



Suboptimal Anticoagulant Treatment to Prevent Stroke Prevalent in Patients with Atrial Fibrillation, Finds Study in Circulation

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The Quest Diagnostics Health Trends™ study of 2.7 million test results is the largest to examine warfarin treatment in patients with atrial fibrillation (Afib) treated in primary care and other non-hospital care settings in the United States
Findings raise prospect that new oral anticoagulants may be more appropriate for some patients

MADISON, N.J., Feb. 4, 2014 /PRNewswire/ -- Approximately one in two patients with atrial fibrillation (Afib) do not optimally reduce their risk of stroke or bleeding when treated with the most widely prescribed oral-anticoagulant therapy, according to a study published online in *Circulation*, the journal of the American Heart Association.

(Logo: <http://photos.prnewswire.com/prmh/20130717/NY48934LOGO>)

The Quest Diagnostics Health Trends™ study by researchers at Quest Diagnostics (NYSE: DGX), Boston University School of Medicine and Lenox Hill Hospital is the largest to examine the efficacy of treatment with the anticoagulant warfarin in patients with Afib in primary-care practices and other non-hospital care settings in the United States. The researchers examined 2.7 million de-identified results of tests performed by Quest Diagnostics' clinical laboratories from more than 138,319 American adults ordered by 37,939 physician practices.

Half of patients with Afib (49.4%) failed to maintain optimal blood clotting levels in the medically recommended therapeutic range to reduce the risk of stroke or potentially dangerous hemorrhage, according to blood tests to assess the International Normalized Ratio (INR; target range is 2.0-3.0). Among these patients, 32.5% had results during therapy that were too low (INR <2.0), predisposing them to an increased possibility of blood clots, while 16.9% were too high (INR >3.0), consistent with heightened bleeding risk.

Physicians periodically assess INR, a globally adopted value that represents the time for blood to clot, with blood tests in patients taking warfarin to monitor and make adjustments to dosing.

"Other research has highlighted the difficulty of achieving optimal anticoagulation control using warfarin, but in smaller populations typically treated by hospitals and other specialty settings," said study investigator Harvey W. Kaufman, M.D., senior medical director, Quest Diagnostics. "The diagnostic insights derived from our study are unique and important because they reveal the magnitude of the challenges of warfarin therapy in a very large, nationally representative population primarily under treatment by non-hospital community practices, which administer the majority of anticoagulation therapy in the U.S."

Afib is a cardiac condition affecting an estimated 2.2 million Americans that can cause blood clots, increasing the risk of strokes and other adverse cardiac events. Anticoagulants inhibit the formation of blood clots and are commonly prescribed for patients with Afib. Despite the introduction of new anticoagulants in recent years, warfarin (brand name Coumadin) continues to be the most commonly prescribed, with about 33 million prescriptions written in 2012 in the United States.

Physician Experience Correlates with Anticoagulation Control

Despite its widespread use, warfarin must be carefully administered, as diet, medications and other factors influence and change its effect on blood clotting. Dosing that is too high may prompt dangerous hemorrhage, while dosing that is too low may fail to prevent blood clots. Based on INR testing, the effectiveness of warfarin dosing is assessed by the optimal time in the therapeutic range (TTR), an indicator of the quality of anticoagulation.

The researchers found that the more experience a physician had administering warfarin treatment (based on patients with Afib referred for INR testing), the greater the likelihood a patient was to achieve optimal TTR. Among patients with Afib treated with warfarin, the average TTR was 54.2% if their physician had only two to four Afib patients within the study period, compared to 72.8% for physicians with case loads of 72 or more patients with Afib during the study period.

The vast majority of physicians in the study – nearly 95% – had a case load of 10 or fewer patients treated with warfarin for Afib, according to an analysis of warfarin-related testing.

"Many other industrialized countries outperform the U.S. in anticoagulant control, perhaps due to more specialized management centers and their support of patient self-management," said investigator Jack Ansell, M.D., a specialist in anticoagulant therapy in New York. "Our study's findings suggest the United States healthcare system could potentially improve the quality of warfarin treatment by adopting provisions that direct individuals with atrial fibrillation to specialists or generalists with significant experience with warfarin and other anticoagulant therapies, such as is practiced in specialized anticoagulation centers."

The investigators also determined that patients taking warfarin for fewer than six months generally experienced less time in the therapeutic range (TTR) than those using the medication for six or more months. Younger age, female gender, and lower income (estimated by zip code of patient) also independently correlated with a greater likelihood of suboptimal anticoagulant control.

Warfarin versus New Anticoagulants: Balancing Costs and Efficacy

In recent years, new anticoagulants intended in part to reduce the warfarin's dosing challenges have been introduced in the U.S. The costs of these medications, however, are typically several multiples of warfarin, which is no longer patent protected. Other research has suggested that new anticoagulants may be more cost-effective in Afib populations at high risk of stroke or hemorrhage and which achieve poor anticoagulation control with warfarin.

"Healthcare institutions and patients are increasingly seeking avenues to reduce their medical costs without sacrificing quality or favorable outcomes," said investigator Elaine Hylek, M.D., of Boston University School of Medicine. "While warfarin may be a highly suitable therapy for many patients, the

widespread suboptimal anticoagulation control reflected in our findings suggests some patients may be more appropriately treated with newer oral anticoagulants."

"For patients with Afib taking warfarin, the implications of our study's findings are clear: Find a physician with significant anticoagulation therapy experience, and be particularly vigilant during the first few months of therapy, when achieving optimal anticoagulation control with warfarin is the most challenging," said lead investigator Dr. Jeffrey S. Dlott, M.D., medical director, coagulation, Quest Diagnostics. "Patients may also want to consider discussing the pros and cons of treatment with warfarin versus other anticoagulant drugs with their physician."

The Quest Diagnostics Health Trends™ study, [A National Assessment of Warfarin Anticoagulation Therapy for Stroke Prevention in Atrial Fibrillation](#), was published on February 3, 2014.

The study's strengths include its size and national scope based on results from the national Quest Diagnostics database and the uniformity of the INR assay across the company's clinical laboratories. The study represents patients under medical care for atrial fibrillation and not the general American population. The investigators required an Afib diagnosis code, two or more months of serial INR measurements, and two or more INR results of >1.2, to minimize misclassification of warfarin exposure. However, the investigators did not have access to prescription drug data. Data was de-identified prior to analysis and the Western Institutional Review Board exempted the study from review.

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Contacts:

Wendy Bost, Quest Diagnostics (Media): 973-520-2800

Dan Haemmerle, Quest Diagnostics (Investors): 973-520-2900

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