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## Limited English Proficient Patients and Time Spent in Therapeutic Range in a Warfarin Anticoagulation Clinic

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**Background**—While anticoagulation clinics have been shown to deliver tailored, high-quality care to patients receiving warfarin therapy, communication barriers with limited English proficient (LEP) patients may lead to disparities in anticoagulation outcomes.

**Methods and Results**—We analyzed data on 3770 patients receiving care from the Massachusetts General Hospital Anticoagulation Management Service (AMS) from 2009 to 2010. This included data on international normalized ratio (INR) tests and patient characteristics, including language and whether AMS used a surrogate for primary communication. We calculated percent time in therapeutic range (TTR for INR between 2.0 and 3.0) and time in danger range (TDR for INR <1.8 or >3.5) using the standard Rosendaal interpolation method. There were 241 LEP patients; LEP patients, compared with non-LEP patients, had a higher number of comorbidities (3.2 versus 2.9 comorbidities,  $P=0.004$ ), were more frequently uninsured (17.0% versus 4.3%,  $P<0.001$ ), and less educated (47.7% versus 6.0%  $\leq$ high school education,  $P<0.001$ ). LEP patients compared with non-LEP patients spent less TTR (71.6% versus 74.0%,  $P=0.007$ ) and more TDR (12.9% versus 11.3%,  $P=0.018$ ). In adjusted analyses, LEP patients had lower TTR as compared with non-LEP patients (OR 1.5, 95% CI [1.1, 2.2]). LEP patients who used a communication surrogate spent less TTR and more TDR.

**Conclusion**—Even within a large anticoagulation clinic with a high average TTR, a small but significant decrease in TTR was observed for LEP patients compared with English speakers. Future studies are warranted to explore how the use of professional interpreters impact TTR for LEP patients. (*J Am Heart Assoc.* 2013;2:e000170 doi: 10.1161/JAHA.113.000170)

**Key Words:** adverse drug events • limited English proficiency • outcomes research • quality of care • warfarin

The United States is increasingly diverse with growing populations of racial and ethnic minorities and immigrants, many of whom have difficulty communicating in English. According to recent estimates, over 55 million Americans, or 20% of the total population, speak a language other than English at home.<sup>1</sup> Of these individuals, over half self-report speaking English less than “very well” and are considered to have Limited English Proficiency (LEP).<sup>2</sup>

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Patients with communication problems due to language barriers are at high risk for preventable adverse events.<sup>3–7</sup> Similarly, drug complications in outpatients are more common in patients who speak a primary language other than English.<sup>8</sup>

Warfarin, a commonly prescribed anticoagulant, has a narrow therapeutic range and therefore requires frequent, long-term monitoring and close communication between patients and providers. Warfarin is indicated for patients with atrial fibrillation and venous thromboembolism in order to prevent ischemic stroke and other adverse outcomes.<sup>9,10</sup> Low literacy levels and limited English proficiency have been associated with poor anticoagulation control.<sup>11–14</sup> Monitoring time in therapeutic range (TTR) can serve as an indicator of the quality of anticoagulation and a surrogate for markers of anticoagulation complications.<sup>13,15–18</sup> Studies have demonstrated that patients who spend less time in TTR are at increased risk for serious bleeding complications, including higher risk of intracranial hemorrhage.<sup>13,19,20</sup> To our knowledge, there have been no previous studies showing the relationship between LEP status and TTR.

Due to the proven clinical importance of high-quality warfarin control for preventing adverse outcomes, understanding how

patients with communication barriers perform is of critical importance. Using detailed clinical data from a large anticoagulation clinic, we sought to answer 3 questions: (1) Do differences in TTR exist between LEP and non-LEP patients? (2) Are LEP patients more likely to spend time in the danger range (ie, sub- or supratherapeutic international normalized ratios [INRs]) compared with non-LEP patients? (3) Does the use of communication surrogates impact TTR? Answering these questions may have important implications for how warfarin management clinics could be organized.

## Methods

### Study Population

The Massachusetts General Hospital Anticoagulation Management Service (AMS) is a large, nurse-run anticoagulation service that provides comprehensive education on anticoagulation management, monitors each patient's INR, and recommends follow-up dosing changes using standardized protocols. Both primary care physicians and specialists, from both inpatient and outpatient settings, refer patients to the AMS. Patient follow-up is based on the prescribed duration of warfarin therapy. Referring physicians complete annual therapy reviews to confirm the current treatment plan and evaluate the risks and benefits of continued therapy. AMS uses a standardized process to monitor adherence, including a series of automated reminder calls and letters to inform patients of missed INR dates. AMS regularly uses medical interpreters to collect information and deliver dosing information to patients. AMS nurses collaborate with the referring physician to promote adherence and safety and, as a result, AMS discharges few patients for nonadherence.

We linked data from the AMS with the Research Patient Data Repository (RPDR) through each patient's unique medical number. The RPDR gathers clinical information from patients' electronic medical records at various hospitals and stores them in a central data registry.<sup>21</sup> We obtained data on patients who received care from AMS from January 1, 2009 through December 31, 2010 for all clinical indications with an INR target between 2 and 3. We collected data on English language proficiency, INR, patient sociodemographic characteristics, site of primary care, and whether or not they used a surrogate for primary communication with the providers.

### Study Variables

Based on randomized trials and clinical guidelines, an INR between 2.0 to 3.0 is the standard target anticoagulation intensity for patients with atrial fibrillation or venous thromboembolism.<sup>22,23</sup> Using each patient's INR data, we calculated the time in therapeutic range (TTR defined as time with an INR

between 2.0 and 3.0) and time in danger range (TDR defined as INR <1.8 or >3.5) for each patient using the standard Rosendaal interpolation method.<sup>20,24</sup> Prior research has demonstrated that stroke risk for patients with AF increases markedly at INR levels below 1.8 and the risk for intracranial hemorrhage increases at INR levels above 3.5.<sup>19,20</sup> We defined TTR as the number of person-days with an INR of 2.0 to 3.0 divided by the total number of person-days on warfarin. This is presented as the average TTR for each individual.

LEP patients were identified as those who reported speaking English less than "very well," as self-reported in their registration documentation. Secondary predictors included self-designated use of a communication surrogate, defined as a family member or other person identified as the primary contact with whom AMS nurses communicate to manage warfarin dosing and frequency of INR monitoring. A communication surrogate is not limited to telephonic communication with AMS, but may also have broader responsibilities such as administration of warfarin, appointment transportation, and other patient medical needs.

Sociodemographic variables included age, gender, race/ethnicity (self-reported as white, Hispanic, black, Asian, other or unknown), education (less than high school, high school or GED, college, or more than college) and insurance status (commercial, Medicare, Medicaid, self-pay, or free care).

A comorbidity index based on a count of comorbid conditions was used for risk adjustment. We included comorbid conditions present at enrollment to AMS based on ambulatory billing data, as have been used by other studies.<sup>25,26</sup> These included atrial fibrillation, chronic obstructive pulmonary disease, coronary artery disease, depression, diabetes mellitus, congestive heart failure, hypertension, osteoarthritis, or a cerebral vascular accident. This study protocol was approved by the Massachusetts General Hospital's Institutional Review Board and informed consent was waived since we analyzed deidentified, retrospective data.

### Statistical Analyses

We compared LEP and non-LEP patient characteristics using 2-sample *t* tests or chi-square tests. We conducted bivariate analyses to explore the associations between LEP status and outcomes using 2-sample *t* tests for percent time in range and chi-square tests for the percentage of patients above or below a cutoff point.

We dichotomized TTR at 65% and TDR at 15% because these levels are considered to represent adequate anticoagulation control based on data from recent clinical trials.<sup>27</sup> We utilized multivariable logistic regression models to examine the relationship between LEP status and these 2 dichotomized outcomes, controlling for demographic and clinical covariates.

We repeated the regression analyses stratified by LEP status and the use of surrogates. SAS version 9.3 (SAS Institute Inc) was used for all analyses. All reported *P* values are 2-tailed and values <0.05 were considered statistically significant.

### Results

Among 3770 total patients enrolled in the anticoagulation clinic in 2009 and 2010, the most common primary indications for anticoagulation were atrial fibrillation (68.4%) and venous thrombosis or thromboembolism (14.1%) (Table 1). There were 241 LEP patients in our sample (6.4%). LEP patients, compared with non-LEP patients, were more likely to be women (42.7% versus 30.1%, *P*=0.002), minorities (45.6% versus 5.2%, *P*<0.001), underinsured (17.0% versus 4.3% with Medicaid, free Care or self-pay, *P*<0.001), and less educated (47.7% versus 6.0% with less than a high school education, *P*<0.001), and had a higher number of comorbidities (3.2 versus 2.9, *P*=0.004).

The overall mean TTR for all patients enrolled in the AMS clinic was 73.8% (median 76.1%). The overall TDR mean was

**Table 1.** Study Population Characteristics (n=3770)

Characteristic	LEP (n=241)	Non-LEP (n=3529)	<i>P</i> Value
Age, mean (SD)	73.0 (13.8)	71.5 (13.0)	0.12
Women, %	42.7%	30.1%	0.002
White, %	47.7%	89.2%	<0.001
Insurance			<0.001
Commercial	14.9%	20.5%	
Medicare	49.8%	48.4%	
Medicaid/self-pay/free care	17.0%	4.3%	
Less than high school education	47.7%	6.0%	<0.001
Comorbidity count, mean (SD)	3.2 (1.5)	2.9 (1.6)	0.004
Surrogate, %	61.4%	12.4%	<0.001
Indication for anticoagulation			0.11
Atrial fibrillation	70.5%	68.3%	
Venous thromboembolism	13.7%	14.2%	
CVD/CAD	10.0%	8.3%	
CHF	2.1%	1.4%	
Valvular disease	2.1%	2.6%	
Other	1.6%	5.2%	

LEP indicates limited English proficient; SD, standard deviation; CVD, cardiovascular disease; CAD, coronary artery disease; CHF, congestive heart failure.

11.4% (median 8.6%). The primary predictor of TTR was LEP status as a binary variable. In unadjusted analyses, LEP patients had a lower mean TTR than non-LEP patients (71.6% versus 74.0%, *P*=0.007) and a higher mean TDR (12.9% versus 11.3%, *P*=0.018) (Table 2). More LEP patients spent <65% of the TTR as compared with non-LEP patients (27.8% versus 20.6%, *P*=0.008). LEP patients were also more likely to spend more than 15% of total TDR as compared with non-LEP patients (32.4% versus 24.3%, *P*=0.005).

After adjusting for sociodemographic and clinical factors, LEP patients were more likely to spend less TTR (OR 1.5, 95% CI 1.1, 2.2) but were not at greater risk of spending more TDR (OR 1.3, 95% CI 0.9, 1.9) (Table 3).

A total of 585 patients (16% of the study sample) reported using a communication surrogate, representing 61.4% of LEP patients and 12.4% of the non-LEP patients. Patients who

**Table 2.** Time in Therapeutic Range and Time in Danger Range for LEP Versus Non-LEP Patients

Characteristic	LEP	Non-LEP	<i>P</i> Value
% TTR, mean (SD)	71.6 (13.1)	74.0 (13.9)	0.007
% TDR, mean (SD)	12.9 (10.2)	11.3 (11.0)	0.018
% Time INR <1.8, mean (SD)	9.5 (8.8)	8.1 (9.5)	0.023
% Time INR >3.5, mean (SD)	3.5 (3.5)	3.2 (4.2)	0.26
% of patients with TTR <65%	27.8	20.6	0.008
% of patients with TDR >15%	32.4	24.3	0.005

LEP indicates limited English proficiency; TTR, time in therapeutic range; TDR, time in danger range; SD, standard deviation; INR, international normalized ratio.

**Table 3.** Multivariable Logistic Regression Models\*

Predictor	TTR <65%, OR (95% CI)	TDR >15%, OR (95% CI)
LEP vs non-LEP	1.5 (1.1, 2.2)	1.3 (0.9, 1.9)
LEP surrogate vs non-LEP surrogate	1.2 (0.6, 2.2)	1.2 (0.6, 2.2)
LEP no surrogate vs non-LEP no surrogate	1.5 (0.9, 2.6)	1.3 (0.8, 2.3)
LEP surrogate vs LEP no surrogate	1.2 (0.6, 2.3)	1.2 (0.6, 2.2)
LEP surrogate vs non-LEP no surrogate	1.8 (1.1, 2.8)	1.6 (1.1, 2.5)

TTR indicates time in therapeutic range; TDR, time in danger range; OR, odds ratio; CI, confidence interval; LEP, limited English proficiency.

\*Adjusted for sociodemographic (age, gender, education, insurance) and clinical factors (comorbidity counts).

used a surrogate were older (mean age 77.1 versus 70.6,  $P<0.001$ ), more likely to be underinsured (7.5% versus 4.7% with Medicaid, Free Care, or Self-pay,  $P<0.001$ ), and more likely to have less than a high school education (23.1% versus 6.1%,  $P<0.001$ ). Additionally, these patients had a higher comorbidity count as compared with patients without a communication surrogate (3.3 versus 2.9,  $P=0.007$ ). The interaction analyses for LEP and surrogate use were significant for both TTR ( $P=0.0297$ ) and TDR ( $P=0.005$ ). There were no significant differences among LEP patients in TTR or TDR with and without surrogate use. Both LEP and non-LEP patients who used a communication surrogate spent less TTR and more TDR, as compared with non-LEP patients who did not use a communication surrogate (Table 3). As compared with non-LEP patients without a surrogate, LEP patients who used a surrogate were more likely to spend less TTR (OR 1.8, 95% CI [1.1, 2.8]) and a greater amount of TDR (OR 1.6, 95% CI [1.1, 2.5]).

## Discussion

Using data from a high-quality anticoagulation clinic, we found that patients had a high average TTR at 74%. However, LEP patients spent more time with suboptimal TTR and in TDR compared with non-LEP patients. In adjusted analyses, LEP patients spent significantly more time in subtherapeutic INR values  $<1.8$ . In addition, the use of a communication surrogate was associated with less TTR and more TDR for both LEP and non-LEP patients.

High-quality anticoagulation with warfarin demands communication with patients and close monitoring of INR levels for dose adjustment. Prior studies have documented that anticoagulation clinics improve patient outcomes, with patients spending more TTR and sustaining fewer complications.<sup>28–31</sup> This suggests that a systematic approach for adherence to a complex medication regimen with a narrow therapeutic window such as warfarin may yield the best outcomes. Nonetheless, we found significant disparities for LEP patients enrolled in the AMS clinic. Our study is one of the few to explore the quality of anticoagulation among LEP patients and supports evidence from prior studies that have documented higher adverse outcomes in patients with language barriers.<sup>3–5,32–35</sup> We found the largest disparity between LEP patients compared with non-LEP among those with subtherapeutic INR values  $<1.8$ . This is consistent with large, international analyses of TTR that have demonstrated that the main variation in INRs is among those patients at INR levels  $<2.0$ .<sup>36</sup> Similar to other studies, our finding may be due to the fact that there were very few participants who had INRs  $>3.5$ .

Interestingly, the use of a surrogates was associated with more unfavorable anticoagulation profiles (lower mean% TTR and higher mean% TDR) for LEP patients. For older LEP

patients, the use of a surrogate may indicate a particularly vulnerable population who, in addition to having a language barrier, may also face cognitive impairments and/or other health literacy problems that further impede their ability to adequately adhere to a complex medication regimen.<sup>14,37,38</sup> Anticoagulation clinics should be aware that the use of a surrogate might identify a higher-risk subset of patients who may need closer and more intensive monitoring. For LEP patients, surrogates may represent clinically untrained family members who themselves also lack health literacy on warfarin administration, side effects, and the importance of maintaining a narrow therapeutic window. Not surprisingly, studies have shown that the use of untrained ad hoc interpreters such as family members and friends may lead to worse outcomes for LEP patients.<sup>39,40</sup>

Our study suggests that, even in an AMS clinic with excellent overall INR goal achievement, further strategies to improve TTR for LEP patients are warranted. For example, more intensive interventions such as language concordant home visits, the use of patient navigators, education sessions with the surrogate at the time of AMS enrollment, as well as visual aids to promote improved patient comprehension may provide useful adjuncts to existing AMS services.<sup>15,41</sup> Alternatively, our study suggests that LEP patients, particularly those who require a communication surrogate, may benefit from the use of newer anticoagulants that require less intensive monitoring. Future studies should explore the role of these newer anticoagulants for LEP patients who may find it particularly challenging to monitor and adjust their warfarin dosing.<sup>42,43</sup>

There are several limitations to our study that warrant mention. In our study, we were unable to account for the type of surrogate used by patients or the exact communication and management role of the surrogate with LEP patients. Similarly, the use of data from a single anticoagulation clinic at an academic institution limits generalizability to other clinical settings. We were also unable to measure adverse events (ie, bleeding or stroke) associated with sub- or supratherapeutic anticoagulation. However, published studies have documented the association of suboptimal TTR with bleeding and stroke complications.<sup>13,19</sup> Finally, we were unable to take into account the intensity of contact with the anticoagulation clinic during the study period.

## Conclusion

Our study suggests that, overall, patients managed by a dedicated anticoagulation clinic can achieve a high average TTR. Still, a small but significant disparity exists for LEP patients, particularly those who require communication surrogates. To our knowledge, there have been no previous studies showing the relationship between LEP status and TTR.

Future studies should further explore the proper role of communication surrogates, including medical interpreters, in reducing disparities for LEP patients taking warfarin anticoagulation, and the potential benefit from more simplified anticoagulation regimens that do not require intensive monitoring.

## Disclosures

Daniel E. Singer has received research grants from Daiichi Sankyo and Johnson and Johnson and served as a consultant to Bayer Healthcare, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Johnson and Johnson, and Pfizer, all manufacturers of novel anticoagulants. The other authors have no conflicts to declare.

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