Aetiology and treatment of venous thromboembolism
Bank, I.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Social Aspects of Genetic Testing for Factor V Leiden Mutation in Healthy Individuals and Their Importance for Daily Practice

Ivan Bank¹, Michael P.R.B. Scavenius², Harry R. Bülker¹, Saskia Middeldorp¹

¹Department of Vascular Medicine and ²Department of Social Medicine, Academical Medical Center, University of Amsterdam, The Netherlands.

Submitted for publication
Abstract
To explore social aspects of asymptomatic carriehood of factor V Leiden mutation (FVL) and how carriers have experienced procedure of screening for FVL we have performed a qualitative study using semi-structured interviews. Seventeen carriers of FVL without history of venous thromboembolism (VTE) were interviewed.
Carriership of FVL has the potential to influence daily life by inducing concerns, stigmatisation and problems with insurances. Furthermore, proper procedure of screening is important because carriers have many questions concerning progeny, risk factors for VTE and preventive measures.
Both health worker and the individual to be screened for FVL need to be fully aware of the possible consequences of screening and the fact that proper screening comprises more than only the collection of a blood sample or explaining the amount of risk for VTE induced by a genetic defect. Any guideline to be developed for the screening for FVL should take this into account too.
Introduction

During the last two decades the increase in knowledge about the pathophysiology and epidemiology of inherited thrombophilia has been impressive. However, despite this progress and the fact that presently patients and their families are frequently screened, no attention has been paid to the social aspects of carriership of these inherited risk factors; at least not in the available biomedical or social scientific literature 1. This is remarkable because in general, informing an individual on his carrier status has the potential of causing negative effects on psychological status and may lead to social stigmatisation 2,3. Furthermore, carriership may influence daily life and work. For instance, knowledge of a genetic defect may cause distress and genetic discrimination. The latter has shown to exist in many social institutions, especially in health and life insurance industries 3,4.

Insight in psychosocial aspects of screening for a genetic defect related to venous thromboembolism (VTE) is also necessary for the management of these patients. In the case of screening of patients with VTE and their families for thrombophilia, knowledge of psychosocial effects should be used to develop guidelines on this issue. Guidelines may improve screening 3.

We have therefore conducted an explorative study in asymptomatic carriers of the factor V Leiden mutation (FVL), the most common inherited thrombophilic factor leading to an increased risk for VTE, to investigate whether screening for this defect had any social consequences. Because no research has been performed on this issue, and because of the nature of our study questions, a qualitative study design was chosen for this purpose 6,7.

Here we describe the social aspects of screening for thrombophilia that are relevant for clinical practice. Furthermore, we propose how knowledge derived from our study could be implemented.

Firstly, we focused on the procedure of screening itself. Secondly, we explored possible FVL influences on daily life. It is important for daily practice to know how individuals experience screening from the day at which blood was collected for DNA analysis until the day their carriership was revealed, as is to know what kind of questions usually occur after screening. This may provide tools to deal with these aspects.

More specific, we developed the following questions:

1. How did participants experience the procedure of screening and the information provided?

2. Did the knowledge on FVL status have any influence on asymptomatic individuals concerning daily life, work, insurances and progeny?
Methods

Recruitment

Participants were recruited from a large study cohort in which the incidence of VTE in first degree relatives above the age of 1.5 of symptomatic carriers of FVL was assessed. Between 1995 and 1997 they have all been informed the same way and seen in the same place as would be individuals for purposes of clinical practice. After stratified sampling, 26 carriers of FVL without a history of VTE from different families, living in the area of Amsterdam, were invited by letter to participate in this study.

Of the potential participants, 6 individuals did not wish to participate, while 3 could not be reached because of change of residence.

Of the 17 individuals that were interviewed, 8 were women and 9 men, varying in age between 26 and 56 years, with various backgrounds and levels of education.

Data Collection and Analysis

All participants were interviewed by either a sociologist (MS) or a medical doctor (IB), both experienced in in-depth interviewing. Nine interviews took place at the participants' homes, while 8 persons were interviewed in the Medical Faculty building. All interviews were tape-recorded with consent and transcribed later. Topics were generated on the basis of a study of literature concerning genetic screening in general, including stigmatisation, assessment of risk, responsibility, prevention and procedure of screening. The investigators conducted the semistructured in-depth interviews following a checklist of these topics. Two investigators (IB, MPRBS) carried out the analysis independently by the established rules of performing qualitative data analysis. Their independent results were compared and the central themes were used for further analysis.

Data processing and analysis was an ongoing process in which central questions were identified through a preliminary analysis. Later on, data from different interviews were categorised by these themes and compared by constant comparison. Since quotations are a rendering of spoken language, not all are grammatically correct.
Findings

Procedure of Screening

*Day of Screening*

Before they consented to participate, participants had received written information on study objectives, blood collection and FV L in general. Some of them had asked their relatives who had participated earlier about what they were to expect. The visit to the hospital, including the blood collection, had not been stressful. In fact, it was as the participants had expected it to be: they knew how long their visit to the hospital would last, how much tubes of blood would be taken and how long they would have to wait for the (written) result. All appreciated the fact that they had received plain and detailed information, also because most of them had never visited a medical specialist.

*Genetic Status Result*

The result of testing for FV L was often discussed with partners and close relatives first, sometimes also with close friends, and in a few cases with colleagues. Relatives were the first line of support. Unfortunately, most participants did not remember which topics concerning FV L they had discussed. They did remember that directly after having received the result the fact whether FV L was also present in others or not seemed most important. Other issues concerning implications of carrier ship were discussed later on. Most questions concerning carrier ship occurred immediately after reading the letter containing their genetic status, as illustrated by participant X:

'Questions, real questions, they come as soon as you know that you are a carrier.'

These 'real questions' mostly concerned issues involving children, their own risk for thrombosis and possible preventive measures. Nearly all participants consulted the study-physicians in the period following disclosure of carrier status. It appeared that participants were aware of the most common transient risk factors for VTE such as surgery and pregnancy. They indicated that their present knowledge concerning these risk factors was mostly derived from the explanations given at the day of screening, or later after receiving the result.

Influences of Carriership on Daily Life

*Concerns*

Participants revealed that FV L has not changed their daily life or work. However,
this sometimes contradicted with certain remarks during the interviews. For example, one woman mentioned that FVL was not important. However, she appeared to be afraid for the need to start anticoagulant treatment just like her mother who had a history of recurrent episodes of VTE. Furthermore, she had adapted some lifestyle habits (like walking, cycling more often than before and quitting use of oral contraceptives). Another example concerns two other participants who discussed FVL often and had concerns about carriership. Therefore, they had decided not to tell their children anything about FVL because ‘it might influence them negatively too’. One of them (Participant X) said:

‘This factor results in thrombosis or pulmonary embolism when you become older and not likely before 14 or 15 years of age; for that reason I do not want to let weigh on their mind yet that knowledge [about FVL] so that they have to be worrying about that now while they are still so young.’

Finally, we found that some participants seemed to be very aware of their increased risk for thrombosis in the fact that they often associated their (minor) complaints with the possibility of FVL causing thrombosis.

**Stigmatisation**

Some carriers felt that others were sometimes more concerned than they were, resulting in a kind of stigmatisation. One woman had been welcomed by her general practitioner with ‘You have got a problem’, while she had been visiting him for another medical issue. The general practitioner knew about her carriership because she had sent him a copy of the result a couple of months earlier. After another participant had told some friends that she was carrying FVL, they had advised her to go to a doctor although she was feeling just fine, because they connected some of her skin lesions to FVL.

**FVL and Insurances**

One of our participants had been discriminated by an insurance company because of the FVL mutation. He would not have received a 100% disability insurance in case he would have become unable to work because of VTE. He solved this problem by asking the research physician to help. However, it has to be mentioned that none of the other participants had given information on carriership to insurance companies.
A frequently asked question concerning genetic disorders in clinical practice is 'do my children have to be screened too?' Our studied population did not differ; for example participant VII:

Interviewer: ‘But what was the first thing you thought about when you received that letter (with the result)?’
Participant: ‘My children. That is the only thing’
Interviewer: ‘Could you explain that?’
Participant: ‘Well, you are worried about the health of your children. Fortunately the medical world does not come to a standstill. It is developing more and more. We then called to ask if it was necessary to screen our children too.’

Many wanted to screen their children because they thought it to be useful. Nevertheless, only few explained exactly why they wanted to know the genetic status of their children. They indicated that they wanted to decrease their daughters’ risk caused by pregnancy or use of oral contraceptives.

**Discussion**

In this qualitative study, we observed that a well organised procedure of screening is important and that carriership of FVL has the potential to influence daily life. Carriership raises various questions concerning risk, progeny and preventive measures while stigmatisation and problems with insurances do occur. Thus, screening for FVL should not be considered as ‘only a DNA test for the assessment of a risk profile’.

It is well established that screening for markers associated with increased risk for a disease or a disability has psychological impact 11. However, this has never been explored in asymptomatic individuals with a thrombophilic disorder, a condition with incomplete penetrance. Although our participants have not experienced anxiety or changes of mood, concerns induced by FVL and a family history of VTE influenced their lives. The fact that our participants had some time to adjust to the fact that they were carriers could however have softened the impressions we have observed.

Problems with insurances do occur, while genetic status is often not disclosed to insurance companies. This latter could induce problems for screened individuals,
also because laws are often inadequate to prevent forms of genetic discrimination, in particular by the health insurance industry \textsuperscript{12}. Research has shown that discrimination occurs \textsuperscript{13,14}. For example, a study on perceptions with respect to occurrence of genetic discrimination by health insurers showed that about 25\% of participants were discriminated with respect to life or health insurances \textsuperscript{13}. Government guidelines for insurance companies should stipulate that an asymptomatic carrier of FVL is at risk for a mostly treatable condition, without a shortened life expectancy \textsuperscript{1,13}. Finally, we observed that individuals screened for FVL do appreciate explanations and information on the procedure of screening, the genetic defect, and risk factors for VTE. Because more questions arised after screening than before, additional support was needed. This is in accordance with the fact that most patients who have little knowledge can only reach a correct interpretation of the information derived from testing by thorough counseling \textsuperscript{16}. A complicating factor is that both patients and professionals have to realise that the annual incidence of VTE in asymptomatic FVL carriers is low (about 0.5 percent per year) and that in most situations risks are only moderately increased as compared to non-carriers \textsuperscript{17,18}. Hence, not much can be offered while there are important non-medical issues. This study was not performed to find out the optimal counseling strategy. Nevertheless, some of our findings may be of importance for proper counseling in order to minimise potential non-medical complications of screening. For example, professionals might be able to prevent or diminish some concerns by extensively informing individuals who are to be screened on many issues of FVL and VTE, including psychosocial aspects. They could for instance inform carriers that problems with insurances may occur and advise, but also learn more themselves about this topic \textsuperscript{14,19}. Furthermore, risk for psychological distress is assumed to be increased if adequate patient education, genetic counseling and follow-up are not provided \textsuperscript{20,21}. Although informing on risks and other issues is a central component of any procedure, it will not always be sufficient, like a study showed in which half of people who came in with inaccurate knowledge did not to had accurate knowledge after counseling \textsuperscript{22}. Some findings of this study could be used for screening for FVL, until a guideline for screening for FVL will be developed. These findings could also be combined with some basic principles as proposed by Marteau and Croylene for screening in general \textsuperscript{20}. Basic principles proposed by them, but also found to be of importance in our study, would include 1. a protocol how testing has to be conducted; 2.
discussion of advantages and disadvantages of testing and potential testing results; 3. adequate follow-up for both individual and family. Some venous thrombosis-specific issues should be added to facilitate it for FVL screening (e.g. information about risk factors for VTE, preventive measures and/or inheritance patterns of FVL) (Table 1). By using these principles in a guideline for screening for FVL, we believe that the needs of both individuals to be screened and professionals will be better fulfilled.

<table>
<thead>
<tr>
<th>Table 1 Proposition for a guideline for testing for FVL.</th>
</tr>
</thead>
<tbody>
<tr>
<td>- A protocol should include how laboratory tests are to be conducted and how communication with patients is to be managed</td>
</tr>
<tr>
<td>- General (written) information should be given on venous thrombosis and its risk factors</td>
</tr>
<tr>
<td>- Clear and simple information should be presented about advantages and disadvantages of testing, as well as the meaning of any possible test result</td>
</tr>
<tr>
<td>- Test results should be explained and follow-up should be offered to all those tested, and if necessary to their relatives</td>
</tr>
<tr>
<td>- Most current advises should be given concerning thrombosis prevention, testing of other family members and consequences for insurances</td>
</tr>
</tbody>
</table>

References
1. We searched for all publications correlating thrombophilia in general or individual thrombophilic factors with psychological and social topics. The literature was scanned by a formal search of Medline, Embase and Web of Science from January 1966 till January 2003. Terms that were used for the search were both MeSH terms and (part of) the text words included and were combined with 'factor V Leiden mutation', 'prothrombin mutation', 'antithrombin deficiency', 'thrombophilia', 'genetic disorders', 'inherited factors', 'cardiovascular disease', 'venous thrombosis', 'thromboembolism', 'stigmatisation', 'labelling', 'insurance', 'social implications', 'psychological implications', 'psychological responses', 'genetic screening', 'genetic counseling', 'genetic discrimination', 'laws'. The search results were limited to 'English language'. Reference lists of articles were scanned for additional potentially relevant publications. Distinguished colleagues working in the field of Thrombosis & Haemostasis were also consulted.


