

Motivating Factors for Physician Ordering of Factor V Leiden Genetic Tests

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Background: The factor V Leiden (FVL) genetic test is used by many physicians despite its uncertain clinical utility.

Methods: We investigate whether self-reported motivations and behaviors concerning FVL genetic testing differ between 2 groups of primary care physicians defined by frequency of previous FVL test use. In January 2007, 112 physicians (60 frequent and 52 infrequent FVL test users) at Group Health, a large health care delivery system, were surveyed. Survey content areas included primary reasons and motivating factors for ordering the FVL test, the likelihood of ordering the FVL test for hypothetical patients, potential barriers to genetic testing, and practices and skills regarding FVL test ordering.

Results: Responses between groups agreed concerning most clinical- and patient-related factors. Frequent-FVL physicians were more likely than infrequent-FVL physicians to report ordering the FVL test for hypothetical patients with mesenteric venous thrombosis (ad-

justed odds ratio, 4.57; 95% confidence interval, 1.55-13.53) or venous thrombosis after hospital discharge (adjusted odds ratio, 3.42; 95% confidence interval, 1.30-8.95). Frequent-FVL physicians were also less likely to identify several items on the survey as barriers to genetic testing and were more likely to report high confidence in interpreting and explaining FVL test results.

Conclusions: Generally, both physician groups reported similar motivating factors for ordering FVL tests, and reported behaviors were consistent with existing guidelines. More striking differences were observed for measures such as barriers to and confidence in using genetic tests. Although additional research is necessary to evaluate the impact of these results, they inform several knowledge-to-practice translation issues that are important for the successful integration of genetic testing into primary care.

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FACTOR V LEIDEN (FVL) IS A genetic variant that confers resistance to activated protein C and a predisposition to venous thromboembolism (VTE). At present, evidence for the clinical utility of the FVL test is limited.¹ Among those who carry the FVL variant, the risk of a first VTE is increased,² but the implications for risk of VTE recurrence and patient management are less clear.^{3,4} Current recommendations suggest evaluation on a case-by-case basis. Two US working groups, the College of American Pathologists and the American College of Medical Genetics, have released consensus statements related to the appropriate clinical use of FVL testing.⁵⁻⁷ Indications for FVL testing are generally the same as those for other thrombophilias and include recommendations based on age,

site, and the presence of precipitating factors (previous VTE, a strong family history, pregnancy, and exogenous hormone use) for patients with VTE and unexplained late pregnancy loss in women. The clinical goal of testing is not specified in these guidelines.

The FVL test is the third most readily available genetic test in the United States, as judged by the number of laboratories that offer FVL testing.⁸ Genetic tests are predicted to become an increasingly important component of clinical care on the presumption that genetic susceptibility information will guide disease prevention and clinical management. Primary care practitioners may be early adopters or gatekeepers of this technology. However, data on factors that affect FVL testing in clinical practice are limited. Previous studies⁹⁻¹¹ have observed that primary care phy-

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sicians are generally supportive of integrating genetics into clinical care but may be hesitant to go beyond traditional roles, such as specialty referral, taking a family history, and supportive counseling. In addition, physician confidence in performing these roles is not high.⁹ Assessing motivating factors for and potential barriers to ordering genetic tests such as FVL may be early but necessary steps in the process of translating genetic knowledge to clinical care, especially in the context of uncertain clinical utility. On a practical level, this understanding could inform the development of practice guidelines or help individual physicians decide how best to integrate genetic testing into their own practices.

The primary objective of this study is to determine whether self-reported motivations for ordering an FVL genetic test differed among groups of primary care physicians, defined by previous clinical use of the test at Group Health (GH), a large, integrated health care delivery system based in western Washington State. At GH, venous thrombosis (VT) treatment guidelines recommend FVL testing for women with VTE who are pregnant and suggest that FVL testing be considered for patients younger than 50 years with an idiopathic VTE or for those who have a strong family history of VTE.¹² These guidelines acknowledge that the appropriateness of such testing has yet to be clarified, but they may inform patient-physician discussions regarding prognosis and duration of anticoagulation. Physicians from 2 groups defined by their FVL test-ordering experience were sampled separately. We hypothesized that previous clinical use of FVL testing is associated with differences in the perceived purpose and motivating factors for test ordering, the likelihood of ordering an FVL test for a hypothetical patient, favorable attitudes toward genetic testing, and greater confidence in ordering and understanding the test.

METHODS

STUDY SETTING AND PARTICIPANTS

Group Health serves as the setting for several case-control studies of heart disease in persons with pharmacologically treated hypertension and in postmenopausal women.^{13,14} Medical records and an automated laboratory database were used to identify which primary care physicians had ever ordered an FVL test for any of these case-control study participants. We then divided the physicians into 2 groups: those who had ever ordered a test at GH for a participant in these case-control studies ($n=69$) and those who had never ordered an FVL test at GH ($n=39$). To increase the power of the study, we supplemented the first group with 16 additional physicians who most frequently ordered FVL testing in the 12 months preceding the survey (December 1, 2005, to December 1, 2006; range, 2-4 tests) and the second group with 46 additional physicians who had not ordered a test at GH during that same period and had the fewest number of FVL tests ever ordered (range, 1-3 tests). For ease of reference, we refer to the first group as frequent FVL test use (frequent FVL) and the second group as infrequent FVL test use (infrequent FVL). Physicians were unaware of the intentional sampling on previous test use. Primary care was defined as any of the following categories: internal medicine, family medicine, and other (obstetrics/gynecology and gerontology/geriatrics; $n=3$). Physicians who were retired, lacked a contact address, or were specialists were ineligible. This study was approved

by the GH institutional review board, and physicians who returned surveys gave implicit informed consent.

After the initial population was supplemented, 170 physicians (85 in each group) were selected to receive surveys; 114 physicians responded (67%). After the exclusion of 2 responders (1 retiree and 1 essentially blank survey), the analysis included 60 frequent-FVL and 52 infrequent-FVL physicians.

SURVEY INSTRUMENT AND DATA COLLECTION

The survey instrument, (available at <http://depts.washington.edu/chru/appendices.htm>) comprised 9 pages and took approximately 20 minutes to complete. The survey was divided into 6 content sections with differing response formats (some questions had multiple parts): (1) 9 questions on the primary reasons for ordering the FVL test (checkbox); (2) 14 questions on the importance of motivating factors (5-point scale); (3) 13 questions on the likelihood of ordering the FVL test for hypothetical patients (5-point scale); (4) 11 questions on potential barriers to the implementation of genetic testing (5-point scale); (5) 3 questions on confidence in practices and skills related to FVL test ordering (5-point scale); and (6) 8 questions on physician characteristics (a combination of open- and closed-ended questions).

Physicians received up to 5 interoffice mailings: (1) an introductory letter, (2) a survey packet that included an incentive (bookstore gift card), (3) a reminder letter for nonrespondents after 2 weeks, (4) an additional copy of the survey for nonrespondents after 2 additional weeks, and (5) a thank you letter to respondents. Responses were double-entered into an electronic database by abstractors who were masked to physician FVL test use group. The data set was closed 8 weeks after the last reminder letter was mailed.

STATISTICAL ANALYSIS

Statistical analyses were performed using a software program (Intercooled Stata 8; StataCorp, College Station, Texas). Statistical significance was declared at $P \leq .05$ (2-sided). Responses phrased on a 5-point scale (eg, very high, high, fair, low, and very low) were dichotomized for analysis (eg, very high/high vs fair/low/very low). Responses at the positive end of the scale (eg, high, important, or agree) were considered affirmative. Between-group differences in the proportion of affirmative responses were assessed using a χ^2 test (unadjusted). Multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) after adjustment for self-reported age, sex, specialty, and number of patients with VT per year.

Rasch analysis was used to estimate the tendency for positive response across all items in a section while accounting for physician-specific variation in the degree of affirmative response.¹⁵ Questions in each section can be ranked according to the logit term for each item, yielding a relative ordering from highest to lowest tendency for an affirmative response. An interaction model suggested that the overall response to all items in a table did not differ significantly between frequent-FVL and infrequent-FVL physicians (Rasch interaction test $P > .11$). Thus, Rasch model variables are reported for the combined population.

RESULTS

The 2 physician groups did not differ significantly according to age; sex; time spent in practice, research, or teaching; or graduation from a US medical school (**Table 1**). However, compared with infrequent-FVL physicians, more frequent-FVL physicians reported practicing

ing internal medicine and fewer reported practicing family medicine. Frequent-FVL physicians were also more likely to spend less time in administration, to report seeing more patients with VT per year, and to order the FVL test at GH in the 12 months preceding the survey and at any time. The mean number of FVL tests ever ordered was higher in the frequent-FVL group (7.8 vs 1.1). Among the various specialties composing primary care and adjusted for FVL test use group, internal medicine physicians were likely to report a mean of 13.8 more patients with VT (95% CI, 9.8-17.8) in a typical year compared with family medicine physicians. "Other" physicians reported approximately the same number of patients with VT as family medicine physicians (adjusted mean difference, -1.7; 95% CI, -11.0 to 7.7).

In the frequent-FVL and infrequent-FVL groups, more than half the participants identified the following primary reasons for ordering the FVL test: to advise patients about risk of recurrence, to make treatment decisions, to make clinical decisions about VT prevention, or to explain the occurrence of VT (**Table 2**). A higher proportion of the frequent-FVL physicians compared with the in-

frequent-FVL group tended to identify each reason, but responses did not differ significantly between the 2 groups when adjusted for age, sex, specialty, and number of patients with VT. A family history of VT, a personal history of VT, and consultation with a specialist were the patient- and clinical care-related factors that were identified by most of those physicians (**Table 3**). After adjustment, frequent-FVL physicians were less likely to identify inclusion of the FVL test on a thrombophilia panel as important (adjusted OR, 0.38; 95% CI, 0.14-0.97).

Thirteen hypothetical clinical scenarios were presented (**Table 4**). The 4 scenarios with the strongest tendency for FVL test ordering were a 45-year-old man diagnosed as having testicular cancer, a 67-year-old man with mesenteric VTE, a 32-year-old woman taking oral contraceptives who is diagnosed as having deep VT, and a healthy 29-year-old woman whose 35-year-old sister was found to be heterozygous for FVL. More than half the physicians in either group were likely to order the test for these hypothetical patients. After adjustment, frequent-FVL physicians were significantly more likely than infrequent-FVL physicians to order the test for a man with mesenteric VT (adjusted OR, 4.57; 95% CI, 1.55-13.53) and for a young man diagnosed as having lower-extremity deep venous thrombosis a week after discharge from an extended hospital stay (adjusted OR, 3.42; 95% CI, 1.30-8.95).

Among possible barriers to the integration of genetic testing into routine clinical care, lack of availability of genetic counseling services, uncertainty about the effect on patient management, and the low number of applicable patients were ranked as the 3 most affirmative statements (**Table 5**). More than half the physicians in both groups agreed with the lack of availability of genetic counseling as a potential barrier. After adjustment, several statements were more likely to reflect a significantly lower proportion of frequent-FVL compared with infrequent-FVL physicians in agreement. These included lack of genetic counseling services (adjusted OR, 0.37; 95% CI, 0.15-0.93), few relevant patients (adjusted OR, 0.24; 95% CI, 0.10-0.60), and lack of professional society guidelines in favor of genetic testing (adjusted OR, 0.13; 95% CI, 0.03-0.59).

Finally, a greater proportion of frequent-FVL physicians reported high confidence in interpreting and communicating FVL test results (**Table 6**). After adjustment for age, sex, specialty, and number of patients with VT, these

Table 1. Characteristics of Physician Participants

Category	Infrequent-FVL Physicians (n=52)	Frequent-FVL Physicians (n=60)
Age, mean (SD), y	51.4 (7.6)	49.8 (8.3)
Female sex, %	40.4	35
Specialty, %		
Family medicine	90.4	66.7 ^a
Internal medicine	9.6	28.3 ^a
Other	0	5.0
Time spent, %		
In practice	87.5	93.7
In research	0	2.2
In administration	9.3	1.6 ^a
In teaching	2.4	0.8
No. of patients with venous thrombosis per year, mean (SD)	7.3 (6.5)	11.6 (11.5) ^a
Ever ordered test, %	61.5	100 ^a
No. of tests ever ordered, mean (SD)	1.1 (1.1)	7.8 (1.0) ^a
Ordered test in 12 mo before survey, %	0	61.7 ^a
Medical school in United States, %	96.2	88.1

Abbreviation: FVL, factor V Leiden.

^a*P* < .05.

Table 2. "In Clinical Practice, What Would Be Your Primary Reasons for Ordering the FVL Test in the Context of Venous Thrombosis?"^a

Statement	Logit (SE)	Infrequent-FVL Group, %	Frequent-FVL Group, %	Adjusted OR (95% CI) ^b
To advise patients about risk of recurrence	-6.7 (0.76)	82.7	91.7	2.42 (0.68-5.21)
To make treatment decisions	-5.9 (0.72)	75	85	1.88 (0.68-8.53)
To make clinical decisions about venous thrombosis prevention	-4.9 (0.69)	67.3	68.3	1.06 (0.45-2.49)
To explain the occurrence of venous thrombosis	-4.9 (0.69)	57.7	75	1.78 (0.76-4.13)
To satisfy a patient request	-3.0 (0.66)	28.8	38.3	1.61 (0.68-3.78)
To make a diagnosis of venous thrombosis	0 [Reference]	3.8	10	2.94 (0.54-16.10)
To teach medical students, residents, etc	0.72 (0.72)	3.8	5	0.96 (0.13-7.08)

Abbreviations: CI, confidence interval; FVL, factor V Leiden; OR, odds ratio.

^a Responses are ordered from highest to lowest tendency for an affirmative response on a logit scale.

^b The ORs are adjusted for age, sex, specialty, and number of patients with venous thrombosis per year.

Table 3. "When Deciding Whether to Order a FVL Test, How Important Would the Following Factors Be to You?"^a

Factor	Logit (SE)	Important, %		Adjusted OR (95% CI) ^b
		Infrequent-FVL Group	Frequent-FVL Group	
Family history of venous thrombosis	-3.5 (0.52)	88.5	91.7	1.76 (0.40-7.79)
Personal history of venous thrombosis	-3.0 (0.44)	84.6	90	1.63 (0.47-5.61)
Consultation with a specialist	-0.92 (0.29)	61.5	60	1.27 (0.55-2.91)
Presence of established risk factors for venous thrombosis	-0.29 (0.29)	50	45	0.70 (0.31-1.62)
Age	0 [Reference]	42.3	40	0.78 (0.34-1.81)
Site	0.39 (0.30)	34.6	31.7	1.15 (0.49-2.69)
Group Health guidelines	0.48 (0.30)	30.8	31.7	1.34 (0.54-3.32)
Family history of arterial thrombosis	0.48 (0.30)	34.6	28.3	0.83 (0.35-1.97)
Professional society guidelines	0.53 (0.30)	30.8	30	0.85 (0.35-2.04)
Inclusion of the FVL test on a thrombophilia panel	0.73 (0.31)	36.5	18.3 ^c	0.38 (0.14-0.97)
Patient preference or request	0.93 (0.31)	19.2	26.7	2.01 (0.74-5.45)
Patient access to genetic counseling	1.6 (0.35)	13.5	15	1.34 (0.42-4.23)
Sex	2.3 (0.43)	9.6	6.7	0.95 (0.22-4.05)

Abbreviations: CI, confidence interval; FVL, factor V Leiden; OR, odds ratio.

^a Responses are ordered from highest to lowest tendency for an affirmative response on a logit scale.

^b The ORs are adjusted for age, sex, specialty, and number of patients with venous thrombosis per year.

^c $P < .05$.

Table 4. "Estimate the Likelihood That You Would Order a FVL Test for Each Hypothetical Clinical Scenario"^a

Scenario	Logit (SE)	Likely to Order, % ^b		Adjusted OR (95% CI) ^c
		Infrequent-FVL Group	Frequent-FVL Group	
A 45-year-old man is diagnosed as having testicular cancer and is scheduled to receive chemotherapy	-2.4 (0.37)	80.8	83.3	1.19 (0.43-3.31)
A 67-year-old man is diagnosed as having mesenteric venous thrombosis	-1.9 (0.34)	65.4	85 ^d	4.57 (1.55-13.53)
A 32-year-old woman taking oral contraceptives is diagnosed as having deep venous thrombosis	-1.6 (0.33)	65.4	76.7	2.23 (0.88-5.63)
A healthy 29-year-old woman reports that her 35-year-old sister was found to be heterozygous for FVL; she would like to know if she also carries the mutation	-1.6 (0.33)	67.3	75	1.42 (0.59-3.44)
A 68-year-old man is diagnosed as having deep venous thrombosis; he frequently travels on long flights and wants to know whether he should be tested	-0.34 (0.31)	44.2	53.3	1.47 (0.64-3.38)
A 55-year-old woman without any known predisposing risk factors is diagnosed as having idiopathic venous thrombosis	-0.10 (0.31)	36.5	51.7	1.94 (0.85-4.40)
A pregnant 35-year-old woman is diagnosed as having lower-extremity deep venous thrombosis	0 [Reference]	34.6	50	1.77 (0.74-4.22)
A 45-year-old man is diagnosed as having lower-extremity deep venous thrombosis a week after discharge from an extended hospital stay	0.20 (0.32)	26.9	50 ^d	3.42 (1.30-8.95)
A 77-year-old man is diagnosed as having pulmonary embolism and reports that his father had venous thrombosis at age 48 years	0.25 (0.32)	32.7	43.3	1.56 (0.65-3.77)
An asymptomatic 75-year-old man with a family history of venous thrombosis is scheduled for elective surgery	2.0 (0.38)	9.6	16.7	1.50 (0.44-5.17)
A 57-year-old woman with a history of deep venous thrombosis is considering hormone therapy for postmenopausal symptoms	2.3 (0.41)	11.5	10	0.79 (0.22-2.78)
A 65-year-old woman is diagnosed as having a second occurrence of deep venous thrombosis	3.7 (0.64)	0	6.7	NE
A 70-year-old woman is diagnosed as having pancreatic cancer	4.9 (1.0)	0	3.3	NE

Abbreviations: CI, confidence interval; FVL, factor V Leiden; NE, not estimable; OR, odds ratio.

^a Responses are ordered from highest to lowest tendency for an affirmative response on a logit scale.

^b "Likely to order" denotes whether the likelihood of ordering the FVL test was "very high" or "high."

^c The ORs are adjusted for age, sex, specialty, and number of patients with venous thrombosis per year.

^d $P < .05$.

associations were not statistically significant (OR, 1.96; 95% CI, 0.73-5.31 and OR, 2.20; 95% CI, 0.80-6.04, respectively). The results differed according to specialty: a greater proportion of internal medicine vs family medicine physicians expressed high confidence in interpreting results (infrequent-FVL group: 40% vs 15%; frequent-FVL group: 59% vs 28%) and in communicating results to patients (in-

frequent-FVL group: 60% vs 11%; frequent-FVL group: 53% vs 28%). Fewer than 40% of physicians in either FVL group expressed high confidence in any of the 3 areas.

Analyses excluding the supplemental physicians yielded similar results, although 95% CIs were wide owing to limited power, and multivariable adjustment was not possible for several items.

Table 5. "A Range of Opinions Exists About Possible Barriers to Integration of Genetic Testing in Clinical Care; Please Check the Appropriate Box"^a

Statement	Logit (SE)	Agree, % ^b		Adjusted OR (95% CI) ^c
		Infrequent-FVL Group	Frequent-FVL Group	
Genetic counseling services are not well integrated into my practice	-1.5 (0.32)	76.9	53.3 ^d	0.37 (0.15-0.93)
It is unclear whether the test result would alter patient management	-0.27 (0.30)	42.3	38.3	0.76 (0.35-1.71)
I do not see enough patients for whom genetic testing would be applicable	0 [Reference]	50	21.7 ^d	0.24 (0.10-0.60)
Current guidelines at GH do not encourage genetic testing	0.60 (0.32)	28.8	20	0.66 (0.25-1.69)
I am concerned about potential genetic discrimination based on my patients' genetic test results	0.66 (0.32)	23.1	23.3	1.05 (0.41-2.69)
I am concerned about my patients' privacy/confidentiality of genetic test results	1.0 (0.34)	21.2	15	0.48 (0.16-1.44)
Current guidelines from professional societies do not encourage genetic testing	1.3 (0.36)	23.1	6.7 ^d	0.13 (0.03-0.59)
It is inconvenient (for either patients or practitioners) to obtain the test	1.3 (0.36)	17.3	11.7	0.77 (0.24-2.45)
Sensitivity or specificity of the test is too low	1.8 (0.40)	13.5	6.7	0.46 (0.12-1.79)
Patients must first express an interest in the test	2.0 (0.42)	13.5	3.3 ^d	0.29 (0.05-1.55)
Genetic testing is not necessary because a family history tells me similar information	2.9 (0.57)	7.7	0 ^d	NE

Abbreviations: CI, confidence interval; FVL, factor V Leiden; GH, Group Health; NE, not estimable; OR, odds ratio.

^a Responses are ordered from highest to lowest tendency for an affirmative response on a logit scale.

^b "Agree" denotes whether the participant designated the corresponding factor as "strongly agree" or "agree."

^c The ORs are adjusted for age, sex, specialty, and number of patients with venous thrombosis per year.

^d $P < .05$.

Table 6. Physician Confidence in Ordering FVL Tests^a

Question	Logit (SE)	High, % ^b		Adjusted OR (95% CI) ^c
		Infrequent-FVL Group	Frequent-FVL Group	
How would you rate your confidence in interpreting the results of FVL tests?	-2.0 (0.58)	17.3	36.7 ^d	1.96 (0.73-5.31)
How would you rate your confidence in communicating information about the results of FVL tests to your patients?	-1.7 (0.56)	15.4	35 ^d	2.20 (0.80-6.04)
How would you rate your confidence in determining when it is appropriate to test for FVL?	0 [Reference]	7.7	16.7	0.77 (0.17-3.51)

Abbreviations: CI, confidence interval; FVL, factor V Leiden; OR, odds ratio.

^a Responses are ordered from highest to lowest tendency for an affirmative response on a logit scale.

^b "High" denotes whether the participant rated the corresponding question as "very high" or "high."

^c The ORs are adjusted for age, sex, specialty, and number of patients with venous thrombosis per year.

^d $P < .05$.

COMMENT

In this survey of practicing primary care physicians, we identified several clinical patient- or physician-related factors associated with FVL test ordering. These differences between groups were generally small in magnitude. The FVL test-ordering status was associated with increased likelihood of ordering of FVL testing in 2 hypothetical scenarios: mesenteric VT in a 67-year-old man and deep venous thrombosis in a 45-year-old man after an extended hospital stay. Larger differences between FVL groups were observed for other features of the survey. The FVL test-ordering status was associated with more favorable attitudes toward genetic testing. Frequent-FVL physicians were less likely to agree on the survey with several items stating perceived barriers to genetic testing, although a substantial proportion of both groups

agreed that genetic counseling services and unclear impact on patient management were potential barriers. A greater proportion of frequent-FVL physicians expressed high confidence in communicating and interpreting FVL test results, although these results were not statistically significant after adjustment.

Physician responses to the motivating factors and clinical vignettes were generally consistent with existing recommendations based on expert clinical opinion.^{5,6} Most physicians were likely to order the FVL test in the context of VTE that presents at an unusual site (mesenteric VT) or concurrently with oral contraceptive use. Physicians in both groups were also likely to order the test for asymptomatic patients if there was an affected relative or if cancer developed at an early age, contexts for which recommendations in the College of American Pathologists, American College of Medical Genetics, and GH guide-

lines are less clear. Only 50% of frequent-FVL physicians and 35% of infrequent-FVL physicians said that they would be likely to order FVL testing for the young pregnant woman, the only scenario included in GH guidelines.

Although most physicians in both groups did not identify any of the 11 potential barriers to integrating genetic tests into clinical care (except for genetic counseling), the level of confidence in interpreting and communicating test results was low even in the frequent-FVL group. The fact that frequent-FVL physicians were less likely to identify several items on the survey as barriers to genetic testing and were more confident in using FVL test results than were infrequent-FVL physicians suggests some internal consistency in this group of physicians. These data are consistent with reports that physicians are open to the integration of genetic testing into primary care, although this integration may require additional training.^{9,10,16-18}

A key strength of this study was the selection of comparison groups based on previous clinical use of the FVL test, allowing us to evaluate which factors were important to either group and those that differed between groups. However, several limitations deserve mention. The 2 FVL test-use comparison groups reflect a low level of difference in the self-reported number of patients with VTE seen annually and likely show a low level of variability in test-ordering experience. This may explain the lack of association between the FVL-ordering group and the clinically motivated factors for ordering the test. We controlled for the self-reported number of patients with VTE, but residual confounding due to a specific mix of patients may have remained (eg, frequent-FVL physicians may have tended to see the patients with the most compelling cases of VTE). In addition, we queried physicians about possible and likely actions, which may not reflect actual behavior or predict future behavior. The survey was lengthy, and false-positive results are possible. In light of the hypothesis-generating nature of this study, we did not statistically control for multiple comparisons, and the results should be interpreted accordingly.

These results suggest several areas for future research that focuses on the translation of knowledge into practice. First, regardless of FVL test-use group, most of the physicians in this study ordered the FVL test at some point, although the mean yearly number of patients with VT was low, and despite a generally low level of confidence in their own ability to interpret or communicate test results. The 2 groups similarly ranked the clinical indications for testing and in a manner that does not correspond precisely to recommendations of professional societies or even of their own clinical group. The fact that FVL test-use groups were similar with respect to clinical- and patient-centered motivational factors but differed according to measures such as perceived barriers to genetic testing or confidence is striking. Not all guidelines are evidence based, but even when sufficient scientific knowledge is available to make a best practice recommendation or guideline, integration of genetic testing into clinical care requires physician awareness and support to achieve best practices. Understanding why physicians do or do not comply with clinical guidelines is a first step; adherence to practice guidelines is known to

be affected by many factors.¹⁹ These results suggest that the availability of counseling or other referral services, frequency of relevant presenting patients, and a physician's ability to explain results are all important to primary care physicians. This study suggests that confidence levels may vary by specialty within primary care, an observation that requires further investigation. Additional research is needed to determine whether interventions or updated practice guidelines targeting areas identified by this survey, such as providing access to specialty referral or education, will improve physician performance and patient health. A key question will be how to achieve higher levels of confidence and better performance; studies that identify such translational factors are needed for the successful deployment of genetic tests in primary care. Ultimately, primary care physicians and their patients will benefit if physicians have the confidence and skills to use these tests properly.

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