Impact of a Quality Improvement and Education Initiative on 'Appropriate' Use of Anticoagulant Therapy in Women with Atrial Fibrillation

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ABSTRACT

Purpose: 1) Quantify the potential net clinical benefit resulting from improved decision-making about antithrombotic therapy in patients with atrial fibrillation (AF); and 2) reduce their risk of stroke by developing and implementing a computerized decision support tool for individual patient-level decision-making about oral anticoagulant therapy.

Scope: Ambulatory setting, 1,876 adults with non-valvular AF or flutter. Total targeted health care professionals: 200.

Methods: Multipart study design. 1) Retrospective cohort study of patients seen in primary care settings between December 2012 and January 2014. Projections for quality-adjusted life expectancy (QALE) were calculated by a decision analytic model that integrates patient-specific risk factors for stroke and hemorrhage and examines strategies of no antithrombotic therapy, aspirin, or oral anticoagulation with warfarin. Net clinical benefit was defined by the gain or loss in QALE between current treatment and treatment recommended by an **A**trial **F**ibrillation **D**ecision **S**upport **T**ool (AFDST). 2) Prospective randomized controlled study in which practices comprising roughly half of all AF patients were randomized to early intervention arm (EIA) and the remaining practices received the intervention at a later time. The later practices functioned as a control during the initial project period. EIA and control practices received the same educational intervention and academic detailing. EIA practices received patient-level reports when current therapy was discordant with that recommended by AFDST.

Results: Current treatment was discordant from that recommended by the AFDST in 931 patients. A clinically significant gain in QALE was projected in 832 patients. In the randomized trial the AFDST report was reviewed in 240 patients in the EIA. Among those, discordant treatment dropped from 63.33% to 58.53% one year later. Among the 90 patients who were actually seen in follow-up primary care visits, discordant treatment dropped from 96.67% to 80.00%. Among patients whose treatment was discordant in 2014, patients cared for by resident physicians and by Medicine-Pediatrics physicians had lower rates of discordant antithrombotic therapy one year later. Non-stratified analyses demonstrated that changes in the proportion of patients with discordant care were not significantly different between the early intervention group and the control group. In multivariate regression models predicting persistently discordant therapy at one-year follow-up, assignment to the early intervention group resulted in a non-significant trend toward decreased discordance; being a patient of a resident physician, and a higher HASBLED score predicted decreased discordance; while female gender and CHADSVASc score predicted increased discordance. In a separate analysis, female gender and increasing age were significantly associated with an increased risk of discordant therapy. In summary, use of a decision support tool that integrates patient-specific stroke and bleeding risk can result in significant gains in QALE for a primary care population of patients with AF. Among patients whose physicians actually reviewed reports and recommendations of the decision support tool, discordant therapy decreased significantly over a one-year timeframe. This effect was even more pronounced among patients who were seen in follow-up. However, in non-stratified analyses the intervention did not result in significant improvements in discordant antithrombotic therapy.

Key Words: Atrial fibrillation, anticoagulation, clinical decision support, outcomes research, decision sciences methods, performance improvement

Purpose

Our objective was first to quantify the potential net clinical benefit resulting from improved decision-making about antithrombotic therapy in patients with atrial fibrillation (AF) and, second, to reduce their risk of stroke by developing and implementing a computerized decision support tool for individual patient-level decision-making about oral anticoagulant therapy. To accomplish these goals, we studied the impact of a combination of education related to anticoagulation therapy and adding a quality-improvement (QI) intervention to an educational package (for practice staff and clinicians) using a computerized aid, the **A**trial **F**ibrillation **D**ecision **S**upport **T**ool (AFDST) for individual patient-level decision-making about oral anticoagulant therapy in patients with non-valvular AF. The QI tool incorporates individual patients' risk factor profiles for ischemic stroke and bleeding. The fundamental question being addressed is: *Does addition of a QI intervention utilizing an AF decision support tool result in larger improvements in "appropriate" antithrombotic therapy and provider knowledge about stroke and bleeding risk than an educational intervention alone as an adjunct to ordinary care?*

Scope

Atrial fibrillation (AF) is the most common significant cardiac rhythm disorder and is also the most powerful common risk factor for stroke: about 15% of all strokes in the U.S. are attributable to AF. Its frequency increases with age, reaching a prevalence of 10% in persons over age 80. With the aging of the U.S. population, the prevalence of AF will increase substantially from over 2.2 million to more than 3 million by the year 2020. In particular, the risk of stroke in women with AF is underappreciated.[1] A recent study by Conen and colleagues showed middle-aged women to be at significantly increased risk of death from AF.[2] Furthermore, studies have shown that populations of women at equivalent risk of stroke are less likely to receive anticoagulant therapy than men.[3] Over the past decade, numerous randomized trials have established that anticoagulation can significantly reduce the stroke risk posed by AF. However, studies have documented widespread underutilization of this therapy, or, at times, inappropriate use. As a result, the recognition of stroke risk from AF and its prevention have become a high profile issue for many organizations. The American College of Physicians recently moved ahead with an initiative on atrial fibrillation and stroke prevention. Similar initiatives have been promulgated by the American Heart Association, and treatment guidelines continue to be publicized by the American College of Chest Physicians (ACCP) and the American College of Cardiology.

Target Audience

The UCHealth Primary Care Network (PCN) consists of 16 primary care practices (general internal medicine, internal medicine/pediatrics, and family medicine). These practices include two urban residency training sites and 14 urban and suburban locations, including several practices that provide services to Medicaid and underserved populations. All practices in the PCN use a common electronic health record (EHR). A centralized data warehouse containing clinical information for the entire PCN is housed

in the University's Center for Health Informatics (CHI). There were 37,000 unique patients with at least two primary care visits in the 12 month time period between December 2012 and January 2014.

Although appreciation of stroke risk and appropriate preventive treatment with anticoagulation therapy is a significant issue for women, it would be short-sighted to develop an intervention that excludes men. Therefore our ***target patient audience*** included female and male patients with non-valvular AF. Furthermore, we recognize that a patient's clinical course is a dynamic process over time. Factors that influence the risk of stroke or bleeding may change; therefore we will continually reexamine the anticoagulation decision in light of new and changing clinical information. We focused our intervention on prevalent (rather than incident) AF in the **ambulatory setting**. In order to be respectful of clinicians' and patients' time, our implementation strategy focused a reexamination of the decision on patients for whom the current anticoagulation decision **may not** be optimal.

Our ***target audience for the educational intervention*** included clinicians and clinical staff at the 16 UCHealth PCN practice sites involved in the study (more than 50 primary care physicians and their clinical staff). The intervention arm deploying the QI initiative addressed some of the recognized physician barriers to the appropriate prescribing of warfarin by providing timely and patient-specific information regarding the patient's risk for thromboembolic stroke and major hemorrhage, along with a decision analytic projection of gain or loss in quality-adjusted life expectancy resulting from the use of oral anticoagulant therapy compared with aspirin or no treatment, and a patient-specific guideline recommendation from the most recent 2014 update of the American College of Cardiology, American Heart Association, Heart Rhythm Society (ACC/AHA/HRS) AF guideline.

Current Assessment of Need

The recognition of stroke risk from AF and its prevention have become a high profile issue for many organizations. The ACP recently has moved ahead with an initiative on atrial fibrillation and stroke prevention. Similar initiatives have been promulgated by the AHA, and treatment guidelines continue to be publicized by the ACCP and the ACC. Despite steady improvements over the past two decades,[4,5] studies continue to document substantial underutilization and at times inappropriate utilization of oral anticoagulant therapy.[6-9]

Preliminary Data:

Our own data on the use of anticoagulation therapy in an Ohio Medicaid population show that only 9.7% of all patients and 11.9% of those without apparent contraindications filled prescriptions for warfarin in the period from 7 days proceeding, to 30 days after, the development of AF.[10,11] We assembled a retrospective, observational cohort of Ohio Medicaid patients from January 1, 1997 through May 31, 2002 analyzing 6,123 Ohio Medicaid recipients with two or more claims containing an International Classification of Diseases, Ninth Revision, Clinical Modification code (ICD-9-CM) for AF

(427.31) during the study period. We used pharmacy claims data to verify use of warfarin. We utilized a decision analytic tool that incorporates patient-specific risks for ischemic stroke and major bleeding events and calculates expected outcomes for patients with atrial fibrillation with and without warfarin treatment.[12,13] This decision support tool (DST) explicitly accounts for the risk of bleeding and formally addresses the balance of risk of bleeding with the benefit of stroke prevention. It is designed to individualize treatment recommendations based upon a patient's age, gender, and different degrees of risk for thromboembolism and hemorrhage by predicting quality-adjusted life years (QALYs).

The mean (SD) age of the study population was 76.2 (13.4) years. The majority of patients were women and were white. The population had numerous comorbidities known to increase the risk of stroke in AF, particularly hypertension, congestive heart failure, diabetes mellitus, and prior myocardial infarction. The DST recommended warfarin for 3,008 patients (49%); however, only 298 (9.9%) of these were prescribed warfarin. In particular, of 2,278 women for whom the DST suggested oral anticoagulant treatment, only 209 (9%) were receiving such therapy. In contrast, 89 of 432 (21%) men for whom oral anticoagulant was suggested were receiving such therapy.

Regarding the consequences of underutilization or inappropriate oral anticoagulation therapy, we calculated hazard ratios for strokes and bleeding events among the two groups with treatment that was either concordant or discordant with the recommendations of the DST. The first group included patients recommended for anticoagulation by the DST and receiving warfarin, compared to those recommended for anticoagulation, but not actually receiving warfarin. In this group there was a trend toward a decreased hazard for stroke (0.9, 95% CI: 0.58 – 1.41) with actual warfarin treatment. The lack of a statistically significant difference in stroke hazard may be secondary to the low overall use of warfarin in this cohort. In patients for whom withholding anticoagulation was recommended by the decision support tool (compared to those NOT recommended for anticoagulation and not receiving warfarin) there was a statistically significant increased hazard of gastrointestinal bleeding. In the final adjusted Cox proportional hazards model using the covariate of propensity for warfarin prescribing, the relative hazard for gastrointestinal bleeding was 1.54 (p=0.031). Thus, for this group of patients oral anticoagulant therapy may actually result in more harm than benefit.

A recent systematic review comparing current treatment practices for stroke prevention in AF with published guidelines showed underuse of oral anticoagulants in high risk patients in the majority of 54 studies reviewed.[9] Among patients in 29 studies with a history of prior stroke or transient ischemic attack (TIA) who should all be receiving anticoagulant therapy, treatment levels averaged less than 60% (range 19% - 81.3%). Among high risk patients with a $CHADS_2$ score[1] ≥ 2, treatment levels averaged less than 70% (range 39% - 92.3%). While there has been a trend toward improvement in utilization of anticoagulant therapy over the past decade,[5] a study of community-based practices in the Christiana Care Health System in northern Delaware published just this

[1] Stroke risk score based on **C**ongestive heart failure, **H**ypertension, **A**ge ≥ 75, **D**iabetes, and previous **S**troke.

year, continued to show substantial underutilization with almost one-third of high risk patients ($CHADS_2$ score ≥ 2) never receiving anticoagulant therapy despite the absence of identified barriers to such treatment.[7] Interestingly, in an analysis of predictors of warfarin use among the 1,141 patients studied there was a trend among men to be more likely to receive treatment. In an analysis of predictors of warfarin interruptions, there was a trend towards an increased risk in women.

Surveys exploring barriers to optimal anticoagulation have identified numerous issues. In our own analysis of Ohio Medicaid recipients with AF, we identified several factors including alcohol or other drug abuse or dependence, psychiatric disease, homelessness or inadequate housing, and lack of a caregiver as significant predictors of warfarin non-prescribing.[10] Clinician awareness of the benefit of anticoagulation therapy in stroke prevention has been identified as a barrier in a study by Cohen and collegues.[14] Beyth and colleagues noted that physicians were less likely to prescribe warfarin for older patients.[15] Others have shown that advanced age, female sex, and rural residency predicted underuse of oral anticoagulant therapy.[16] The pivotal physician-related factor seems to be an insufficiently balanced evaluation of the risk versus benefit of oral anticoagulant therapy.[17]

Several studies have shown that women, particularly older women, are less likely to receive oral anticoagulant therapy for AF.[18-20] Fang and colleagues explored this issue in the large community-based AnTicoagulation and Risk factors In Atrial fibrillation (ATRIA) cohort of 13,559 AF patients in the Kaiser Permanente system of northern California. They found that women not taking oral anticoagulants were at higher risk for stroke than men at both younger and older ages, with an adjusted relative risk of 1.6 (95% CI – 1.0 – 2.3) and 1.8 (95% CI – 1.4 – 2.3) respectively among patients ≤ 75 years of age and > 75 years of age.[21] Several mechanisms have been proposed for this observed difference in AF-related stroke, including observations that women with AF may have higher levels of von Willebrand factor, prothrombin factor F1.2, and tissue plasminogen activator antigen. Addressing this issue, the more contemporary stroke risk prediction tool CHA_2DS_2VASc[2], provides additional discrimination in risk score calculation on the basis of female gender.[22]

Regarding the inappropriate use of oral anticoagulant therapy, in low risk patients for whom current practice guidelines would not recommend anticoagulation (ie., age < 65 years, without a history of diabetes, hypertension, congestive heart failure, or previous TIA or ischemic stroke), upwards of 30% have been identified as receiving anticoagulant therapy.[5] In summary, both underutilization and inappropriate use of oral anticoagulant therapy occur in substantial numbers of patients. Furthermore, patients differ in their underlying risk for ischemic stroke, and their risk of major bleeding from anticoagulants. Thus, the decision to treat AF patients with antithrombotic therapy is ideally suited to a patient-centered decision analytic approach.[23]

[2] Adds **V**ascular disease, **A**ge 65-74 years, **S**ex category to $CHADS_2$ score.

Methods

Our goal was to study the impact of adding a quality-improvement (QI) intervention to an educational package (for practice staff and clinicians) using a computerized decision support tool for individual patient-level decision-making about oral anticoagulant therapy in patients with non-valvular AF. The QI tool incorporates individual patients' risk factor profiles for ischemic stroke and bleeding. We accomplished this by performing a cluster randomized clinical trial of an educational package, with and without the addition of the QI intervention.

Specifically, this project aimed to:

1. *Improve clinician and staff knowledge and ability to assess stroke and bleeding risk in the treatment of patients with AF.*
2. *Improve appropriate prescribing of oral anticoagulant therapy in patients with AF; and answer the following question:*
3. *Does addition of a QI intervention utilizing an AF decision support tool result in larger improvements in "appropriate" antithrombotic therapy and provider knowledge about stroke and bleeding risk than an educational intervention alone as an adjunct to ordinary care?*

We queried our health system's clinical data store to identify 9,270 patients with an ICD-9-CM diagnosis of atrial fibrillation (427.31) or atrial flutter (427.32) who did not have diagnoses of mitral valve disease (394.x), aortic valve disease (395.x), heart valve transplant (V42.2) or heart valve replacement (V42.3). Of these, 4,021 had a visit within the 12 month period January 1, 2013 – December 30, 2013, and 1,876 were seen in the PCN. The number of patients with AF in any single practice ranged between 4 and 366. The institutional review board at the University of Cincinnati approved this study.

Patient Characteristics

Information needed to calculate risk for stroke (CHA_2DS_2VASc),[24] major hemorrhage (HAS-BLED),[25] and intracerebral hemorrhage (ICH),[25] and to analyze the patient-specific decision model was extracted from the clinical data store using the active problem list and a combination of laboratory values and clinical measurements. Time in therapeutic range, needed to calculate the HAS-BLED score, was determined by interpolating INR values through time over the past one year, similar to the Rosendaal method.[26]

Atrial Fibrillation Decision Support Tool (AFDST)

We used structured query language (SQL) to generate a batch file containing values for clinical and demographic parameters needed to analyze the patient-specific decision model. We used a standard computer program (Decision Maker, Boston, Massachusetts) to build the decision analytic model and analyze results. Once the annual stroke and major hemorrhage rates were calculated, we used Decision Maker's remote control function to run a script file containing the required information for each

patient through a decision analytic model that estimates the quality-adjusted life expectancy with each of three strategies - 1) no antithrombotic therapy; 2) aspirin; and 3) oral anticoagulant therapy (warfarin in the base case) for each individual patient.[27] Results for the batch file run were stored to a text file which was then loaded into a SQL database. The strategy recommended by the decision support tool was the one resulting in the largest expected utility in QALYs (see text box). Current antithrombotic therapy was classified as either concordant or discordant with model recommendations. Using a decision analytic model allowed us to incorporate patient values (utilities) into the decision making process. Life spent in less-than-perfect states of health, such as a non-fatal stroke, can be valued through multi-attribute metrics, such as quality-adjusted life expectancy, to facilitate explicit tradeoffs between the risks and benefits of therapies. Population based average utilities were used for the health states considered in the model for this analysis.[32] Details of the 29-state Markov decision analytic model are described in our manuscript and on-line supplement - *Integrating real-time clinical information to provide estimates of net clinical benefit of antithrombotic therapy for patients with atrial fibrillation*.[33]

> ***QALYs (Q**uality **A**djusted **L**ife **Y**ears**)** have been used as a metric for decision making in a variety of clinical contexts including individual patient-level decision making, particularly when a model considers outcomes with very different implications and impact upon quality of life.[28-30] A strategy is not considered to be better if it results in a gain of less than 0.1 QALYs.[31] The choice of a 0.1 gain in QALYs as our threshold for a minimum clinically significant difference was empirical. There is no clear definition of how large a gain constitutes a clinically significant gain. When the gain is too small to matter clinically, the decision is considered a "toss-up."[31] Theoretically, if all factors have been considered in a decision analysis, any gain in QALYs would be sufficient to identify the optimal strategy. However, a model never captures all elements of a decision problem and parameter values have associated uncertainty. Thus, the AFDST will not recommend one treatment over another unless the gain exceeds a threshold of 0.1 QALYs.*

Development and Dissemination of Didactic Materials

The clinician experts on the project worked to develop a set of major topics and from that a 2-session conference series (see appendix – Outline of Topics for Educational Conference Series). This educational package was delivered as two didactic noon conferences on atrial fibrillation with a review of up-to-date anticoagulation guidelines for stroke prevention, and distribution of educational materials (e.g., pocket cards with CHA_2DS_2VASc stroke risk assessment and HAS BLED risk factors – see appendix). These activities all were certified for 1 *AMA Category 1 PRA credit(s)™* and/or AAFP Prescribed Credit. Physicians delivering the noon conference series at all of the general internal medicine and primary care practice sites included 3 stroke neurologists, 2 cardiologists, and a general internist (PI) who were co-investigators in this study. Internists who were faculty at the University of Cincinnati and Internal Medicine residents also had an opportunity to participate in the first of the noon conferences in a special Department of Internal Medicine (DOIM) Grand Rounds delivered by the PI.

All practices (intervention and control groups) received the educational package focused on physicians and clinical and non-clinical staff who would be involved in this QI process.

As part of the conference series, a 21 question knowledge survey was distributed to attendees at the DOIM Grand Rounds and at the first didactic noon conferences held at the community practice sites (see appendix – AF Knowledge Survey). This survey was completed before the lectures began. A follow-up knowledge survey was distributed to all prior attendees approximately one year later, in the Spring of 2015.

Design of the Clinical Trial

We cluster randomized practices to an early and late intervention group. The late intervention group served as the control. Six practices containing 35 clinicians and 918 patients with AF served as the early intervention group, while 9 practices containing 35 clinicians and 958 patients were randomized to the control or late intervention group.

For patients in the intervention group, a practice-level and physician-level summary report was designed for all patients with treatment recommendations that were discordant with current therapy, along with an explanation for the recommendation, the gain or loss in QALYs predicted by the decision model, and the current 2014 ACC/AHA/HRS guidelines. Practices were encouraged to revisit the anticoagulation decision in these patients, and processes to accomplish this were developed in collaboration with the UCHealth Quality Manager and local practice leadership. The culmination of this process was a retreat in which lead physicians from each practice, along with their practice managers, participated. At the retreat we presented and discussed an early prototype of the report, received feedback and modified the report. We also discussed ideas for how best to manage the information flow for the performance improvement intervention, seeking particular input from the practice managers who would need to supervise the process on site.

We next developed a secure web site which we used to communicate patient information to the clinicians in the early intervention arm. All physicians who had patients with care determined to be discordant from the recommendation of the AFDST received an email with a personal login and password to the secure website. The initial login screen provides an overview of the performance improvement initiative (see Figure 1).

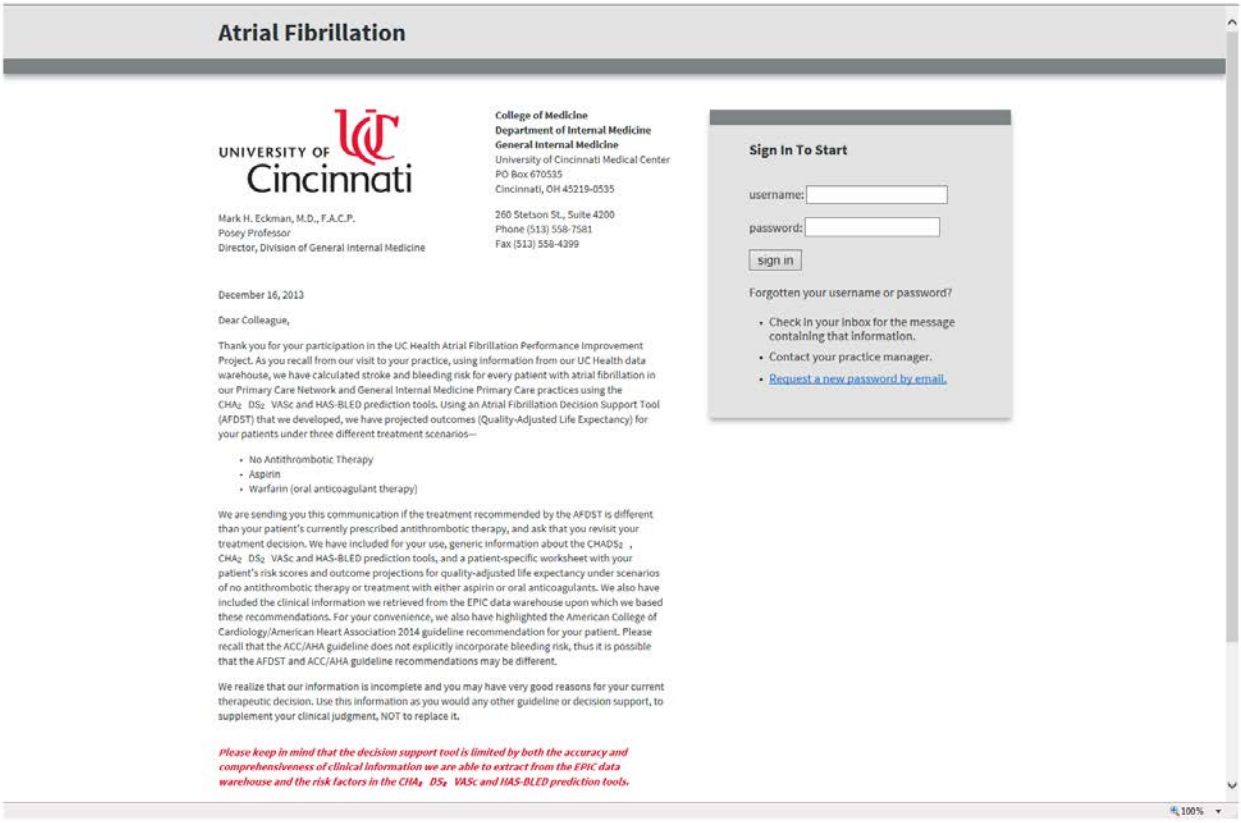

Figure 1. Secure web site login screen.

Once the clinician logs in, they encounter a list of their patients (see Figure 2). They then have the opportunity to indicate if any of the patients on their list are not in fact theirs. Once this is done, the clinicians are asked to review the clinical risk factors and current treatment plan that we obtained from our Clarity® database queries to ensure the information was accurate.

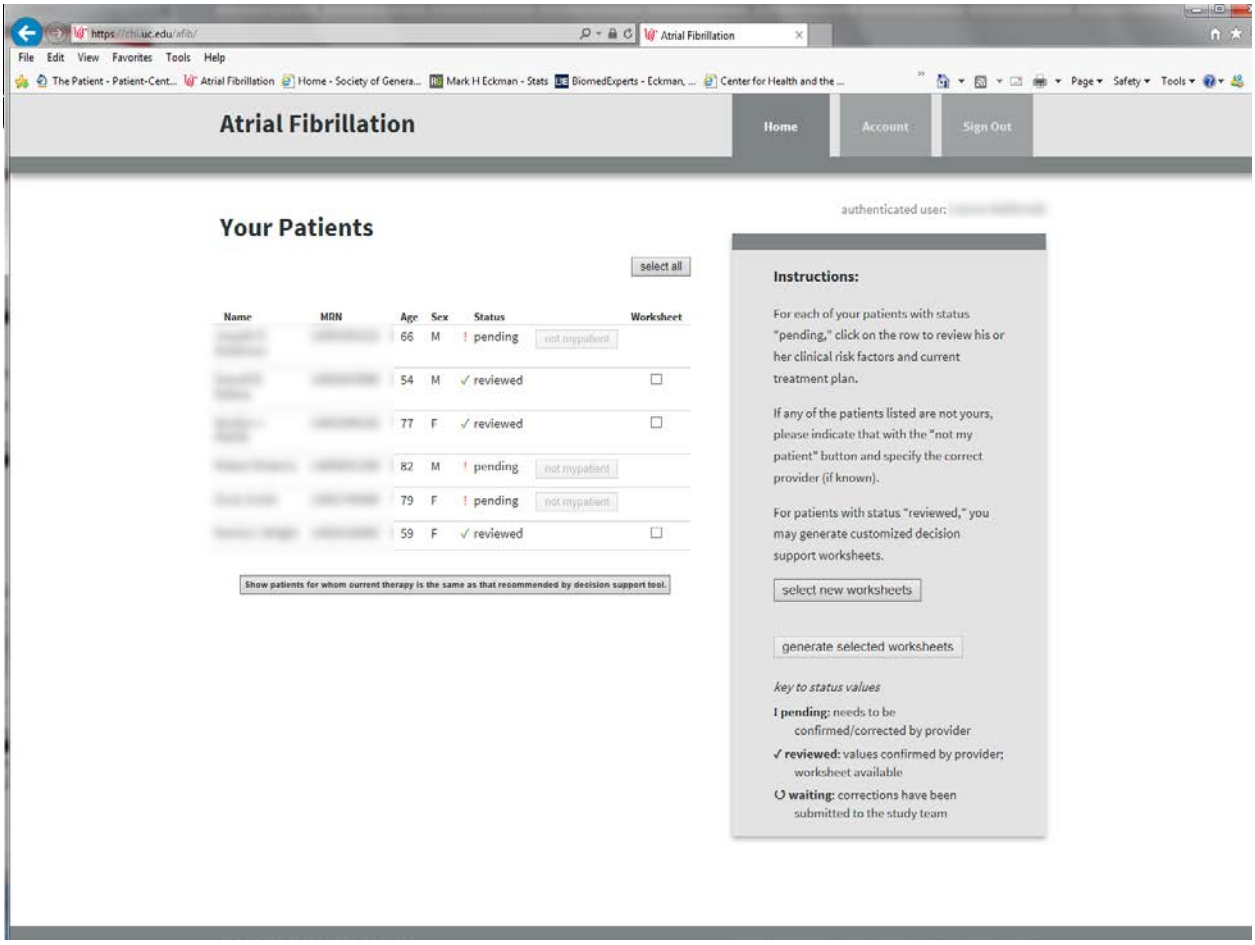

Figure 2. List of patients for each physician with current treatment that is discordant with recommended treatment.

This is accomplished by clicking on the patient's name, taking them to the view shown in Figure 3.

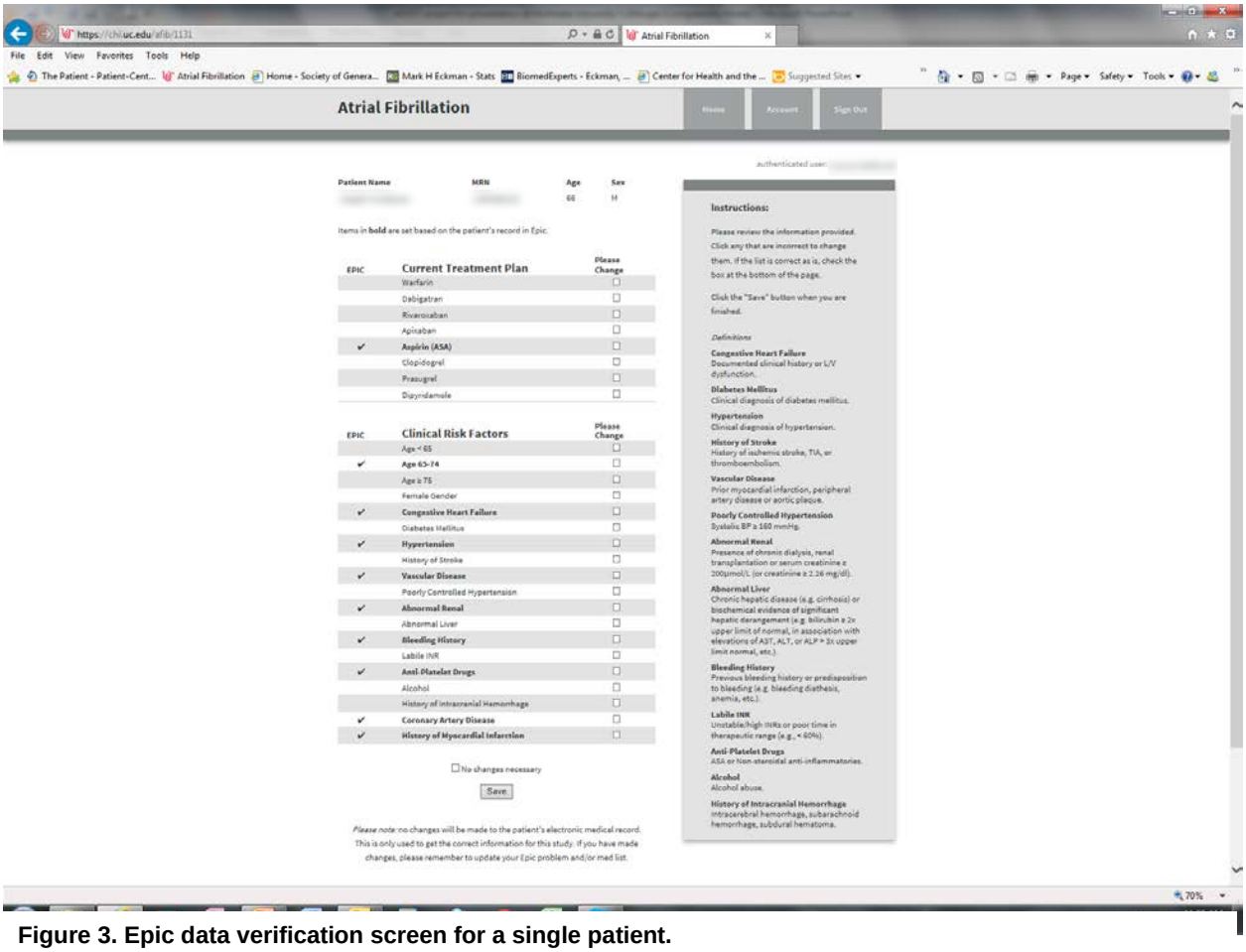

Figure 3. Epic data verification screen for a single patient.

Clinical information obtained from the electronic health record is highlighted by a check mark in the column to the far left, labeled “EPIC”, and by bolding of the text. Information about the specific meaning of each clinical variable/risk factor is provided to the far right of the screen. The clinician can correct this information by adding or deleting treatments or risk factors. If changes are made, we re-analyze that patient’s recommendation through the AFDST and repost the information and report. If no changes are required, the clinician clicks the appropriate box and is taken to the view shown in Figure 4, which summarizes the confirmed values for information being used to generate the report.

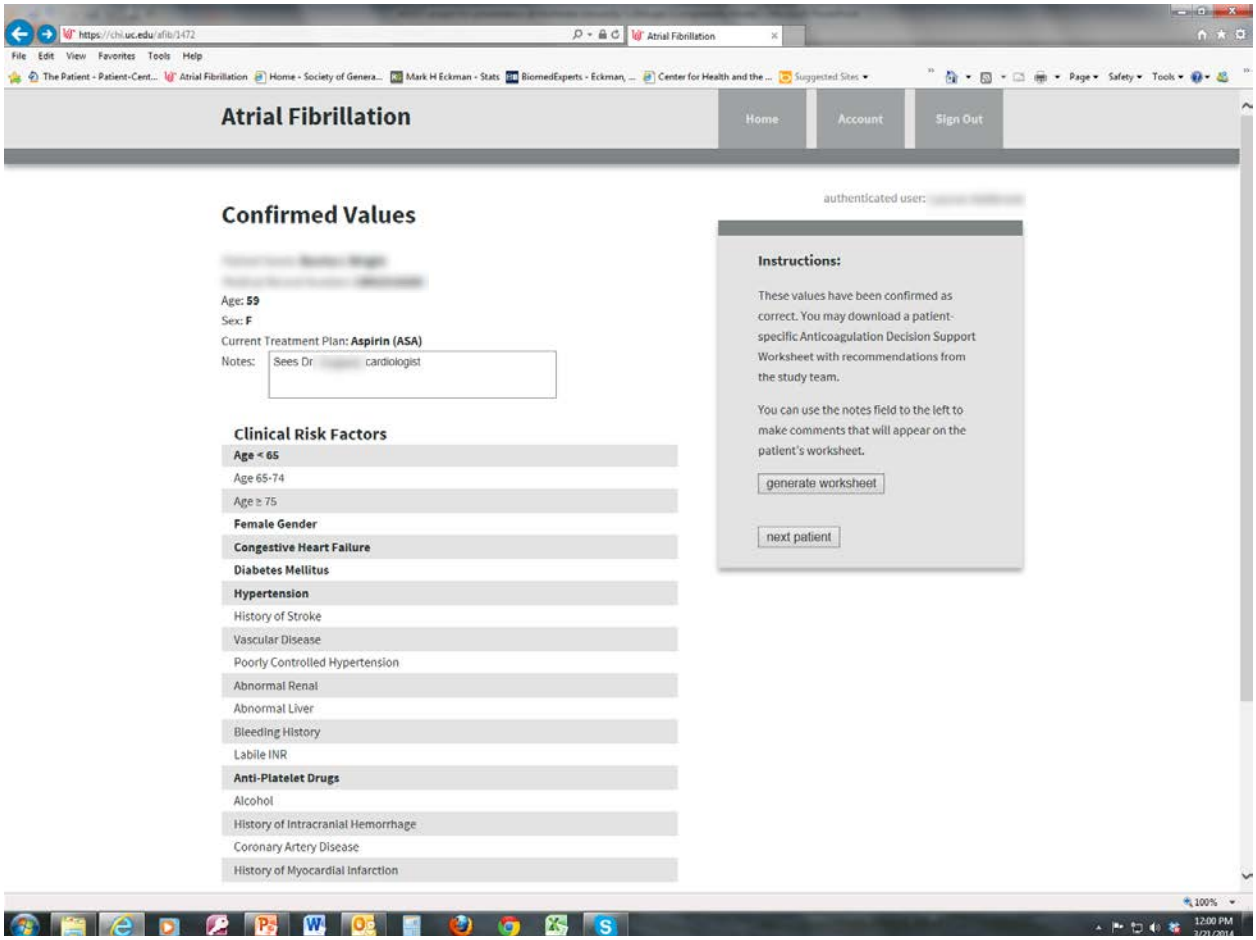

Figure 4. Confirmed values for clinical information being used to generate the patient-specific treatment report.

By clicking on the box labeled “generate worksheet” they next see a 2-page, patient report which is a dynamically generated pdf file. The first page (Figure 5) contains a review of the CHA_2DS_2VASc, $CHADS_2$, and HAS-BLED scores along with the physician’s and patient’s names. The second page (Figure 6) is the worksheet which reviews the clinical factors upon which the stroke and bleeding risk scores are calculated, the patient’s CHA_2DS_2VASc, $CHADS_2$, and HAS-BLED scores, and the patient-specific projections for quality-adjusted life expectancy with each of three strategies – no treatment, oral anticoagulant therapy, and aspirin. The far right side of

the worksheet contains a condensed summary of the ACC/AHA/HRS guideline. The appropriate recommendation for each patient is highlighted based upon the CHA_2DS_2VASc score. In order to get feedback on the design and functionality of the secure web site, and the plans for information flow within the practice for the performance improvement intervention and primary care physician notification, we first performed a pilot study in the largest practice included in the early intervention arm of the study. We discovered many issues and revised our processes and the web site design in response to feedback from the physicians in that practice.

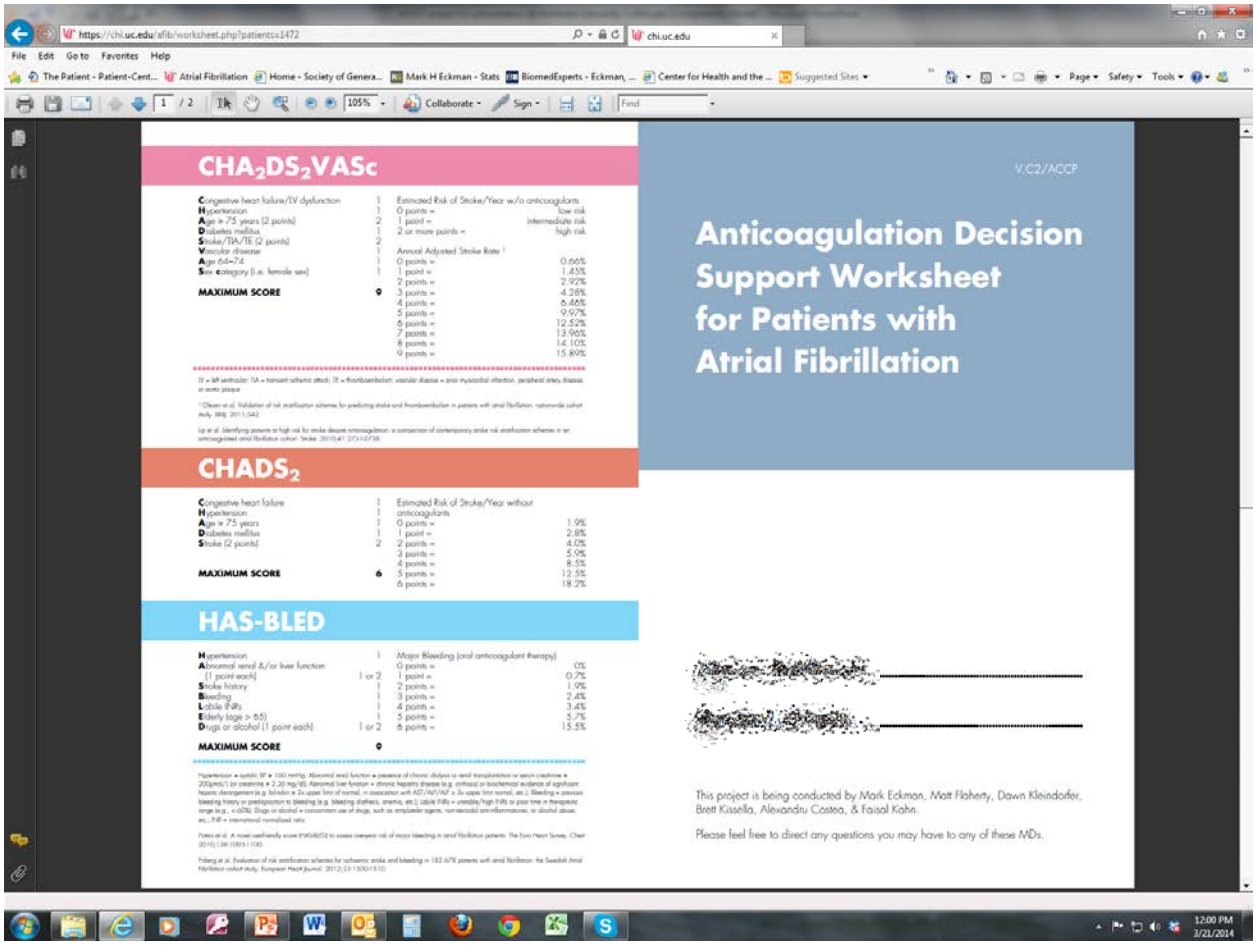

Figure 5. Title page for patient report.

Near the conclusion of this pilot phase (early March 2014), the AHA/ACC/HRS published their guideline update for atrial fibrillation. The report we created initially had displayed the American College of Chest Physicians (ACCP) guideline whose recommendations were based upon the $CHADS_2$ score. We were concerned about possible cognitive dissonance and confusion as the AFDST recommendations were based upon stroke risk calculations using the more recent CHA_2DS_2VASc score. The updated ACC/AHA/HRS guideline was the first guideline published in the United States to use the CHA_2DS_2VASc score. Consequently, we immediately updated our patient reports to use this more recent guideline. Figure 6 displays this updated report format.

After completing the pilot phase and updating our processes and report format, we extended the performance improvement project to the remaining 5 practices in the early intervention group on April 2, 2014.

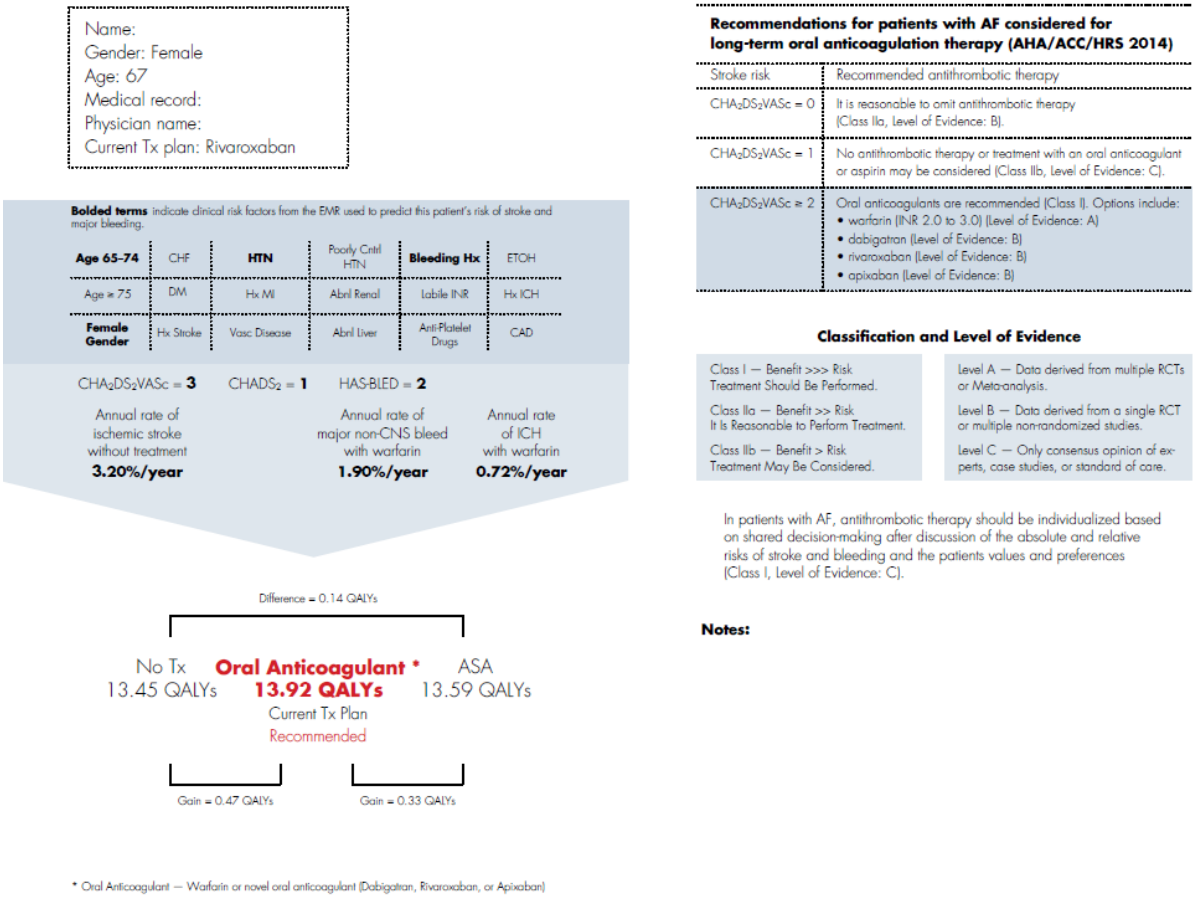

Figure 6. Patient report containing review of clinical data and risk factors, CHA2DS2VASc, CHADS2, and HAS-BLED scores, AFDST treatment recommendation, and AHA/ACC/HRS guideline.

Performance Improvement Procedures

We implemented the following processes and procedures for the intervention. Our study coordinator reviewed a report from our EHR every Friday that summarized all upcoming visits in the next week for patients whose current therapy is discordant with the treatment recommended by the AFDST. (Providers receive information on each of their patients on the list in order to verify the data extracted from the EHR. Treatment discordance is verified when the physician has confirmed the data retrieved from our EHR and reviewed the patient report.) Our study coordinator used this information to notify both the physicians and the practice managers involved. The practice managers maintained a tickler file of already printed patient reports. On the morning of the patient

visit, she/he gave the report to the physician so it could be reviewed and fresh in the physician's mind prior to the visit.

Our study coordinator also received a report from the EHR every Friday that summarized all scheduled patient visits on her list that had been completed in the prior week. This was used to trigger an email to the physician with a link to a REDCap® survey (see appendix – Post-Visit Physician Survey).

Results

Results are presented on the following pages for the three major components of the study.

Net Clinical Benefit of Antithrombotic Therapy for Patients with Atrial Fibrillation -

Risk Factors for Stroke and Bleeding - Figure 7 shows distributions of $CHADS_2$, CHA_2DS_2VASc, and HAS-BLED scores, along with annual predicted rate of ICH. 63% of the cohort had a $CHADS_2$ score ≥ 2, 85% had a CHA_2DS_2VASc score ≥ 2, and 67% had a HAS-BLED score ≥ 2. We tested the calibration of our decision model by simulating an observational study of future events in our cohort (first order Monte Carlo),

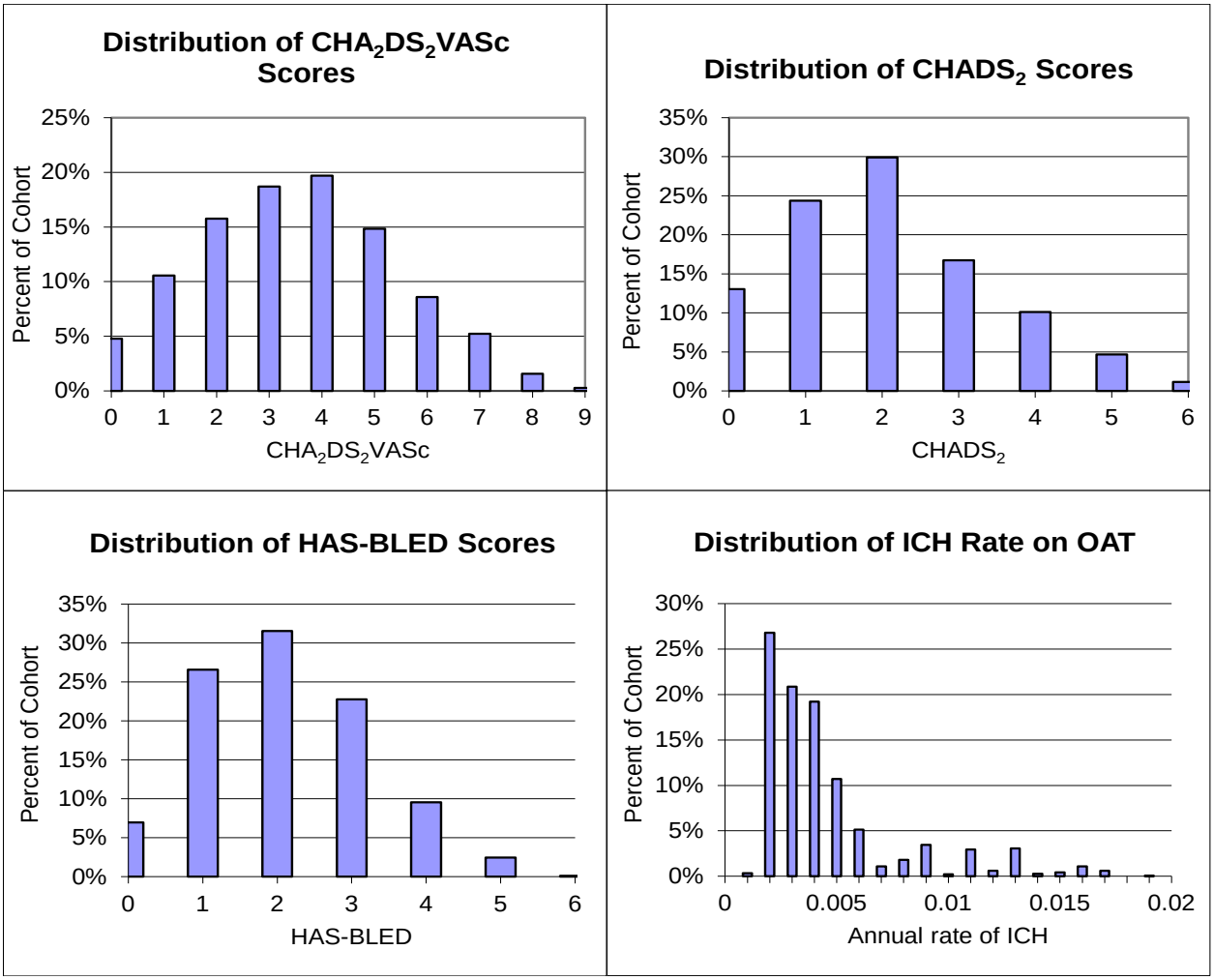

Figure 7. Distribution of Stroke Risk and Bleeding Risk Scores Among Patients with Atrial Fibrillation in the Primary Care Network.

comparing event rates for ischemic stroke and ICH across strata of stroke risk using $CHADS_2$ scores to those reported in a contemporary AF cohort, ATRIA over a similar period of time.[4] Stroke and ICH risk at all $CHADS_2$ scores were not significantly different, indicating good calibration (see on-line supplement of manuscript).

Projections of Quality-Adjusted Life Expectancy - QALE was calculated for each of the 1,876 AF patients in the PCN. An example of one such calculation is shown in Figure 6. Across the cohort of 1,876 AF patients, the AFDST recommended no antithrombotic therapy for 158 (8%) patients, aspirin for 89 (5%) patients, and oral anticoagulant therapy for 1,629 (87%) patients. Table 1 describes results in patients for whom AFDST-recommended treatment and current treatment were discordant. There were 931 (50%) such patients, 832 (44%) of whom were projected to gain more than 0.1 QALYs were treatment concordant with decision model recommendations. For instance, oral anticoagulant therapy was recommended for 188 who currently were receiving no antithrombotic therapy. Of these 188 patients, 179 would be expected to achieve a clinically significant gain of > 0.1 QALYs. Were their treatment to be changed to oral anticoagulant therapy, the projected aggregate gain in expected utility for this group of patients would be 209.4 QALYs, while the average gain per patient in this group would be 1.17 QALYs. To put this in context, the average projected quality-adjusted life expectancy for the entire cohort was 12.82 QALYs for "No Treatment," 13.16 QALYs for "Aspirin," and 13.74 QALYs for "Oral Anticoagulant Therapy." Of particular interest, our analysis suggested that we have the potential to gain roughly 736 QALYs among the 931 AF patients in our system's PCN whose current treatment is discordant with the recommendations of the AFDST if we improve our practice patterns for prescribing antithrombotic therapy.

Projected gains in quality-adjusted life expectancy among patient groups for whom AFDST-recommended treatment is discordant with current treatment

Recommended Treatment	Current Treatment	Number of Patients (n)	Patients with gain > 0.1 ‡ QALYs (n)	Average Gain per Patient (QALYs)	Gain for Group with > 0.1 gain (QALYs)
Oral Anticoagulant Therapy	None	188	179	1.17	209.38
	Aspirin	575	547	0.83	455.21
Aspirin	None	19	17	0.60	10.22
	Oral Anticoagulant Therapy†	41	31	0.60	18.73
None	Aspirin	59	30	0.21	6.15
	Oral Anticoagulant Therapy†	49	28	1.31	36.55
Total for Primary Care Network Population		931	832		736.24

Table 1.

Projected gains in quality-adjusted life expectancy among patient groups for whom current treatment is discordant with AHA/ACC/HRS 2014 guideline-recommended treatment

Treatment Recommended by AHA/ACC/HRS Guideline	Current Treatment	Number of Patients (n)	Average Gain per Patient (QALYs)	Total Gain for Group (QALYs)
OAT†	OAT	887		
	Aspirin	553	0.78	433.42
	None	165	1.04	171.22
No Antithrombotic Tx, Aspirin, or OAT‡	OAT	54		
	Aspirin	80		
	None	55		
None¥	OAT	12	1.51	18.07
	Aspirin	30	0.17	5.22
	None	36		
Total for Primary Care Network Population				627.93

† $CHA_2DS_2VASc \geq 2$. ‡ $CHA_2DS_2VASc = 1$. ¥ $CHA_2DS_2VASc = 0$.

Table 2.

We also determined the potential gain in QALE across our AF cohort were patients to be treated in accordance with the recently released 2014 AHA/ACC/HRS guidelines.[34] This is the first U.S. guideline to utilize the CHA_2DS_2VASc scoring algorithm. As shown in Table 2, of 1,605 patients with a $CHA_2DS_2VASc \geq 2$, 887 (55%) were receiving guideline-concordant treatment with oral anticoagulant therapy. The 553 who were receiving aspirin could gain an average 0.78 QALYs each, for an aggregate gain of 433 QALYs for the group, were they to receive oral anticoagulant therapy. The 165 who were receiving no antithrombotic therapy could gain an average of 1.04 QALYs each, for an

aggregate gain of 171 QALYs were they to receive guideline-concordant treatment. The guideline recommends that any treatment is reasonable for patients with a CHA_2DS_2VASc score of 1; therefore no patients in this group had treatment that was discordant from the guideline. Finally, a total of 78 patients had a CHA_2DS_2VASc score of zero. A total of 23 QALYs could be gained were patients in this group who were receiving either oral anticoagulant therapy or aspirin NOT to receive antithrombotic therapy in concordance with the guideline. In Table 3 we compare the CHA_2DS_2VASc-based treatment recommendations of the AHA/ACC/HRS guideline with the AFDST. While there is a high level of agreement between the guideline and the decision support tool, there are some patients with a $CHA_2DS_2VASc \geq 2$ for whom either aspirin (41) or no antithrombotic therapy (65) is recommended. This discrepancy is due to the incorporation of bleeding risk into the projections made by the AFDST. While the AHA/ACC/HRS guideline makes no specific recommendation for patients with a CHA_2DS_2VASc of 1, the AFDST specifies oral anticoagulant therapy, aspirin, or no antithrombotic therapy for 54, 80, and 55 patients respectively.

Comparison of AFDST recommended treatment with AHA/ACC/HRS 2014 guideline-recommended treatment

CHA_2DS_2VASc	Treatment Recommended by AHA/ACC/HRS Guideline	Decision Support Tool Recommendation	Number of Patients (n)
≥ 2	OAT	OAT	1,503
		Aspirin	41
		None	65
1	No Antithrombotic Tx, Aspirin, or OAT	OAT	54
		Aspirin	80
		None	55
0	None	OAT	0
		Aspirin	2
		None	76

Table 3.

Use of Dual Antithrombotic Therapy in Patients with Atrial Fibrillation -

As part of our system-wide performance improvement initiative focused on improving antithrombotic therapy decisions for patients with atrial fibrillation (AF), we discovered a large number of patients who were receiving dual therapy with both aspirin and warfarin. Our goal was to determine the indications for dual therapy and possibly identify patients who might reasonably be treated with oral anticoagulant therapy alone. We hypothesized that the majority of these patients likely had a prior indication for antiplatelet therapy, such as stable coronary artery disease or diabetes, subsequently developed AF and had warfarin added to their regimen without discontinuing aspirin. There have been multiple studies examining outcomes of dual therapy in patients with indications for both antiplatelet and anticoagulant therapy. All have demonstrated an increased risk of major bleeding compared with either treatment alone; and among patients with stable CAD, in particular, dual therapy has not been shown to reduce ischemic events. The 2012 AF guidelines from the American College of Chest Physicians (ACCP) recommends against the use of dual therapy for AF patients with

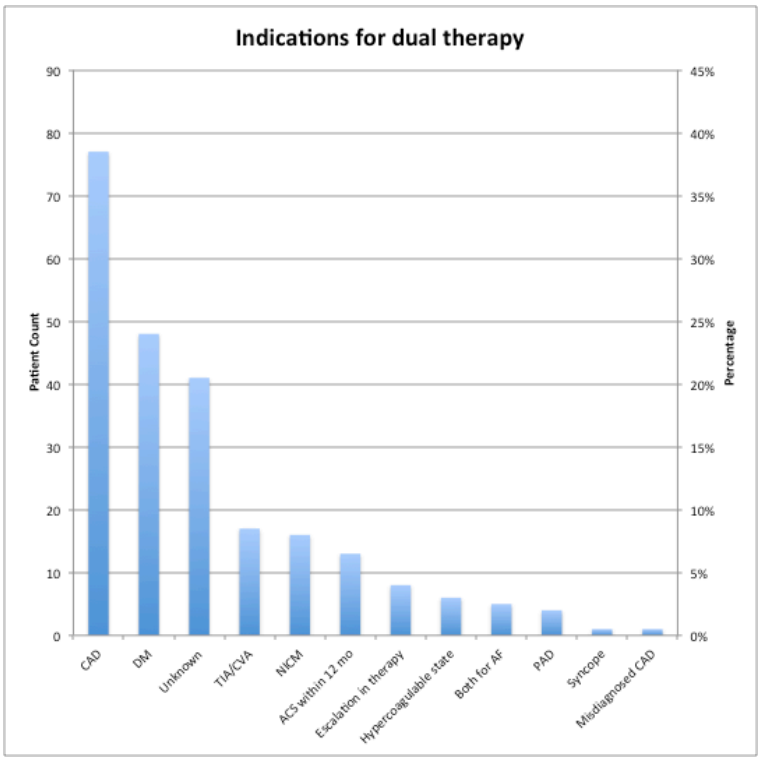

Figure 8. This graph depicts the indications for dual therapy grouped into several general categories.

stable CAD, indicating that warfarin alone within a therapeutic INR range of 2-3 is sufficient. We identified 348 patients (23% of the total AF cohort) in the UC Health Primary Care Network who were receiving dual therapy with an antiplatelet as well as antithrombotic agent as of 1/7/2014. We randomly sampled 200 charts to evaluate and categorize the indication(s) for dual antithrombotic therapy and collected information describing the time course of events that led to the initiation this treatment.

Of the 200 patients reviewed, 77 (38.5%) had stable CAD and 48 (24%) had DM as co-morbidities resulting in dual therapy. 41 patients (20.5%) were classified as unknown, meaning patients whose charts had insufficient information to determine the reason for dual therapy. 36 patients (18%) had diagnoses of both CAD and DM and were counted in both categories (Figures 8 and 9). Thus the total added up to more than 100%.

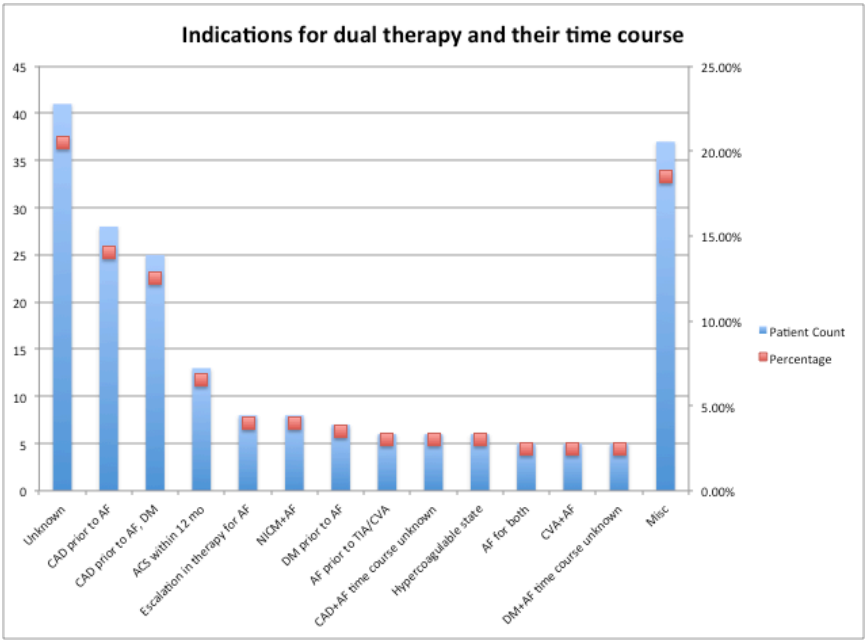

Figure 9. This graph further details the indications for dual therapy and the time course of events that led to its initiation.

Our data show that the majority of patients receiving dual antithrombotic therapy had a diagnosis of stable CAD or DM. Of interest, in a significant proportion of patients aspirin had been initiated due to a prior diagnosis of either stable CAD or DM and was not discontinued when warfarin was started for their AF (73% and 14.58% respectively). The 2012 ACCP guidelines indicate that there is insufficient evidence to warrant dual therapy in AF patients with

stable CAD. A number of recent studies have examined outcomes in AF patients with stable CAD receiving dual therapy, and have concluded that dual therapy increased bleeding risk without reducing the risk of ischemic events, defined as stroke or myocardial infarction. Withdrawing aspirin from the antithrombotic regimens of these patients may provide an opportunity to improve clinical outcomes.

Randomized Trial: Does the Addition of a QI Intervention Improve "Appropriate Antithrombotic Therapy?" -

Characteristics of patients and practices in each of the arms of the study are described in Table 4 below. For the most part, the patients in both groups were demographically comparable and a similar proportion were receiving oral anticoagulant therapy (OAT). There was a slightly higher proportion of faculty members and a lower proportion of residents in the control practices. There was a higher proportion of family medicine and medicine-pediatrics physicians in the control group and a higher proportion of internal medicine physicians in the early intervention group.

Table 4. Patient and Practice Characteristics

	Early Intervention Practices	Control Practices
Patient Characteristics		
Number	801	692
Age (mean)	70.2	69.8 (*p=0.56*)
Female (%)	44	48 (*p=0.19*)
CHA_2DS_2VASc (mean)	3.60	3.74 (*p=0.14)*
HAS-BLED (mean)	2.07	2.18 (*p=0.06)*
Proportion receiving oral anticoagulant therapy (%)	50	50 (*p=0.92)*
Practice Characteristics		
Faculty (%)	37	47 (*p=0.05)*
Non-Faculty (%)	12	24 "
Residents (%)	51	29 "
Internal Medicine	88	13 (*p<0.0001)*
Family Medicine	9	37 "
Medicine-Pediatrics	4	50 "

Changes in discordant prescribing of antithrombotic therapy – How did the overall proportion of patients with discordant treatment change between 2014 and 2015?

For the UCHealth PCN practices overall (see Table 5), the proportion of patients whose treatment was discordant with the recommendations of the AFDST dropped from 41.93% (626/1493) to 40.59% (606/1493), *p=0.10*. The 84 patients who died over the year were censored from these numbers. At baseline, 41.82% (335/801) of the early intervention practices' patients had discordant care, while 42.05% (291/692) of patients in the control practices had care that was discordant from AFDST recommendations. At one year follow-up, the proportion of patients with discordant care dropped to 41.07% (329/801) and 40.03% (277/692) in the early intervention and control practices, respectively. When we looked at subgroups based upon the AFDST recommendation, we also did not see significant differences.

Table 5. Antithrombotic Therapy discordant from AFDST recommendations.

Intervention Group	Antithrombotic Therapy	
	Discordant in 2014 (%)	Discordant in 2015 (%)
All Practices	41.9	40.6 (*p=0.10)*
Early Intervention Practices	41.8	41.1 (*p=0.51)*
Control Practices	42.1	40.0 (*p=0.07)*
Aspirin or No Anticoagulant Therapy Among Patients for whom OAT was recommended		
Early Intervention Practices	44.7	44.5 (*p=0.59)*
Control Practices	44.8	43.5 (*p=0.27)*
Antithrombotic Therapy Among Patients for whom No Antithrombotic Therapy was recommended		
Early Intervention Practices	60.0	59.1 (*p=0.65)*
Control Practices	43.2	32.5 (*p=0.56)*
Oral Anticoagulant Therapy Among Patients for whom No Antithrombotic Therapy was recommended		
Early Intervention Practices	22.7	21.1 (*p=0.56)*
Control Practices	14.3	10.9 (*p=1.00)*

As shown in Table 6 below, we also looked at how the proportion of patients with treatment that was discordant from the AFDST recommendation changed over time, stratified by various subgroups describing practice and physician characteristics. Practice characteristics included an assessment of their readiness for change and enthusiasm for participating in performance improvement (PI) activities. This assessment was made by the director of performance improvement for the Primary Care Network on a 3-item scale ranging from high enthusiasm to low enthusiasm. There was a provocative but not statistically significant trend towards a larger decrease in discordant therapy among the practices with a high level of enthusiasm for PI work. Physician characteristics included faculty type (academic faculty, non-faculty, or resident). There was a significant decrease in discordant care among faculty. In addition, there was an interesting trend among residents, with discordant therapy decreasing from 44.19% in 2014 to 39.53% in 2015. Although the p-value did not reach statistical significance, the total number of patients cared for by the residents was only 172, the smallest sub-group of the category. When physicians were categorized by specialty (Internal Medicine, Family Medicine, or Medicine-Pediatrics), only the Medicine-Pediatrics physicians had a significant decrease in discordant care, from 47.73% in 2014 to 40.91% in 2015. Finally, among physicians in the early intervention group, we also looked at the impact of whether the physician reviewed the AFDST report and whether the patient was ultimately seen in follow-up. Recommendations of the AFDST were reviewed for a total of 240 patients. Among those patients, there was a significant decrease in the proportion with discordant care, declining from 63.33% in 2014 to 58.33% in 2015. There was a highly significant decrease in discordant care among the 90 patients who actually were seen in follow-up, declining from 96.67% to 80%.

Table 6. Antithrombotic Therapy discordant from AFDST recommendations – by subgroup		
Intervention Group	Antithrombotic Therapy	
	Discordant in 2014 (%)	Discordant in 2015 (%)
Practice Rating (readiness for change) –		
high enthusiasm	41.1	39.2 (*p=0.09)*
moderate enthusiasm	42.9	41.1 (*p=0.25)*
low enthusiasm	43.3	44.5 (*p=0.51)*
Faculty type –		
Faculty	42.0	40.0 (*p=0.04)*
Non-faculty	41.6	43.4 (*p=0.24)*
resident	44.2	39.5 (*p=0.14)*
Faculty Specialty –		
Internal Medicine	42.4	42.1 (*p=0.75)*
Family Medicine	38.8	37.2 (*p=0.27)*
Medicine-Pediatrics	47.7	40.9 (*p=0.01)*
Among Patients for whom AFSDT Report was reviewed	63.3	58.3 (*p=0.02)*
Among Patients seen in Follow-up	96.7	80.0 (*p=0.0001)*

Persistence of discordant prescribing of antithrombotic therapy – How did the proportion of patients with discordant treatment change between 2014 and 2015, among patients with discordant treatment in 2014?

We next looked at the proportion of patients with discordant treatment in 2015 among the group who had discordant treatment in 2014. As shown in Table 7 below, differences in the proportion with discordant treatment in 2015 were not significantly different between the early intervention and control practices. Looking at practice sites, there was an interesting, but not statistically significant trend towards a clinically meaningful decrease in discordant therapy in the Internal Medicine Resident practice, with a decrease to 74.6% among patients who had discordant treatment in 2014. Looking at practice readiness for change and enthusiasm to participate in PI activities, the practices rated as having low enthusiasm had the highest proportion with discordant treatment in 2015, but the differences were not significant. Looking at type of faculty, there was a significantly lower proportion of discordant treatment among resident

physicians (75%) and faculty (86.98%) compared with non-faculty (92.96%) physicians. Looking at physician specialty, there was a significantly lower proportion of patients with discordant treatment among Medicine-Pediatrics physicians (78.57%), compared with Internal Medicine (88.21%) and Family Medicine (88.00%).

Table 7. Discordant Care in 2015, among patients with Discordant Care in 2014.

Intervention Group	Discordant in 2015 (%)
All Practices	86.6
Treatment Group –	*(p=0.79)*
Early Intervention Practices	86.6
Control Practices	87.3
Practice Site –	(*p=0.08*)
A	89.1
B	90.1
C	100
D	88.4
E	88.9
Resident Practice	74.6
Practice Rating (readiness for change) –	(*p=0.27*)
high enthusiasm	85.6
moderate enthusiasm	86.8
low enthusiasm	91.6
Faculty type –	(*p=0.001*)
Faculty	87.0
Non-faculty	93.0
resident	75.0
Faculty Specialty –	(*p=0.05*)
Internal Medicine	88.2
Family Medicine	88.0
Medicine-Pediatrics	78.6
Among Patients for whom AFSDT Report was	(*p=0.74*)
Reviewed	

Not Reviewed	87.3
	86.0
Among Patients	(*p=0.23*)
seen in follow-up	82.8
not seen in follow-up	87.9

Lastly, we performed multivariable regression analyses examining the impact of patient, physician, and practice characteristics on the persistence of discordant therapy. These analyses predicted discordance in 2015 treatment decisions among patients who had discordant therapy in 2014. The purpose of these models was multifold – 1) to control for confounding in order to isolate the impact of the intervention on outcomes; 2) to better understand the impact of factors that influenced the outcomes; and 3) to specifically examine the impact of age and gender on therapeutic decisions. Factors included in the development of these models included –

Patient factors:

- CHA_2DS_2VASc
- HASBLED
- Gender
- Age

Physician factors:

- Specialty (IM, MP, FP)
- Faculty status (faculty, non-faculty, resident)

Practice factors:

- Readiness for change/enthusiasm for involvement in PI activities.

Impact of Intervention on Treatment:

Final models were developed to predict the proportion of patients in 2015 with antithrombotic therapy that was discordant from recommended therapy among patients whose treatment was discordant in 2014. We forced variables into the model that made clinical sense. These included gender, HASBLED score, CHA_2DS_2VASc score, faculty status, physician specialty, and practice enthusiasm for PI work. We also forced the variable representing the intervention group assignment into the model, although it was not statistically significant. As shown in table 8 below, being in the early intervention group showed a trend toward a decrease in the predicted level of discordant therapy in 2015. In addition, a higher HASBLED score, and being a resident physician decreased the probability of discordant treatment in 2015. Female gender and a higher CHA_2DS_2VASc score increased the probability of discordant therapy.

Table 8. Multivariable Model including Assignment to Early Intervention Group.		
Variable	Beta	P-value
Assignment to Early Intervention Group	-0.42	0.29
Female Gender	0.72	0.01
HASBLED score	-0.29	0.03
CHA_2DS_2VASc score	0.16	0.10
Faculty status –		0.02
resident physician	-0.915	
faculty	0	
non-faculty	0.83	
Physician Specialty		0.19
Internal Medicine	0.92	
Family Practice	0.33	
Medicine-Pediatrics	0	
Practice Rating (readiness for change) –		0.67
high enthusiasm	0.5534	
moderate enthusiasm	0.40	
low enthusiasm	0	

Impact of Practice, Physician, and Patient factors on Treatment:

We next explored models without forcing assignment to the early intervention group as a covariate, to better understand the impact of practice, physician, and patient factors on the persistence of discordant therapy. As shown in Table 9 below, only faculty status as a resident, CHA_2DS_2VASc score, and HASBLED score remained in this model. As before, the higher the CHA_2DS_2VASc score the more likely treatment was discordant in 2015, while a higher HASBLED score and faculty status as a resident physician decreased the likelihood of discordant therapy.

Table 9. Multivariable Model Exploring Practice, Physician, and Patient Factors.		
Variable	Beta	P-value
HASBLED score	-0.35	0.008
CHA_2DS_2VASc score	0.286	0.0012
Faculty status –		0.0013
resident physician	-0.831	
faculty	0	
non-faculty	0.69	

Impact of Gender and Age on Treatment:

Finally, we explored a model that only contained gender and age to investigate the hypothesis that female gender and advanced age were associated with an increased risk of discordant therapy. This analysis was performed on all patients, not just those who had discordant treatment in 2014. While the impact of female gender supported our initial hypothesis, we were surprised to find the opposite effect of increasing age. As shown below in Table 10, increasing age was actually associated with a decreased probability of discordant treatment.

Table 10. Multivariable Model Exploring Patient Gender and Age.

Variable	Beta	P-value
Female Gender	0.50	< 0.0001
Age	-0.019	< 0.0001

Changes in Need for Treatment Over Time

For this analysis we wished to see how often physicians reacted to changes in a patient's clinical status that prompted a changed AFDST recommendation over the 1-year follow-up period. For instance, the occurrence of a major bleed and the resultant increase in the HASBLED score could alter the balance of risk and benefit and result in an AFDST recommendation changing from oral anticoagulant therapy to no antithrombotic therapy. Similarly, if a patient developed new risk factors for stroke, the AFDST recommendation could change from either no antithrombotic therapy or aspirin to oral anticoagulation. Although these events did not occur often, clinicians rarely responded to changes in the clinical status that prompted the AFDST to make a recommendation change. As shown in Table 11 below, the AFDST recommendation changed from Oral Anticoagulant Therapy to No Antithrombotic Therapy in 11 patients. Of the 7 patients who were receiving oral anticoagulant therapy in 2014, treatment was changed to no antithrombotic therapy in 3, to aspirin in 1, and not changed in 3. As shown in Table 12, the AFDST recommendation changed from No Antithrombotic Therapy to Oral Anticoagulant Therapy in a total of 34 patients. Of the 8 patients who were receiving no antithrombotic therapy in 2014, 2 were switched to oral anticoagulation, 1 was switched to aspirin, and 5 remained on no antithrombotic therapy. These results underscore that changes in patients' clinical status that warrant a reconsideration of antithrombotic therapy are likely not being recognized and acted upon.

Table 11. Patients for whom the AFDST Treatment Recommendation Changed from Anticoagulant Therapy in 2014 to No Antithrombotic Therapy in 2015.

	2015 Treatment Plan			Total
2014 Treatment Plan	No Antithrombotic Therapy	Aspirin	Oral Anticoagulant Therapy	
No Antithrombotic Therapy	0	0	0	0
Aspirin	0	3	1	4
Oral Anticoagulant Therapy	3	1	3	7
Total	3	4	4	11

Table 12. Patients for whom the AFDST Treatment Recommendation Changed from No Antithrombotic Therapy in 2014 to Anticoagulant Therapy in 2015.

	2015 Treatment Plan			Total
2014 Treatment Plan	No Antithrombotic Therapy	Aspirin	Oral Anticoagulant Therapy	
No Antithrombotic Therapy	5	1	2	8
Aspirin	1	10	0	11
Oral Anticoagulant Therapy	0	1	14	15
Total	6	12	16	34

Accuracy of Medical Information Obtained from EHR –

When physicians first viewed their patient's information in the AFDST secure web-site, we asked them to confirm the data we pulled from the EHR before providing the worksheet/report (see Figure 3). Physicians were able to add, remove or modify information. In the 240 patients in the early intervention group who were reviewed by their primary care physicians, changes were made on information for 79 patients (approximately 1/3). Of interest, the most common addition of a risk factor that was not captured by our search of diagnostic codes on the active problem list was coronary artery disease. Table 13 details a full listing of all risk factors and antithrombotic therapies physicians added or deleted.

Table 13. Corrections Made by Physicians in Clinical Information Gathered from the Electronic Health Record.

Additions:		Deletions:	
Risk Factor or Treatment	frequency	Risk Factor or Treatment	frequency
coronary artery disease	24	Poorly controlled hypertension	4
Bleeding history	13	Aspirin	4
Aspirin	10	Bleeding history	3
Clopidogrel	5	History of myocardial infarction	2
Warfarin	5	Abnormal renal function	2
Congestive heart failure	4	Congestive heart failure	1
Rivaroxaban	3	Rivaroxaban	1
Antiplatelet drugs	3	Labile INR	1
History of intracranial hemorrhage	3	Hypertension	1
Hypertension	3	Warfarin	1
Alcohol use	3	Clopidogrel	1
Apixaban	3	Diabetes mellitus	1
History of stroke	3		
Labile INR	3		
Vascular disease	2		
Abnormal renal function	1		
Diabetes mellitus	1		
History of myocardial infarction	1		
Poorly controlled hypertension	1		

Qualitative Analysis -

In order to investigate physician decision making about therapeutic decisions for their patients who were discordant with the model recommendations, we designed a qualitative study within the larger project to examine two questions:

- When the AFDST makes a recommendation that is discordant with current antithrombotic therapy, does use of the tool lead physicians to change treatment to that recommended by the decision support tool?
- What barriers exist for using the tool in the two-communication exchanges that occur between patients and doctors in the shared-decision medical encounter?

For the qualitative study we conducted semi-structured interviews with the 4 physicians members of the research team who reviewed charts of the discordant patients and 12 physicians/residents participating in the project.

We are currently coding and analyzing the de-identified physician interview notes. The process of coding, naming segments of data with labels that categorize and summarize chunks of data is being undertaken by a member of the research team and a second individual to ensure internal consistency.

We are using a two-step coding process. In the first cycle. coders worked independently to assign coded themes to text in each interview transcript. We started with a list of provisional codes taken from the survey and added other codes as themes emerged from the data. The provisional codes included:

- Did not have time to discuss with the patient
- Cost Issues
- Clinical contraindication(s)
- Patient preferences
- Disagree with the decision support tool or guideline recommendation
- Patient does not have atrial fibrillation
- Refers all atrial fibrillation patients to specialists for anticoagulation therapy

The coders then met to try to resolve any inconsistencies in coding. Currently the coders are performing a second cycle of coding to finalize all the major codes and sub-codes. Once this cycle is complete, we will assess inter-rater reliability using Cohen's kappa. Disagreements in coding will be mediated through discussions between the 2 coders until consensus about correct application of the code is reached. The following table shows the first cycle of coding for major themes.

Rater 1 Codes	Rater 2 Codes
time	time
cost	
contraindications	
inaccurate diagnosis	inaccurate diagnosis
patient preference	patient preference
clinical judgment	doctor judgment
sees specialist	
not familiar with patient	
comorbidities	
literacy	
compliance	
	Integrated into workflow
	Patient behavior

Table 14. Recurring themes in qualitative analyses.

Post-Visit Survey of Primary Care Physicians - The project coordinator submitted a weekly list of discordant AF patients who had been seen by their primary care provider to the project evaluator. An email containing a link to a REDCap® survey was sent to providers asking them to provide an assessment of the recent patient encounter. Slightly more than half (51.6%) of these surveys were returned by the providers. The survey found that over 70% of the providers received the therapy recommendations prior to the patient visit and almost all of those providers (68.8% of 70.1%) reviewed the report prior to seeing the patient (Table 15). Over half of the providers (51.1%) discussed anticoagulation treatment with their patients, however, only a small percentage (6.3%) actually made a change in therapy at that visit.

Table 15. Provider responses to post-visit surveys.

Survey Question	"Yes" responses (%)
Did you receive the antithrombotic therapy recommendations prior to your patient's visit?	70.2%
Did you review the recommendations prior to seeing this patient?	68.8%
Was this report helpful to you in the care of this patient?	42.4%
Would you like to receive a reminder for this patient's next appointment	46.7%
Did you discuss the atrial fibrillation anticoagulation treatment decision with this patient?	51.1%
Did you make changes in the patient's antithrombotic therapy?	6.3%

Providers were asked to comment on why they did not change antithrombotic therapy when indicated by the AFDST. The most frequent explanations were: patient preferences (26.7%) and specialists are managing anticoagulation therapy (24.4%). Cost was never indicated as a reason for not changing therapy. Interestingly, 9% of the respondents indicated that they did not change therapy because they disagreed with the support tool recommendation. Providers were also asked to provide other general comments about the tool and changing therapy for patients. Several commented that the tool was cumbersome or could be improved. There were also a number of comments regarding the patient's condition such as risk of a fall in an elderly patient, patient is not currently in afib, and patient is managed by a cardiologist for afib.

Conclusions:

Net Clinical Benefit of Antithrombotic Therapy for Patients with Atrial Fibrillation - Our analysis comparing current antithrombotic therapy to that recommended by an AF decision support tool suggests that significant improvement in clinical outcomes can be achieved by improving treatment decisions. At a population level, for a cohort of more than 1,800 patients in our primary care network, more than 700 quality-adjusted life years could be gained by improving antithrombotic therapy. This finding should not be surprising. At a national level we still find significant underutilization of anticoagulant therapy for patients with AF. A recently published systematic review comparing current treatment practices with guidelines showed underuse of oral anticoagulants in high risk patients in the majority of 54 published articles.[9] More concerning, among patients in 29 studies with a history of prior stroke or TIA, treatment with anticoagulant therapy averaged less than 60%. Among high risk patients with a $CHADS_2$ score ≥ 2 treatment levels averaged less than 70%.[9] Finally, risk factors profiles for stroke or bleeding are dynamic, changing over time. A decision about anticoagulant therapy made several years ago may not remain the best option today. Therefore, it is reasonable to revisit the anticoagulation decision, particularly when new and significant diagnoses are made.

Current guidelines for anticoagulant therapy are based upon stroke risk as calculated by either the $CHADS_2$, (American College of Chest Physicians)[35] or the CHA_2DS_2VASc scores (European Society of Cardiology and more recently American Heart Association/American College of Cardiology).[34,36] While mentioning that bleeding risk is a consideration, these guidelines do not integrate bleeding risk in a formal, quantitative manner. If one makes decisions based upon overall event rates for bleeding and stroke, choosing to treat with anticoagulants only if the stroke risk in untreated patients exceeds the risk of major hemorrhage in treated patients, there is an implicit assumption that outcomes following both stroke and bleeding events are equivalent. However, most bleeds are extracranial and have less significant long-term consequences than strokes. Furthermore, intracerebral hemorrhage (ICH) while receiving anticoagulant therapy generally results in worse clinical outcomes than ischemic stroke.[37] Singer and colleagues dealt with this later issue by differentially weighting ischemic stroke and ICH in their calculations of net clinical benefit of warfarin anticoagulation, using an impact weight of 1.5 for the latter.[4] Using a similar weighting scheme for ICH, Friberg and colleagues studied a large Swedish AF cohort of 182,678 patients. They found that in almost all patients the risk of ischemic stroke without anticoagulant therapy was higher

than the risk of ICH, and concluded in their analysis of net clinical benefit that more patients may benefit from anticoagulant treatment and should be offered this treatment.[38] The AFDST used in this study is able to integrate both stroke risk and bleeding risk along with their longer term sequelae in a formal quantitative manner by utilizing a decision model as the analytical "engine." The projections of QALE generated by the AFDST for each individual patient and therapeutic alternative capture both the differential clinical outcomes following these events and their impact on patients' quality of life. For quality assurance or performance improvement purposes, estimates of potential aggregate gains in quality-adjusted life expectancy over a population of patients in a health care system may provide a more informative picture than the proportion of high risk patients (e.g., with a CHA_2DS_2VASc score ≥ 2) not receiving anticoagulant therapy.

The AFDST has a number of limitations. Most significantly, the tool assumes that the information extracted from the electronic health record is accurate and complete. One obvious concern is the underreporting of over the counter medications such as aspirin or non-steroidal anti-inflammatory drugs. Therefore when we communicate AFDST recommendations to clinicians as part of our system's performance improvement project, we have them first verify the accuracy of the clinical data upon which recommendations are based. Furthermore, there may be extenuating circumstances not captured by the AFDST and our focused data extraction that affect the decision to use antithrombotic therapy. Current risk prediction models for major hemorrhage, such as $HEMORR_2HAGES$ and HAS-BLED, do not incorporate psychosocial and socio-demographic information that may bear on the risk of bleeding with anticoagulant therapy.[39,40] Therefore, the recommendations of the AFDST cannot be interpreted as a mandate that replaces clinical judgment. Rather, they must be interpreted holistically within the broader clinical context of the whole patient. We must make sure to appropriately communicate these limitations to clinicians using such decision **support** tools.

Over the past 2 years, several novel anticoagulants have come on the scene. Three—dabigatran, rivaroxaban, and apixaban—have received FDA approval for use in patients with AF. At this time, knowledge regarding the use of these agents outside of selected populations within randomized trials is limited. Decisions among the various oral anticoagulants are nuanced and complex and the benefits and circumstances in which one agent may be better than another for an individual patient remain unclear. Furthermore, the most recent guidelines from the both the ACCP and the AHA/ACC/HRS focus on the decision to use anticoagulant therapy rather than specifying a particular anticoagulant. Therefore, the AFDST does not address choices among competing anticoagulants. In this manner, we have biased the recommendations for anticoagulation to be conservative; thus if a recommendation is made for warfarin, as in the ACCP or AHA/ACC/HRS guideline, the use of any of the novel agents would also be reasonable.

Finally, the AFDST uses population-based average utilities for health states and clinical outcomes such as stroke and major hemorrhage. Ideally, in the future, individuals will be able to assign their own values to different treatments and potential disease states or outcomes.

Given the increasing availability of real-time clinical information from electronic health records and clinical data warehouses, tools like the AFDST can be used by health care systems for both retrospective reviews of the quality of care around anticoagulant therapy for patients with AF, and prospectively to improve performance about decision-making for these patients. Our next steps are to provide practices and clinicians in our system, patient and practice-level reports (see sample report – Figure 2) when current antithrombotic therapy and that recommended by the AFDST are significantly discordant. Performance improvement processes will be developed, utilizing concepts of the patient-centered medical home to support revisiting the anticoagulation decision for these patients. This project also helped us understand the importance of centralizing data from diverse sources into a single access node at the point of care. As data from patients, other health record systems, pharmacies, and other sources become increasingly important to coordinating care, it is critical that providers have easy access to coordinated data through a single portal. The AFDST, while valuable, was still considered an "add on" piece of information that had to be integrated into data that are typically available via the EHR. Several providers commented on the awkwardness of using the AFDST information during a patient visit.

Use of Dual Antithrombotic Therapy in Patients with Atrial Fibrillation **-** The majority of patients in our AF cohort who were receiving dual antithrombotic therapy had a diagnosis of stable coronary artery disease (CAD) or diabetes mellitus (DM). Of interest, in a significant proportion of patients aspirin had been initiated due to a prior diagnosis of either stable CAD or DM and was not discontinued when warfarin was started for their AF (73% and 14.58% respectively). The 2012 ACCP guidelines indicate that there is insufficient evidence to warrant dual therapy in AF patients with stable CAD. A number of recent studies have examined outcomes in AF patients with stable CAD receiving dual therapy, and have concluded that dual therapy increased bleeding risk without reducing the risk of ischemic events, defined as stroke or myocardial infarction. Withdrawing aspirin from the antithrombotic regimens of these patients may provide an opportunity to improve clinical outcomes.

Randomized Trial: Does the Addition of a QI Intervention Improve "Appropriate Antithrombotic Therapy?" - A randomized controlled trial examining the impact of implementing the **A**trial **F**ibrillation **D**ecision **S**upport **T**ool demonstrated no significant improvement in discordant antithrombotic therapy compared with a group of control practices that did not receive the tool. However, within the early intervention practices, among patients whose physicians actually reviewed the reports and recommendations of the decision support tool, discordant therapy decreased significantly over a 1-year period of time. This effect was even more pronounced among patients who were seen in follow-up. This suggests that the AFDST can have a beneficial impact on clinical care if it is used.

There are many potential explanations for the less than expected impact of our QI intervention. Most obvious is the nuance and complexity of real-world clinical situations. In interviews with physicians who used the tool, a common explanation for antithrombotic therapy decisions that were discordant with both AFDST and ACC/AHA

guideline recommendations was that their patients had many competing medical problems that increased the risks associated with antithrombotic therapy and complicated the decision-making process. These competing clinical issues included among others, frailty, a history of frequent falls, and other significant comorbidities that limited life expectancy and/or quality of life. Many of these physicians added however, that even if they didn't change treatment, it was useful to review their patient's situation and that it prompted them to have a discussion about their treatment choice with the patient. An unexpected issue that came up was that many primary care physicians indicated that they were not generally making antithrombotic therapy decisions for their patients with AF, rather they were deferring these decisions to their cardiologist colleagues to whom they referred the patients. In other cases, patients had been discharged from an inpatient setting already started or not on an antithrombotic therapy and the primary care physicians felt that the decisions had already been made. Another issue we suspect played a role is therapeutic or clinical inertia.[41-44] Clinical inertia is a particular challenge in the management of chronic diseases and may contribute to hesitancy or delays in intensifying treatment. While making an initial therapeutic decision is hard enough, it is even more difficult to get clinicians to reconsider treatment decisions once made. This is what we have asked them to do by reviewing the antithrombotic therapy decision in patients with prevalent rather than newly incident AF. Relevant to this point, we found that the treatment recommendation made by the AFDST changed over the 1-year follow-up period in 45 patients. We also found that physicians responded to these changes in the clinical balance of risk factors by changing treatment in only a minority of cases, identifying another important gap in clinical care and decision-making. Bringing decision support to bear on these fewer but more relevant cases, in terms of asking physicians to reconsider their current treatment plans, may be a more effective approach. Finally, a number of physicians commented about the difficulty of using a separate, non-integrated web-site for the AFDST. They suggested that it would be more convenient to have the decision support tool fully integrated as part of the EHR.

All of these findings suggest next steps we must take to focus on decreasing barriers to the convenient and more effective use of the AFDST, perhaps by improving its integration into the EHR as a fully embedded application; by better targeting high yield clinical situations, perhaps by generating best practice alerts within the EHR when evolution in clinical risk factors results in a recommendation change by the decision support tool instead of asking physicians to review all AF patients with discordant therapy; and finally to consider targeting different clinician groups as decision makers, cardiologists instead of primary care physicians; and focusing on decision-making for incident rather than prevalent AF, when initial therapeutic decisions are first being made.

IMPACT OF GENDER AND AGE ON ANTITHROMBOTIC THERAPY IN PATIENTS WITH ATRIAL FIBRILLATION

(Copy of abstract presented at the 2014 Annual Meeting of the Society for Medical Decision Making –in Miami, FL.)

Purpose – Female gender has been associated with a decreased likelihood of receiving anticoagulant therapy among patients with atrial fibrillation.

Guidelines for anticoagulant therapy in patients with atrial fibrillation (AF) are based upon stroke risk as calculated by either the $CHADS_2$ or the CHA_2DS_2VASc scores and do not integrate bleeding risk in an explicit, quantitative manner. Our objective was to quantify the net clinical benefit resulting from improved decision-making about antithrombotic therapy.

Methods - Retrospective cohort study of 1,876 adults with non-valvular AF or flutter seen in primary care settings of an integrated healthcare delivery system between December 2012 and January 2014. Projections for QALE were calculated by a decision analytic model that integrates patient-specific risk factors for stroke and hemorrhage and examines strategies of no antithrombotic therapy, aspirin, or oral anticoagulation with warfarin. Net clinical benefit was defined by the gain or loss in quality-adjusted life expectancy (QALE) between current treatment and treatment recommended by an **A**trial **F**ibrillation **D**ecision **S**upport **T**ool (AFDST).

Results - Recommended treatment was discordant from current treatment in 931 patients. A clinically significant gain in QALE (defined as ≥ 0.1 quality-adjusted life years or QALYs) was projected in 832 patients. Subgroups were examined. For example, oral anticoagulant therapy was recommended for 188 who currently were receiving no antithrombotic therapy. For the entire cohort, a total of 736 QALYs could be gained were treatment changed to that recommended by the AFDST.

Conclusions - Use of a decision support tool that integrates patient-specific stroke and bleeding risk could result in significant gains in quality-adjusted life expectancy for a primary care population of patients with AF.

Using an Atrial Fibrillation Decision Support Tool (AFDST) for Thromboprophylaxis in Atrial Fibrillation: Impact of Gender and Age

(Copy of abstract submitted to the Society for Medical Decision Making – for presentation at 2015 Annual Meeting in St. Louis, MO.)

Purpose – Among patients with atrial fibrillation (AF), female gender has been associated with both an increased risk of stroke and paradoxically a decreased likelihood of receiving anticoagulant therapy. There also is a perception that the elderly are less likely to receive anticoagulant therapy due to concerns about falling and frailty. We wished to assess the appropriateness of antithrombotic therapy among women and the elderly, looking for patterns of either under-treatment or unnecessary treatment.

Methods - Retrospective cohort study of 1,586 adults with non-valvular AF or flutter seen in primary care settings of an integrated healthcare system between December 2012 and March 2014. Treatment recommendations were made by an **A**trial **F**ibrillation **D**ecision **S**upport **T**ool (AFDST) based on projections for QALE calculated by a decision analytic model that integrates patient-specific risk factors for stroke and hemorrhage and examines strategies of no antithrombotic therapy, aspirin, or oral anticoagulation.

Results – Current treatment was discordant from recommended treatment in 45% (326/725) of women and in 39% (338/860) of men ($p = 0.02$). Among the elderly (age ≥ 85) current treatment was discordant from recommended treatment in 35% (89/258), while treatment was discordant among 43% (575/1328) of patients < 85 years of age ($p = < 0.01$). We further examined age categories in 5-year increments and found that discordant therapy was as high as 60-70% in those between the ages of 31 and 50. Among 326 women with discordant treatment 99% (322/326) was due to under-treatment and 1% (4/326) was due to overtreatment. Among 338 men with discordant treatment 81% (274/338) was due to under-treatment, while 19% (64/338) was due to overtreatment. Among 89 elderly patients with discordant treatment 98% (87/89) of discordance was due to under-treatment and 2% (2/89) was due to overtreatment, whereas in those < 85 years of age, 88% (509/575) was due to under-treatment and 12% (66/575) of was due to overtreatment.

Conclusions – Women are still undertreated with antithrombotic therapy for AF. Somewhat surprisingly, compared with older patients, a larger proportion of patients < 85 years of age are receiving treatment that is discordant from recommended therapy. Furthermore, in women and the elderly the major reason for discordant therapy is under-treatment; whereas in men and younger patients, a larger proportion of discordance is due to overtreatment.

Combined Antiplatelet and Anticoagulant Therapy in Patients with Atrial Fibrillation- a Descriptive Study

(Copy of abstract presented at the 2015 Annual Meeting of the Society of General Internal Medicine –in Toronto, Ontario, Canada.)

Background: As part of a system-wide performance improvement initiative focused on improving antithrombotic therapy decisions for patients with atrial fibrillation (AF), we discovered a large number of patients who were receiving dual therapy with both aspirin and warfarin. Our goal was to determine the indications for dual therapy and possibly identify patients who might reasonably be treated with oral anticoagulant therapy alone. We hypothesized that the majority of these patients likely had a prior indication for antiplatelet therapy, such as stable coronary artery disease or diabetes, subsequently developed AF and had warfarin added to their regimen without discontinuing aspirin. There have been multiple studies examining outcomes of dual therapy in patients with indications for both antiplatelet and anticoagulant therapy. All have demonstrated an increased risk of major bleeding compared with either treatment alone; and among patients with stable CAD, in particular, dual therapy has not been shown to reduce ischemic events. The 2012 AF guidelines from the American College of Chest Physicians (ACCP) recommends against the use of dual therapy for AF patients with stable CAD, indicating that warfarin alone within a therapeutic INR range of 2-3 is sufficient.

Methods: We identified 348 patients (23% of the total AF cohort) in the UC Health Primary Care Network who were receiving dual therapy with an antiplatelet as well as antithrombotic agent as of 1/7/2014. We randomly sampled 200 charts to evaluate and categorize the indication(s) for dual antithrombotic therapy and collected information describing the time course of events that led to the initiation this treatment.

Results: Of the 200 patients reviewed, 77 (38.5%) had stable CAD and 48 (24%) had DM as co-morbidities resulting in dual therapy. 41 patients (20.5%) were classified as unknown, meaning patients whose charts had insufficient information to determine the reason for dual therapy. 36 patients (18%) had diagnoses of both CAD and DM and were counted in both categories. Thus the total added up to more than 100%.

Conclusions: Our data show that the majority of patients receiving dual antithrombotic therapy had a diagnosis of stable CAD or DM. Of interest, in a significant proportion of patients aspirin had been initiated due to a prior diagnosis of either stable CAD or DM and was not discontinued when warfarin was started for their AF (73% and 14.58% respectively). The 2012 ACCP guidelines indicate that there is insufficient evidence to warrant dual therapy in AF patients with stable CAD. A number of recent studies have examined outcomes in AF patients with stable CAD receiving dual therapy, and have concluded that dual therapy increased bleeding risk without reducing the risk of ischemic events, defined as stroke or myocardial infarction. Withdrawing aspirin from the antithrombotic regimens of these patients may provide an opportunity to improve clinical outcomes.

List of Publications and Products

Publications in peer-reviewed medical literature

1. Eckman MH, Wise RE, Naylor K, Arduser L, Lip GYH, Kissela B, et al. Developing an Atrial Fibrillation Guideline Support Tool (AFGuST) for Shared Decision Making. *Current Medical Research and Opinion* 2015;31:603-614.
2. Eckman MH, Wise RE, Speer B, Sullivan M, Walker N, Lip GY, et al. Integrating real-time clinical information to provide estimates of net clinical benefit of antithrombotic therapy for patients with atrial fibrillation. *Circ Cardiovasc Qual Outcomes* 2014;7(5):680-6.

Abstracts presented at national meetings (see above for full abstracts)

1. Eckman MH, Wise RE, Speer B, Sullivan M, Walker N, Lip GYH, Kissela B, Flaherty ML, Kleindorfer D, Khan F, Kues J, Baker P, Ireton R, Hoskins D, Harnett BM, Aguilar C, Leonard A, Prakash R, Arduser L, Costea A. Real-Time Estimates of Net Clinical Benefit of Antithrombotic Therapy for Patients with Atrial Fibrillation. Annual Meeting of the Society for Medical Decision Making. Miami, FL, October 2014.
2. So C, Eckman MH. Combined Antiplatelet and Anticoagulant Therapy in Patients with Atrial Fibrillation- a Descriptive Study. Annual Meeting of the Society of General Internal Medicine. Toronto, CA. April 2015.
3. Eckman MH, Fitzgerald A. Barriers, Solutions and Critical Issues for Interprofessional Research – What We've Learned from UC Health's Atrial Fibrillation Decision Support Tool Team; Panel on Interdisciplinary Research. Annual Meeting of the Society of General Internal Medicine. Toronto, CA. April 2015. (See attached link for video) - http://www.cincinnatichildrens.org/research/divisions/b/bmi/video/

Abstracts submitted and pending for presentation at national meetings

1. Eckman MH, Wise RE, Speer B, Sullivan M, Walker N, Lip GYH, Kissela B, Flaherty ML, Kleindorfer D, Khan F, Kues J, Baker P, Ireton R, Hoskins D, Harnett BM, Aguilar C, Leonard A, Arduser L, Costea A. Using an Atrial Fibrillation Decision Support Tool (AFDST) for Thromboprophylaxis in Atrial Fibrillation: Impact of Gender and Age. Annual Meeting of the Society for Medical Decision Making. St. Louis, MO. October 2015.

Invited Lectures – local, national and international

1. Update on Anticoagulation Issues in Atrial Fibrillation. Medical Grand Rounds, University of Cincinnati, Cincinnati, OH. August 2013.
2. Brain Injury From Bleeding and Stroke in Atrial Fibrillation. Research Week Symposium on Brain Injury and Epigenetics. University of Cincinnati, Cincinnati, OH. October 2013.

3. Update on Anticoagulation Issues in Atrial Fibrillation. Two part lecture series delivered to multiple practices in the UCHealth Primary Care Network between August 2013 and April 2014.
4. The Development and Implementation of an Atrial Fibrillation Decision Support Tool. Clinical Epidemiology and Biostatistics Grand Rounds at McMaster University, Hamilton, Ontario. May 2014.
5. The Development and Implementation of an Atrial Fibrillation Decision Support Tool. Cardiology Grand Rounds, University of Cincinnati, Cincinnati, OH. September 2014.
6. The Development and Implementation of an Atrial Fibrillation Decision Support Tool. Medical Grand Rounds at Albany Medical Center, Albany, NY. October 2014.
7. Integrating Real-Time Clinical Information to Provide Net Benefits of Antithrombotic Therapy in Patients with Atrial Fibrillation. Video conference to Pfizer Global Health Values, Outcomes and Effectiveness Group. November 2014.
8. The Development and Implementation of an Atrial Fibrillation Decision Support Tool. Alumni Weekend, University of Cincinnati, Cincinnati, OH. April 2015.
9. Integrating Real-Time Clinical Information to Provide Net Benefits of Antithrombotic Therapy in Patients with Atrial Fibrillation. Ohio Chapter, American College of Physicians Annual Meeting. October 2015.

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