

# Direct Oral Anticoagulant Prescription Trends, Switching Patterns, and Adherence in Texas Medicaid

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**A**nticoagulants prevent the clotting process by inhibiting thrombin formation and, ultimately, fibrin formation. This reduces blood clots that may lead to venous thromboembolism, stroke, and death.<sup>1-3</sup> Warfarin, a coumarin derivative, is the most commonly used oral anticoagulant.<sup>1,2</sup> However, the use of warfarin has long been associated with challenges, including the need for close monitoring and frequent dosage adjustments due to the narrow therapeutic index and other factors that influence response to the medication.<sup>1,2</sup> This conventional approach to anticoagulation is changing with the availability of direct oral anticoagulants (DOACs).<sup>4</sup>

DOACs have been approved by the FDA in recent years—dabigatran, October 2010; rivaroxaban, July 2011; apixaban, December 2012; edoxaban, January 2015; betrixaban, June 2017—with indications for risk reduction for stroke and embolism in nonvalvular atrial fibrillation (AF).<sup>5</sup> DOACs have also been approved for prophylaxis and treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE).<sup>6-8</sup> This new generation of anticoagulants does not require frequent laboratory monitoring or dosage adjustments. Additionally, DOACs have fewer drug interactions, food interactions, and adverse effects compared with warfarin.<sup>3,9</sup> The promising efficacy and safety profiles of the DOACs demonstrated in clinical trials have been reflected in guideline updates, and the use of DOACs is anticipated to increase.<sup>10</sup> Nevertheless, there are limited data on the actual adoption of, and adherence to, these agents in clinical practice, particularly regarding utilization patterns of the different agents.<sup>11,12</sup>

Previous studies that examined the use of DOACs compared with warfarin found an increase in DOAC use and a decrease in warfarin use.<sup>11,13-15</sup> One study reported that the costs of DOACs in terms of patient out-of-pocket and insurance spending were 5 and 15 times higher compared with warfarin, respectively.<sup>11</sup> The same study also reported that DOACs accounted for more than 90% of one private insurer's spending on anticoagulants. On the other hand, Medicaid patients have been described as having a greater comorbidity burden and higher stroke risk, but contrastingly lower odds of receiving oral anticoagulants, compared with patients not insured by Medicaid.<sup>16</sup>

## ABSTRACT

**OBJECTIVES:** To compare prescription trends, costs, switch patterns, and mean adherence among oral anticoagulants in the Texas Medicaid population.

**STUDY DESIGN:** Secondary analysis of Medicaid prescription claims data.

**METHODS:** All oral anticoagulant prescriptions for patients aged 18 to 63 years with 1 or more prescription claims for an oral anticoagulant from July 1, 2010, to December 31, 2015, were included in utilization and expenditure trend analyses. Switch patterns and adherence, measured by the proportion of days covered (PDC), were analyzed over 1 year for patients newly initiated on oral anticoagulant therapy.

**RESULTS:** Over the 5.5-year study period, direct oral anticoagulant (DOAC) use increased steadily and the proportion of oral anticoagulant prescription expenditures accounted for by DOACs increased substantially. By December 2015, DOACs accounted for one-third of anticoagulant prescription claims and more than 90% of total oral anticoagulant prescription expenditures. The mean cost per prescription was 30 times higher for DOACs than warfarin. A higher proportion of patients with a DOAC as an index drug switched drugs. The overall mean  $\pm$  SD PDC was  $0.71 \pm 0.21$ , with no significant differences among patients on dabigatran, rivaroxaban, and apixaban. Using a PDC cutoff point of 0.80 to indicate adherence (vs nonadherence), 42% of patients were categorized as adherent.

**CONCLUSIONS:** Texas Medicaid prescription data show a gradual increase in DOAC use with a rapid increase in prescription expenditures. Further exploration of the causes of higher switch rates among DOAC initiators compared with warfarin initiators and nonadherence to DOACs is needed to understand the challenges related to DOAC adoption in practice and to improve patient outcomes.

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## TAKEAWAY POINTS

Direct oral anticoagulants (DOACs) are changing the practice of anticoagulation and are associated with increased prescription costs. This study examined the prescription trends, switching patterns, and adherence to DOACs in the Texas Medicaid population.

- ▶ DOACs imposed a high cost burden on Medicaid. Specifically, in 2015, more than 90% of Texas Medicaid oral anticoagulant prescription spending was for DOACs.
- ▶ Among new users, patients initiated on a DOAC had higher switch rates than warfarin initiators.
- ▶ Poor adherence among patients taking DOACs should be further investigated to optimize the efficiency of DOACs.

An 8-month adherence study in patients with AF conducted in 2011 found that almost 70% of Medicaid patients were adherent to dabigatran (average medication possession ratio [MPR], 0.87). However, about one-fifth of the patients switched to warfarin after initiating treatment with dabigatran.<sup>12</sup> There are limited data about DOAC adherence, yet having actual practice evidence is important in understanding patient adherence and, subsequently, patient outcomes. Finally, no current literature has described the use of all 4 DOACs in the Medicaid population. Therefore, this study aims to contribute to the growing literature on utilization of, expenditures on, and adherence to DOACs, with a focus on the Texas Medicaid population.

## OBJECTIVES

To compare trends in prescription utilization, expenditures, switching patterns, and adherence among oral anticoagulants in the Texas Medicaid population.

## METHODS

This was a secondary analysis of prescription claims data from Texas Medicaid from July 1, 2010, to December 31, 2015. Texas Medicaid provides coverage for more than 4 million beneficiaries.<sup>17</sup> This joint federal–state program provides low-income Texans with access to healthcare. These prescription claims data include

unique patient identifiers (not actual patient identification numbers), drug name/strength, dispense date, paid amount, National Drug Code, quantity dispensed, days supplied, and patient gender and age. The first part of the study examined utilization and prescription expenditure trends of oral anticoagulants. All Medicaid prescription claims data for patients aged 18 to 63 years with at least 1 prescription claim for an oral anticoagulant (ie, dabigatran, rivaroxaban, apixaban, edoxaban, warfarin)

during the study period were included in these analyses.

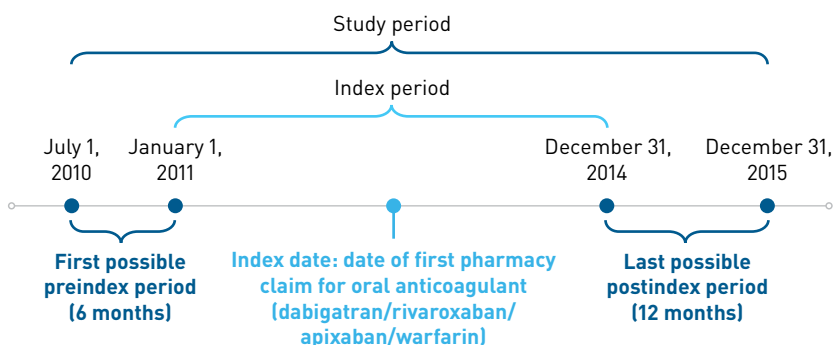
The second part of the study analyzed switching patterns and adherence for patients who were newly initiated on oral anticoagulant therapy between January 1, 2011, and December 31, 2014 (index period). The index date was defined as the earliest anticoagulant prescription drug claim during the index period, and patients were followed for 1 year (365 days) after the index date. Continuous Medicaid enrollment was required during the 6-month period prior to and the 12-month period following the index date, defined as the pre- and postindex periods, respectively. Only patients defined as new initiators of anticoagulant therapy were included (ie, no anticoagulant claim in the preindex timeframe). **Figure 1** illustrates the study timeline.

Patients who met the following criteria were included for switching and adherence analyses: (1) had at least 2 prescription claims for an oral anticoagulant (dabigatran, rivaroxaban, apixaban, warfarin) during the index period, (2) had no prescription for an oral anticoagulant during the 6-month preindex period, (3) were aged 18 to 63 years at the index date, and (4) were continuously enrolled in Texas Medicaid during their pre- and postindex periods.

Continuous enrollment was determined based on the presence of any prescription drug claim in 3 consecutive 6-month periods (6 months preindex, 0–6 months post index, and 7–12 months post index). Patients having only 1 prescription claim for an oral anticoagulant during the index period, patients not continuously enrolled in Texas Medicaid, patients with any prescription claim(s) for an oral anticoagulant during the 6-month period before the index date, and patients with more than 1 type of oral anticoagulant claim on the same day were excluded from the study.

Switching was defined as the presence of a claim for any oral anticoagulant in the follow-up period that was different from the index drug. Adherence was estimated using proportion of days covered (PDC), defined as total days the drug was available divided by 365 days. When dispensings overlapped, the full length of each filled prescription was accounted for and the start date of the second prescription was forwarded to be at the end of

**FIGURE 1.** Study Period and Index Period



the previous prescription.<sup>18</sup> Because warfarin users can have frequent dose adjustments to therapy, prescription claims may not accurately estimate warfarin adherence.<sup>19</sup> For that reason, adherence was only calculated for patients newly initiating anticoagulant therapy with a DOAC and who were determined to be nonswitchers during the postindex follow-up period.

According to the American College of Chest Physicians Clinical Guidelines for Antithrombotic Therapy and Thrombosis (2012), at least 3 months of anticoagulation therapy is recommended for the treatment of DVT and PE.<sup>20</sup> However, durations of treatment are variable according to specific patient needs and preferences. According to the product information for rivaroxaban<sup>8</sup> and apixaban,<sup>7</sup> the recommended treatment duration for DVT and PE is at least 6 months. Therefore, in order to more accurately calculate adherence to DOACs, we further limited our adherence calculations to individuals with at least 1 prescription for the index oral anticoagulant during the 6-month period starting 6 months after the index anticoagulant prescription. This was our attempt at capturing adherence in chronic users of these medications.<sup>18</sup>

To illustrate trends, drug utilization and prescription expenditures were plotted against time in months. For continuous variables, means and SDs were reported and analysis of variance (ANOVA) was used to determine if differences existed among groups. Scheffe's post hoc test was used to identify differences among specific groups. For categorical variables, frequencies were reported and proportions were compared using  $\chi^2$  tests. All analyses were performed at a .05 level of significance using STATA version 14 (STATACorp; College Station, Texas). Human subjects approval was granted by the Institutional Review Board of the University of Texas at Austin.

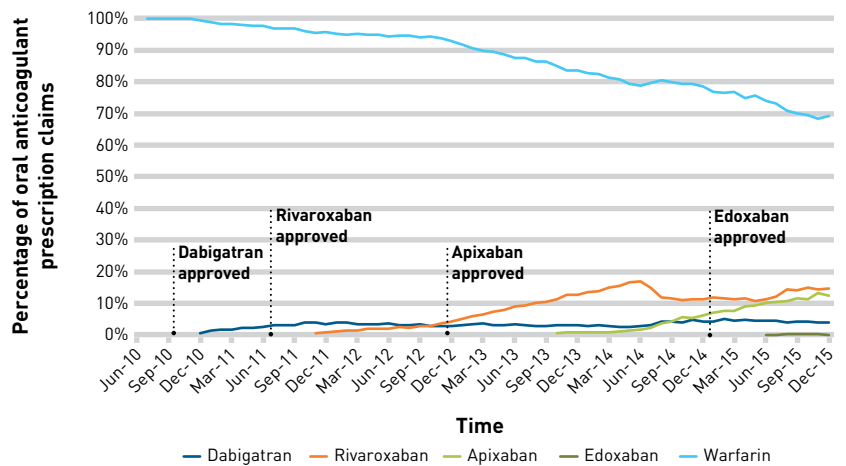
## RESULTS

### Trends of Oral Anticoagulant Utilization

Over the 5.5-year study period, there were 277,147 oral anticoagulant prescription claims. The average monthly number of prescription claims for oral anticoagulants increased consistently from 2460 (July–December 2010) to 4672 (January–December 2015). Warfarin was the only oral anticoagulant available before the introduction of the first DOAC, dabigatran. Since its introduction in October 2010, dabigatran has consistently accounted for less than 5% of total monthly anticoagulant prescription claims (Figure 2).

The uptake of rivaroxaban as measured by prescription claims increased at a higher rate than that of dabigatran (Figure 2; eAppendix Table 1 [eAppendix available at [ajmc.com](http://ajmc.com)]). By October 2012,

**FIGURE 2.** Trends in Proportions of Monthly Oral Anticoagulant Prescription Claims in Texas Medicaid (July 2010–December 2015)



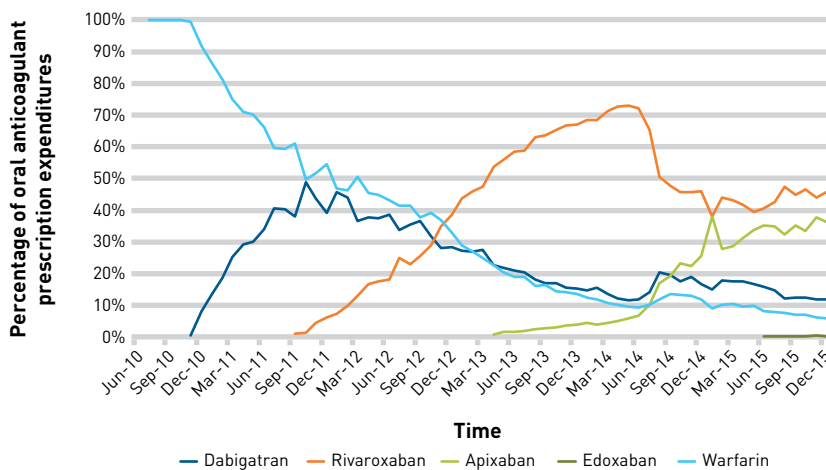
rivaroxaban usage surpassed that of dabigatran, and it alone has accounted for more than 10% of total monthly anticoagulant prescription claims since August 2013. Apixaban followed a similar trend. In December 2015, rivaroxaban and apixaban accounted for 14% and 13% of oral anticoagulant claims, respectively. The number of warfarin prescription claims increased during the study period, from 36,206 in 2011 to 41,015 in 2015, but the overall proportion of oral anticoagulant claims for warfarin decreased by 24%. From 2011 to 2015, the total annual number of prescription claims for DOACs increased almost 15-fold, from 1053 to 15,043. By the end of 2015, warfarin usage had steadily declined to about 70% of total oral anticoagulant claims, with DOACs accounting for about 30% of the claims.

Chi-square analysis showed statistically significant ( $P < .001$ ) relationships between drug type and gender and drug type and age category. There were higher proportions of claims for dabigatran ( $n = 4633$ ; 52.4%) and edoxaban ( $n = 20$ ; 55.6%) among males (eAppendix Table 2). Conversely, female patients accounted for greater proportions of claims for rivaroxaban ( $n = 12,314$ ; 56.5%), apixaban ( $n = 3819$ ; 51.9%), and warfarin ( $n = 121,316$ ; 54.1%). There were more claims for patients in the older age group (aged 45–63 years) ( $n = 193,809$ ; 73.9%) than the younger group (aged 18–44 years) ( $n = 68,581$ ; 26.1%) for all drug types.

### Trends of Prescription Expenditures

In October 2011, 1 year after its initial availability, dabigatran accounted for about 5% of the total prescription claims but almost half of the total oral anticoagulant prescription expenditures covered by Texas Medicaid (Figures 2 and 3). Rivaroxaban continued to account for an increasing proportion of DOAC prescription expenditures, with dabigatran and rivaroxaban accounting for about 30% (\$30,000) and 40% (\$41,000), respectively, of total oral anticoagulant expenditures

**FIGURE 3.** Trends in Proportions of Monthly Oral Anticoagulant Prescription Expenditures in Texas Medicaid (July 2010–December 2015)<sup>a</sup>



<sup>a</sup>Approximate total oral anticoagulant prescription expenditures: July–December 2010, \$0.29 million; January–December 2011, \$0.76 million; January–December 2012, \$1.06 million; January–December 2013, \$2.48 million; January–December 2014, \$3.61 million; January–December 2015, \$5.20 million.

**TABLE 1.** Frequencies and Proportions of Patients Who Switched Oral Anticoagulant Therapies, by Gender and Age Category (N = 843)

Demographic Variables (n)	Warfarin to DOAC, n (%)	DOAC to Warfarin, n (%)	DOAC to DOAC, n (%)	$\chi^2$	P
Gender					
Female (485)	329 (67.8)	78 (16.1)	78 (16.1)	0.92	.631
Male (358)	232 (64.8)	61 (17.0)	65 (18.2)		
Age category, years					
18–44 (260)	189 (72.7)	45 (17.3)	26 (10.0)	3.03	.001
45–63 (583)	372 (63.8)	94 (16.1)	117 (20.1)		

DOAC indicates direct oral anticoagulant.

**TABLE 2.** Comparison of Mean Adherence to DOACs Among Non-switchers as Measured by PDC Among Anticoagulants (N = 595)<sup>a</sup>

DOAC	Dabigatran (n = 168)	Rivaroxaban (n = 322)	Apixaban (n = 105)	P
PDC, mean (SD)	0.70 (0.21)	0.70 (0.21)	0.73 (0.21)	.359

DOAC indicates direct oral anticoagulant; PDC, proportion of days covered. <sup>a</sup>F = 1.03; df = 2, 592.

in December 2012. Apixaban contributed to the increasing proportion of prescription expenditures, driving the combined DOAC prescription expenditures to exceed 87% (>\$219,000) and 88% (>\$320,000) of the total Texas Medicaid expenditures for oral anticoagulants in December 2013 and December 2014, respectively. In 2015, DOAC utilization accounted for more than \$4.7 million (90%) of the total

oral anticoagulant prescription expenditures in Texas Medicaid.

Two-way ANOVA showed that the mean cost per prescription of dabigatran, rivaroxaban, and apixaban increased significantly ( $P < .001$ ) each year from 2011 to 2015, except from 2011 to 2012, when that of dabigatran decreased (eAppendix Table 3). Based on the latest data in 2015, dabigatran, rivaroxaban, and apixaban cost more than \$300 per prescription, about 30 times the cost of warfarin.

### Switching Patterns

Overall, 3.5%, 11.7%, 2.1%, and 82.8% of new users were started on dabigatran, rivaroxaban, apixaban, and warfarin, respectively. Among new users of oral anticoagulants who were followed for 1 year, the proportions of patients who switched to another oral anticoagulant were 17.9%, 24.5%, 15.6%, and 9.2%, respectively (eAppendix Table 4).

Chi-square analysis showed a statistically significant relationship ( $P < .001$ ) between drug type and switch status. Compared with patients who were initiated on warfarin, a higher proportion of patients with a DOAC as an index drug switched during the 12-month postindex period ( $P < .001$ ).

Further examination of the switching patterns using  $\chi^2$  analysis revealed a significant relationship between age group and switch patterns. A higher proportion of younger patients versus older patients switched from warfarin to a DOAC (72.7% vs 63.8%) and from a DOAC to warfarin (17.3% vs 16.1%) (Table 1). Conversely, older patients accounted for a higher proportion of patients who switched from a DOAC to another DOAC compared with younger patients (20.1% vs 10.0%). Overall, switching to a DOAC occurred more frequently than the reverse: 704 patients switched from warfarin to a DOAC or from the index DOAC to a different DOAC, whereas only 139 patients switched from a DOAC to warfarin.

### Adherence

The mean adherence was compared among nonswitcher DOAC patients, using PDC as the adherence measure. The overall mean  $\pm$  SD PDC was  $0.71 \pm 0.21$ . Using an adherence cutoff point of 0.80 to indicate adherence/nonadherence, 42% of patients were categorized as adherent. One-way ANOVA showed no significant differences in mean PDC among the patients on dabigatran, rivaroxaban, and apixaban ( $P = .359$ ) (Table 2).

## DISCUSSION

To the best of our knowledge, this is the first study to describe the utilization of all currently available DOACs in a Medicaid population.

Other studies' conclusions apply to more limited patient populations that include either those with comorbid AF or patients older than 65 years.<sup>18,21,22</sup> Therefore, this study adds meaningful information on an expanded group of patients: patients who are younger and patients prescribed oral anticoagulants regardless of medical condition(s).

### Trends of Oral Anticoagulant Utilization and Prescription Expenditures

Consistent with prior reports, our study findings showed a gradual increase in the uptake of new oral anticoagulation medications, although there were a few months of delay in the uptake of each DOAC after FDA approval.<sup>10,13,23</sup> According to a national audit, dabigatran prescriptions increased to about 18% of all oral anticoagulant visits in US ambulatory practice by the end of the first year after its introduction.<sup>13</sup> Following rivaroxaban introduction, the trends in utilization and expenditures are analogous with those found in the study conducted by Desai et al, in terms of the increasing uptake of rivaroxaban and decreasing proportion accounted for by dabigatran and warfarin.<sup>11</sup>

In addition, rivaroxaban utilization was observed to increase at a much higher rate (>5000 prescriptions in 2013) (eAppendix Table 1) compared with dabigatran. This may be due to rivaroxaban's FDA-approved indications at the time of approval and once-daily dosing in patients with AF.<sup>5,8</sup> The results in this study suggest that apixaban may follow a similar trajectory, as it had (as of 2015) already started to displace the earlier drugs. It should also be noted that the increasing use of newer DOACs may be encouraged by the changes in guidelines that prefer DOACs over warfarin, growing physician experience, and approval of new indications.<sup>10</sup>

As of July 2016, all DOACs were classified as preferred drugs on the Texas Medicaid Preferred Drug List, except for edoxaban, which requires prior authorization. It is interesting to note that rivaroxaban was moved to nonpreferred agent classification from July 2014 to July 2015.<sup>24</sup> Correspondingly, there was a slight reduction in rivaroxaban prescription claims and expenditures during this period.

Compared with men, women generally have a higher risk of thromboembolism and lower odds of receiving both DOACs and warfarin.<sup>11,25,26</sup> Our unadjusted analysis shows a higher proportion of rivaroxaban, apixaban, and warfarin claims for women compared with men. Recent studies suggest that women treated with warfarin experience safety and efficacy similar to that experienced by men when treated with DOAC agents.<sup>27,28</sup> Therefore, our results suggest that the practice of anticoagulation treatment for female patients may be moving in a positive direction with the availability of DOACs, which have favorable safety and efficacy profiles compared with warfarin.

The adoption of DOACs into practice imposed a significantly higher cost burden to Texas Medicaid between 2010 and 2015. However, these higher expenditures have been demonstrated to be cost-effective relative to warfarin.<sup>29-32</sup> Nevertheless, more research is needed to better understand the cost impact and cost-effectiveness of DOACs in actual practice.<sup>32,33</sup>

### Switching Patterns

This study reports a switch rate of 18% among patients initiated on dabigatran compared with 3 studies that reported dabigatran switch rates of less than 10%, 16%, and 21%, respectively.<sup>12,22,34</sup> Analyses of Texas Medicaid data revealed that the switch rates for patients initiated on any DOAC ranged from 15% to 25%, as opposed to a switch rate of less than 10% for patients initiated on warfarin. Although this study did not have information on why patients switched drugs, common reasons for switching include an occurrence of bleeding complications, nontolerance of therapy, and patient's or physician's preference.<sup>35,36</sup> The higher switch rate among DOAC users compared with warfarin users demonstrates the need for further research to understand DOAC management.

A Dutch study reported that the rate of patients who switched from warfarin to a DOAC is double that of the reverse.<sup>21</sup> Similarly, our findings show that switching off of initial anticoagulant therapy in patients starting warfarin occurred at a rate twice that of DOACs. The switch rate to a DOAC is anticipated to increase in the future with more availability, as well as improved safety and efficacy profiles, of DOACs.

### Adherence

Our study found a relatively low mean adherence for anticoagulant therapy as measured by PDC (mean  $\pm$  SD = 0.71  $\pm$  0.21), with no significant difference among dabigatran, rivaroxaban, and apixaban. However, 2 recent studies reported that rivaroxaban users have higher adherence compared with dabigatran and apixaban users.<sup>18,37</sup> An earlier study on dabigatran in Medicaid reported an average MPR of 0.87.<sup>12</sup> Other actual practice studies have demonstrated similar nonadherence to DOACs or a high proportion ( $\geq$ 25%) of nonadherent patients.<sup>21,22,34,38,39</sup> It should be noted that the nonadherence to DOACs in this study may also be attributed to the younger patient population examined, as younger patients have been associated with lower adherence.<sup>37,39</sup>

The poor adherence to DOACs found in this study calls for further investigation into the risk factors for nonadherence to DOACs, particularly in view of poor adherence even when medications are provided at no cost to Medicaid patients. Additionally, health professionals and other stakeholders should look for opportunities to improve adherence with DOACs, such as delivering patient education and using technology aids as reminders, to optimize the safety and effectiveness of these promising agents.<sup>40,41</sup>

### Limitations

This retrospective data analysis has several limitations. First, because the data were from prescription claims databases, inaccuracies and coding errors may have occurred. Second, our analyses were limited to the study period specified and the utilization trends may change over time. On the same note, we were unable to provide detailed information on edoxaban use, because it had just recently been introduced into the market at the time of our study. Third,

## ORIGINAL RESEARCH

measurements of switching and adherence were based on prescription claims data, assuming that the patient is taking the medication. Fourth, the results from this study may not be generalizable beyond the Texas Medicaid population. Fifth, no comparison could be made between warfarin and DOAC adherence. This is because patients on warfarin typically have frequent dosage adjustments, and prescription claims may not accurately estimate PDC.

## CONCLUSIONS

Overall, the data show a gradual increase in new oral anticoagulant use in the Texas Medicaid population with a rapid increase in oral anticoagulant prescription costs. This study's findings show that the cost per DOAC prescription is markedly higher (30 times higher) than that of warfarin. There is a need to further explore the causes of higher switch rates among DOAC users and nonadherence to DOACs. These findings provide an early utilization trend profile in the Medicaid population and aid in our understanding of the challenges accompanying DOAC adoption in practice. ■

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## REFERENCES

1. Turckington C, Mitchell D, eds. *The Encyclopedia of Poisons and Antidotes*. 3rd ed. New York, NY: Facts On File; 2010.
2. Warckentin TE. Anticoagulants. In: Offermanns S, Rosenthal W, eds. *Encyclopedia of Molecular Pharmacology*. Berlin, Germany: Springer; 2008:107-112.
3. Wigle P, Hein B, Bloomfield HE, Tubb M, Doherty M. Updated guidelines on outpatient anticoagulation. *Am Fam Physician*. 2013;87(8):556-566.
4. Lip GY, Wang KL, Chiang CE. Non-vitamin K antagonist oral anticoagulants (NOACs) for stroke prevention in Asian patients with atrial fibrillation: time for a reappraisal. *Int J Cardiol*. 2015;180:246-254. doi: 10.1016/j.ijcard.2014.11.182.
5. FDA website. fda.gov. Accessed April 29, 2018.
6. Pradaxa [package insert]. Ridgefield, CT: Boehringer Ingelheim; 2015.
7. Elixquis [package insert]. Princeton, NJ: Bristol-Myers Squibb; 2015.
8. Xarelto [package insert]. Titusville, NJ: Janssen Pharmaceuticals; 2014.
9. Bauer KA. Pros and cons of new oral anticoagulants. *Hematol Am Soc Hematol Educ Program*. 2013;2013:464-470. doi: 10.1182/asheducation-2013.1.464.
10. Weitz JI, Semchuk W, Turpie AGG, et al. Trends in prescribing oral anticoagulants in Canada, 2008-2014. *Clin Ther*. 2015;37(11):2506-2514. e4. doi: 10.1016/j.clinthera.2015.09.008.
11. Desai NR, Krumme AA, Schneeweiss S, et al. Patterns of initiation of oral anticoagulants in patients with atrial fibrillation—quality and cost implications. *Am J Med*. 2014;127(11):1075-1082.e1. doi: 10.1016/j.amjmed.2014.05.013.
12. Trask N, Kotadiya PN, Gagnon J, et al. Adherence measurement and incidence of bleeding and systemic embolism with dabigatran in a Medicaid population. Poster presented at: University of Massachusetts Center for Clinical & Translational Science 4th Annual Research Retreat; May 8, 2013; Worcester, MA. escholarship.umassmed.edu/cgi/viewcontent.cgi?article=1176&context=cts\_retreat.
13. Kirley K, Qato DM, Kornfield R, Stafford RS, Alexander GC. National trends in oral anticoagulant use in the United States, 2007 to 2011. *Circ Cardiovasc Qual Outcomes*. 2012;5(5):615-621. doi: 10.1161/CIRCOUTCOMES.112.967299.

14. Jani SM, Gosch K, Schneider P, et al. Uptake of novel oral anticoagulants in patients with non-valvular and valvular atrial fibrillation: results from the NCDR-PINNACLE registry. *J Am Coll Cardiol*. 2014;63(suppl 12):A324. doi: 10.1016/S0735-1097(14)60324-7.
15. Shah N, Gosch K, Chan P, Marzec L, Ting H. Use of novel oral anticoagulants for patients with non-valvular atrial fibrillation: results from the NCDR PINNACLE registry. *J Am Coll Cardiol*. 2014;63(suppl 12):A332. doi: 10.1016/S0735-1097(14)60332-6.
16. O'Brien EC, Kim S, Thomas L, et al. Clinical characteristics and treatment patterns of Medicaid patients with atrial fibrillation: insights from the ORBIT-AF I Registry. *Circ Cardiovasc Qual Outcomes*. 2015;8(suppl 2):A14.
17. Healthcare statistics. Texas Health and Human Services website. hhs.texas.gov/about-hhs/records-statistics/data-statistics/healthcare-statistics. Accessed May 2, 2017.
18. Crivera C, Nelson WW, Bookhart B, et al. Pharmacy Quality Alliance measure: adherence to non-warfarin oral anticoagulant medications. *Curr Med Res Opin*. 2015;31(10):1889-1895. doi: 10.1185/03007995.2015.1077213.
19. Proportion of days covered (PDC): percentage of patients who filled at least two prescriptions for a non-warfarin oral anticoagulant on two unique dates of service at least 180 days apart, received greater than 60 days supply of the medication, and who met the PDC threshold of 80% during the measurement period. National Quality Measures Clearinghouse website. qualitymeasures.ahrq.gov/summaries/summary/47502/proportion-of-days-covered-pdc-percentage-of-patients-who-filled-at-least-two-prescriptions-for-a-non-warfarin-oral-anticoagulant-on-two-unique-dates-of-service-at-least-180-days-apart-received-greater-than-60-days-supply-of-the-medication-and-who-met-the-pdc-t-q-pdc. Updated July 2015. Accessed June 20, 2016.
20. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines [erratum in *Chest*. 2012;142(6):1698-1704. doi: 10.1378/chest.12-2089]. *Chest*. 2012;141(suppl 2):e419S-e494S. doi: 10.1378/chest.11-2301.
21. Hanemaaijer S, Sodihardjo F, Horikx A, et al. Trends in antithrombotic drug use and adherence to non-vitamin K oral anticoagulants in the Netherlands. *Int J Clin Pharm*. 2015;37(6):1128-1135. doi: 10.1007/s11096-015-0174-4.
22. Zhou M, Chang H-Y, Segal JB, Alexander GC, Singh S. Adherence to a novel oral anticoagulant among patients with atrial fibrillation. *J Manag Care Spec Pharm*. 2015;21(11):1054-1062. doi: 10.18553/jmcp.2015.21.11.1054.
23. Martinez C, Katholing A, Wallenhorst C, Freedman SB. Therapy persistence in newly diagnosed non-valvular atrial fibrillation treated with warfarin or NOAC: a cohort study. *Thromb Haemost*. 2016;115(1):31-39. doi: 10.1160/TH15-04-0350.
24. Health and Human Services Commission: Texas Medicaid preferred drug list (PDL) and prior authorization (PA) criteria. Community First Health Plans website. cfhp.com/images/uploads/2015-0723-pdl.pdf. Published July 2015. Accessed June 20, 2016.
25. Raji MA, Lowery M, Lin YL, Kuo YF, Baillargeon J, Goodwin JS. National utilization patterns of warfarin use in older patients with atrial fibrillation: a population-based study of Medicare Part D beneficiaries. *Ann Pharmacother*. 2013;47(1):35-42. doi: 10.1345/aph.1R515.
26. Thompson LE, Maddox TM, Lei L, et al. Gender differences in the use of oral anticoagulants for atrial fibrillation: a report from the National Cardiovascular Data Registry (NCDR) PINNACLE Registry. *J Am Heart Assoc*. 2017;6(7):e005801. doi: 10.1161/JAHA.117.005801.
27. Dentali F, Sironi AP, Gianni M, et al. Gender difference in efficacy and safety of nonvitamin K antagonist oral anticoagulants in patients with nonvalvular atrial fibrillation or venous thromboembolism: a systematic review and a meta-analysis of the literature. *Semin Thromb Hemost*. 2015;41(7):774-787. doi: 10.1055/s-0035-1564042.
28. Panchoy SB, Sharma PS, Panchoy DS, Patel TM, Callans DJ, Marchlinski FE. Meta-analysis of gender differences in residual stroke risk and major bleeding in patients with nonvalvular atrial fibrillation treated with oral anticoagulants. *Am J Cardiol*. 2014;113(3):485-490. doi: 10.1016/j.amjcard.2013.10.035.
29. Freeman JV, Zhu RP, Owens DK, et al. Cost-effectiveness of dabigatran compared with warfarin for stroke prevention in atrial fibrillation. *Ann Intern Med*. 2011;154(1):1-11. doi: 10.7326/0003-4819-154-1-201101040-00289.
30. Lee S, Anglade MW, Pham D, Pisacane R, Kluger J, Coleman CI. Cost-effectiveness of rivaroxaban compared to warfarin for stroke prevention in atrial fibrillation. *Am J Cardiol*. 2012;110(6):845-851. doi: 10.1016/j.amjcard.2012.05.011.
31. You JHS. Novel oral anticoagulants versus warfarin therapy at various levels of anticoagulation control in atrial fibrillation—a cost-effectiveness analysis. *J Gen Intern Med*. 2014;29(3):438-446. doi: 10.1007/s11606-013-2639-2.
32. Harrington AR, Armstrong EP, Nolan PE Jr, Malone DC. Cost-effectiveness of apixaban, dabigatran, rivaroxaban, and warfarin for stroke prevention in atrial fibrillation. *Stroke*. 2013;44(6):1676-1681. doi: 10.1161/STROKEAHA.111.000402.
33. Kamel H, Easton JD, Johnston SC, Kim AS. Cost-effectiveness of apixaban vs warfarin for secondary stroke prevention in atrial fibrillation. *Neurology*. 2012;79(14):1428-1434. doi: 10.1212/WNL.0b013e31826d5f68.
34. Tsai K, Erickson SC, Yang J, Harada ASM, Sotow BK, Lew HC. Adherence, persistence, and switching patterns of dabigatran etexilate. *Am J Manag Care*. 2013;19(9):e325-e332.
35. Beyer-Westendorf J, Förster K, Ebertz F, et al. Drug persistence with rivaroxaban therapy in atrial fibrillation patients—results from the Dresden non-interventional oral anticoagulation registry. *Europace*. 2015;17(4):530-538. doi: 10.1093/europace/euu319.
36. Abo-Salem E, Becker R. Transitioning to and from the novel oral anticoagulants: a management strategy for clinicians. *J Thromb Thrombolysis*. 2014;37(3):372-379. doi: 10.1007/s11239-014-1060-y.
37. Nelson WW, Song X, Coleman CI, et al. Medication persistence and discontinuation of rivaroxaban versus warfarin among patients with non-valvular atrial fibrillation. *Curr Med Res Opin*. 2014;30(12):2461-2469. doi: 10.1185/03007995.2014.933577.
38. Cutler TW, Chuang A, Huynh TD, et al. A retrospective descriptive analysis of patient adherence to dabigatran at a large academic medical center. *J Manag Care Spec Pharm*. 2014;20(10):1028-1034. doi: 10.18553/jmcp.2014.20.10.1028.
39. Shore S, Carey EP, Turakhia MP, et al. Adherence to dabigatran therapy and longitudinal patient outcomes: insights from the Veterans Health Administration. *Am Heart J*. 2014;167(6):810-817. doi: 10.1016/j.ahj.2014.03.023.
40. Abdou JK, Auyeung V, Patel JP, Arya R. Adherence to long-term anticoagulation treatment, what is known and what the future might hold. *Br J Haematol*. 2016;174(1):30-42. doi: 10.1111/bjh.14134.
41. Di Minno A, Spadarella G, Tufano A, Prisco D, Di Minno G. Ensuring medication adherence with direct oral anticoagulant drugs: lessons from adherence with vitamin K antagonists (VKAs). *Thromb Res*. 2014;133(5):699-704. doi: 10.1016/j.thromres.2014.01.016.

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**eAppendix Table 1.** Frequency and Proportion of Prescription Claims by Year for Oral Anticoagulants in Texas Medicaid (2011-2015), n (%)

Anticoagulants	Year					$\chi^2$	<i>P</i>
	2011	2012	2013	2014	2015		
Dabigatran	992 (2.7)	1573 (3.2)	1926 (3.1)	1935 (3.4)	2418 (4.3)	25,000	<.001
Rivaroxaban	61 (0.2)	1175 (2.4)	5685 (9.1)	7826 (13.6)	7058 (12.6)		
Apixaban	-	-	214 (0.3)	1617 (2.8)	5531 (9.9)		
Edoxaban	-	-	-	-	36 (0.1)		
Warfarin	36,206 (97.2)	46,182 (94.4)	54,761 (87.5)	46,179 (80.2)	41,015 (73.2)		
Total	37,259 (100)	48,930 (100)	62,586 (100)	57,557 (100)	56,058 (100)		

**eAppendix Table 2.** Frequencies and Proportions of Oral Anticoagulant Prescription Claims by Gender and Age Category

<b>Demographic Variables</b>	<b>Total, n (%)</b>	<b>Dabigatran, n (%)</b>	<b>Rivaroxaban, n (%)</b>	<b>Apixaban, n (%)</b>	<b>Edoxaban, n (%)</b>	<b>Warfarin, n (%)</b>	$\chi^2$	<i>P</i>
<b>Gender</b>								
Female	141,676 (54.0)	4211 (47.6)	12,314 (56.5)	3819 (51.9)	16 (44.4)	121,316 (54.1)	214.1	<.001
Male	120,714 (46.0)	4633 (52.4)	9491 (43.5)	3543 (48.1)	20 (55.6)	103,027 (45.9)		
<b>Age category, years</b>								
18-44	68,581 (26.1)	1278 (14.4)	5775 (26.5)	1428 (19.4)	8 (22.2)	60,092 (26.8)	849.5	<.001
45-63	193,809 (73.9)	7566 (85.6)	16,030 (73.5)	5934 (80.6)	28 (77.8)	164,251 (73.2)		



**eAppendix Table 3.** Mean Cost Per Prescription (\$) of Oral Anticoagulants by Year in Texas Medicaid (2011-2015)

Drug	Mean Cost Per Prescription (SD)				
	2011	2012	2013	2014	2015
Dabigatran (n = 8844)	258.6 <sup>a</sup> (137.2)	239.9 (75.1)	256.7 <sup>a</sup> (40.5)	290.2 (49.1)	312.4 (60.5)
Rivaroxaban (n = 21,805)	153.2 (79.5)	203.1 (81.2)	257.9 (82.9)	278.2 (94.2)	318.8 (105.1)
Apixaban (n = 7362)	-	-	251.7 (42.8)	285.4 (51.4)	305.4 (77.0)
Edoxaban (n = 36)	-	-	-	-	278.1 (28.4)
Warfarin (n = 224,343)	13.6 (13.8)	9.5 (10.8)	8.5 (11.1)	8.9 (11.6)	10.5 (13.7)
Total (N = 262,390)	20.3 (47.8)	21.6 (54.0)	39.6 (87.0)	62.7 (115.1)	91.6 (142.2)

Analysis of variance showed overall significant model.  $F = 120,000$ ;  $df = 18, 262,389$ ;  $P < .001$ .

There was a significant interaction between year and drug.  $F = 2070.34$ ;  $df = 10, 262,371$ ;  $P < .001$ .

Scheffe's post hoc test showed that all group means are significantly different except <sup>a</sup>.

Year 2010 data was excluded due to incomplete data.

**eAppendix Table 4.** Proportions of Patients Who Switched Oral Anticoagulant Therapy by Index Drug

<b>Index Drug</b>	<b>Switch n (%)</b>	<b>No Switch n (%)</b>	$\chi^2$	<i>P</i>
Dabigatran	46 (17.9)	211 (82.1)	190.9	<.001
Rivaroxaban	212 (24.5)	653 (75.5)		
Apixaban	24 (15.6)	130 (84.4)		
Warfarin	561 (9.2)	5560 (90.8)		