Aetiology and treatment of venous thromboembolism
Bank, I.

Citation for published version (APA):
A Qualitative Study of Carriers’ Perception of Having a Genetic Risk Factor for a Common Disease: Uncertainty, Control and Stigma

Michael P.R.B. Scavenius¹, Ivan Bank², Saskia Middeldorp² and Nick S. Klazinga¹

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

Submitted for publication
Abstract

This paper describes a qualitative study of carriers of a genetic risk factor for a common disease. As with many such risk factors of common diseases, this genetic risk factor has limited predictive value. Thus, knowledge of being a carrier of such a genetic risk factor is inherently problematic: The context of 'genetics' conveys the notion of a blueprint for the future whereas 'limited predictive value' contradicts this. Thus, uncertainty characterises the carriers' notion of risk. Besides an uncertain notion of risk, carriers had also developed different types of control given this uncertainty. This basic uncertainty also made different types of stigmatisation processes possible. It is argued that the nature of the effect of knowledge of carriernship is essentially relationally determined because of the hereditary aspects of this type of risk factor. Finally, it is argued that the only way to avoid the negative effects of such knowledge of carriership is to clarify the paradigm of the gene-environment interaction to both carriers and health professionals.
Introduction

Common diseases are neither purely genetic nor environmental, but dependent on interactions between genetics and environment. The concept of gene-environment interaction, therefore, is becoming a central theme in studies assessing causes of common diseases in population. The research focus on this interaction acknowledges that genetic risk factors for most of the common diseases generally have limited predictive value (low penetrance). Because of this limited predictive value, knowledge of having a genetic risk factor for a common disease does not imply clear-cut health benefits for the carrier of the risk factor. Therefore, what becomes all the more important to investigate, is how knowledge of such genetic risk factors is shaped by the social environment in which it is disclosed. In this paper we report on a qualitative case study of this (cognitive) gene-social environment interaction as expressed by participants in a research study who turned out to be carriers of an inherited thrombophilic factor: the factor V Leiden mutation (FVL).

FVL contributes to risk for venous thromboembolism. Much research on FVL has already been performed which might explain why FVL is often used as an example in scientific articles when discussing the scientific and policy implications of genetic risk factors for common diseases. Curiously however, to date there has been no study of how carriers of FVL deal with their knowledge in spite of the fact that it is the DNA-based test most commonly ordered in the United States. Also, knowledge of how carriers of FVL deal with their carriership seems very pertinent when using FVL as an example in discussing the wider scientific and policy implications of genetic research for common diseases. The absence of such studies of how carriers of FVL manage their carriership defines the present study as a preliminary study having all the markings of being explorative.

Other genetic risk factors with limited predictive value have been studied for the effect this knowledge has for the carrier. There is the useful study of familial hypercholesterolaemia which concluded that there were no important adverse quality of life effects in the short or long term for the participants. However, effective lipid lowering therapy exists for this risk factor. For FVL, on the other hand, there is no medical control available in the sense of a daily therapy that can be used indefinitely.

Therefore, informing participants in a research study that they are carriers of FVL is problematic since they themselves have to come to grips with the knowledge in the absence of medical control. In these cases, predictive medical testing has, for the individual being tested, the function of producing uncertainty. Hence
predictive medicine, in these cases, produces for the individual the need to manage this uncertainty.

Within a cohort study we explored the ways in which carriers responded to such uncertainty. Their responses have implications not only for testing for FVL and other inherited thrombophilia factors, but also implications for future research studies of genetic risk factors for common diseases in which standard preventive measures are absent. Such type of genetic testing is bound to increase as more genetic risk factors are used in studies of the gene-environment interaction basic to most common diseases.

In other words, the following three characteristics of testing for FVL are of importance in understanding the impact that knowledge of having this genetic marker has for the carriers:

1. Because of the limited predictive value of this genetic marker the knowledge of being a carrier is not linked to knowledge on clear-cut consequences. This in contrast to genetic markers with strong predictive value, as for example the genetic marker of Huntington’s disease, the knowledge of which produces certainty.

2. Because there are no standard accepted preventive measures available, the knowledge of being a carrier cannot be managed, and thus to a certain extent neutralised, through medical control as is possible in e.g. genetic screening for familial hypercholesterolemia. Carriers of FVL have to develop their own notions of management.

3. The amount of people receiving the information that they are carriers of a common genetic marker (with limited predictive value and limited medical control) of a common disease will very likely increase. This is because so much can be gained through research studies of such genetic markers to determine which combination of gene-environment interaction are most causative in the multifactorial basis of common diseases. Such knowledge can lead to diagnosis and treatment in the future tailored to individual variation in risk factor constellations.

Methods

Participants

Participants were recruited in 2001 from a large study cohort in which the incidence of venous thromboembolism in first-degree relatives above the age of 15 of symptomatic carriers of FVL was assessed between 1995 and 1998.
After stratified sampling, 26 carriers of FVL, without a history of venous thromboembolism 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 provide informed consent, while 3 could not be reached because they had changed 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.

Interviews
All participants were interviewed by either a sociologist (MPRBS) 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.

Four different interrelated topics were covered during the semi-structured interview with the carriers; their developing knowledge and experience of having the FVL risk factor, their general experience of health and disease, their relation to others (family, work, insurance etc) and their notion of prevention. The sequence of questions were meant to support a chronological story of the carrier (starting with; ‘when did you first hear about FVL?’). Although the answers were sometimes extensive, such a chronological story did not, however, develop. This reflects the fact that FVL did not appear to be a big issue for them and did not seem to have much of an impact in their lives. It became clear to us that it would not be possible to analyse their experience with FVL in terms like ‘anxiety’, ‘coping’, ‘depression’ etc. simply because nothing they said concerning FVL could fall under the heading of one of these ‘serious’ terms. So we realised that our analysis of the interviews had to be straightforward and explorative.

Data Analysis
The interviews were digitally recorded and transcribed verbatim. We analysed the data in three steps. Firstly, using open coding, we identified passages of the text that related to carrier’s perception of their genetic risk, and, any change (in conduct of life or outlook) that might be construed to be a consequence of this knowledge of genetic risk. Secondly, using axial coding we further analysed the changes by comparing them with each other. Through this comparison the two common denominators of ‘control’ and ‘stigma’ emerged as characterising these changes. Thirdly, through a conceptual analysis of the instances expressing these
two denominators, the different types of control and the different types of stigma emerged that are reported on in this study. In other words, analyses of the passages in the interviews that fell under the heading of either 'control' or 'stigma' revealed that these passages signified a specific type of control or stigma. For example, the passages in the interviews that expressed a stigma conferred by medical doctors was subsequently labelled 'medical stigmatisation'; a specification of the common denominator 'stigma'.

Results
Analyses of the interviews revealed three interrelated areas, namely, uncertainty, control and stigma, in which the carriers had processed their knowledge of being a carrier of FVL. Briefly, the nature of this interrelatedness; as a point of departure, their perception of the risk of venous thrombosis itself was uncertain and vague. This uncertainty was, on the one hand, seemingly countered by notions of how it might be controlled. On the other hand, this uncertainty had made stigmatisation possible.

Uncertain Knowledge
On the day that their blood had been tested in the hospital (anywhere between 1995 and 1998) all participants had been extensively informed about FVL and venous thromboembolism. Furthermore, all participants had been informed by mail in the summer of 2001 of the main research results of the study programme: that the annual incidence of venous thromboembolism is 6 per 1000 carriers, that this is 5 to 6 times higher than the general population but not enough to warrant routine family screening of suspected carriers. Our interviews took place six months to one year after they had received this information. In the course of the interview it became clear that the risk perception of all the participants, except one, was very unclear. All participants were asked to explain, in their own words, what they took to be their risk of thrombosis given the fact that they were carriers of FVL. The interviewer always applied probing questions if the first response was vague. But respondents either drew a blank or kept giving a vague answer:

‘No, I don’t really know how big the risk is.’;

‘Well, it is a risk, but I can’t really say; I’ll get it, or, I won’t get it.’;
‘The only thing I know is that it is quite a bit.’;
‘Well, less than 30%,...this is a bit of a pointer to indicate that I don’t think the chance is very big.’

The impression of a vague answer was often amplified when they seemed to undo their own estimation:

‘I would gamble about 20 to 30%, but I really don’t know for sure. I hope that the chance is very small. I actually don’t have any idea.’;

‘The chance is big. I don’t have any idea how big.’

A certain measure of fatalism could sometimes be discerned in the way they conveyed what they took to be the amount of risk involved:

‘Like if I come under a bus tomorrow. Yes. You understand? That’s how I see it. Anyway it’s hereditary and you can’t do anything about it. You just have to learn to live with it and that’s it.’

So the participants had a vague knowledge of a chance of a possible great misfortune but without being able to elaborate on the specific chance, circumstance or context. The one exception was a biochemist who stated that the chances of a carrier developing thromboembolism was relative to bodily condition, pregnancy or immobility, in fact, exemplifying the gene-environment interaction.

It is significant that, in general, such possible contextualisations are not part of their definition of risk. This fact underlines the vagueness and thus uncertainty, because the risk is unclear not only as an absolute measure but also unclear as a risk relative to a specific context. This does not mean that they were ignorant of possible risk contexts (see next section), we can merely assume that it is not part of their standard evaluation, or fixed idea, of their risk.

In the context of health and illness, uncertainty is logically connected to ‘control’ and ‘stigma’. Control is a means of countering the threat of uncertainty, while stigma may very well develop in connection with illness when the basis of illness is uncertain (as for example the stigma that appeared in the early phase of the AIDS epidemic when the public knowledge was uncertain). The negative connotations implied by ‘illness’ may then easily push aside uncertainty in a social environment dealing with uncertain knowledge.
Control

Medical Control

All participants were aware of the fact that the special circumstances of a medical situation implied the possibility of medical control. So being a carrier had the positive function that health workers could be informed, thus providing some measure of control in medical situations, especially with respect to operations, but also accidents or emergency situations were mentioned. The advantage of having this knowledge, however, was deflated if the participants had undergone surgery:

Interviewer: ‘So you did just mention that if there is an operation then it’s up front in your head.’

Participant: ‘No, not really, not really, I’ve had a few and then you get, just like every body else, an injection needle in your stomach or pills to anticoagulate your blood, and after a few days it stops and then it’s finished.’

We also encountered the assumption that medical control could be indefinite; as a (possible) standard preventive measure by means of anticoagulants. One woman was puzzled and somewhat perplexed when the drug was withdrawn from her grandfather who subsequently developed thrombosis. Two other participants were sure that they would be on anticoagulants when they got older. They had not been informed about this by health workers, but simply assumed that this was what was going to happen because the relative who suffered from thrombosis was given anticoagulants.

Three women had stopped taking oral contraceptives, one on her own accord and two following the orders of their general practitioner. For example one of these women, upon informing her general practitioner that she was a carrier, was simply told that she should not have the pill and that she should try to stop smoking.

Finally, it should be mentioned that the future possibility of developing medical control was the main reason mentioned for participating. Mostly, they first mentioned that they had participated for the sake of science, or for the sake of the relative first found to be a carrier. After probing these answers, possible future medical control was mentioned as for example:

‘Maybe something will come out of it so that my children can receive some preventive measure, that’s the way we have been talking about this.’
This illustrates the extent to which participation in genetic screening programmes is motivated by altruistic motives, familial altruistic motives. Furthermore, for the medical scientist, this points to social mechanism responsible for motivating people to participate, a mechanism that is specific to genetic screening.

Control through Relativising

Often, respondents defined their personal appreciation of the risk by comparing it with something much worse, thus relativising FVL, which meant for them that the threat was weakened. For example, one respondent had rheumatic arthritis:

‘Actually, I haven’t thought much about it, because that other thing, the rheumatic pain, dominates everything.’

And a respondent who had no disease:

‘I don’t think its such a burden to know it. I find the threat of cancer much worse than this. More life threatening.’

Another was very afraid of Alzheimer’s disease, so the FVL was in no way a problem according to him. Relatives who have not yet been tested may also draw conclusions based on a comparison:

Interviewer: ‘How old are your children?’
Participant: ‘Five, ten and twelve.’
Interviewer: ‘Do they know that you have a genetic risk factor?’
Participant: ‘Yes, but they believe that a genetic risk factor for cancer is much worse than that something in your blood is maybe a bit different than in another person’s blood.’

A special variant of relativising the risk is the use of humour. A man related:

‘When I got the letter I started to make jokes like; “God, I have a big risk....’

All these cases concern a relativisation of FVL, making it more insignificant in the process than if FVL had remained a new and thus strange defining term of their body. Genetic testing also affects others than the ones who have been tested. Therefore, children who are informed also participate in this process of relativising,
thus making the term more manageable.

**Temporal Control**

There were two ways in which their concerns were future concerns and therefore, at the present moment at least, under control in the sense of not being an immediate threat. Firstly, the actual development of thrombosis was connected to old age:

'I know it's something I will be involved with when I get older, but at the moment I don't think about it.'

We see here that pushing the concern into the future was coupled with minimisation of the threat implied by carrier knowledge (on minimisation in connection with genetic testing, see Marteau and Croyle 7). Secondly, their children. Given that they themselves had been screened, it was not surprising that all parents had thought about screening their children, although they varied in the extent to which they had brought it up with their general practitioner, and they varied with respect to the age they believed it might be appropriate to screen. Discussion was spent on describing the different pros and cons of having them screened. In these discussions there was no indication of minimisation of the risk, but sometimes there was relief that the decision had to be taken in the future and need not be resolved now. They were content-wise concerned with when and if their children should be tested, and in this there was no relativisation, there was no mention that they therefore were not concerned in the present, as was the case with the abovementioned form of temporal control in which there is an expressed absence of present concern. This distinction between two forms of temporal control may seem circumstantial, but this last form of future control does point to the distinctive problems of genetic testing in contrast to non-genetic testing; concern with the future possibility of testing children.

On the basis of the present study it is, of course, not possible to conclude on the level that this felt need to decide in the future concerning children is a burden for these parents, nor the level to which guilt might be felt in (possibly) passing this future threat on to their children. But children did seem to be a relatively big issue, children were often mentioned as the reason why they participating in screening for FVL. For example, one man related that the only reason why he participated in the screening was because of his children; to find out if they had a chance of having it because he thought that was much more important then finding out for himself if he had it.
Stigmatisation Processes
Four different types of stigmatisation processes could be distinguished: stigmatising the future, familial stigmatisation, institutional stigmatisation and medical stigmatisation.

Stigmatising the Future
Apart from present parenthood, there is also future parenthood; a person with no children but at an age that parenthood is a possibility in the future. In such cases, knowledge of being a carrier of FVL can stigmatising the notion of parenthood, thereby, in fact, questioning future parenthood. A woman of 27 years old:

‘If in the future I want to have children, then I know of course that I may be passing this on, and you’re conscious about that. You have to think it through very well, do you want to do that to your children, yes or no.....’

This example highlights the central difference between genetic and non-genetic testing. It is common knowledge in medicine that non-genetic testing can have stigmatising effect on the participants. There is the well-known study of changes in absenteeism among working men due to hypertension screening. But the lay person’s risk perception of a genetic risk factor, on the other hand, obviously includes a hereditary aspect and can therefore have strong and direct relational implications, as for example in this case, stigmatising the future relationship found in the concept parenthood.

Familial Stigmatisation
A different form of familial stigmatisation was that found with respect to present family members. For example, other family members who had refused to participate in the screening were seen to have made a ‘sticking your head in the sand’ decision. But familial stigmatisation could also take the form of experiencing ‘felt stigma’; a carrier feels himself as being inferior to his brothers because they turned out not to be carriers, whereas he, besides the other illnesses he already has and they do not have, is again the victim. He related that he had avoided his brothers after he learned that he was a carrier so that this topic of his being a carrier would not be raised.
Institutional Stigmatisation

A special variant of stigma is what might be called institutional stigma; an insurance company excludes a client from insurance after obtaining information that the client is a carrier of FVL. One participant described his indignation at being excluded from life insurance because he had truthfully written down that he was a carrier of FVL. Luckily, in this particular case, the carrier was able to bring the power of his employer to bear on the insurance company, thus undoing his exclusion. Another participant wanted to raise his mortgage, which would have meant revising his present mortgage conditions. He abstained from doing it, explaining that one of the reasons was that he was afraid that he would have to mention the fact that he was a carrier of FVL. In other words, financial institutions need not necessarily discriminate, nevertheless, the (imagined or real) possibility of discrimination can have a stigmatising effect.

Medical Stigmatisation

The cases of stigma arising from interpersonal interaction all involve medical doctors.

For example, one woman worked with different doctors in the area of medical insurance:

‘At my work suddenly people started reacting like; ‘oh, how terrible’. And I thought ‘how terrible’? I don’t have anything. And then they start noticing things about me, for example I get a lot of blue spots, you just have to look at me and I get a blue spot, and then suddenly all these doctors at my work started to see connections....’

and

‘I have a new general practitioner, and I enter his office, and he begins immediately with ‘you have a problem’, he was very interested in genetic research, he said he was very involved, also in his own general practice.. I found that very strange, that one’s general practitioner reacts like that.’

and

‘they tested ... and I thought it was a cryptic letter, because they wrote, ‘you have
a defect', and I didn’t really think it was the way it should be circumscribed.’
It is significant that in all these cases the participants reacted to the proposed
stigma by deflating the possible stigmatising effect. Deflating through denial (‘I
don’t have anything’) feigned astonishment (‘I found that very strange’) or a simple
negative definition (wrong circumscription) of the stigma.

Discussion
This qualitative study has shown that knowledge of being a carrier of a genetic
risk factor with limited predictive value has a small but important effect on the
carrier. This effect would probably not have been detected if the more
conventional survey research method, using quality of life scales, anxiety scales
or depression scales, had been applied. Nevertheless, the limitations of this type
of qualitative study should be acknowledged. Analyses of a limited number of
cases says little about the overall prevalence in a larger population of carriers of
the effect we have found. Our ambition was more limited; to explore the nature
of the effect of knowledge of carriership.
We suggest that the results of this qualitative study point to a basic social
mechanism that is set in motion when a genetic risk factor, with limited predictive
value, is processed by carriers. A genetic risk factor, in spite of having limited
predictive value, may have an impact on the social environment in which it is
disclosed precisely because ‘hereditary’ means by definition relational and thus
social. For an individual, therefore, the social environment of the family is what
shapes the meaning of a genetic risk factor for a common disease. This back and
forth conferring of meaning, that is, the genetic risk factor is shaped by the social
environment, and, the social environment in turn may be shaped by the genetic
risk, raises a number of issues that are specific to genetic testing as opposed to
non-genetic testing.
Most problematic is how the social environment may be shaped by the knowledge
of having FVL. This was illustrated by the woman who was of the opinion that
the future decision of whether or not to conceive a child needed serious
consideration. This points to a very important area which the medical doctor
should be aware of. Genetic risk factors with limited predictive value generally
do not fall under the responsibility of clinics for genetic counseling. The medical
doctor receives the information that a patient is a carrier and has to process this
information with the carrier. It is obviously vital that the medical doctor is aware
of the difference between a genetic and a non-genetic risk factor. With respect to
a genetic risk factor, the present and future family situation needs to be considered with the carrier. This implies quite a work burden for the medical doctor. It is not enough to simply inform the carrier of the risks involved. Since the perception of the carrier may change over time due to a different family situation or due to being informed of new scientific developments, the medical doctor may have to repeat with the carrier the discussion of the subject. This cannot be limited to carriers who might wish to be a parent in the future, the medical doctor also has to be involved with parents whose children are growing up and who may be changing their perception of the need to have their children tested. This calls for subtle communication; it should be appreciated that informing a carrier of a genetic risk factor with limited predictive value is difficult. As Baird writes: 'It is much easier to transmit the idea that 'genetic makeup interacts over a lifetime with life circumstances and exposure to determine health' than the idea that genes causes illness' than the idea that genetic makeup interacts over a lifetime with life circumstances and exposure to determine health". It is certainly important that this contextual concept of genetic risk factors for common diseases is well understood by both lay people and health professionals. Only then can the research paradigm of the gene-environment interaction be implemented without producing the various types of stigmatisation processes that we have encountered in our study.

References