Direct-to-consumer genetic testing for factor V Leiden and prothrombin 20210G>A: the consumer experience

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Introduction

Venous thromboembolism (VTE) is a condition characterized by the formation of blood clots in veins. VTE affects 300,000 - 600,000 individuals in the U.S. each year, can cause long-term complications, and is associated with high morbidity and mortality (*1*, *2*). Variants in clotting factor genes are responsible for inherited predisposition (thrombophilia). The two most common genetic risk factors are factor V Leiden (c.1691G>A) in the *F5* gene (*3*), and prothrombin 20210G>A in the *F2* gene (*4*).

Since VTE risk is compounded by numerous acquired and situational factors, known thrombophilia status may influence clinical recommendations, including decisions about contraception and hormone replacement therapy (HRT), and may prompt increased vigilance and/or prophylaxis during pregnancy and postpartum (*4*–*8*).

There is limited consensus about which individuals should be tested for *F5* and *F2* variants to inform treatment and prevention decisions. Clinical guidelines recommend testing only in circumstances where test results are likely to influence clinical management and discourage routine testing for patients with VTE and their family members (*4*, *9*–*11*). However, there are indications of consumer interest in testing (*12*), and there have been public health efforts to raise awareness of VTE (*1*).

Given the gap between clinical guidelines and consumer and public health organizations' interest in greater awareness, it is useful to assess the impact of direct-to-consumer (DTC) testing for thrombophilia. Here we report data from a nine-month study on consumer response to DTC genetic testing for variants in *F5* and *F2*.

Methods

Study participants were customers of 23andMe who obtained 23andMe's personal genomic services, including a VTE genetic risk report, between November 2007 and November 2013. The study was conducted according to 23andMe's IRB-approved research protocol.

We defined cases as participants whose results indicated having one or more *F5* or *F2* variant, and controls as having neither of these variants.

Study participation consisted of responding to at least one of two online surveys. Survey 1 addressed participants' recall of test results and subsequent perception of VTE risk, personal and family history of VTE, sharing of results with health care providers (HCPs) and family, behavioral and emotional responses to testing, and demographics. Survey 2, sent nine months later, further interrogated participants' health outcomes, attitudes, and understanding of the causes and consequences of VTE. Tables 1, 3-5, 6A and 6C include data from Survey 1; Tables 1, 2,and 6B include data from Survey 2. 8536 mutation-positive cases and 11,353 mutation-negative controls were invited to participate in the study. 1244 cases and 1110 controls responded to Survey 1; 751 cases and 574 controls took both surveys (**Table 1**).

	Cases			Controls		
	female	male	total	female	male	total
Survey 1 contacted (N)	3961	4575	8536	5273	6080	11353
Survey 1 responded (N)	680	564	1244	581	529	1110
Survey 1 response rate (%)	17.2%	12.3%	14.6%	11.0%	8.7%	9.8%
Average age of participants who took Survey 1 (years)	57.4	56.5	57.0	58.2	55.9	57.1
Prior history of VTE (%)	8.3%	8.8%	8.5%	2.9%	2.7%	2.8%
Previously viewed 23andMe VTE report (%)	79.8%			45.8%		
Prior knowledge of genetic risk for VTE (%)	9.8%			1.0%		
Survey 2 contacted (N)	617	470	1087	495	434	929
Survey 2 responded (N)	404	347	751	316	258	574
Survey 2 response rate (%)	65.5%	73.8%	69.1%	63.8%	59.4%	61.8%
Average age of participants who took Survey 2 (years)	56.7	56.9	56.8	59.5	57.7	58.7

Table 1. Study population.

Results

Risk perception: Cases demonstrated awareness of VTE risk (**Table 2**).

Perception of VTE risk	Cases (n=622)	Controls (n=273)
Lower	2.9%	19.4%
Average	5.8%	27.5%
Higher	83.0%	18.7%
I'm not sure	8.4%	34.4%

Table 2. Risk perception among participants who had viewed their VTE report. Response distribution to the question: Compared to others of the same sex and ethnicity, what is your chance of developing VTE during your lifetime?

Outcomes of receiving 23andMe genetic test results for VTE: Cases reported moderate rates of sharing test with results family members and HCPs (**Table 3**). HCPs offered risk-reducing recommendations to approximately one third of cases (**Table 4**). A majority of cases reported making changes based on results of their VTE reports (**Table 5**).

VTE results shared with the following:	Cases (n=910)	Controls (n=456)
Spouse or significant other	60.2%	21.9%
Mother	33.4%	5.7%
Father	19.9%	3.3%
Sister(s)	31.3%	5.7%
Brother(s)	24.4%	3.5%
Child(ren)	25.2%	5.9%
Aunt(s)	5.6%	0.2%
Uncle(s)	3.6%	0.0%
Grandparent(s)	1.5%	0.0%
Cousin(s)	8.7%	1.1%
Friend(s)	33.6%	7.0%
Health care provider(s)	**41.4%**	**7.0%**
Online forum (23andMe or other)	4.3%	0.7%
None of the above	15.5%	67.1%

Table 3. Sharing genetic test results with family and HCPs. Response distributions to the question: Since you received your 23andMe results, with whom have you discussed your genetic risk for VTE? Please check all that apply.

A

HCP(s) recommended changes?	Cases (n=375)	Controls (n=35)
Yes	31.2%	14.3%
No	68.8%	85.7%

B

HCP recommendations	Cases (n=117)
Wear compression socks/stockings	35.9%
Exercise more	34.2%
Lose weight	28.2%
Repeat F5 and F2 testing in a clinical laboratory	21.4%
Take medication to prevent blood clots	17.9%
Use a blood thinner (anticoagulant) such as heparin or warfarin after surgery	17.1%
Discontinue or change estrogen-containing contraceptive	14.5%
Suggest relatives have testing for clotting disorders	14.5%
Have testing for other clotting disorders	12.8%
Use a blood thinner (anticoagulant) such as heparin or warfarin for a longer duration	11.1%
Discontinue or change hormone replacement therapy	10.3%
Stop smoking	5.1%
Use heparin during pregnancy	5.1%
Other or None of the above	30.8%

Table 4. HCP recommendations. Response distributions to the questions: When you shared your 23andMe results with your healthcare provider(s), did he/she recommend any changes to your lifestyle, any changes to your medications, or additional testing? (A); What did your health care provider recommend? Please check all that apply. (B)

Behavioral and medication changes	Cases (n=911)	Controls (n=457)
Exercise more	29.6%	12.3%
Took steps to lose weight	24.9%	10.5%
Started wearing compression socks/stockings	12.1%	1.5%
Discontinued or changed estrogen-containing contraceptive	4.6%	0.2%
Took a blood thinner (anticoagulant) such as heparin or warfarin for a longer duration	3.8%	0.2%
Discontinued or changed hormone replacement therapy	3.7%	0.4%
Took a blood thinner (anticoagulant) such as heparin or warfarin after surgery	3.1%	0.2%
Stopped smoking	2.1%	0.7%
Started taking medication to prevent blood clots	2.0%	0.2%
Took a blood thinner (anticoagulant) such as heparin during pregnancy	0.8%	0.0%
Other	17.1%	6.1%
Made no changes	42.6%	78.8%

Table 5. Changes made due to 23andMe VTE report. Response distributions to the question: Have you made any of the following changes as a result of your 23andMe report on genetic risk for VTE? Please check all that apply.

Emotional response to testing: Participants were satisfied with knowing their genetic risk for VTE and would choose to learn their risk if they could do it again, despite potential for more worry (**Table 6**).

A

Satisfaction with knowing genetic risk for VTE	Cases (n=906)	Controls (n=447)
Satisfied	81.1%	67.1%
Unsatisfied	1.2%	1.3%
Neither satisfied nor unsatisfied	17.5%	31.5%

B

Would choose to learn genetic risk for VTE again	Cases (n=610)	Controls (n=263)
Yes	96.7%	93.5%
No	0.8%	1.5%
I'm not sure	2.5%	4.9%

C

Worry more or less about developing VTE	Cases (n=899)	Controls (n=443)
Worry less	11.7%	35.7%
Worry more	36.3%	8.4%
Worry same	51.9%	56.0%

Table 6. Emotional responses to VTE test results. Response distributions to the questions: Are you satisfied or unsatisfied that you know your genetic probability for VTE? (A); If you could do it all over again, would you choose to learn your genetic risk for VTE? (B); Does knowing your genetic probability for VTE make you worry more or worry less about developing VTE? (C).

Discussion

This study builds on previous investigations into consumer reactions to DTC testing for disease risk (*13*), in this instance providing insight into outcomes of testing for VTE risk. We observed moderate rates of cases taking action following receipt of test results (*e.g.*, sharing results with a medical provider or making behavioral changes) and high rates of satisfaction with test results. Further, cases reported positive impacts of receiving test results, including ability to take preventative measures, to inform medical providers, and to recognize signs and symptoms, as well as increased knowledge of VTE and personal risk (data not shown). Taken together, these results suggest that consumers may experience personal benefit from receiving DTC genetic results for VTE risk, even if clinical actionability is limited.

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