Impact Of Transportation Barriers On High-Quality Anticoagulation Management In Underserved Patients

BY

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THESIS
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LIST OF ABBREVIATIONS

INR  International Normalized Ratio
CYP2C9 cytochrome P450, family 2, subfamily C, polypeptide 9
VKORC1 vitamin K epoxide reductase complex subunit 1
SES socioeconomic status
ATC  Antithrombosis Clinic
EHR  electronic health record
VTE  venous thrombosis
AF   atrial fibrillation
CVA  cerebrovascular accident
MVR  mechanical valve replacement
VHD  valvular heart disease
TTR  within-patient proportion of INR levels spent in therapeutic range
Y outcome variable
M mediator variable
X predictor variable
SD  standard deviation
SUMMARY

The objective of this study was to evaluate the relationship between transportation barriers to anticoagulation monitoring visits and the quality of anticoagulation control in an inner-city underserved population. We conducted a cross sectional survey of patients treated with warfarin and managed at the University of Illinois at Chicago Hospital and Health Sciences System Antithrombosis Clinic, between September 2010 and February 2011. A 23-item survey questionnaire was administered to participants to elicit responses to variables such as access to health care barriers, socio-economic characteristics, and opinions regarding anticoagulation patient-centered management models. Additional data on patient demographics, clinical characteristics and outcomes were extracted from the EHR for each patient for a total follow-up period of 12 months (February 2010 to February 2011) prior to survey administration. Descriptive statistics were performed to characterize the sample stratified by transportation barriers.

Chi-square, Fisher’s exact, student’s t-test, and Wilcoxon signed rank test, were used as appropriate to examine differences between covariates and the exposure variable. Multivariate linear regression analysis was used to determine the association between transportation barriers and TTR, while adjusting for potential confounders. Patients with transportation barriers compared to patients without transportation barriers were older (57.89 ± 17.37 vs. 51.24 ± 16.55), more likely to be female (72.67% vs. 61.42%), more likely to be African American (64.67% vs. 58.27%) or Hispanic (24% vs. 18.11%), more likely to have their primary language other than English (14.67 vs. 7.20), more likely to have
less than a 12th grade education (41.38% vs. 21.26%), more likely to have an annual income of < $15,000 (52.82% vs. 31.45%), less likely to have private insurance (8.67% vs. 38.58%), and more likely to be dependent on a caregiver (48.99% vs. 3.97%), all values significant (p<0.05). After adjusting for confounders, TTR was lower in patients with transportation barriers than in those without transportation barriers (absolute difference 6.04%, p=0.009).

Our study is significant in that it is among the first to evaluate the relationship between transportation barriers and anticoagulation related clinical outcomes such as quality of anticoagulation control in a largely minority, underserved population. Understanding this relationship is especially important in underserved, minority patients who are at highest risk for anticoagulation related complications. Future studies should focus on elucidating the feasibility of adopting alternate models of anticoagulation monitoring such as telehealth guided patient-centered interventions such as self-testing and self-monitoring.
I. INTRODUCTION

Despite the emergence of several novel target specific oral anticoagulants, warfarin remains the most commonly prescribed oral anticoagulant with over 30 million prescriptions dispensed and 2.5 million patients treated annually in the United States.(1) At the same time, warfarin is among the top ten medications with the highest incidence of serious adverse event reports and the leading cause of drug-related hospitalizations and emergency room visits among older adults.(2) Due to its narrow therapeutic index and inter-patient variability in dose-response, warfarin requires frequent monitoring of its anticoagulant effect by measurements of the International Normalized Ratio (INR) and dose adjustments to maintain patients within the therapeutic range. Adherence to monitoring is critical in order to ensure safe and effective anticoagulation. The time in therapeutic INR range (TTR) is a common measure used to evaluate the quality of anticoagulation control and can serve as a surrogate marker for anticoagulation complications.(3) Low TTR can result in complications of therapy such as bleeding, clotting, and hospitalizations. (4-8) Data demonstrate that minority patients are more prone to complications of warfarin therapy due to inadequate TTR. (9-11) Patients with low TTR require more intensive laboratory testing leading to increased health care costs. (12-13) Thus, increasing TTR should be a priority for clinicians managing patients on warfarin therapy.
Specialized anticoagulation clinics provide a mechanism for frequent patient monitoring and have been reported to improve TTR and clinical and resource utilization outcomes compared to patients managed by routine medical care. (14-18) However, patient access to clinic appointments for monitoring may be limited by several socioeconomic, clinical and demographic factors. Transportation barriers comprise a major impediment to health care access, especially in those with lower socioeconomic status (SES) and the under or uninsured. (19) While associations of several socioeconomic, demographic, clinical and genetic factors with quality of anticoagulation control have been studied, the impact of transportation barriers to anticoagulation monitoring visits has not been evaluated. (20-23) Therefore, the objective of this study was to evaluate the relationship between transportation barriers to anticoagulation monitoring visits and the quality of anticoagulation control in an inner-city underserved population. (Figure 1)
Figure 1: Conceptual Framework.

- Socio-Demographic
- Clinical Factors

**Exposure**
- Patients with Transportation Barriers
- Patients without Transportation Barriers

**Confounders**

**Outcome**
- Quality of Anticoagulation Control: Time in Therapeutic Range
II. METHODS

A. Study Population

Patients treated with warfarin and cared for at the clinical pharmacist managed Antithrombosis Clinic (ATC) at the University of Illinois at Chicago Hospital and Health Sciences System (UI Health) were enrolled in the study. The ATC serves approximately 500 warfarin treated patients and provides approximately 750 patient visits per month, with 35 to 40 patients seen in clinic each day. The majority of the population served by the clinic is African American (60%), followed by Hispanics (20%), Caucasians (17%), and Asians and those of other ethnicities (3%). Clinical pharmacists in ATC follow a structured process of care and all patients receive targeted assessment and education that includes the indication and duration of warfarin therapy, INR and other pertinent laboratory assessment, dosing adjustment and instruction, importance of adherence with therapy and monitoring clinic appointments, tablet recognition and refill procedures, signs and symptoms of thrombosis, potential food and drug interactions and how to manage consistent intake of vitamin K containing foods, procedures for emergencies, and notifying ATC of any changes in therapy or disease status. Once a stable warfarin dose is reached after initiation of therapy, patients are seen in clinic approximately every 4 weeks with shorter intervals for unstable patients and with longer intervals for more stable patients. Data on laboratory tests including the INR, warfarin dose, adherence status, any missed clinic appointments, fluctuations in vitamin K intake, any acute illness, alcohol intake, smoking status, changes in concurrent medications (prescription and over the counter), and bleeding and
thromboembolic complications are routinely collected at each clinic visit using a standardized data collection and documentation form and entered into an electronic health record (EHR), Cerner Millenium Data Repository.

B. Study Design and Data Collection

We conducted a cross sectional survey of patients treated with warfarin and managed at the UI Health ATC between September 2010 and February 2011. A 23-item survey questionnaire was developed and administered to participants to elicit responses to variables such as access to health care barriers, socio-economic characteristics, and opinions regarding anticoagulation patient-centered management models. Specifically, the survey contained 5 questions about access barriers to the ATC which included the type of transportation used to arrive at the clinic, distance from the clinic, time taken to travel to the clinic, dependency on a caregiver, and the need for travel assistance. We established face validity by pre-testing the questionnaire in 10 patients managed at ATC and 5 clinical pharmacist anticoagulation specialists who were not members of the research team. Survey revisions were based on respondent feedback and pre-test results. Additional data on patient demographics, clinical characteristics and outcomes were extracted from the EHR for each patient for a total follow-up period of 12 months (February 2010 to February 2011) prior to survey administration. A 12 month follow-up period was chosen to allow a sufficient window to capture the incidence of temporal factors associated with anticoagulation control. Patients were eligible for the study if they were treated with warfarin
and received care in the ATC for ≥ 3 months. Patients were excluded from the study if they were < 18 years old (unless a caregiver or family member recorder the responses) and if they had difficulty in communicating or completing the survey. The local institutional review board approved this study (IRB 2010-0500).

C. **Measurements and Study Variables**

The primary outcome variable was the quality of anticoagulation control measured as the percentage of time patients spent within the therapeutic INR range (TTR), a commonly accepted method of reporting quality of anticoagulation management. (3, 24) The exposure variable was the presence of transportation barriers to anticoagulation clinic monitoring visits. Patients were categorized to have transportation barriers if they depended on travel assistance (from a family member, friend, or relative), needed to borrow or rent a vehicle, or relied on state Medicaid supported transportation services such as a medical car to travel to clinic. Additional socio-demographic and pertinent clinical variables (age, gender, race, primary language spoken, marital status as a proxy for social support, housing status, living arrangements, education level, income level, insurance status, dependence on caregivers, travel time to clinic, distance to clinic, indication for therapy, length of therapy, interest in alternate methods of monitoring such as self-testing, concurrent medications, total number of clinic appointments, missed clinic appointments, and non-adherence with therapy over the 12 month follow-up period) known to affect anticoagulation outcomes were included for testing as covariates. (Table I)
# TABLE I

## STUDY VARIABLES

<table>
<thead>
<tr>
<th>Variable</th>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Key outcome variable</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time in therapeutic range</td>
<td>Continuous</td>
<td>Within-patient proportion of INR levels spent in therapeutic range / 12 months</td>
</tr>
<tr>
<td><strong>Key exposure variable</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transportation barriers</td>
<td>Categorical</td>
<td>Indicator variable for having transportation barriers</td>
</tr>
<tr>
<td><strong>Covariates</strong></td>
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<td></td>
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<tr>
<td>Age</td>
<td>Continuous</td>
<td>Values in years</td>
</tr>
<tr>
<td>Gender</td>
<td>Categorical</td>
<td>Indicator variable for being male</td>
</tr>
<tr>
<td>Race</td>
<td>Categorical</td>
<td>Indicator variables for being Caucasian, African American, Hispanic, other</td>
</tr>
<tr>
<td>Language</td>
<td>Categorical</td>
<td>Indicator variable for speaking English</td>
</tr>
<tr>
<td>Marital status</td>
<td>Categorical</td>
<td>Indicator variables for being married, single, divorced, widowed or separated</td>
</tr>
<tr>
<td>Education level</td>
<td>Categorical</td>
<td>Indicator variable for having education level of &lt; 9th grade, 9-12th, high school diploma, some college, college graduate or above</td>
</tr>
<tr>
<td>Income level</td>
<td>Categorical</td>
<td>Indicator variables for having income &lt; $15,000, $15,000-$25,000, &gt; $25,000-$50,000, &gt; $50,000-$75,000, other</td>
</tr>
<tr>
<td>Insurance status</td>
<td>Categorical</td>
<td>Indicator variables for having Private, Medicare, Medicaid or no insurance</td>
</tr>
<tr>
<td>Distance to travel to clinic</td>
<td>Continuous</td>
<td>Distance in miles calculated using zip codes</td>
</tr>
<tr>
<td>Travel time to clinic</td>
<td>Continuous</td>
<td>Time to travel to clinic (minutes)</td>
</tr>
<tr>
<td>Housing status</td>
<td>Categorical</td>
<td>Indicator variable for owning home</td>
</tr>
<tr>
<td>Living arrangements</td>
<td>Categorical</td>
<td>Indicator variable for living with someone</td>
</tr>
<tr>
<td>Dependence on caregiver/s</td>
<td>Categorical</td>
<td>Indicator variable for being dependent on caregiver/s</td>
</tr>
<tr>
<td>Indication for therapy</td>
<td>Categorical</td>
<td>Indicator variables for being treated for VTE, AF, CVA, MVR/VHD, other</td>
</tr>
<tr>
<td>Concurrent medications</td>
<td>Continuous</td>
<td>Total number of concurrent medications</td>
</tr>
<tr>
<td>Length of therapy</td>
<td>Continuous</td>
<td>Duration of therapy in years</td>
</tr>
<tr>
<td>Missed clinic appointments</td>
<td>Continuous</td>
<td>Percentage of missed clinic appointments / 12 months</td>
</tr>
<tr>
<td>Non-adherence to therapy</td>
<td>Continuous</td>
<td>Percentage of clinic appointments with documented non-adherence to prescribed therapy / 12 months</td>
</tr>
<tr>
<td>Total appointments</td>
<td>Continuous</td>
<td>Total number of clinic monitoring appointments</td>
</tr>
<tr>
<td>Interest in self-testing</td>
<td>Categorical</td>
<td>Indicator variable for being interested in self-testing</td>
</tr>
</tbody>
</table>
D. Sample Size and Power Calculation

A range of sample sizes were calculated using G*Power 3.1.3 to detect a difference in TTR in patients with and without transportation barriers to anticoagulation monitoring visits. The parameters used for input were effect size ($F^2$) (25) and the number of predictors. Three standard effect sizes were used to calculate the sample size. For a one-tailed t-test with significance (alpha) set to 0.05 and power set to 80%, the required sample size to detect a small effect of 0.02 was 1022, a medium effect of 0.15 was 150, and a large effect of 0.35 was 74.

E. Data Analysis

Statistical analyses were conducted in SAS® 9.2 (SAS Institute, Cary, NC). We conducted descriptive statistics to characterize the sample stratified by transportation barriers. Chi-square, Fisher’s exact, student’s t-test, and Wilcoxon signed rank test, were used as appropriate to examine differences between covariates and the exposure variable. Multivariate linear regression analysis was used to determine the association between transportation barriers and TTR, while adjusting for potential confounders. Covariates considered for inclusion were initially selected using prior literature / clinical knowledge (as also described in section C and Table I above) and were then tested using a change in coefficient approach. (26) After determining the crude parameter estimate between transportation barriers and TTR, we then calculated an adjusted parameter estimate for transportation barriers by adding to the model one covariate at a time. The confounders included in the final model were the ones that altered
the crude estimates of the independent-dependent variable relationship by > 10%. We evaluated the main effects and all 2-way interactions between exposure and covariates.
III. RESULTS

A. Description of Study Cohort

A total of 291 patients completed the survey and 277 patients provided information on transportation status. (Figure 2) A total of 150 patients reported to have transportation barriers to anticoagulation monitoring visits, while 127 patients reported having no transportation barriers.

Figure 2. Study Cohort.

- 303 patients approached to complete survey
- 12 patients refused to participate
- 291 patients completed the survey
- 277 patients responded to transportation status
  - 127 with no transportation barriers
  - 150 with transportation barriers
B. Characteristics of the Study Cohort

The study cohort was mainly comprised of females (67%) and the average age was 54.6 years. The majority of patients were African Americans (61.5%), followed by Hispanics (21.05%), Caucasians (13.63%) and other race (3.85%). Table II presents baseline socio-demographic characteristics of the study population stratified by the presences or absence of transportation barriers. Patients with transportation barriers compared to patients without transportation barriers were older (57.89 ± 17.37 vs. 51.24 ± 16.55), more likely to be female (72.67% vs. 61.42%), more likely to be African American (64.67% vs. 58.27%) or Hispanic (24% vs. 18.11%), more likely to have their primary language other than English (14.67 vs. 7.20), more likely to have less than a 12th grade education (41.38% vs. 21.26%), more likely to have an annual income of < $15,000 (52.82% vs. 31.45%), less likely to have private insurance (8.67% vs. 38.58%), and more likely to be dependent on a caregiver (48.99% vs. 3.97%), all values significant (p<0.05).

Table III presents baseline clinical characteristics of the study population stratified by the presences or absence of transportation barriers. Patients with transportation barriers compared to patients without transportation barriers had worse anticoagulation control as expressed by the TTR (47.50 ± 20.67 vs. 52.22 ± 19.58, p=0.05), were on a higher number of concurrent medications (10.58 ± 6.53 vs. 7.45 ± 5.38, p<0.0001), were more likely to be non-adherent with their warfarin therapy (14.09 ± 14.23 vs. 11.64 ± 12.17, p=0.07), and were on warfarin therapy for a shorter duration of time (3.09 ± 5.23 years vs. 3.67 ± 3.75 years, p=0.01). Other characteristics were similar between the 2 groups.
<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>No Transp. Barriers (n=127)</th>
<th>Transp. Barriers (n=150)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>51.24 (16.55)</td>
<td>57.89 (17.37)</td>
<td>0.0020</td>
</tr>
<tr>
<td>Gender (n, %)</td>
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<td></td>
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<tr>
<td>Male</td>
<td>49 (38.58)</td>
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<tr>
<td>Female</td>
<td>78 (61.42)</td>
<td>109 (72.67)</td>
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<td>Race (n, %)</td>
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<td>Caucasian</td>
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<td>African American</td>
<td>74 (58.27)</td>
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<td>&lt; $15,000</td>
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<td>75 (52.82)</td>
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<td>16 (11.27)</td>
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<td>Travel Time to Clinic, minutes (mean, SD)</td>
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<td>38.52 (24.79)</td>
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<td>11.39 (13.66)</td>
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<td>Own Home</td>
<td>56 (44.09)</td>
<td>53 (36.30)</td>
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<tr>
<td>Rent Home</td>
<td>63 (49.61)</td>
<td>75 (51.37)</td>
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<td>Other</td>
<td>8 (6.30)</td>
<td>18 (12.33)</td>
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<td>Living arrangements (n, %)</td>
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<td>Live Alone</td>
<td>28 (22.22)</td>
<td>27 (18.37)</td>
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<tr>
<td>Live with Someone</td>
<td>96 (77.78)</td>
<td>120 (81.63)</td>
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<td>Caregiver Depend. (n, %)</td>
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<td>Yes</td>
<td>5 (3.97)</td>
<td>73 (48.99)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>121 (96.03)</td>
<td>76 (51.01)</td>
<td></td>
</tr>
</tbody>
</table>
### TABLE III

CLINICAL CHARACTERISTICS OF THE STUDY POPULATION STRATIFIED BY TRANSPORTATION BARRIERS

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>No Transp. Barriers (n=127)</th>
<th>Transp. Barriers (n=150)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VTE</td>
<td>85 (66.93)</td>
<td>103 (68.67)</td>
<td>0.8279</td>
</tr>
<tr>
<td>AF</td>
<td>14 (11.02)</td>
<td>20 (13.33)</td>
<td></td>
</tr>
<tr>
<td>CVA</td>
<td>7 (5.51)</td>
<td>9 (6.00)</td>
<td></td>
</tr>
<tr>
<td>MVR/VHD</td>
<td>7 (5.51)</td>
<td>7 (4.67)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>14 (11.02)</td>
<td>11 (7.33)</td>
<td></td>
</tr>
<tr>
<td>Concurrent Medications (mean, SD)</td>
<td>7.45 (5.38)</td>
<td>10.58 (6.53)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Length of therapy, years (mean, SD)</td>
<td>3.67 (3.75)</td>
<td>3.09 (5.23)</td>
<td>0.0141</td>
</tr>
<tr>
<td>Time in Therapeutic Range (mean, SD)</td>
<td>52.22 (19.58)</td>
<td>47.50 (20.67)</td>
<td>0.0535</td>
</tr>
<tr>
<td>Self-Testing Interest (n, %)</td>
<td></td>
<td></td>
<td>0.5937</td>
</tr>
<tr>
<td>Yes</td>
<td>108 (85.04)</td>
<td>124 (82.67)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>19 (14.96)</td>
<td>26 (17.33)</td>
<td></td>
</tr>
<tr>
<td>Total No. of Monitoring Appointments /INRs (mean, SD)</td>
<td>18.09 (9.10)</td>
<td>18.43 (9.66)</td>
<td>0.7339</td>
</tr>
<tr>
<td>Missed Monitoring Appointments (mean, SD)</td>
<td>17.24 (18.17)</td>
<td>15.15 (17.68)</td>
<td>0.2785</td>
</tr>
<tr>
<td>Non-Adherence Warfarin (mean, SD)</td>
<td>11.64 (13.17)</td>
<td>14.09 (14.23)</td>
<td>0.0799</td>
</tr>
</tbody>
</table>
C. Multivariate Linear Regression Analysis of Association Between Transportation Barriers and Quality of Anticoagulation Control

The variables retained in the final model were age and its interaction term, non-adherence with warfarin regimen, length of warfarin therapy (> 12 months vs < 12 months), an interest/preference for self-testing of anticoagulation, and missed clinic appointments for anticoagulation monitoring. Table IV displays the multivariate regression analysis of the association between transportation barriers and quality of anticoagulation control. After adjusting for confounders, TTR was lower in patients with transportation barriers than in those without transportation barriers (absolute difference 6.04%, p=0.009).
### TABLE IV

**MULTIVARIATE REGRESSION ANALYSIS OF THE ASSOCIATION BETWEEN TRANSPORTATION BARRIERS AND QUALITY OF ANTICOAGULATION CONTROL**

<table>
<thead>
<tr>
<th></th>
<th>Model 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 3&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \beta ) (SE)</td>
<td>( p )-value</td>
<td>( \beta ) (SE)</td>
</tr>
<tr>
<td><strong>Transportation barriers</strong></td>
<td>-4.72 (2.43) 0.05</td>
<td>-6.04 (2.31) 0.009</td>
<td>-5.81 (2.35) 0.01</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>-</td>
<td>0.38 (0.10) 0.0003</td>
<td>0.44 (0.10) &lt;0.0001</td>
</tr>
<tr>
<td><strong>Age*transportation barriers [Interaction]</strong></td>
<td>-</td>
<td>-0.36 (0.13) 0.007</td>
<td>-0.38 (0.14) 0.005</td>
</tr>
<tr>
<td><strong>Non-adherence with warfarin</strong></td>
<td>-</td>
<td>-0.16 (0.08) 0.05</td>
<td>-0.20 (0.08) 0.01</td>
</tr>
<tr>
<td><strong>Interest in self-testing</strong></td>
<td>-</td>
<td>-7.54 (3.07) 0.01</td>
<td>-6.75 (3.11) 0.03</td>
</tr>
<tr>
<td><strong>Length of therapy &gt; 12 months vs. &lt; 12 months</strong></td>
<td>-</td>
<td>7.95 (2.70) 0.003</td>
<td>7.47 (2.75) 0.006</td>
</tr>
<tr>
<td><strong>Missed clinic appointments</strong></td>
<td>-</td>
<td>-0.22 (0.07) 0.0008</td>
<td>-</td>
</tr>
<tr>
<td><strong>Intercept</strong></td>
<td>52.22</td>
<td>&lt;0.0001</td>
<td>53.86</td>
</tr>
<tr>
<td>( R^2 )</td>
<td>0.01</td>
<td>0.18</td>
<td>0.15</td>
</tr>
</tbody>
</table>

<sup>a</sup> Model 1: Crude estimate from the unadjusted regression analysis

<sup>b</sup> Model 2: Multivariate regression model controlling for all confounders that altered the crude estimate of the independent-dependent variable relationship by > 10%

<sup>c</sup> Model 3: Multivariate regression model controlling for all confounders that altered the crude estimate of the independent-dependent variable relationship by > 10% minus missed appointments

Interestingly, the missed clinic appointments covariate was found to alter the crude estimates of the independent-dependent variable relationship by > 10% and was included as one of the confounders in the final model. Based on clinical experience and existing literature (19) we would expect that the presence of transportation barriers would lead to missed clinic appointments, Thus, missed clinic appointments could potentially be a mediator of the relationship between our predictor (transportation barriers) and outcome variable (TTR). Even after removing the missed appointments variable from the model, TTR was lower in patients with transportation barriers than in those without transportation.
barriers (absolute difference 5.81%, p=0.01). It is fair to ask however: to what extent (if any) is the effect of transportation barriers on anticoagulation control transmitted through missed appointments? To further elucidate this question, we conducted a 4-step mediation analysis (27) and found that while both transportation barriers and missed appointments were independently associated with TTR, missed appointments did not meet the criteria of mediator of the association between transportation barriers and TTR. Table V and Figure 3 depict the results of our mediation analysis.

### TABLE V

RESULTS OF THE 4-STEP MEDIATION ANALYSIS

<table>
<thead>
<tr>
<th>Analysis Steps</th>
<th>β (SE)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y = B₀+B₁X+e</td>
<td>-4.72 (2.43)</td>
<td>0.05</td>
</tr>
<tr>
<td>M=B₀+B₁X+e</td>
<td>-2.09 (2.16)</td>
<td>0.33</td>
</tr>
<tr>
<td>Y=B₀+B₁M+e</td>
<td>-0.26 (0.07)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Y=B₀+B₁X+B₂M+e</td>
<td>-5.45 (2.37)</td>
<td>0.02</td>
</tr>
<tr>
<td>Transportation Barriers</td>
<td>-0.27 (0.07)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Missed Appointments</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Y=outcome variable; M=mediator variable; X=predictor variable
Figure 3: Mediation Analysis.

Other Factors:
- Patient Beliefs
- Behaviors
- Attitudes
- Self-Reliance
- Organizational skills
- Access to Pharmacy
- Dietary Stability
- Patient Preference
- Alternate models of monitoring

Y=outcome variable; M=mediator variable; X=predictor variable
IV. DISCUSSION

Safe and effective management of warfarin requires frequent visits for INR monitoring and dosing adjustments, however barriers to transportation can result in delays to timely health care access and clinical interventions. Such delays can result in disease exacerbations and complications of anticoagulation therapy such as thromboembolism and bleeding. While previous studies have shown that transportation barriers are a major impediment to health care access especially in those with lower SES and ethnic minorities (19) and that minority patients have worse anticoagulation control compared to non-minorities (21), studies to date have not evaluated the impact of transportation barriers on anticoagulation related clinical outcomes. Our study is significant in that it evaluated the relationship between transportation barriers and anticoagulation related clinical outcomes such as quality of anticoagulation control in a largely minority, underserved population. We found that patients with transportation barriers had significantly lower TTR compared to those without transportation barriers, effect which remained significant after controlling for socio-demographic and clinical confounders.

As minority patients are at particularly high risk for poor outcomes as a result of non-therapeutic anticoagulation (9-11), our findings highlight the importance of addressing barriers to transportation and finding alternate methods of increasing TTR in these patients. One option that could lessen the burden of frequent clinic visits for monitoring are the target specific oral anticoagulants (apixaban, dabigatran, edoxaban, and rivaroxaban). However, due to their higher acquisition costs and lack of generic alternatives, warfarin is projected to
remain a mainstay therapy for the prevention and treatment of venous and arterial thrombosis especially in the underinsured and disadvantaged minorities who can’t readily access these agents.

In our study, the association between transportation barriers and TTR was not explained by a higher number of missed clinic appointments suggesting that other factors such as patients’ beliefs and attitudes, self-reliance and organizational skills, access to pharmacies and medications, time between clinic visits, and preference for alternate models of monitoring maybe driving this effect. Another consideration is that our definition of transportation barriers reflected whether patients “relied on” or “depended on” someone else for their transportation to clinic and did not only reflect cases that had no transportation available at all. There is no consistently, accepted definition of transportation barriers to health care/clinic appointments. (19) It is possible that a modified definition of transportation barriers could have found a mediation effect of missed appointments. In addition, we did not assess genotype and dietary vitamin K, which can contribute to variation in INR, however we excluded the 1st 3 months of therapy which excludes the dose response variably attributed by genotype.

In summary, our results suggest a negative association between the presence of transportation barriers and quality of anticoagulation control, even after controlling for socio-demographic and clinical factors associated with anticoagulation control. Understanding this relationship is especially important in underserved, minority patients
who are at highest risk for anticoagulation related complications. Our work serves as a first step towards understanding this relationship. Future studies should focus on elucidating additional factors that are potentially driving this effect and the feasibility of adopting alternate models of anticoagulation monitoring such as telehealth guided patient-centered interventions such as self-testing and self-monitoring.


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EDUCATION / POST GRADUATE TRAINING:

2011 – 2014 Master in Clinical and Translational Science
University of Illinois at Chicago
School of Public Health
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1995 - 1996 Primary Care Specialty Residency - ASHP Accredited
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College of Pharmacy
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1994 - 1995 Pharmacy Practice Residency - ASHP Accredited
Lutheran General Hospital/Advocate Health Care
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1990 - 1994 Doctor of Pharmacy, graduated with high-honors
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1989 - 1990 Pre-Pharmacy Curriculum
Wilbur Wright College
Chicago, Illinois

1983 - 1988 Chemical Engineering - Bachelor of Science Program
Politechnical Institute of Bucharest
Bucharest, Romania

LICENSURE: Registered Pharmacist, Illinois # 051-039827
ACADEMIC APPOINTMENTS:

<table>
<thead>
<tr>
<th>Year Range</th>
<th>Position</th>
<th>Department/Center</th>
<th>University</th>
<th>College</th>
<th>Location</th>
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<tbody>
<tr>
<td>2011 - Present</td>
<td>Clinical Professor</td>
<td>Department of Pharmacy Systems Outcomes and Policy</td>
<td>University of Illinois at Chicago</td>
<td>College of Pharmacy</td>
<td>Chicago, Illinois</td>
</tr>
<tr>
<td>2009 - Present</td>
<td>Clinical Professor</td>
<td>Department of Pharmacy Practice</td>
<td>University of Illinois at Chicago</td>
<td>College of Pharmacy</td>
<td>Chicago, Illinois</td>
</tr>
<tr>
<td>2009 – Present</td>
<td>Clinical Professor</td>
<td>Center for Pharmacoepidemiology &amp; Pharmacoeconomic Research (CPR)</td>
<td>University of Illinois at Chicago</td>
<td>College of Pharmacy</td>
<td>Chicago, Illinois</td>
</tr>
<tr>
<td>2008 – 2009</td>
<td>Clinical Associate Professor</td>
<td>Center for Pharmacoeconomic Research (CPR)</td>
<td>University of Illinois at Chicago</td>
<td>College of Pharmacy</td>
<td>Chicago, Illinois</td>
</tr>
<tr>
<td>2004 - 2009</td>
<td>Clinical Associate Professor</td>
<td>Department of Pharmacy Practice</td>
<td>University of Illinois at Chicago</td>
<td>College of Pharmacy</td>
<td>Chicago, Illinois</td>
</tr>
<tr>
<td>2005 – 2008</td>
<td>Affiliate Faculty</td>
<td>Center for Pharmacoeconomic Research (CPR)</td>
<td>University of Illinois at Chicago</td>
<td>College of Pharmacy</td>
<td>Chicago, Illinois</td>
</tr>
<tr>
<td>1996 - 2004</td>
<td>Clinical Assistant Professor</td>
<td>Department of Pharmacy Practice</td>
<td>University of Illinois at Chicago</td>
<td>College of Pharmacy</td>
<td>Chicago, Illinois</td>
</tr>
</tbody>
</table>
PROFESSIONAL AND CLINICAL EXPERIENCE:

2013 – Present  
Co-Director  
Center for Pharmacoepidemiology & Pharmacoeconomic Research (CPR)  
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2012 - Present  
Co-Director  
UI-Health Pharmacogenetics Service  
University of Illinois Hospital & Health Sciences System  
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1996 - Present  
Clinical Director  
Antithrombosis Center (ATC), Heart-Center  
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2007 - Present  
Clinical Pharmacist - Ambulatory Care  
Services covered: Heart Center – Antithrombosis Clinic / Pharmacogenetics  
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2000 – 2008  
Assistant Director, Wellness Center Clinics  
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Clinical Pharmacist Ambulatory Care – Wellness Center  
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1994 - 1997  
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POST-DOCTORAL FELLOWS/RESIDENTS AND GRADUATE STUDENTS MENTORED:

- Juan Blackburn, MD; Pharmacoeconomics Research Fellow (research emphasis in cardiovascular-antithrombotic therapy). University of Illinois at Chicago. 2003-2005.
- Zenobia Dotiwala, BS Pharm, MS Candidate - Graduate Student. University of Illinois at Chicago. 2009-2011.
- Sacheeta Bathia, BS Pharm, MS Candidate - Graduate Student. University of Illinois at Chicago. 2010-2013.
- Vardhaman Patel, PhD Candidate – Graduate Student. University of Illinois at Chicago. 2011-2013
- Adam Bress, Pharm.D. – Cardiovascular-Pharmacogenetics Fellow, MS Candidate. University of Illinois at Chicago. 2012-2013
- Christine Rash, Pharm.D. – Primary Care Specialty Resident. University of Illinois at Chicago. 2012-2013
- Wei-Han Cheng, MS, PhD Candidate – Graduate Student. University of Illinois at Chicago. 2012-2014
- Beenish Manzoor, MPH, PhD Candidate – Graduate Student. University of Illinois at Chicago. 2012-
- Katarzyna Drozda, Pharm.D. – Cardiovascular-Pharmacogenetics Fellow, MS Candidate. University of Illinois at Chicago. 2012-2013
- Deval Gor, MS, PhD Candidate – Graduate Student. University of Illinois at Chicago. 2014-

PUBLICATIONS (RECENT):


ABSTRACTS AND SCIENTIFIC PRESENTATIONS (RECENT):


**GRANTS AND CONTRACTS:**


**HONORS AND AWARDS:**

- American Society of Health System Pharmacists. Distinguished Service Award, December 2010.
- American College of Clinical Pharmacy, Clinical Practice Award, October 2009.
- American College of Clinical Pharmacy, Fellow, October 2007.
- ASHP Foundation’s Antithrombotic Pharmacotherapy Traineeship Program: selected as main preceptor and one of eight national training sites. 2006 – Present.
- Appointed as Vice President of the Anticoagulation Forum, 2007 – Present.
- NQF National Steering Committee for the Prevention and Care of VTE: Appointed as the only pharmacist member on the committee. 2006 -2009.
- Bristol Myers Squibb Antithrombosis Management Service Excellence Award, November, 2002.
- The Illinois Pharmacy Foundation Literature Award, September 1998.

EDITORIAL BOARDS:

- Thrombosis. Editorial Board Member, 2011 – present.
- Pharmacotherapy. Editorial Board Member, 2011 – present.

PROFESSIONAL SERVICE (RECENT):

Service to the University:

- Mentoring Program: Mentor to 2 faculty members. (Voluntary) The University of Illinois at Chicago, College of Pharmacy, Department of Pharmacy Practice. 2011-present.
- Promotion and Tenure Committee. (Appointed). The University of Illinois at Chicago, College of Pharmacy, Department of Pharmacy Practice. 2010 – Present.
- Faculty Advisory Committee. (Elected). The University of Illinois at Chicago, College of Pharmacy, Department of Pharmacy Practice. 2009 – 2011.
- Clinical Track Promotion Review Committee (Appointed). The University of Illinois at Chicago, College of Pharmacy, Department of Pharmacy Practice. 2010.
• Clinical Tenure Track Ad-hoc Committee (Appointed). The University of Illinois at
  Chicago, College of Pharmacy, Department of Pharmacy Practice. 2011.
• Translational Research Academy. (Appointed). The University of Illinois at Chicago,
• Research and IRB Review Committee. (Appointed). The University of Illinois at
  Chicago, College of Pharmacy, Department of Pharmacy Practice. 2008 – Present.
• Reimbursement for Clinical Services and Payment Task Force. Chair. (Appointed).
  The University of Illinois at Chicago, College of Pharmacy, Department of Pharmacy
• Anticoagulation Task Force. Co-Chair. (Appointed). The University of Illinois Medical
  Center Chicago. 2007 - Present.
• ACPE Self-Study Committee on Faculty and Staff. (Appointed). The University of

Service to the Profession:

• National Blood Clot Alliance (www.stoptheclot.org). Medical and Scientific Advisory
  Board. Member. 2011 – present.
• American College of Clinical Pharmacy Practice Based Research Network –
  Community Advisory Panel. Chair 2011-2012; Co-Chair 2009-2010.
• American College of Clinical Pharmacy. Ambulatory Care PRN. Treasurer. 2008 -
  2010.
• American College of Clinical Pharmacy. Ambulatory Care PRN. Education
• National Institutes of Health, Office of Dietary Supplements: Expert Committee on
• Anticoagulation Forum. Member, Board of Directors, 2006 – Present. Vice President,
• American Society of Health-System Pharmacists, Section of Home, Ambulatory, and
  Chronic Care Practitioners - Cognitive Services Reimbursement Resources Advisory
• American Society of Health-System Pharmacists, Section of Home, Ambulatory, and
  Chronic Care Practitioners – Programming Committee (2006 Midyear Clinical
• American College of Clinical Pharmacy. Ambulatory Care PRN - Frontiers Fund
• American Society of Health System Pharmacy. Section of Clinical Specialists and
  Scientists – Committee on Nominations. Member. 2004 – 2005; 2005 – 2006; 2006-

PROFESSIONAL AFFILIATIONS:

• International Society for Pharmacoeconomics and Outcomes Research, 2013 - present.
• International Society of Thrombosis and Haemostasis, 2001 - present.
• American Association of Colleges of Pharmacy, 1997 - present.
• Anticoagulation Forum, 1997 - present.
• American College of Clinical Pharmacy, 1994 - present.
• Illinois Council of Health System Pharmacists, 1994 - present.
• American Society of Health System Pharmacists, 1994 – present.