarin therapy, respectively.

Outcomes included admissions and inpatient hospital costs for any reason as well as reasons known to be influenced by anticoagulants, including ischemic stroke, systemic embolism, GI bleeding, other major bleeding, acute myocardial infarction, or heart failure (HF), as defined previously (1). Inpatient hospital costs reflected the payer perspective and were assessed as the total paid by Medicare to the admitting hospital. Patient demographics; comorbidities; stroke and bleeding risk; concurrent medication use; and prior health services utilization were derived from claims incurred within 12 months prior to AF diagnosis, based on recommended protocols (1).

Analysis used 3-way propensity matching to create groups of patients receiving dabigatran, rivaroxaban, or warfarin who were balanced with respect to patient covariates and were therefore plausible candidates for all 3 anticoagulants (2). Covariate balance was achieved by ensuring that standardized differences between groups were <10%. For each outcome, we then used 2-part models consisting of a discrete-time survival analysis for the likelihood of admission over 30-day intervals and a generalized linear regression with a log link to

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estimate expected costs when an admission occurred (3). Censoring occurred due to death, end of observation, or medication termination (defined as the last refill date plus the number of days supplied at the last refill date). Ultimately, predicted values from the 2 models were multiplied together to estimate expected costs per patient-year. Confidence intervals were estimated using 1,000 bootstrap replications.

Table 1 shows admission rates per 1,000 patient-years and inpatient costs per patient-year for each outcome by drug. Overall inpatient admission rates were 560, 544, and 617 admissions per 1,000 patient years for dabigatran, rivaroxaban, and warfarin, respectively. Inpatient costs per person-year were $399 lower for dabigatran and $346 lower for rivaroxaban, compared to warfarin. The largest reductions in costs relative to warfarin occurred with HF ($172 and $192 lower with dabigatran and rivaroxaban, respectively). Costs for all thromboembolic, major bleeding, and acute cardiovascular events combined were also lower for dabigatran and rivaroxaban compared to that for warfarin. There were few differences in outcomes between dabigatran and rivaroxaban, although rivaroxaban users experienced more GI bleeds than dabigatran users.

Although we did not evaluate all health care services, it has been estimated that roughly one-half of resources used by patients with AF are hospital costs (4). We also did not account for the cost of DOACs, which were higher than those for warfarin. Nevertheless, the higher cost for DOACs will change once manufacturer's patents expire.

Our study included only standard doses of DOACs (dabigatran, 150 mg; rivaroxaban, 20 mg), which may, in part, explain discrepancies between our findings and those of clinical trials. For example, 20% of patients in the ROCKET-AF (Rivaroxaban Once daily oral direct factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism) trial received rivaroxaban 15 mg; that trial found no significant decrease in stroke with rivaroxaban relative to warfarin. In contrast to the RE-LY (Randomized Evaluation of Long-term anticoagulant therapY) trial, we did not find risk of GI bleeding with dabigatran that was higher than that with warfarin, which may be due to the increasing use of low-dose dabigatran in patients with high risk for bleeding (5).

Our data suggest that patients with new AF taking dabigatran, 150 mg, or rivaroxaban, 20 mg, experience lower annual inpatient costs than patients taking warfarin, largely due to fewer admissions for stroke, non-GI-related hemorrhage, and HF events.

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TABLE 1

Mean (95% CI) Admission Rates and Inpatient Costs for Dabigatran, Rivaroxaban, and Warfarin

				p Values for Drug Comparisons*		
	Dabigatran	Rivaroxaban	Warfarin	Dabigatran Relative to Warfarin	Rivaroxaban Relative to Warfarin	Rivaroxaban Relative to Dabigatran
Inpatient admissions per 1,000 patient-years						
Stroke	24 (20-28)	21 (18-24)	31 (25-35)	0.002	<0.001	0.12
Embolism	4.1 (2.9-5.6)	3.6 (2.5-4.8)	5.3 (3.9-6.9)	0.24	0.067	0.53
GI hemorrhage	35 (32-39)	44 (40-48)	34 (31-38)	0.65	<0.001	0.002
Other major hemorrhage	4.6 (3.4-6.0)	6.6 (5.1-8.1)	11.8 (10.0-14.0)	<0.001	<0.001	0.049
Acute myocardial infarction	15 (12-17)	12 (10-14)	19 (17-22)	0.007	<0.001	0.089
Heart failure	69 (64-75)	66 (61-71)	93 (86-100)	<0.001	<0.001	0.34
Any stroke, embolism, hemorrhage, or acute cardiovascular event	154 (147-162)	151 (143-159)	197 (188-206)	<0.001	<0.001	0.65
Any admission	560 (551-569)	544 (535-551)	617 (608-626)	<0.001	<0.001	0.005
Inpatient hospital costs per patient-year						
Stroke	$141 (110-229)	$129 (99-208)	$192 (147-316)	0.007	0.002	0.22
Embolism	$38 (25-55)	$32 (21-46)	$43 (30-58)	0.32	0.13	0.25
GI hemorrhage	$246 (215-278)	$270 (239-303)	$229 (199-261)	0.23	0.035	0.14
Other major hemorrhage	$74 (47-110)	$59 (40-83)	$110 (77-150)	0.13	0.015	0.46
Acute myocardial infarction	$176 (128-227)	$125 (94-159)	$205 (161-152)	0.32	0.006	0.08
Heart failure	$556 (492-620)	$536 (474-601)	$728 (649-816)	<0.001	<0.001	0.65
Any stroke, embolism, hemorrhage, or acute cardiovascular event	$1,234 (1,136-1,338)	$1,154 (1,066-1,263)	$1,511 (1,403-1,639)	<0.001	<0.001	0.22
Any admission	$4,519 (4,372-4,660)	$4,572 (4,413-4,739)	$4,918 (4,766-5,071)	<0.001	0.002	0.61

*95% confidence intervals (CIs) around mean admission rates and costs are based on the actual 2.5 and 97.5 percentiles in the distribution of admission rates and inpatient costs from 1,000 bootstrap iterations. p Values are two-sided tests of the null hypothesis that the difference in admission rates (or differences in annual costs) between 2 drugs is 0, and is based on the distribution of differences between each pair of drugs over 1,000 bootstrap iterations.

GI = gastrointestinal.