Chapter 1

General introduction
General introduction
Common chronic diseases (e.g. cardiovascular diseases, and type 2 diabetes) are becoming progressively more prevalent due to growing physical inactivity and unhealthy eating patterns, resulting in an overweight population (Mokdad et al., 2003). These common diseases are multifactorial in nature due to a complex interaction of genetic and environmental influences. As a result of genomics research, new susceptibility genes for common chronic diseases are being discovered every day (for an overview, see www.genome.gov/gwastudies/). This gives rise to expectations on applications based on the knowledge about susceptibility genes in population health and community-based interventions by personalized disease prevention (Khoury & Mensah, 2005). These applications will enable people to know at a much earlier stage whether they are at risk of developing a certain disease. However, testing based on these genetic variants, even in addition to traditional disease risk factors, such as obesity and hypertension, still shows limited predictive value for disease (Dupuis & O'Donnell, 2007; Janssens & van Duijn, 2008). While we await the identification of more genetic variants that do show higher predictive value together, family history can be used as a proxy for genetic susceptibility (Burke et al., 2011; Yoon et al., 2003). In disease risk assessment, family history is traditionally associated with monogenic disorders (e.g. Huntington’s disease and hereditary forms of cancer). So far, there is little attention for the use of family history information in prevention programmes for common chronic diseases (Khoury & Mensah, 2005). It is however suggested that family history can also play an important role in risk assessment and prevention of common chronic diseases (Claassen et al., 2010; Yoon et al., 2003), as numerous studies show that familial risk is an important and independent risk factor for these common diseases (Valdez et al., 2010). Being at familial risk reflects genetic susceptibility, common behaviours, and shared environment. In this thesis we will explore the role of family history information in common disease prevention, taking type 2 diabetes as an example.

The need to address individuals at familial risk for diabetes
Type 2 diabetes is characterised by prolonged asymptomatic hyperglycaemia, resulting in many vascular complications including coronary heart disease, cerebrovascular disease, and peripheral vascular disease. With about 65,000 new cases each year, diabetes is one of the most common chronic diseases in the Netherlands (Dekker et al., 2003). There is convincing evidence from intervention studies in high-risk groups that weight loss, healthy diet, and physical activity can delay or even prevent the onset of diabetes (Gillies et al., 2007; Tuomeolito et al., 2001). However, current behavioural programmes aimed at type 2 diabetes prevention that use general health messages have limited effect (Kinmonth et al., 2008). Besides lifestyle factors, family history is an important and independent risk factor for type 2 diabetes. If a familial risk is present, the risk of getting diabetes increases with an odds ratio of 3 for one affected parent (mother 3.4 (Confidence Interval (CI) 2.3–4.9) father 3.5 (CI 2.3–5.2)) to 6 fold (CI 2.9–13.0) when both parents are affected (Meigs et al., 2000).

Although family history is commonly used, for example to identify individuals at risk for disease and improve early detection, there is no common definition of family history (Berg et al., 2009), and a positive family history is often defined in several ways (Qureshi et al., 2009a). Findings of a review suggest no useful step up in discriminatory accuracy is achieved with extension of family history enquiry beyond first-degree relatives (Qureshi et al., 2009a). In this thesis, having a positive family history is thus defined as having (or having reported) at least one first-degree relative with diabetes.

Besides the use of family history as a risk identification tool, it has been suggested that family history information can be used to increase risk awareness and personalize health messages for individuals at risk, which may be more effective in motivating individuals at familial risk to adopt and
maintain a healthy lifestyle than general health messages (Claassen et al., 2010; Yoon et al., 2003). Studies show that people with a family history of type 2 diabetes perceive a higher risk of getting diabetes compared with those at average risk (Hariri et al., 2006; Acheson et al., 2010), but they still often underestimate their actual risk (Adriaanse et al., 2003). Furthermore, only about half of these people believe that diabetes is preventable (Harwell et al., 2001; Pierce et al., 2001). Walter and Emery (2005) have shown that in comparing perceptions of people with a family history of diabetes, cancer, or heart disease, diabetes was generally seen as the least threatening. More in-depth information about these perceptions of people with a family history of diabetes is needed so that effective targeted prevention strategies can be designed.

Requirements for assessing diabetic family history
As most people have access to their family history of diabetes, assessing a family history is considered a simple and cost-effective tool (Valdez et al., 2010). However, in order to determine personal diabetes risk, accurate methods to assess the risk associated with a given family history are required. It is suggested that the accuracy of reporting is greater for first-degree relatives than second-degree or beyond (Qureshi et al., 2007). Furthermore, the accuracy of reporting is influenced by the self-reported personal health status of relatives (Janssens et al., 2011), and by factors relating to the method of capturing the family history data (Qureshi et al., 2007). Systematic assessment of a family history with a computer-based tool was shown to prompt the information better than a short enquiry of family history by a physician or the information from medical reports (Sweet et al., 2002). It is expected that there is also a difference in accuracy of a diabetes risk assessment for which detailed familial history information is assessed in a comprehensive family history tool (Yoon et al., 2009) compared to the use of a single-item question that is integrated into a diabetes risk assessment (Alssema et al., 2008). Individuals who have a relative with diabetes are not always aware of their family history and of being at familial risk (Walter & Emery, 2005). Since diabetes can be delayed or prevented by adopting a healthy lifestyle, being aware of family history as a risk factor is a prerequisite. Thus, assessing diabetic familial risk and informing individuals about their risk not only results in identification of people at risk, but also might result in these individuals showing increased risk awareness. In this thesis, the additional value of using a detailed diabetic family history questionnaire compared to a simple enquiry for diabetes risk identification is evaluated.

Raising risk awareness and motivating lifestyle change by using familial risk information
There is evidence that people who are aware of having a diabetic family history engage more in risk-reducing behaviour (Hariri et al., 2006; Qureshi & Kai, 2008; Walter & Emery, 2005; Zlot et al., 2009; Chang, 2011). However, in general people at familial risk have little awareness of being at risk. It is thus important to know how familial risk should be communicated to improve their risk awareness and to change behaviour. Although lay understanding of disease risk is partly based upon factors similar to epidemiological knowledge (e.g. the level of kinship and number of affected relatives), other important factors have also been identified. These include the experience of a relative's illness, feelings of closeness to the affected relative, and perceived differences between themselves and the affected relative (e.g. gender, age, personality, lifestyle and physical characteristics) (Hunt et al., 2000; Pierce et al., 2001; Walter et al., 2004; Walter & Emery, 2005). Since people's illness and risk perceptions seemingly do not correspond to the epidemiological models, increasing awareness by explaining the multifactorial nature of diabetes and the role of family history may be essential (Harrison et al., 2003). This thesis was designed to investigate the impact of communicating familial risk of diabetes on illness
and risk perceptions and behavioural outcomes. The following paragraph describes the conceptual model that was used in the studies performed in this thesis.

**Conceptual model**

Theoretical behavioural models can be used to describe the effects of risk information on illness and risk perceptions and behaviour. Two of these models are addressed here. The common sense model of self-regulation of health and illness (Leventhal et al., 1997) explains how a person processes an illness threat. This model is centred around the idea of ‘lay’ beliefs about illness or illness perceptions (e.g. beliefs about the causes of the illness). New information concerning this illness threat is integrated within these existing beliefs. The Protection Motivation Theory proposes that a person decides to protect him- or herself based on the perceived threat (threat appraisal) and the perceived controllability of that threat (coping appraisal) (Floyd et al., 2000). Illness perceptions (Leventhal et al., 1997), as well as threat and coping appraisals (Floyd et al., 2000) are suggested to influence motivation to engage in preventive behaviours. The conceptual model used in this thesis integrates both theories and is described in Figure 1.

![Conceptual model used in this thesis]

The assumption is that providing people with familial risk information, in addition to general diabetes risk information, raises awareness of both the genetic and behavioural causes (causal beliefs) of diabetes and the interaction between them. In turn, this awareness is suggested to influence the threat appraisal, i.e. the perception of the risk (or relative risk) of getting diabetes. Because of the increased understanding of family history as a risk factor, individuals with a family history might experience a higher risk as compared to those without familial risk.

When familial risk information is provided, the belief that diabetes is determined mainly by genetic predisposition may, however, prevent individuals from engaging in risk-reducing behaviour as a result of fatalism, e.g. the thought that preventive measures will not help to reduce the risk (Marteau, Lerman, 2001; Shiloh et al., 2002). Diabetes is multifactorial in nature. Explaining to people with a positive family history that both lifestyle and genetic risk factors play a role in the development of diabetes, and that they can reduce their risk by changing their lifestyle, might enhance their sense of control. Thus, a better understanding of the multifactorial nature of the risk may affect a person’s coping appraisal (personal control over the risk of getting diabetes), besides the perception of risk.

Finally, according to the Protection Motivation Theory, both the perception of being at risk and the feeling of control over the risk of getting diabetes are important factors associated with (the intention to) changing behaviour, such as increasing physical activity and eating more healthily, in order to prevent or delay the onset of diabetes. Since an individual’s perceived risk of diabetes does not correspond to their actual risk and their causal beliefs are not always correct, interventions need to...
be developed to reduce the mismatch, and to improve awareness of the multifactorial nature of diabetes.

From individual prevention to a public health approach

Personal risk communication is the preferred way to communicate familial risk information and appropriate preventive measures, as the health care provider can respond to possible misconceptions of the patient. This way of communicating family history information corresponds with so-called selective prevention, e.g. the general practitioner selects people based on their positive family history of diabetes and provides these individuals an individualized prevention programme (see definitions in the Netherlands at www.preventweb.nl).

Another way of using family history information is to address the entire general population (so-called universal prevention, www.preventweb.nl), additionally screen individuals for having a family history, and provide lifestyle information when necessary, thus using the information as a public health strategy. When using this approach, it is necessary to develop a tool that is simple, easily applied, and adaptable to different settings (Yoon et al., 2003; O’Neill et al., 2009). Computer tailoring is seen as an effective way to mimic interpersonal contact, since personalized feedback is provided by means of questions in digital form, for example by using computer-tailored health education (Kroeze et al., 2006). Family history and disease risk assessments are often offered via the Internet using a public health strategy. An advantage of using Internet as a medium to deliver diabetes risk assessment with integrated familial risk assessment is that more people can be reached at lower costs (Brug et al., 2003). However, there is little evidence concerning the impact of web-based familial diabetes risk communication on illness and risk perceptions and self-reported behavioural outcomes. In this thesis family history is addressed in two different ways: in an individual face-to-face consultation (to mimic everyday general practice), and a public health, universal, approach by using web-based familial risk information.

Adverse effects of diabetic familial risk information

A consequence of using a public health approach and exploring familial risk in the general population is that individuals with no family history will also be informed about the fact that family history is an important risk factor for diabetes. This could be problematic since people without a family history of diabetes might then erroneously believe that having no family history means being less at risk than they actually are, i.e. false reassurance (Marteau et al., 1996). This belief may lead to unintentional adverse effects, such as reduced motivation to change behaviour, justification of unhealthy behaviour, and delayed seeking of medical advice (Paddison et al., 2009). The question is whether diabetic familial risk information does indeed lead to false reassurance (i.e. reduced risk perception and less risk-reducing behaviour) among people without a family history.

Although there has been concern that emphasizing family history may lead to adverse psychological effects such as increased anxiety, there is no evidence that informing people about their familial risk causes psychological harm (Pierce et al., 2000; Qureshi et al., 2001). Research has shown that a genetic risk may be perceived differently compared to other risks because of its potential for fatalism, e.g. the thought that preventive measures will not help to reduce the risk (Senior et al., 1999; Harwell et al., 2001; Pierce et al., 2001). The belief that diabetes is determined mainly by genetic predisposition may prevent individuals from engaging in preventive behaviour to reduce their risks. However, other studies do not support this finding (Collins et al., 2010; Acheson et al., 2010).
Implications of diabetic familial risk information for individuals and their families

Little is known about how users – i.e. people with and without a family history of diabetes – perceive the addition of familial risk information to diabetes risk assessment and information. Is the information perceived as useful and do people with a positive family history appreciate being informed about their familial risk, and should we therefore offer these risk assessments? Besides the evaluation of familial risk information of the user for themselves, there might also be an impact on their families or families in general. Communication about genetic health risks is often difficult within families, due to complex communication patterns and family structures (Wilson et al., 2004; Esch et al., 2011). In addition to familial risk assessment, new developments in genetic predictive medicine are expected (i.e. risk assessment based on DNA test results), and this calls for an understanding of issues related to these tests (Becker et al., 2011). For monogenic diseases, there is many data available on societal issues of testing for and communication of genetic risk information to individuals and families. Important issues are, for example, the right to know or not know one’s genetic status (Sankar, 2003), potential genetic discrimination by insurance companies and employers (Low et al., 1998), privacy issues concerning who has access to sensitive personal genetic information (Lilani, 2005), and freedom of choice, indicating that free and informed consent has to be guaranteed before a genetic test is carried out (Häberlin, 2005). However, very little research has focused on the possible societal issues related to genetic testing for multifactorial diseases (Becker et al., 2011). These issues are expected to be less pronounced, because the aetiology is essentially different. Each gene variation might have an effect on more than one disease or phenotype, the inheritance of an identical pattern of gene variants is low, and there is a high environmental influence on the development of a disease (Janssens & Khoury, 2006). However, new issues may arise. For example, Janssens and Khoury (2006) have expressed their concern about whether it is ethical to perform DNA tests with low predictive value. Other issues may be relevant for family history assessment. For example, Yoon et al. (Yoon et al., 2003) suggested that labelling a family at risk might induce feelings of blame.

The study project

This study project was performed to examine (1) the impact of assessing and communicating familial risk of diabetes on risk awareness and behaviour change, and (2) the possible large-scale positive and negative outcomes of integrating such a family history tool into public health. The results may serve as a model for risk assessment based on other complex chronic diseases with multiple aetiologies, such as cardiovascular diseases.
Research questions
In this thesis the following research questions will be addressed:

1. What are causal beliefs, perceived risk, and perceptions of control among individuals at familial risk for diabetes and do these differ from perceptions of individuals without a family history? (Chapter 2)

2. How do people perceive diabetic risk assessment based on family history assessment?
   a. What issues related to predictive testing based on family history assessment in diabetes prevention do lay individuals perceive? (Chapter 3)
   b. Do these issues differ from the issues with regard to DNA testing? (Chapter 3)
   c. What is the perceived value of diabetic familial risk assessment and information for users of such an intervention and what are the perceived implications for families and society? (Chapter 7)

3. What is the additional value of using a detailed diabetic family history questionnaire compared to a simple enquiry for diabetes risk identification? (Chapter 4)

4. What is the effect on people of assessing and communicating diabetic familial risk?
   a. What is the impact of communicating familial risk of diabetes in a personal consultation on illness and risk perceptions and self-reported behavioural outcomes of people with a family history of diabetes? (Chapter 5)
   b. What is the impact of web-based familial risk information on illness and risk perceptions and risk-reducing behaviour of people with a family history of diabetes? (Chapter 6)
   c. Does an intervention that emphasizes familial risk information result in false reassurance among people without a family history of diabetes? (Chapter 6)
Chapter 2

Family history of diabetes: exploring perceptions of people at risk in the Netherlands

Abstract

Introduction
The aim of this study was to explore the perceptions of causes, risk, and control with regard to diabetes and the role of family history among people at increased risk for type 2 diabetes.

Methods
Semi-structured interviews were conducted among people aged 57 to 72 years with (n=9) and without (n=12) a family history of diabetes.

Results
Participants mentioned different causes for diabetes; these were often a combination of genetic and behavioural factors. Some participants with a family history expressed incoherent causal beliefs; their general ideas about the causes of diabetes did not explain why their relatives were affected. The role of genetics as a cause for diabetes was more pronounced when people perceived diabetes as “running in the family,” and this finding did not necessarily relate to a high number of affected relatives. Although people with a family history were aware of the diabetes in their family, they did not always associate their family history with increased risk, nor did they worry about getting diabetes. The absence of diabetes in the family was often used as a reason to perceive a low risk. Participants who primarily perceived genetic predisposition as a cause felt less able to prevent getting diabetes.

Conclusion
Future diabetes prevention strategies would benefit from giving more attention to individual perceptions, especially in the context of family history, explaining the multifactorial character of diabetes, and highlighting effective ways to reduce the risk.
Introduction
The prevalence of type 2 diabetes mellitus, a serious health problem, is increasing. Several factors contribute to this increase, including increasing obesity and inactivity (Ford, Williamson, Liu, 1997). In high-risk people, the onset of and complications from type 2 diabetes can be delayed or even prevented by adopting a healthy lifestyle (Tuomilehto et al., 2001). Prevention is especially important for people with a family history of diabetes because a family history is one of the strongest risk factors for type 2 diabetes (Valdez et al., 2007; Bjørnholt et al., 2000; Klein et al., 1996). Studies consistently report a 2- to 6-fold increased risk of diabetes associated with a positive family history, depending on the number and closeness of relatives affected (Annis et al., 2005; Pierce, Keen, Bradley, 1995). Family history represents genetic, environmental, and behavioural elements, and the interactions between them.

Despite the high prevalence of type 2 diabetes, little is known about the perceptions of diabetes risk among high-risk populations. Quantitative studies show that people with a family history of type 2 diabetes perceive a higher risk of getting diabetes compared with those at average risk (Hariri et al., 2006), but they still often underestimate their actual risk (Adriaanse et al., 2003). Furthermore, only about half of these people believe that diabetes is preventable (Harwel et al., 2001, Pierce et al., 2001). Walter and Emery (2006) have shown that in comparing perceptions of people with a family history of diabetes, cancer, or heart disease, diabetes was generally seen as the least threatening. More in-depth information about these perceptions of people with a positive family history of diabetes is needed so that effective targeted prevention strategies can be designed.

Although family history is not a modifiable factor, communicating familial risk information may be useful in raising risk awareness, thereby encouraging preventive behaviours (Yoon, Scheuner & Khoury, 2003). At the same time, familial risk information may result in a sense of fatalism if people see familial risks as deterministic, thereby discouraging healthy behaviour. According to Marteau and Weinman (2006), understanding the conditions under which genetic risk information does and does not motivate behaviour change is the first step toward developing ways of communicating such information to maximize its motivational impact. Perceptions about genetic risk are thought to be mainly influenced by causal beliefs, since genetic information is specifically about causes (Marteau, Senior, 1997). In addition, both risk perception (threat appraisal) and perceptions of control (coping appraisal) can be used to explain people’s motivation to improve their lifestyle to reduce their risk for type 2 diabetes (Rippetoe & Rogers, 1987).

The aim of this study is to explore causal beliefs, perceived risk, and perceptions of control among people at increased risk for getting diabetes, and the role of family history in this context. Perceptions of people with and without a family history are explored to compare and contrast these beliefs between groups.
Methods
Participants
A sample was recruited from a database of a population-based targeted diabetes screening study that was carried out from 1998 to 2000 among inhabitants of the West-Friesland region of the Netherlands (for details, see Spijkerman et al. 2002). Participants (N = 2,315) had been at increased risk of developing diabetes on the basis of a self-reported risk questionnaire. However, blood test results excluded them from having developed the disease at that time. The participants had been informed by letter that they did not have diabetes, but no further information was provided. For our study, people older than 75 years were excluded; of all eligible people, 20 people with at least 1 first-degree relative with diabetes and 20 people without a family history of diabetes were randomly selected on the basis of self-reported information.

A municipal official checked the 40 addresses to determine whether people had moved or died. Two people had died and 1 had moved, leaving 37 people who were sent a letter of invitation signed by a general practitioner. Exclusion criteria for the interview study were not speaking the Dutch language and having been told that they had diabetes. In total, 31 of 37 people (84%) responded to the invitation (14 were sent a reminder), and 24 people (65%) agreed to participate. Of the nonparticipants, 1 reported having developed type 2 diabetes; 1 participant was on vacation during the study period; and 5 others did not want to participate and gave no reason for nonparticipation. In the analyses, 3 participants were excluded because they appeared to have only second-degree relatives with diabetes, leaving only 9 people with a positive family history and 12 people without a positive family history.

Methods
The 3 core concepts in this qualitative study — causal beliefs, risk perception, and perceptions of control — were used to construct a semi-structured interview guide. Additional themes were participants’ personal family history of diabetes and perceived consequences of diabetes. Two researchers (M.P. and L.C.) conducted the interviews in the participants’ homes. Interviews were held in June 2005 and lasted 30 to 60 minutes. The interview guide was refined after the first 2 interviews, following discussion among 4 researchers (M.P., L.H., L.C., and D.T.) using the taped interviews. The Medical Ethical Committee of the VU University Medical Center approved the study, and every participant signed an informed consent form before participation.

Analysis
All interviews were audiotaped and transcribed. Content analyses were conducted on the transcripts (Pope, Ziebland, Mays, 2000). On the basis of found codings, further analyses were conducted to detect correspondence and differences between people with and without a family history. Coding was subsequently completed by 2 of the authors (M.P. and L.H.). To ensure uniform coding, the 2 authors coded each transcript and then discussed the codings until agreement was reached. For the analysis, we used Kwalitan version 5.0 (Department of Research Methodology, Radboud University, Nijmegen, the Netherlands). The most important themes are presented, and quotations are used to illustrate the meanings that participants attached to a theme. Participants’ identification number (#), age in years, sex, and family history (FH) are presented. Perceptions of people without a family history are used to compare and contrast the findings among people with a family history and are not described in detail.
Results

The characteristics of the participants with (n = 9) and participants without (n = 12) a family history of diabetes who were interviewed are shown in table 1. Participants with a family history of diabetes reported 1 to 4 affected relatives among first- and second-degree relatives. The mean age in the group of people with a positive family history was 67 years (range 62-72), and for the group without a family history was 66 years (range 57-71). Participants varied in educational level, and in both groups approximately a quarter of the participants were highly educated.

Table 1 – Participant Characteristics, Semi-structured Interviews on Perceptions of People at Familial Risk of Diabetes in the Netherlands, 2005

<table>
<thead>
<tr>
<th>Participant #a</th>
<th>Aye, y</th>
<th>Sex</th>
<th>Relative with Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>101</td>
<td>70</td>
<td>Male</td>
<td>None</td>
</tr>
<tr>
<td>105</td>
<td>70</td>
<td>Female</td>
<td>None</td>
</tr>
<tr>
<td>106</td>
<td>64</td>
<td>Female</td>
<td>Father, mother, mother’s sister</td>
</tr>
<tr>
<td>107</td>
<td>67</td>
<td>Male</td>
<td>Brother</td>
</tr>
<tr>
<td>108</td>
<td>69</td>
<td>Female</td>
<td>Mother’s mother, mother</td>
</tr>
<tr>
<td>112</td>
<td>69</td>
<td>Female</td>
<td>None</td>
</tr>
<tr>
<td>113</td>
<td>71</td>
<td>Female</td>
<td>Mother’s mother, mother</td>
</tr>
<tr>
<td>115</td>
<td>65</td>
<td>Female</td>
<td>Mother’s father, father, brother, sister</td>
</tr>
<tr>
<td>117</td>
<td>69</td>
<td>Male</td>
<td>None</td>
</tr>
<tr>
<td>118</td>
<td>62</td>
<td>Female</td>
<td>Mother</td>
</tr>
<tr>
<td>119</td>
<td>57</td>
<td>Male</td>
<td>None</td>
</tr>
<tr>
<td>121</td>
<td>57</td>
<td>Female</td>
<td>None</td>
</tr>
<tr>
<td>124</td>
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</tr>
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<td>59</td>
<td>Male</td>
<td>None</td>
</tr>
<tr>
<td>132</td>
<td>64</td>
<td>Male</td>
<td>Brother, sister</td>
</tr>
<tr>
<td>133</td>
<td>68</td>
<td>Female</td>
<td>Mother</td>
</tr>
<tr>
<td>134</td>
<td>61</td>
<td>Female</td>
<td>None</td>
</tr>
<tr>
<td>136</td>
<td>72</td>
<td>Male</td>
<td>Mother, daughter of sister</td>
</tr>
</tbody>
</table>

*aAll people who were eligible to participate in the study were numbered. Only numbers of participants included in the article are listed in the table, so the numbers are not sequential.*
Causal beliefs

*Both genetic and behavioural causes*

Participants in both groups were often able to name several causes for diabetes, including genetic and behavioural causes. Causes mentioned were genetic predisposition (including family history), unhealthy food (too much fat and sugar, unvaried diet), lack of physical activity, stress, alcohol intake, and age. Participants often mentioned genetic predisposition as a cause of diabetes in combination with an unhealthy lifestyle, whether they had a family history or not. For example, this man said:

*I think [diabetes] has to do with eating habits, if I understood it correctly. But I think that it’s also a hereditary matter, that someone inherits it. That the mother or father possibly had it.*

(#131, 59, M, no FH)

*General ideas about causes do not explain diabetes in the family*

Compared with people without a family history, those with a family history sometimes expressed less coherent thoughts about the causes of diabetes. The following quotation is from a woman who had explained earlier in the interview that she predominantly saw genetic predisposition as a cause of diabetes, though when she explained why her relatives developed diabetes, she had another perception:

*I think that it’s always genetically determined whether you get it. . . . I think that for my mother it was caused by stress, when my father died. . . . For my father, it was his lifestyle. I think that the diabetes that my father had wasn’t hereditary for us. Because my father too was always busy.*

(#106, 64, F, FH: father, mother, mother’s sister)

Others who generally perceived an unhealthy lifestyle (e.g. unhealthy diet, overweight) to be the cause of diabetes showed confusion about the cause of the diabetes in their family when lifestyle could not be seen as an explanation for their affected relative. For example, this man commented:

*People with overweight have a high risk of getting diabetes. It has to do with food. . . . My brother has had diabetes since years. He’s very slim, and he was also skinny when he got it, so that’s miraculous. Yes, in this case [heredity] could play a role.*

(#107; 67; M; FH: brother)

*Diabetes runs in my family, thus genetic cause*

For people with a family history of diabetes, the role of genetics as a cause for diabetes was seen as more pronounced when people perceived diabetes as “running in the family,” particularly when diabetes was passed on from generation to generation in the same lineage. For example, this woman has a family that is heavily affected with diabetes, and therefore she believed that she has inherited the predisposition for diabetes:

*Diabetes runs in our family, because my old grandmother suffered from it to a lesser extent, my father had it very severely, my sister injects, and my brother controls it with medication. So then you do think there’s something inside you.*

(#115; 65; F; FH: mother’s father, father, brother, sister)

However, this phenomenon also occurred when only 1 relative was affected, as in the following example of a woman who mentioned that diabetes has a genetic cause:

*So I think it’s just genetic, that you can’t prevent it. My risk is somewhat higher [than that of a random man or woman of the same age], because I have diabetes in the family.*

(#118; 62; F; FH: mother)
Behaviour triggers the course of diabetes
Although some believed that behavioural factors, such as an unhealthy diet, were not the cause of diabetes, they thought that these factors might influence the course of the disease (i.e., causing an earlier onset of diabetes or more severe symptoms) in case of genetic predisposition. The following quotation from a woman illustrates this perception:

I think it’s in your genes. I don’t think if you eat too many sweets that you get [diabetes]. You will just get fat. Well, if you have diabetes you shouldn’t eat sweets. It maybe just makes [the diabetes] worse. (#118; 62; F; FH: mother)

“Inherited lifestyle”
One participant believed that the diabetes in his family was caused by an “inherited lifestyle,” in particular their diet:

My sister’s lifestyle is sloppy, that might be the cause [of her diabetes]. Being rather overweight, quite a lot of food, never exercising. [As to the cause of diabetes for my brother,] the only possible thing is that he has the same lifestyle as my sister. Eating a lot of sweets and a lot of food, lots of fat. That might be an inherited factor. (#132; 64; M; FH: brother, sister)

Perceived risk
Diabetes in my family, therefore increased risk
Only 4 of 9 participants with a positive family history perceived a slightly higher risk when comparing themselves with other people of the same age, because of the diabetes in their family.

Maybe I have a higher risk [of getting diabetes] because my mother had diabetes. (#108, 69, F, FH: mother, mother’s mother)

Diabetes in my family, but no risk for me
Although participants with a family history did mention that they had diabetes in their family, they did not always seem to associate this information with their own risk. For example, this woman said:

The risk of getting diabetes is on my mind. I do have a mother and a grandmother who had it. But [my chance of getting diabetes] is the same, everybody can get it, I don’t think my risk is higher or lower. (#113; 71; F; FH: mother, mother’s mother)

Diabetes not in my family, so no risk for me
Most of the participants without a family history perceived a low risk of getting diabetes. Only a few (3/12) perceived themselves at a slightly higher risk than average because they considered themselves to be overweight and to have an unhealthy lifestyle. Moreover, the absence of diabetes in the family was often (7/12) mentioned as a reason to perceive a low diabetes risk. For example, this woman:

The [diabetes] risk must be very low, because at home there were 7 of us, and none of us has it! (#130; 71; F; no FH)

Despite high risk-awareness, low emotional response
Participants who did mention severe consequences of diabetes and sometimes even perceived a high risk due to an extensive number of affected family members still did not worry about getting diabetes. The following quotation is from a woman who mentioned in the interview that she perceived a high risk of getting diabetes:

Blindness, the legs, the muscles or nerves in the legs of my father were affected. . . . No
severe illness, they say you can become 100 years old with it, but I think the side effects are very hard. I never think about getting diabetes. [Having diabetes] is not a problem; I mean, you just pay more attention to what you eat. (#115; 65; F; FH: mother’s father, father, brother, sister)

Perceptions of control
Although some people correctly stated that having a healthy diet and being physically active can delay the onset of or even prevent diabetes, most participants in both groups were unaware of ways to prevent diabetes. Participants with a family history held different beliefs about ways to control their risk, depending on their causal beliefs.

Genetic cause, cannot control risk
Participants with a family history of diabetes who mainly perceived genetic causes for getting diabetes all felt that they were not able to prevent it. At most, they thought they might be able to postpone the disease by adopting a healthy lifestyle, like this woman:

I think that it’s always genetically determined whether you get [diabetes]. I think there’s little you can do about it then. You might be able to postpone it a little, if you know you can get it, by paying attention to what you eat. (#106; 64; F; FH: father, mother, mother’s sister)

Behavioural cause, can control risk
In contrast, those with a family history who predominantly saw lifestyle as a cause of diabetes did believe there were ways to prevent diabetes, as this man's comments illustrate:

Of course you always have an influence [on the chance of getting diabetes] by not doing things that can cause diabetes . . . like having lots of fat and drinking sweet cola. (#107; 67; M; FH: brother)

Discussion
Both people with and without a family history of diabetes mentioned several causes for diabetes, including genetic and behavioural causes. This finding suggests that people correctly see diabetes as a multifactorial disease. Walter and Emery (2005) earlier described the multifactorial model of familial disease risk. They also showed that people at risk for diabetes view lifestyle factors as triggering an underlying risk, for example, genetic risk. In our study, some participants thought that lifestyle could worsen the diabetes or that it would develop sooner in case of genetic predisposition. None of them mentioned that an unhealthy lifestyle alone would trigger an underlying risk. One participant, however, pointed out that lifestyle might be an inherited factor. This may imply that some people identify behaviour as heritable. Because only 1 participant mentioned this aspect, it is difficult to draw such a conclusion.

A contrast between both groups concerning causal beliefs was that people with a family history of diabetes were less coherent and more confused when talking about the causes of diabetes, since their general beliefs about the causes did not always explain why their relatives were affected. Being incoherent about causal beliefs has been identified previously for diabetes patients. Though aware of possible risk factors for diabetes (e.g. being overweight, physically inactive, having a family history), patients without these risk factors could not understand how they had developed the disease (Tessaro, Smith & Rye, 2005). Thus, their general ideas about the causes of diabetes did not explain why they were affected. It seems that people have difficulty in understanding the interplay between genes and environment or behaviour (e.g. unhealthy lifestyle). Possibly people have more difficulty in
integrating risk information from more than 1 source than when there is a single risk factor for a disease, as Marteau and Weinman (2006) have suggested.

People mostly perceived a genetic cause for getting diabetes when they perceived diabetes as “running in the family.” This belief was reported when several affected relatives were of the same lineage, as one might expect. However, a woman with only 1 affected relative also perceived diabetes as running in the family and perceived a higher risk of getting diabetes. In a quantitative study designed to identify determinants of familial risk perception of common diseases (cancer, coronary heart disease, and diabetes), Walter et al. (2008) found that believing the disease “runs in the family” is an important predictor of perceiving a familial risk, together with believing the disease has a genetic cause and diabetes is a serious condition. People without a family history often see not having a family history as protective, which might indicate that they also perceive diabetes is caused by a genetic predisposition when it runs in the family.

Some people who saw diabetes as running in the family indeed perceived an increased risk of getting diabetes because of the occurrence of diabetes in the family. This finding might indicate that people associate their beliefs about heredity of diabetes with their perception of being at risk. Participants with a family history perceiving behavioural causes for getting diabetes had a different risk perception. Though they acknowledged their family history, when comparing themselves with other people of the same age, they still did not perceive a higher risk. In line with these findings, Harrison et al. (2003) found that less than 40% of the people with a family history of diabetes perceived themselves to be at increased risk. Despite their family history of diabetes, participants in this study did not feel worried about getting it. Walter and Emery (2006) earlier described that diabetes was not viewed as a serious disease but as a chronic disease of older age and at worst a minor inconvenience. In keeping with these findings, Eborall et al. (2007) described low levels of anxiety among participants of a screening program for type 2 diabetes in the east of England, even those eventually diagnosed with type 2 diabetes.

This study suggests that people with a positive family history, especially people who perceive genetic causes for getting diabetes, are less likely than others to believe that diabetes is preventable, supporting the results of Harwell et al. (2001). In contrast, it seemed that people who perceived behavioural causes for developing diabetes did believe that diabetes was preventable. A previous study by Senior et al (Senior et al., 2002), considering perceptions about an inherited predisposition to heart disease (familial hypercholesterolemia), showed evidence for fatalistic beliefs when the underlying cause of a positive test result was seen as genetic, and no such evidence was found for perceptions of underlying behavioural causes.

Some limitations of our study need to be addressed. Participants were older adults who might consider health risks a part of getting older, may be less engaged in preventing disease, and may have had fewer concerns about getting premature disease due to their family history. The participants had been in a stepwise-based screening study some years earlier; therefore, their knowledge about diabetes might have been better than that of the average population. Nevertheless, these results suggest that, even in this group, knowledge about diabetes and especially ways to prevent it were suboptimal. Although the small sample size of the study may limit conclusions, we have gained a deeper understanding of the perceptions and beliefs of people with a family history of diabetes.

This study suggests that people probably used causal beliefs to construct their perceptions of risk and control (i.e., when people perceive genetic causes for diabetes, they tend to have a higher perception of risk and lower perception of control). Perceptions of risk and control in turn may be important motivating factors for preventive health behaviours (Rippetoe & Rogers, 1987). People with a family history of diabetes seem to have incoherent causal beliefs; therefore, prevention programs
should promote correct understanding of the multifactorial causes of type 2 diabetes among people at high risk due to their family history, which might have a positive effect on their perceptions of risk and control and, directly or indirectly, on preventive behaviours. In addition, people without a family history would also benefit from clear information on this topic. The findings of the study point to the need for more research on this topic, for example, on the relationship between causal beliefs and both risk perception and perception of control.
Chapter 3

Lay perceptions of predictive testing for diabetes based on DNA test results versus family history assessment: a focus group study

Abstract

Background
This study assessed lay perceptions of issues related to predictive genetic testing for multifactorial diseases. These perceived issues may differ from the "classic" issues, e.g. autonomy, discrimination, and psychological harm that are considered important in predictive testing for monogenic disorders. In this study, type 2 diabetes was used as an example, and perceptions with regard to predictive testing based on DNA test results and family history assessment were compared.

Methods
Eight focus group interviews were held with 45 individuals aged 35-70 years with (n = 3) and without (n = 1) a family history of diabetes, mixed groups of these two (n = 2), and diabetes patients (n = 2). All interviews were transcribed and analysed using Atlas-ti.

Results
Most participants believed in the ability of a predictive test to identify people at risk for diabetes and to motivate preventive behaviour. Different reasons underlying motivation were considered when comparing DNA test results and a family history risk assessment. A perceived drawback of DNA testing was that diabetes was considered not severe enough for this type of risk assessment. In addition, diabetes family history assessment was not considered useful by some participants, since there are also other risk factors involved, not everyone has a diabetes family history or knows their family history, and it might have a negative influence on family relations. Respect for autonomy of individuals was emphasized more with regard to DNA testing than family history assessment. Other issues such as psychological harm, discrimination, and privacy were only briefly mentioned for both tests.

Conclusion
The results suggest that most participants believe a predictive genetic test could be used in the prevention of multifactorial disorders, such as diabetes, but indicate points to consider before both these tests are applied. These considerations differ with regard to the method of assessment (DNA test or obtaining family history) and also differ from monogenic disorders.
Background

As a result of genomics research, a growing number of genetic variants that contribute to the multifactorial aetiology of many common disorders, such as diabetes and coronary heart disease, are being identified. Multifactorial diseases are, however, characterised by complex gene-environment interactions (Collins et al., 2003). Testing based on these genetic variants alone (DNA-based test), or in addition to traditional disease risk factors, such as obesity and hypertension, still shows limited predictive value for disease (Dupuis & O'Donnell, 2007; Janssens & van Duijn, 2008). While we await the identification of more genetic variants that do show higher predictive value together, family history might be used as a ‘genomics’ tool for disease prevention (Yoon, Scheuner & Khoury, 2003).

Numerous studies show that familial risk is an important and independent risk factor for multifactorial diseases (Valdez et al., 2010). Family history reflects the consequences of a genetic predisposition, a shared environment, and common behaviour. Family history information may be used to determine personal disease risk (family history assessment), raise risk awareness and motivate individuals to adopt preventive behaviour (Claassen et al., 2010). So far, there is little attention for the use of genetic information (DNA test results or a family history assessment) in prevention programmes for common diseases (Khoury & Mensah, 2005). Nevertheless, new developments in predictive medicine are expected, and this calls for an understanding of issues related to these tests (Häberlin, 2005).

Little is known about how people compare and contrast predictive testing based on DNA test results to family history assessment, e.g. in terms of perceived utility or perceived drawbacks, and how they compare genetic tests for multifactorial diseases to monogenic diseases. So far, most predictive genetic tests have been used to detect predispositions for single-gene diseases with a strong genetic influence, such as hereditary forms of cancer. For these monogenic diseases there are many data available on the ethical, legal and social issues of testing for and communication of genetic risk information to individuals and families. Important issues are, for example, the right (not) to know one’s genetic status (Sankar, 2003), freedom of choice, indicating that free and informed consent has to be guaranteed before a genetic test is carried out (Häberlin, 2005), potential genetic discrimination by insurance companies and employers (Low, King, Wilkie, 1998), and privacy issues concerning who has access to sensitive personal genetic information (Lilani, 2005). Yet, limited research has focused on the possible ethical, legal and social issues related to genetic testing for multifactorial diseases (van El & Cornel, 2011). These issues are expected to be less pronounced, because the aetiology is essentially different. Each gene variation might have an effect on more than one disease or phenotype, the inheritance of an identical pattern of gene variants is low, and there is a high environmental influence on the development of a disease (Janssens & Khoury, 2006). New issues may, however, arise. For example, Janssens and Khoury (2006) have expressed their concern about whether it is ethical to perform DNA tests with low predictive value. Other issues may be relevant for family history assessment. For example, Yoon et al. (2003) suggested that labelling a family at risk might induce feelings of blame, or induce anxiety associated with knowledge of affected relatives.

Moreover, there is still little evidence about the clinical utility of DNA testing and family history assessment for multifactorial diseases (Yoon, Scheuner & Khoury, 2003; Marteau et al., 2010), i.e. how likely is the test to significantly improve patient outcomes and motivate people to engage in preventative behaviour to reduce their disease risk (Haddow, Palomaki, 2003).

In this study we used type 2 diabetes as an example of a multifactorial disease, and focussed on both DNA test results and family history assessment to predict the risk for developing diabetes. Diabetes is an important health problem, which has an increasing prevalence due to physical inactivity and unhealthy diet (Mokdad et al., 2003). It has been shown that modest changes in lifestyle can delay or even prevent the onset of diabetes in high risk populations (Gillies et al., 2007). In addition to
behavioural factors, genetic factors also influence the development of type 2 diabetes (De Silva, Frayling, 2010), but with limited predictive value (van Hoek et al., 2008). In contrast, a familial risk of diabetes reflects a 2 to 6-fold increase in the odds of developing diabetes, depending on the number and closeness of affected relatives (Meigs, Cupples & Wilson, 2000; Valdez et al., 2007).

In order to be able to develop effective prevention programmes for multifactorial diseases, such as diabetes, based on genetic risk information, it is important to explore the opinions and expectations of potential users. Therefore the aim of this study was to assess lay perceptions of issues related to predictive genetic testing (DNA test results or family history assessment) in diabetes prevention.

Methods
To gain insight into lay perceptions of predictive testing for diabetes, focus group interviews were held. Focus groups aim to promote a variety of opinions and self-disclosures, i.e. group members influence each other by responding to comments made by others (Krueger & Casey, 2000). The Medical Ethics Committee of the VU University Medical Center approved the study protocol.

Participants and procedure
Eight focus group interviews were held with 45 individuals with (n=3), and without (n=1) a family history of diabetes, mixed groups of these two (n=2) and diabetes patients (n=2). Participants were recruited by means of an advertisement in a regional newspaper, inviting people between 35 and 70 years of age to participate in a group discussion about the prevention of diabetes. It was indicated that they would receive an incentive of €25 (gift card) for participation. No further information was provided. The responders were asked via the telephone whether they had diabetes, and subsequently whether they had a first-degree relative with diabetes. Additionally, one group with a family history of diabetes was recruited among participants in an earlier diabetes screening study in 1999 (Spijkerman et al., 2002). In that study, participants had been informed by letter that they did not have diabetes, but no further information about diabetes prevention was given. The diabetes patients were primarily recruited by means of an advertisement in a magazine distributed by the regional Diabetes Patient Organisation. All participants gave written informed consent before participation.

All the focus groups were facilitated by the same moderator (LH), and an assistant (MWP) made notes during each session. The focus groups lasted for approximately 90 minutes, and were held at the University Medical Center and a community facility between June and October 2008. Since the questions addressed in the focus groups required some knowledge about the concepts that were referred to, these were briefly explained at the start of the session using a PowerPoint presentation. The presentation included information about diabetes, such as causes and consequences, and information about the difference between diabetes risk assessment and a blood glucose test to indicate diabetes. Table 1 shows the information that was given about the DNA test and the family history assessment. It was emphasised that the aim of both tests is to inform people about an increased risk for developing diabetes and to provide them with preventive options to reduce the risk, i.e. a healthy diet and physical activity. No specific risk percentages were given.
Table 1 - Information given to participants during the focus group sessions concerning both genetic risk assessments

<table>
<thead>
<tr>
<th>DNA test</th>
<th>Family history assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Risk is increased by genetic predisposition</td>
<td>- Includes genetic predisposition, common behaviour, and shared environment</td>
</tr>
<tr>
<td>- Assessed by taking a sample of blood or saliva</td>
<td>- Risk increases with number and closeness of affected family members</td>
</tr>
<tr>
<td>- Test result does not depend on the occurrence of diabetes within the family</td>
<td>- Assessed by asking about the number and relatedness of affected family members</td>
</tr>
</tbody>
</table>

A semi-structured interview guide was used to assess perceptions. The participants were asked to indicate the possible advantages, disadvantages, and barriers related to both tests in diabetes prevention. Subsequently, the effect on individuals and their families (stigmatisation, discrimination, worry), and privacy issues when using genetic risk information in diabetes prevention were introduced if the participants did not bring these subjects up (see Additional file 1). In addition, two hypothetical vignettes were used to stimulate discussion. The vignettes described two males aged 55 years with a high risk of developing diabetes as a result of: a) two first-degree family members with diabetes (family history assessment), and b) a positive test result on a DNA test for diabetes (DNA test). The participants were asked to indicate which of these two men would be most or least motivated to adopt healthy behaviour, and why. Characteristics of the participants in the focus groups were obtained by means of a brief self-completed questionnaire (see Table 2).

Table 2 - Characteristics of the participants (n=45) in the focus groups (n=8)

<table>
<thead>
<tr>
<th>Group code</th>
<th>Average age in years (SD)</th>
<th>Total</th>
<th>Gender</th>
<th>Level of education*</th>
<th>Family history of diabetes**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>1NoFam, general population</td>
<td>52 (7)</td>
<td>6</td>
<td>5</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>1Fam, family history</td>
<td>55 (11)</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>2Fam, family history</td>
<td>46 (23)</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>3Fam, family history</td>
<td>66 (3)</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>1Mix, mixed group</td>
<td>63 (6)</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2Mix, mixed group</td>
<td>52 (11)</td>
<td>8</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1Pt, patients</td>
<td>57 (8)</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>2Pt, patients</td>
<td>55 (9)</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>56 (11)</td>
<td>45</td>
<td>34</td>
<td>7</td>
<td>20</td>
</tr>
</tbody>
</table>

* Low level of education refers to people who completed elementary school, lower secondary education or lower vocational education; Intermediate level of education refers to higher secondary education or intermediate vocational education; High level of education refers to university or higher vocational education

** 1st degree refers to having at least one or more first-degree family member(s) with diabetes; 2nd degree refers to having at least one or more second-degree family member(s) with diabetes

*** This person had an extensive family history of people with cardiovascular diseases, but no family members with diabetes.
Preparation of data and analyses
All focus group interviews were audio-taped and transcribed. Atlas-ti software was used for the analyses. First, codings were annotated to the data to structure and analyse the transcripts. The codings were then clustered to define sub-themes and main themes. On the basis of these themes, further analyses were performed to detect and check correspondence and differences between the themes, and to search for the most important messages transmitted by the participants. In order to ensure uniform coding, two authors (MP and LH) coded each transcript, and then discussed the codings until agreement was reached (Pope, Ziebland & Mays, 2000). In the results, quotations are used to illustrate the meanings that participants attached to a theme. Quotations were translated from Dutch and checked by a Dutch to English translator. Characteristics of participants are given in brackets, indicating the type of group (group number (1–3), general population of people with no family history, with a family history, mixed group or diabetes patients (NoFam, Fam, Mix, Pt), [family members with diabetes], gender (male, female), and age in years).

Results
The most important themes that emerged concerning predictive genetic testing for diabetes were: 1) identification of people at risk, 2) positive and negative health outcomes, 3) family issues, 4) informational privacy, and 5) autonomy. These themes and corresponding sub-themes are shown in Table 3. Perceived differences between testing based on DNA test results and family history assessment will be illustrated.

Identification of people at risk
Participants supported both the use of DNA tests and family history assessment in order to identify people who are at risk for diabetes:

If diabetes runs in your family, you don’t assume that you can get it [diabetes] too. If you have a predisposition for diabetes, because family members are affected, then I think it is a good idea to promote such a test [family history assessment], because not everyone will perceive the risk. (2Mix [nephew], male, 43 years)

You know it instantly [whether you’re at risk], by taking some blood. Do I have a predisposition, yes or no? Brief and effective; it’s [DNA test] a good test. (1NoFam, female, 53 years)

However, some believed diabetes was not severe enough for DNA testing:

Genetic testing is [more than for diabetes] for serious diseases like cystic fibrosis, cancer, kidney diseases. Having a family member with one of these diseases can be a reason to have a genetic test. (1Mix [grandmother], female, 69 years)

Participants indicated the advantage that taking a family history can be done quickly. Others questioned this assessment, because information about the presence of diabetes within the family is not always known, it is of no use for people without a family history, and there are other risk factors for diabetes apart from family history:

Having a family member with diabetes implies an increased risk, but it’s limited, information on unhealthy living and physical activity should also be included. (2Mix, female, 52 years)

Some participants emphasised that there should be a reason for risk assessment to be most effective, i.e. that people should be at increased risk before having their risk assessed.

I don’t think that people will think it concerns them. People will only respond to risk information when they have physical complaints and only then they will think “Now I have to be careful.”. (2Fam [mother], female, 65 years)
Positive and negative health outcomes

Motivation to adopt healthy behaviour

A positive outcome of predictive testing for diabetes that was mentioned was that it may motivate to engage in healthy behaviour. Although many participants experienced no difference between DNA test results and family history assessment in the effect on people’s motivation to adopt healthy behaviour, some participants believed that people would be more motivated to adopt risk-reducing behaviour after having had a DNA test. The underlying reason they gave was that to have a DNA test is a deliberate decision, since the first step towards risk reduction has already been taken by having such a test. In addition, this risk was seen as most certain:

The DNA test gives the hardest ‘push’ to live healthier. It will frighten me more than a test based on a family history, because it is the strongest evidence. (1Pt [father, 2 brothers], male, 51 years)

Others believed that familial risk information will motivate people more than a DNA test to adopt healthy behaviour, since these people see examples (of the consequences) of diabetes within their family. The contrary of enhancing motivation, however, was also mentioned. Some believed that a family history assessment will not increase the motivation of people with a familial risk, since these people will already be aware of the risk. It was also believed that for some people genetic risk information, based either on DNA or family history, could reduce motivation. Here an example of the adverse impact of family history assessment is given:

If people are informed that they have a risk, because their father had diabetes, and their grandfather, grandmother, and aunt too; it’s discouraging. They will accept the risk and think they can’t prevent diabetes, since it’s heritable. (2Pt, male, 56 years)

Furthermore, some participants mentioned that people could be falsely reassured if they are told that they have no genetic risk.

There is a chance that if people hear that they have no predisposition [for diabetes], that they will think “I can eat what I want, being fat is no problem, and being physically active, I prefer sitting behind the computer all day.”. (1NoFam, female, 57 years)

Psychological impact

Although some believed that knowing the disease risk could induce worry, most participants believed that diabetes risk assessment, even when genetic risk assessment is used, would cause very little or no psychological harm. Moreover the effect on raising risk awareness was emphasised:

Familial risk information will not necessarily lead to worry [about disease risk], but it can raise awareness about the risk. (1Fam [mother, brother], female, 64 years)

Others, however, thought that people might be worried for and about their children, when family history will be assessed:

A [familial] risk can be threatening. I’ve got a 14 year-old daughter. If she would be tested [family history assessment] and hears that she has an increased risk for diabetes, too, that would be a kind of “Damocles’ sword” hanging above her head. (1Pt [mother], female, 50 years)
<table>
<thead>
<tr>
<th>Themes</th>
<th>DNA test</th>
<th>Family history assessment</th>
<th>Both tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of people at risk</td>
<td>Diabetes is not severe enough</td>
<td>Can be assessed quickly</td>
<td>Can identify people at risk</td>
</tr>
<tr>
<td></td>
<td>Diabetes family history is unknown</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>No use for people with no family history</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>There are other risk factors for diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive and negative health outcomes</td>
<td>Motivation to engage in healthy behaviour</td>
<td>The test is a deliberate decision</td>
<td>Genetic risk cannot be influenced</td>
</tr>
<tr>
<td></td>
<td>Risk is certain</td>
<td></td>
<td>False reassurance</td>
</tr>
<tr>
<td>Psychological impact</td>
<td></td>
<td>People with a family history are</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>already aware of the risk</td>
<td></td>
</tr>
<tr>
<td>Family issues</td>
<td></td>
<td>Worry for and about children</td>
<td>Little or no psychological harm</td>
</tr>
<tr>
<td>Influence on family relationships</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Informing family members</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autonomy</td>
<td>Not performed unasked for</td>
<td>Can be offered to everyone</td>
<td>Risk tests should be voluntary</td>
</tr>
<tr>
<td></td>
<td>No tests on embryos or children</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Informative before having children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Informational privacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discrimination</td>
<td>Ownership of data</td>
<td>Private information</td>
<td></td>
</tr>
<tr>
<td>Sensitive data</td>
<td>No trust in relatively new test</td>
<td></td>
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</tbody>
</table>
Family issues

Impact on family relationships

Participants discussed the possible impact of familial risk information on family relations. On the one hand, some believed that it opens up discussions, and can be used to support each other to adopt healthy behaviour. For example, this woman (diabetes is prevalent in her husband’s family) said:

I think that when you’re aware of diabetes running in your family, it can help to talk about it with each other. I notice that the relationships in our family are not distorted. We talk about it [diabetes in the family] with each other. Not that we get anxious about it, but more to be supportive for other family members. It’s no longer a taboo. (1NoFam, female, 47 years)

On the other hand, some thought that it could also disturb family relationships if family members do not want to be informed about their diabetes risk:

My relatives will get anxious [if our family history is assessed]. [...] There are some who would rather not know that. So, I think that it can cause anxiety for some people. (1Mix, female, 57 years)

One participant mentioned that, if family members are identified to be at risk for diabetes, the patient with diabetes in the family might be blamed for putting the family at risk.

Informing family members

Some diabetes patients felt the obligation to disclose risk information to other members of the family:

I warned my brother and he visited his general practitioner. He had it, in a less severe way, nevertheless. So, I think it’s good to warn family members. (1Pt, [father, mother, brother, uncle, aunt], male, 63 years)

Another issue was that participants, diabetes patients in particular, did not only see the benefit of genetic risk information for themselves, but indicated that knowing their risk will also allow people to raise their children more consciously:

[DNA test results] can be used preventatively, if I know that my little son might be at risk I can be careful about his diet. (2Pt [father, grandmother], female, 46 years)

Autonomy

Issues that would affect autonomy were emphasised more when the DNA test was discussed. While most participants believed that DNA tests should never be performed (or even offered) unless asked for, no such condition was suggested with regard to a family history assessment. Moreover, only one participant mentioned that having a family history assessment should be voluntary. For this test it was even suggested that it should be actively offered to the entire population:

Why are we never approached for such a test [family history assessment]? Now, people themselves must request it, but they don’t go to the doctor for such a thing. [...] So, I think that the government should provide the test.

Moreover, one woman also mentioned that DNA tests should not be performed on embryos or children, possibly referring to the fact that they are not able to properly consent:

They might test [DNA test] young children, and they may even test embryos [...] there is a high risk that they will go further, and one thing may lead to another. (1Fam [mother], female, 58 years)

Another person mentioned that a DNA test could be informative before having children, suggesting that it can be used before conception to give an indication of a possible genetic predisposition for diabetes in the offspring, and thus as a means to reproductive autonomy:

For example, for young people who would like to have children, and diabetes is very common in their family. I think it’s a good thing that they can have a genetic test. (2Fam [mother], female, 65 years)
Informational privacy

Discrimination

Only one participant indicated that a consequence of a genetic test might be discrimination on the basis of the test results:

> How will the [family history] information be used? Now it’s voluntary to provide the information, but these tests may be obligatory in the future. Then you have the risk that people will be unable to get insurance; life insurance and that sort of thing. (3Fam, female, 61 years)

This woman therefore argued that family information should be protected from third parties. Subsequently this belief was picked up and supported by other participants.

Sensitive data

Two participants worried about the safety of the data-storage of DNA test results (ownership of data):

> I can imagine that your whole genetic profile will then be public…I think it should be stored somewhere safe. When it’s stored with the general practitioner, there is at least some privacy. (2Mix, female, 49 years)

In addition, some did not trust DNA test results, because it is a relatively new test:

> If they want to prove that someone is at risk, they can manipulate the results. I don’t know how, since it’s quite new, quite precarious. (1Mix [grandmother], female, 69 years)

With regard to a family history assessment, a diabetes patient indicated that discussing the presence of diabetes in the family can be considered as private information:

> You can get a problem with privacy. When you say my brother has diabetes and my sister has diabetes, and she’s too fat, then you say things about your family that are personal, and some people might have a problem with that. (1Pt, male, 51 years)

Discussion

This study provides an overview of perceived issues that may arise among the public when predictive tests for diabetes, based either on DNA test results or family history assessment, are introduced. Although it was believed that both tests could be used to identify people at risk for diabetes, also drawbacks were mentioned. With regard to the motivational impact, participants perceived differences in the underlying mechanism between a DNA test and family history assessment and both arguments for a positive and a negative impact were mentioned. Respect for autonomy of individuals was emphasized more with regard to DNA testing than family history assessment. Psychological harm, and discrimination, privacy were only mentioned by some participants.

Participants had high expectations about the predictive value of DNA test results. However, until now genetic variants have a marginal improvement in predictive ability above traditional risk factors for diabetes (Dupuis & O’Donnell, 2007; van Hoek et al., 2008). Also, some participants had an unrealistic perception of the possible uses of DNA test results, e.g. they believed that the test result can be manipulated, or believed that information about a genetic risk for diabetes could be used to make a reproductive choice. Earlier studies have shown that many people know little about genetic technology, and have unclear notions about the benefit of genetic testing for multifactorial diseases, but are interested in having these tests (Scheuner, Sieverding & Shekelle, 2008). For example, it has been shown that non-diabetic patients were more likely to request a genetic test to assess future diabetes risk than physicians were to recommend it, and also had higher beliefs that it will motivate people to adopt healthy behaviour (Grant et al., 2009).

Although the participants believed that both assessments could be used to identify high-risk individuals, some thought that diabetes was not severe enough for a DNA test. People in general perceive diabetes as less threatening than other common diseases such as cancer or heart disease (Wang et al., 2009). Other participants in this study questioned the accuracy and reliability of family
history reports, since the presence of diabetes in the family is not always known. An under-reporting of the family history of common chronic diseases for parents and siblings has, indeed, been found in several studies (Qureshi et al., 2009).

Participants gave several underlying reasons for the motivational impact of either a DNA test or a family history assessment, and these differed between both tests. Some believed that people would get more motivated after receiving DNA test results, since a first step has already been made by taking such a test and the test result is considered more certain as compared with a family history test. The perception that a diabetes risk based on DNA test results is more concretely defined and based on evidence has previously been identified among people at risk for getting diabetes (Markowitz, 2011). With regard to family history assessment, participants in this study mentioned that having examples of diabetes patients within the family will motivate people to engage in preventive behaviour. Research has shown that the perceived difference in impact of genetically-based risk information or family history-based risk information on motivation (or intention) to engage in recommended health behaviour is inconsistent (LaRusse et al., 2005; Hicken & Tucker, 2002). Only few studies evaluated the impact of genetic risk information on motivation (or intention) to adopt healthy behaviour and report conflicting effects on actual behaviour change (Marteau et al., 2010; Pijl et al., 2009). Some participants in this study believed that genetic risk information could lead to fatalism, i.e. people being less motivated to change their behaviour. However, there is no evidence for such an effect (Collins, Wright & Marteau, 2010).

In the present study, no prominent distinctions were found between the opinions of people with a family history of diabetes, people without a family history of diabetes, and diabetes patients. It seemed, however, that diabetes patients perceived more benefits of genetic risk information for their children compared to the other participants, and also felt obliged to disclose risk information to other members of the family. Also, participants mentioned that familial risk information can support family members to jointly adopt preventative behaviour. It has indeed been shown that healthy eating habits may be easier to achieve if the entire family is involved in promoting healthy living (Haga, 2009).

Participants placed more emphasis on autonomy with regard to the unrequested offer of a DNA-test, as they do not want to be offered such a test unless asked for, whereas this was not brought up as a condition with regard to a family history assessment. Moreover, with regard to a family history assessment, only one person indicated that it will be important to be able to accept or reject the test, thus stressing that participation should be voluntary. In general, we conclude that being offered a family history test was far less readily considered as a potential threat to autonomy than the offer of a DNA-test. Therefore, the former type of assessment might be more ready for a public health setting, as has been suggested by others (Yoon, Scheuner & Khoury, 2003, Claassen et al., 2010). Khoury (2008) indicated that with the output of the human genome project there has been a shift from gene-assessment for individuals or families (monogenic disorders) to a public health approach (multifactorial diseases). While genetics has traditionally focused on a non-directive way of communicating information to diagnose and manage rare conditions for which there might not be effective interventions (Khoury, 1996). Type 2 diabetes is very common and people can reduce their risk for the disease by adopting healthy behaviour. This may justify a public health approach, i.e. offering a family history risk assessment and health messages to people who did not ask for it. Indeed, the issues mentioned by the participants in the present study are comparable to non-genetic risk assessment and related to issues that are specifically relevant in public health.

In this explorative study, issues related to monogenic diseases, such as discrimination, privacy, and psychological impact, were mentioned by only few participants; for example, the possibility of discrimination by insurance company or employer based on genetic test results, privacy or induced worry. A reason for this might be that the views of people, as far as they are familiar with genetic risks, may be influenced by discussions about genetic testing for monogenic disorders. It is,
however, expected that issues concerning, for example, diabetes risk worry and discrimination, might be less applicable for multifactorial diseases than for monogenic disorders (van El & Cornel, 2011), because of the preventive options that are available. In a review on the delivery of genomic medicine for common chronic diseases it was concluded that there are no well-documented cases of health insurers either asking for or using genetic test results for discriminative purposes (Scheuner, Sieverding & Shekelle, 2008). However, even with existing legislation the fear of genetic discrimination with regard to testing for adult-onset diseases has not greatly reduced (Hall & Rich, 2000).

The findings presented in this paper are not intended to be generalised, rather they give an overview of possible issues related to genetic risk assessment for diabetes as perceived by participants. It can be expected that people who are more interested in health or who are in need of money are more prone to have responded on the study invitation. Besides, more women than men participated in this study, which may have influenced the findings as it has been shown that women, in general, are less favourable towards genetic testing than men (Sanderson et al., 2004; Henneman, Timmermans & van der Wal, 2006). A drawback in the discussions may have been that the current low predictive value of DNA test results was not explained to the participants, since this information was considered to be too complex. Moreover, because of the semi-structured interview guide, the issues that were raised by the participants were also more or less the issues that were addressed during the interviews. Monogenic sub-types of diabetes, such as Maturity Onset Diabetes of the young (MODY), were not considered. The predictive value of genetic testing for these rare sub-types is clearly higher.

Conclusions
The results of this study indicate that individuals believe in the ability of predictive genetic testing to identify people at diabetic risk and enhancing healthy behaviour, but also points to consider before using these tests were identified. With regard to DNA tests these are, e.g. an unrealistic perception of the test results, and a perceived threat for autonomy. It is therefore important to educate people about DNA tests for multifactorial diseases and to inform possible future consumers about the low predictive value, as was also recommended by the European Society of Human Genetics (van El & Cornel, 2011). With regard to the family history assessment, participants indicated drawbacks in identifying people at risk and a possible negative influence on family relations. The results further show that issues that are important in testing for monogenic diseases, such as privacy, discrimination, and psychological harm, are mentioned by some participants with regard to this multifactorial disease. Nevertheless, new issues will most likely become important, which are more related to a public health setting and non-genetic risk information.
Chapter 4

How does a simple enquiry compare to a detailed family history questionnaire to identify familial risk?

Abstract

Purpose
To examine whether a simple enquiry can provide similar family history information compared with a detailed questionnaire for coronary heart disease or diabetes.

Methods
Data from two randomized controlled trials were extracted that assess the clinical value of using family history information for either coronary heart disease (ISRCTN17943542) or diabetes risk assessment (NTR1938) in a community-based population. Outcome measures were percentage agreement, sensitivity, and specificity of self-reported family history for coronary heart disease and diabetes by means of a simple enquiry, when compared with a detailed questionnaire.

Results
Agreement between both family history tools was 76.8% for first-degree relatives with coronary heart disease, and 89.2% and 87.6% for first- and second-degree relatives with diabetes, respectively. The sensitivity was 44.2% for first-degree relatives with coronary heart disease, 81.9% for first-degree relatives with diabetes, and 35.4% for second-degree relatives with diabetes. Specificity was 89.3%, 97.0%, and 94.5%, respectively.

Conclusion
Compared with a detailed questionnaire, the simple enquiry correctly identified the majority of individuals classified as having no significant family history but missed a significant proportion of individuals with positive family history. Incorrect classification of family history, in particular the high false-negative rate, has implications on the utility of a simple enquiry in identifying familial risk in clinical practice.
A positive family history is an independent risk factor for many common chronic diseases, such as cancer, cardiovascular diseases, and diabetes (Qureshi et al., 2009a) family history reflects shared genetic, behavioural, and environmental risk factors. Family history is seen as a useful tool to select high-risk groups and may be used as a tool to raise awareness and target disease prevention in public health and primary care (Claassen et al., 2010; Yoon et al., 2003). Although reporting of the disease family history can be inaccurate, many people have a family history of common diseases (Qureshi et al., 2009b). Family history assessments are part of the national professional guidelines for many common diseases (Wood et al., 2005), such as coronary heart disease (CHD) and diabetes. However, family history is not systematically integrated into risk assessment of clinicians for these diseases in Europe or the United States (Sheridan, Pignone & Mulrow, 2003; Reid et al., 2009), and there is, as yet, no standard method for taking family history.

Comprehensive family history assessment can be achieved, e.g., by drawing a pedigree or family tree or by presenting questions in a tabular form (Qureshi et al., 2009b). A detailed family history assessment is, however, time-consuming, and nonspecialist clinicians, such as primary care practitioners, often have little time per patient. Familial risks, therefore, often go unrecognized, and avoidable risk is recognized too late (Rich et al., 2004; Suther & Goodson, 2003). An alternative approach would be to minimize the detailed assessment to a simple enquiry as first screen for high risk without compromising the sensitivity of the familial risk assessment. The question is, however, whether a simple enquiry will have similar performance to a detailed family history assessment to identify significant family history of CHD and diabetes.

There is a great variation in methods used to collect family history across common diseases (Qureshi et al., 2009a), although little is known about how the accuracy of family history is affected by the method of collection, e.g., paper based, web based, or in person and by simple enquiry or detailed questionnaire (Berg et al., 2009). Measures that have been used to evaluate adequacy of family history assessments include the percentage agreement, sensitivity, and specificity (Qureshi et al., 2009b). Earlier studies indicate that there was reasonable agreement between self-completed family history questionnaires (FHQs) to identify familial cancer risk and measures of optimal approach (e.g., a detailed family history by a trained specialist) or criterion standard (e.g., family history recorded in relatives’ charts) (Qureshi et al., 2009b). Currently, there are no studies comparing simple enquiry to a detailed assessment for common diseases, such as CHD or diabetes. The aim of this study is, therefore, to compare a simple enquiry of family history with a detailed assessment, which is considered to be the “optimal” or “best pragmatic” approach, rather than a criterion standard.

Materials and Methods

In this study, assessing CHD or diabetic family history by means of a simple enquiry and a detailed questionnaire were compared. For this comparison, we conducted subanalyses within two cohorts derived from randomized trials that were conducted in two European countries with comparable health care systems. The first trial, the ADDFAM study, was conducted in the United Kingdom and assessed CHD family history. The second trial, the PreDiCT study, was conducted in the Netherlands and assessed diabetes family history. Both studies were approved by the Institutional Medical Research Ethics Committees, and informed consent of all participants was obtained.

Study design

Coronary heart disease

Subjects were participants of the ADDFAM study (ISRCTN17943542) that assessed the clinical value of incorporating systematic family history information into CHD risk assessment in primary care (Qureshi et al., 2009c). Patients between 30 and 65 years of age, who were offered cardiovascular disease risk assessment and referred for a cholesterol test as part of their normal care, either at their
doctor’s initiative or at their own request, were invited to participate. In line with the Joint British Societies guidelines (Wood, 2005), a positive family history was defined as having at least one first-degree relative (mother, father, and sibling) with a CHD and an early age of onset (male < 55 years; female < 65 years). The FHQs that were used in this trial were as follows:

1. Simple enquiry: As part of the study questionnaire, the CHD family history was assessed by a simple enquiry: “Known family history of heart disease. Please tick box ONLY if you know the following is true. Either my father, or one or more of my brothers, has had heart disease before the age of 55 years/Either my mother, or one or more of my sisters, has had heart disease before the age of 65 years.”

2. Detailed assessment: Detailed CHD family history information was collected by a CHD focused validated FHQ, an instrument that was shown to be effective to identify those with a family history of premature CHD and had acceptable face validity (Qureshi et al., 2005; Qureshi, 2006). Participants completed the FHQ before a risk assessment consultation with a primary care provider. The FHQ collects relevant medical history, medical information about close relatives (mother, father, siblings, children, and grandparents), information on more distant relatives, and information on age of onset of the diseases in a tabulated form. The FHQ enquired about heart disease, i.e., angina, heart attack, myocardial infarction, heart failure, blocked artery, and coronary artery disease. The detailed family history assessment was assessed 6 months before the simple enquiry.

**Diabetes**

Subjects for the diabetic family history family history were participants of the PreDiCT study (NTR1938) that assessed the impact of diabetic familial risk information on self-reported risk-reducing behaviour, by using a tailored web-based tool. Participants included were healthy people from the general population aged 35–65 years with an elevated risk for diabetes because of a body mass index ≥ 25 kg/m², recruited among an online panel maintained by an independent research agency. In line with a validated risk assessment tool for diabetes, the Diabetes Risk Test (Alsema, 2008), a positive family history was defined as having at least one first-degree relative (mother, father, sibling, and children) with diabetes. As having a diabetic family history was an inclusion criterion in this trial, there was an oversampling of people with a family history. There were two ways of assessing diabetic family history in this trial:

1. Simple enquiry: As part of an online version of the Diabetes Risk Test (Alsema, 2008), diabetic family history was assessed by a single-item: "Does diabetes occur within your family? 1) no; 2) yes, with my grandfather, grandmother, uncle, aunt, cousin; 3) yes, with my father, mother, brother, sister, or child."

2. Detailed assessment: Detailed family history was collected by means of a web-based systematic assessment. First, participants had to indicate the number of children and siblings, and the number of both paternal or maternal aunts and uncles. Subsequently, they could indicate for each first-degree relative and second-degree relative and whether these relatives had been diagnosed with diabetes or whether they did not know this. The detailed family history assessment was assessed 3 months after the simple enquiry.

**Analyses**

The first metric assessed was the percentage agreement between both methods of family history collection, defined as the proportion of individuals identified by both approaches with a positive family history and with no significant family history among all participants, presented as a percentage. The discriminatory accuracy of the simple enquiry compared with the detailed assessment was assessed using metrics of sensitivity and specificity. Sensitivity was defined as the percentage of individuals who reported a positive family history based on the simple enquiry among all those who had a positive
family history based on the detailed assessment and similarly for negative family history reports to calculate specificity. The complimentary metrics of false-negative rate and false-positive rate were also presented. The false-negative rate is 1-sensitivity and represents those with a positive family history on detailed assessment that were missed by simple enquiry, whereas the false-positive rate is 1-specificity and indicates those classified as having a positive family history on simple enquiry but no significant family history on detailed assessment.

Results

Characteristics of the study population
Table 1 lists the characteristics of participants who completed the first family history assessment (this is the detailed assessment for the subgroup of people participating in the ADDFAM trial and the simple enquiry in the PreDiCT trial) and the characteristics of the respondents on the second family history assessment. Nonrespondents to the follow-up simple enquiry in the ADDFAM trial were significantly younger ($P < 0.001$) and more likely to be of non-white origin ($P < 0.05$). No further differences between respondents and nonrespondents on the second assessment were found in both trials.

Table 1 - Characteristics of respondents who completed the first and second family history assessment

<table>
<thead>
<tr>
<th></th>
<th>ADDFAM Respondents completing detailed assessment: baseline (n=365)</th>
<th>Respondents completing simple enquiry: 6-month follow-up (n=310)$^b$</th>
<th>PreDiCT Respondents completing simple enquiry: baseline (n=584)</th>
<th>Respondents completing detailed assessment: 3-month follow-up (n=557)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, % female</td>
<td>52.3</td>
<td>54.5</td>
<td>48.5</td>
<td>49.4</td>
</tr>
<tr>
<td>Age (yr), mean ± SD</td>
<td>50.3 ± 9.4</td>
<td>51.4 ± 9.1</td>
<td>53.4 ± 5.6</td>
<td>53.3 ± 5.6</td>
</tr>
<tr>
<td>Ethnicity, % white$^c$</td>
<td>94.0</td>
<td>95.2</td>
<td>97.4</td>
<td>97.3</td>
</tr>
<tr>
<td>Education, % higher education$^d$</td>
<td>61.9</td>
<td>63.9</td>
<td>23.1</td>
<td>23.2</td>
</tr>
</tbody>
</table>

$^a$For ADDFAM and PreDiCT trial, the response rate for the first assessment was 98% and 90%, respectively.  
$^b$For ADDFAM and PreDiCT trial, the response rate for the second assessment was 85% and 95%, respectively.  
$^c$Participants of the ADDFAM study were asked how they would describe their ethnic group, and participants of the PreDiCT study were asked to indicate their country of birth.  
$^d$Higher education refers to higher secondary education, intermediate vocational education, higher vocational education, or university.

Comparison of simple enquiry with detailed assessment
Table 2 presents the percentage agreement of family history obtained from a simple enquiry compared with a detailed assessment for CHD and diabetes. For first-degree relatives with CHD, the agreement was 76.8% (238/310). Agreement was 89.2% (497/ 557) and 87.6% (488/557) for first- and second-degree relatives with diabetes, respectively. Sensitivity was 44.2% (38/86) for first-degree relatives with CHD, 81.9% (236/288) for first-degree relatives with diabetes, and 35.4% (23/65) for second-degree relatives with diabetes. False-negative rates on the single enquiry were 55.8%, 18.1%, and 64.6%, respectively. Specificity was 89.3% (200/224) for first-degree relatives with CHD, 97.0% (261/269) for first-degree relatives with diabetes, and 94.5% (465/492) for second-degree relatives with diabetes. False-positive rates on the single enquiry were 10.7%, 3.0%, and 5.5%, respectively.
Table 2 - Percentage agreement, sensitivity, and specificity (with 95% confidence interval) of a simple enquiry of CHD or diabetes compared with a detailed assessment

<table>
<thead>
<tr>
<th>Assessment of</th>
<th>Agreement (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD first-degree</td>
<td>76.8 (72.1–81.5)</td>
<td>44.2 (34.2–54.7)</td>
<td>89.3 (84.6–92.7)</td>
</tr>
<tr>
<td>Diabetes first-degree</td>
<td>89.2 (86.6–91.8)</td>
<td>81.9 (77.1–86.0)</td>
<td>97.0 (94.2–98.5)</td>
</tr>
<tr>
<td>Diabetes second-degree</td>
<td>87.6 (84.9–90.3)</td>
<td>35.4 (24.9–47.5)</td>
<td>94.5 (92.1–96.2)</td>
</tr>
</tbody>
</table>

CI, confidence interval; CHD, coronary heart disease.

Discussion

There was more than 75% agreement between the simple enquiry and a detailed questionnaire for assessing a family history of CHD or diabetes; however, the simple enquiry can give high false-negative rates. In comparison with the detailed assessment, the simple enquiry correctly identified a greater proportion of individuals with no significant family history than individuals who had a positive family history, i.e., higher specificity than sensitivity. When a simple family history enquiry is used as an initial screening tool, sensitivity is more important than specificity, as we do not want to miss individuals who have a positive family history (i.e., achieve low false-negative rate) (Qureshi et al., 2009a). In a nonspecialist setting, it may be more acceptable for the simple enquiry to incorrectly identify some individuals with positive family histories. These cases will be excluded on a more detailed family history assessment, but the false negatives will be lost to follow-up. Taking this into account, the simple enquiry underperformed for its expected role.

Comparing the different conditions, the discriminatory accuracy for first-degree relatives was better for diabetes than for CHD simple enquiry. The ADDFAM and PreDiCT studies were not designed to assess the accuracy of family history collection against a criterion standard (e.g., recall by relatives, relatives' medical records, and death certificates) but designed to compare two approaches to assess family history. However, benchmarking the sensitivity against studies designed to assess criterion standard provides an indirect comparison. The Framingham Offspring Study, for example, shows higher sensitivity for paternal history reports of a heart attack below the age of 55 years (74%) but lower sensitivity for diabetes (56%) (Murabito et al., 2004), compared with this study. Similarly, the NHLBI Family Heart Study, where age of onset was not identified, shows much greater sensitivity for CHD (85%) but similar levels for diabetes (87%) (Bensen et al., 1999). The findings for CHD in this study might be explained by the number of possible diagnoses that individuals have to consider when recalling relatives’ heart disease diagnosis, compared with only one non-specific disease diagnosis for diabetes. Also, recall error of the age of onset may complicate the accuracy of CHD family history reports (Toren et al., 2007). Adding more details to a single question might make it harder for respondents to understand (Fowler, 1992). A possible solution is thus to break the single-question enquiry into a series of simple questions.

Some methodological drawbacks of this study need to be addressed. Although both samples used a community-based population, recruitment and assessment were different. The ADDFAM trial was performed in a primary care setting using paper-based questionnaires, whereas the PreDiCT trial was done in a public health setting using web-based questionnaires. Moreover, both trials had a different temporal sequence, where ADDFAM started with the detailed assessment and the PreDiCT trial first assessed the simple enquiry. There may have been better recall in the second assessment, and CHD simple enquiry would have performed better; however, the long time period between assessments may have limited this effect. The differences, however, will not obscure the conclusions, as the aim of this article is not to make a comparison between the CHD and diabetes samples but to examine whether a simple enquiry can provide similar family history information compared with a
detailed questionnaire. Previous studies indicate that better educated individuals are more likely to complete family history collection (Qureshi et al., 2009a). This selection bias was also noted in the ADDFAM trial but not in the PreDiCT trial.

Accurate family history reporting is essential if family history is used as a tool to target disease prevention in public health and primary care (Claassen et al., 2010; Yoon et al., 2003). Type of disease, the degree of family members, and the phrasing and details of the question could be important factors for an accurate family history assessment. The implication of the high rate of false-negative family history reports when based on a single enquiry is that a significant proportion of people at familial risk for CHD or diabetes will be missed. When assessing family history, either as part of a multifactorial risk assessment or to identify the single risk factor, the discriminatory accuracy of the simple enquiry needs to be taken into account when interpreting the findings.
Chapter 5

Impact of communicating familial risk of diabetes on illness perceptions and self-reported behavioural outcomes: A randomized controlled trial

Abstract

Objective
To assess the potential effectiveness of communicating familial risk of diabetes on illness perceptions and self-reported behavioural outcomes.

Research design and methods
Individuals with a family history of diabetes were randomized to receive risk information based on familial and general risk factors (n = 59) or general risk factors alone (n = 59). Outcomes were assessed using questionnaires at baseline, 1 week, and 3 months.

Results
Compared with individuals receiving general risk information, those receiving familial risk information perceived heredity to be a more important cause of diabetes (P = 0.01) at 1-week follow-up, perceived greater control over preventing diabetes (P = 0.05), and reported having eaten more healthily (P = 0.01) after 3 months. Behavioural intentions did not differ between the groups.

Conclusions
Communicating familial risk increased personal control and, thus, did not result in fatalism. Although the intervention did not influence intentions to change behaviour, there was some evidence to suggest it increases healthy behaviour.
Prevention of type 2 diabetes is especially important for people with a positive family history of diabetes, because family history is one of the strongest risk factors (Valdez, et al., 2007). Individuals with a positive family history have difficulty understanding the causes of diabetes (Pijl et al., 2009), underestimate their risk (Adriaanse et al., 2003), and are less likely than those without a family history to believe that diabetes is preventable (Harwell et al., 2001). Family history information might be used to raise awareness of individual risk and thereby positively influence preventive behaviours to reduce the risk (Yoon, Scheuner & Khoury, 2003). However, the belief that diabetes is determined mainly by genetic predisposition may prevent individuals from engaging in risk-reducing behaviour as a result of fatalism (Pijl et al., 2009; Marteau & Lerman, 2001; Shiloh et al., 2002). The aim of this study was to assess the potential effectiveness of communicating familial risk of diabetes on illness perceptions and self-reported behavioural outcomes.

Research design and methods
In 2007, a randomized trial was conducted among individuals who were at risk for diabetes and had participated in a diabetes screening program 5 years earlier (Spijkerman et al., 2002). People (n = 233; age ≤ 75 years) with self-reported family history (one or more first-degree relatives) and the highest diabetes risk scores on a symptom-risk questionnaire (Spijkerman et al., 2002) were invited. Exclusion criteria were as follows: being diagnosed with diabetes and not understanding Dutch. The VU University Medical Center Ethical Committee approved the protocol.

Participants were randomly assigned by computerized and concealed block randomization to receive risk information based on familial risk and general risk factors (intervention group) or based on general risk factors alone (control group) during a personal consultation with a researcher (M.P.) at a Diabetes Research Centre. Five-year diabetes risk was estimated using a validated Diabetes Risk Test (Alssema et al., 2008) and communicated to each participant using a graphical bar chart. In the intervention group alone, a family tree was constructed, familial risk was discussed, and the multifactorial character of diabetes was explained, indicating the nature of the risk in the bar chart. All participants received information on diabetes, including preventive measures.

Sample size calculation was performed on intention-to-change behaviour (diet, physical activity, and diabetes testing). With a mean ± SD difference of 2.00 ± 1.6 in the intervention group compared with 1.00 in the control group for 80% power (P < 0.05), 41 individuals per group were needed. Outcome measures were assessed at baseline and at 1-week and 3-month follow-up and included behavioural intentions, self-reported behaviours, illness perceptions (causal beliefs, perceived consequences of diabetes, and personal control over preventing diabetes), perceived susceptibility to diabetes, worry about diabetes risk, and psychological well-being (Table 1). The effect of the intervention on outcome measures was investigated using ANCOVA for follow-up measurements with baseline measures as covariates.
Results
Of 233 participants invited, 187 (80%) responded to the invitation and 118 (51%) agreed to participate and were randomly assigned (n = 59 in each group) (see Figure 1). Ten individuals did not receive the consultation and were excluded. Participants were Dutch Caucasian. Mean ± SD age at baseline was 67.1 ± 5.3 years; 43% were men; 5% completed higher vocational training or university; mean ± SD BMI was 28.3 ± 4.3 kg/m²; and 52 and 31% reported having high blood pressure and high cholesterol, respectively. The median number of first-degree relatives was 1 (range 1–7). At baseline, there were no significant differences in participant characteristics between the groups.

For all variables used in our analyses, 10 and 18% of the data were missing at 1-week and 3-month follow-up, respectively. There were no differences at baseline in outcome variables between participants with missing data at follow-up and those for whom complete data were obtained. The intervention had no effect on behavioural intentions (Table 1). People who had received the...
intervention reported having eaten more healthily than those in the control group in the previous 3 months (P = 0.01). Being more physically active showed a marginal significant difference (P = 0.08). There was a significant increase in perceiving heredity as a cause of diabetes in the intervention group (P < 0.01) compared with the control group at 1 week. Perceived consequences of diabetes increased in the control group and slightly decreased in the intervention group at 1 week (P = 0.02). The intervention group perceived greater personal control over preventing diabetes than the control group at the 3-month follow-up (P = 0.03), an effect that was of borderline significance after 1 week (P = 0.06). Communicating familial risk information did not affect perceived susceptibility, worry, or psychological well-being.

Conclusions
Our study shows that an intervention in which familial risk of diabetes is communicated did not result in fatalism and actually led to increased perceived control over preventing diabetes. Although at 1 week both groups had increased their intentions to change their health behaviour, participants receiving familial risk information reported having eaten more healthily 3 months after the consultation. A possible explanation might be that familial risk information, being more novel and more personally relevant, was better retained. In line with a recent cross-sectional study (Qureshi, Kai, 2008), our study suggests that informing people of their risk of diabetes attributable to their family history could increase their engagement in risk-reducing behaviours. In addition, our results and others (Pierce, et al., 2000) show that discussing familial diabetes risk does not adversely affect psychological well-being.

Although an earlier theory-based behavioural intervention aimed at increasing physical activity of people at familial risk of diabetes was no more effective than information given in an advice leaflet (Kinmonth et al., 2008), it is promising that some positive results of communicating familial risk in our minimal design were found. Both groups received a personal consultation differing only in the type of risk information (familial vs. general risk information) that was given. This study, though small, is one of the first to examine this issue. Because the measures of behaviour and personal control were based on single-items and the measures of behaviour were self-reported, the effects of the intervention must be considered tentative. Additionally, participants were recruited from a previous diabetes screening study, thereby limiting generalization.

More robust trials are needed to confirm these findings, using objective measures of health-related behaviour in larger samples. More research is also needed in the area of risk communication and fatalistic attitudes, particularly with the introduction of more genetic information available in addition to family history.
Table 1 – Outcomes of the ANCOVA analyses at baseline and at 1-week and 3-month follow-up*  

<table>
<thead>
<tr>
<th>Behavioural intentions (scale 1 – 7)</th>
<th>Intervention group</th>
<th>1-week mean (sd)</th>
<th>3-month mean (sd)</th>
<th>Control group</th>
<th>1-week mean (sd)</th>
<th>3-month mean (sd)</th>
<th>p-value baseline and 1-week</th>
<th>p-value baseline and 3-month</th>
</tr>
</thead>
<tbody>
<tr>
<td>healthy diet</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>test for diabetes</td>
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<tr>
<td>Health behaviour (scale 1 – 7)</td>
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<tr>
<td>healthy diet</td>
<td>3.6 (2.2)</td>
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<td>4.0 (2.2)</td>
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<td></td>
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<td>physical activity</td>
<td>3.9 (2.1)</td>
<td></td>
<td>4.4 (2.2)</td>
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<td></td>
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<tr>
<td>Causal beliefs (scale 1 – 5)</td>
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<tr>
<td>heredity</td>
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<td>4.0 (0.6)</td>
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<tr>
<td>lifestyle</td>
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<td>4.1 (0.6)</td>
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<td>Perceived consequences (scale 1 – 5)</td>
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</tr>
<tr>
<td>personal control (scale 1 – 5)</td>
<td>3.7 (0.8)</td>
<td></td>
<td>4.0 (0.6)</td>
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<tr>
<td>Perceived susceptibility (scale 1 – 7)</td>
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<td></td>
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<tr>
<td>diabetes risk worry (scale 1 – 7)</td>
<td>2.7 (1.4)</td>
<td></td>
<td>3.0 (1.5)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Psychological well-being (scale 1 – 5)</td>
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<tr>
<td>PANAS positive</td>
<td>3.1 (0.7)</td>
<td></td>
<td>3.2 (0.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANAS negative</td>
<td>1.7 (0.6)</td>
<td></td>
<td>1.6 (0.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STAI</td>
<td>1.9 (0.6)</td>
<td></td>
<td>1.9 (0.6)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

* Unadjusted analyses are presented, since predefined variables did not affect the outcome of the trial.
† Baseline measures were unavailable for one person in the control group.
‡ Intention to eat more healthily (at least 2 pieces of fruit and 200 grams of vegetables a day and low saturated fat nutrition) or to increase physical activity (at least 30 minutes of moderate activity at least 5 days a week) within the following month were assessed (completely applicable to me (1) – completely inapplicable to me (7)).
§ Participants were asked to indicate whether they had changed their behaviour in the previous 3 months (completely disagree (1) – completely agree (7)).
¶ Participants were asked to indicate the extent to which they believed that a given cause could be a cause of diabetes (definitely not (1) – definitely (5)), based on the revised form of the Illness Perceptions Questionnaire. A heredity sub-scale was comprised of two items: "handedness, diabetes runs in the family" and "predisposition" (a = .62). A lifestyle sub-scale was comprised of three items: "unhealthy diet or eating habit", "lack of physical activity", and "being overweight" (a = .75).
** Perceived consequences was assessed using a 6-item scale (a = .80), based on the revised form of the Illness Perception Questionnaire.
†† Perceived susceptibility was assessed using the mean score of three items (a = .88): "How likely do you think it is that you will get diabetes within the next 5 years?" (very likely (1) – very unlikely (7)), "Based on your feelings, how big is the chance of you getting diabetes within the next 5 years?" (very low (1) – very high (7)), and "In your opinion, what is the chance of you getting diabetes compared to an average man/woman your age?" (a lot lower (1) – a lot higher (7)).
Chapter 6

Using web-based familial risk information for diabetes prevention: a randomized controlled trial

Wijdenes-Pijl M, Henneman L, Qureshi N, Kostense PJ, Cornel MC, Timmermans DRM. Using web-based familial risk information for diabetes prevention: a randomized controlled trial, *submitted*
Abstract
Objective
To determine if diabetic familial risk information by using a web-based tool leads to improved self-reported risk-reducing behaviour among individuals with a diabetic family history, without causing false reassurance among those without a family history.
Research design
An online sample of 1,174 healthy adults aged 35-65 years with a BMI ≥ 25 was randomized (NTR1938). Both arms received general tailored diabetes prevention information, whilst the intervention arm also received familial risk information. Separate analysis was performed for four groups (family history group: 286 control versus 288 intervention; no family history: 269 versus 266).
Primary outcomes were self-reported behavioural outcomes: fat intake, physical activity, and attitudes towards diabetes testing. Secondary outcomes were illness and risk perceptions.
Results
For individuals at familial risk there was no overall intervention effect on risk-reducing behaviour after three months, except for a decrease in self-reported saturated fat intake among low-educated individuals (Beta (\(\beta\)) -1.01, 95% CI -2.01 to 0.00). Familial risk information resulted in a decrease of diabetes risk worries (\(b\) -0.21, -0.40 to -0.03). For individuals without family history no effect was found on risk-reducing behaviour and perceived risk.
Conclusions
Web-based familial risk information appeared to reduce worry related to diabetes risk and decreased saturated fat intake of those at greatest need of preventative care. However, the intervention was not effective for the total study population on improving risk-reducing behaviour. The emphasis on familial risk does not seem to result in false reassurance among individuals without family history.
Type 2 diabetes is increasingly common due to lifestyle factors (physical inactivity, unhealthy diet) (Mokdad et al., 2003). There is convincing evidence from intervention studies in high-risk groups that weight loss, healthy diet and physical activity can delay or even prevent the onset of diabetes (Gillies et al., 2007). However, current behavioural programs aimed at diabetes prevention that use general health messages have limited effect (Kinmonth et al., 2008). Besides lifestyle factors, family history is an important and independent risk factor for diabetes (Meigs, Cupples & Wilson, 2000). Being at familial risk reflects the consequences of genetic predisposition, shared environment and common behaviours. Family history can be used to identify individuals at risk for diabetes and to influence early detection (Yoon, Scheuner & Khoury, 2003). Besides, it has been suggested that family history information can be used to personalize health messages for individuals at risk, which may be more effective in motivating them to adopt a healthy lifestyle than general health messages (Claassen et al., 2010). Individuals with a diabetes family history have difficulty understanding the complex interaction between genetic and behavioural causes of diabetes and have limited concerns about getting the disease (Pijl et al., 2009a; Acheson et al., 2010; Harrison et al., 2003).

Theories of health behaviour show that risk perception (threat appraisal) (Floyd, Prentice-Dunn & Rogers, 2000), as well as illness perceptions, such as causal beliefs and personal control over the risk (Leventhal et al., 1997), are important factors associated with motivation to engage in preventive behaviours. Since individual’s perceived risk of disease does not correspond to their actual risk, interventions need to be developed to reduce the mismatch, and to improve awareness of the multifactorial nature of diabetes (Pijl et al., 2009a; Harrison et al., 2003). The latter includes explaining the nature of a familial risk. Although there has been concern that emphasizing family history may lead to adverse psychological effects, there is no evidence that informing individuals about their familial risk might cause psychological harm (Pierce et al., 2000; Pijl et al., 2009b; Qureshi et al., 2001) or leads to a decrease of perceived personal control over the risk (fatalism) (Collins et al., 2010).

A recent study showed that individuals who received diabetic familial risk in a face-to-face consultation reported to engage more in risk-reducing behaviour (Pijl et al., 2009b). However, if family history information is used as a public health strategy, then it is necessary to develop a tool that is simple, easily applied, and adaptable to different settings (Yoon, Scheuner & Khoury, 2003; O’Neill et al., 2009). Computer tailoring is seen as an effective way to mimic interpersonal contact, since personalized feedback is provided by means of electronic questions (Kroeze et al., 2006). A consequence of exploring familial risk in the general population is that individuals with no family history will also be highlighted. This could be problematic since individuals without a diabetes family history might erroneously believe that having no family history indicates that they are not at risk of diabetes, in other words, lead to false reassurance (Marteau et al., 1996). This belief may lead to unintentional adverse effects, such as reduced motivation to change behaviour, justification of unhealthy behaviour, and delayed seeking of medical advice (Paddison et al., 2009). Among individuals without a family history the question of false reassurance needs further exploration. In the literature, there is no clear operational definition of false reassurance. In this study it is represented by reduced risk perception and as a consequence less risk-reducing behaviour, as has been done in other studies (Maarle, Stouthard & Bonsel, 2003; van Dijk et al., 2005).

The aim of this study was to determine the effect of tailored web-based diabetic familial risk information on risk-reducing behaviour and perceptions of individuals. Research questions are:

1. What is the impact of familial risk information on risk-reducing behaviour and illness and risk perceptions of individuals with a diabetes family history?

2. Does an intervention that emphasizes familial risk information result in false reassurance among individuals without a diabetes family history?
Research design and methods
This Preventing Diabetes Controlled Trial (PreDiCT) was registered at the Dutch Trial Register (NTR1938) and approved by the VU University Medical Center Ethical Committee.

Participants and procedure
Study participants were recruited from an independent certified research agency. The research agency provided credit points that could be redeemed for gift cards to encourage participation. People with one (or more) first-degree relative (23%) were identified using a single-item family history question, a month prior to recruitment for the study (April 2009), as part of a larger online general survey of the research agency sampling frame of 88,568. To ensure the trial was adequately powered, 4,100 people were recruited (see sample size section). This involved block randomization, a random sample of 2,900 individuals with a diabetes family history was drawn and a random sample of 1,200 individuals without a family history. Participants were not aware of being selected because of their familial risk. The study procedure, including the selection and enrolment of participants, is shown in the flow diagram in figure 1. Included were healthy individuals from the general population aged 35 to 65 years with a Body Mass Index (BMI, kg/m\(^2\)) $\geq$ 25, as overweight people have a higher risk of developing diabetes. Exclusion criteria were being diagnosed with diabetes (type 1 or 2), unable to read and complete questionnaires in Dutch, and being Hindustani, Turkish, Creolish, or Moroccan (because these populations have a higher than average risk of getting diabetes and the Diabetes Risk Test was not validated on these populations). From the 4,100 individuals invited, 3,244 (79%) people responded to the study invitation per Email and were assessed for inclusion. Thirty-eight percent (1,236) of individuals with a BMI < 25 were excluded and 145 individuals declined to participate. The remaining 1,863 completed the online baseline study questionnaire (May 2009). From these 1,863, a random sample of 1,300 participants was invited to complete the intervention (June 2009), of which 1,174 (90%) agreed to participate. From the 1,174 sample, participants were randomized into parallel control and intervention arms by means of a concealed computer-generated list of random numbers.

Intervention
The design of the web-based information for the intervention arm was based on the results of earlier studies (Pijl et al., 2009a; Pijl et al., 2009b). Both groups received general tailored diabetes prevention information, whilst the intervention group also received information based on familial risk. All participants were informed that the study was to determine the best way to advise people about their diabetes risk and were thus blinded for study groups.

General web-based information (control group)
- Participants received general information about type 2 diabetes, consisting of a simplified explanation of the metabolic disorder, the diabetes consequences, and main risk factors (not including family history). The effectiveness of preventive options were explained in a bar chart (Figure 2a), indicating that they can reduce their risk by half by adopting a healthy lifestyle.
- Diabetes risk was assessed using a Diabetes Risk Test (Alssema et al., 2008) validated for the Dutch population. Family history in this test was assessed by a simple enquiry: ‘Does diabetes occur within your family? 1) no; 2) yes, with my grandfather, grandmother, uncle, aunt, cousin; 3) yes, with my father, mother, brother, sister, or child’.
- Diabetes Risk Test results are categorized in three risk strata (2 in 100, 10 in 100, and 20 in 100) that refer to people’s risk of getting diabetes within the next five years. Each participant received an individual risk based on the risk test, supported by risk-reducing preventive measures tailored to the three risk strata.
After completing the post-test study questionnaire, all participants were invited to visit an evidence based computer-tailored lifestyle modification tool advising on approaches to reduce saturated fat intake and improve physical activity (www.leefgezondcoach.nl) (Oenema et al., 2008). This lifestyle information was not part of the web-based intervention, but was included to give participants the option to reduce their diabetes risk.

**Intervention web-based information (intervention group)**

As well as general information, described above, the intervention comprised:

- Advise that familial risk increases with the number and kinship of affected relatives. Further, the multifactorial character of type 2 diabetes was explained by presenting the proportion of various risk factors that contributed to the overall risk in a pair of bar charts (Figure 2b), in order to raise awareness about the nature of the risk. The contribution of familial risk (including genetic predisposition) was explicitly identified and it was showed that by adopting a healthy lifestyle the risk could be lowered by half.

- Instead of the simple family history enquiry, participants in the intervention group completed a detailed and systematic family history questionnaire (Wijdenes-Pijl et al., 2011a). First participants had to indicate their number of children and siblings, and the number of both paternal or maternal aunts and uncles. Subsequently, they could indicate for each first and second-degree relative whether they were diagnosed with diabetes or whether they did not know this.

- Besides the Diabetes Risk Test result, participants with a family history also received feedback about the total number of affected relatives based on their family history assessment. The bar chart (Figure 2b) was presented a second time.

**Outcome measures**

Online questionnaires were administered at baseline, immediately post-test and after three months. In the control arm, the 3-month assessment included the detailed questionnaire to assess family history in this group.

**Research question 1: Individuals with family history**

**Primary outcomes**

*Saturated fat intake* was assessed with a validated food frequency questionnaire (FFQ) of 35-items, which measured the intake of food products that contribute most to saturated fat intake in the Netherlands (van Assema et al., 2001). A score for saturated fat intake, ranging from 0 to 80, was computed. *Physical activity* was assessed using the short version of the International Physical Activity Questionnaire (IPAQ) that measures frequency and duration of physical activity in the past 7 days (Craig et al., 2003). According to the IPAQ data processing guidelines, participants were classified in a categorical score of three levels of physical activity: low, moderate, and high. Additionally participants were asked to indicate how many days a week they were physically active altogether for at least 30 minutes with, e.g. walking in fast pace, cycling, severe housekeeping, heavy work, gardening or sports. *Attitudes towards testing for diabetes* were assessed by a statement with 3 attitude items: "I think that regular (e.g. yearly) testing for diabetes with a blood glucose test is..." (not important [1] – important [7]; a bad idea [1] – a good idea [7]; not self-evident [1] – self-evident [7]). The 3 attitude items were combined in a scale, as internal consistency between the items was good (Cronbach’s alpha (α) was 0.88).
Invited to participate (n=4,100)

Assessed for eligibility (n=3,244)

Completed baseline questionnaire (n=1,863)

Random sample (n=1,300)

Excluded (n=1,381)
- Not meeting inclusion criteria
  BMI < 25 (n=1,236)
- Not available (n=63)
- Declined to participate (n=145)
- Not interested (n=26)
- Too much work (n=16)
- GP check sufficient (n=14)
- Diabetes or other disease (n=7)
- Other (n=8)
- No reason (n=11)

Allocated to intervention group (n=586)

Family history (n=308)

Lost to follow-up (n=15)

Analysed (n=288)
  Excluded from analyses
  - Diabetes diagnosis (n=4)
  - BMI < 25 (n=1)

Allocated to control group (n=588)

Family history (n=308)

Lost to follow-up (n=6)

Analysed (n=286)
  Excluded from analyses
  - Diabetes diagnosis (n=2)
  - BMI < 25 (n=2)

Figure 2a – Graphical bar chart presented to the participants in the control group

Figure 2b - Graphical bar chart presented to the participants in the intervention group.
Secondary outcomes
Illness and risk perceptions were assessed at baseline and immediately post-test. To assess causal beliefs participants were asked to indicate the extent to which they believed different items could be a cause of diabetes (definitely not [1] – definitely [5]). This was based on the revised form of the Illness Perception Questionnaire (Moss-Morris et al., 2002) and comprised five items: heredity (diabetes runs in the family), predisposition, physical activity, healthy diet, being overweight. Personal control over developing diabetes was assessed using a 3-items scale (α =0.67): “There is a lot I can do to prevent getting diabetes”, “There is nothing I can do to decrease my risk of getting diabetes” (reversed), “I am definitely able to influence my risk of getting diabetes” (completely disagree [1] – completely agree [5]). Perceived risk was assessed by a single-item: “In your opinion, what is the chance of you getting diabetes compared to an average man/woman your age?” (a lot lower [1] – a lot higher [7]). To assess diabetes risk worry, participants were asked to indicate their feelings when thinking about their chance of getting diabetes using a 7-point rating scale for two worry items (α =0.92) (no fear at all [1] – a lot of fear [7], not worried at all [1] - very worried [7]).

Research question 2: Individuals without family history
The primary outcome measure used to assess false reassurance was risk-reducing behaviour change and secondary outcome was perceived risk.

Socio-demographics
Socio-demographic variables (sex, age, ethnicity, educational level) were provided by the online research agency. Self-reported waist circumference, weight, and length were acquired from the baseline questionnaire.

Sample size
In both research questions we hypothesized that there would be a change in risk-reducing behaviour. Sample size was calculated for all three primary outcome measures. The largest sample was required to demonstrate a change in fat intake, and thus this sample size is presented here. Based on a significance level of 0.05 and a power of 0.80, the needed sample size for change in fat intake between baseline and 3-month follow-up was 291 subjects, based on a relative difference of 1.1 point on fat intake (range 0 – 80). The expectations of this effect (1.1) were based on results of a previous web-based trial (Oenema et al., 2008).

Statistical analyses
To identify predictors of participation and loss to follow-up, logistic regression analyses, with participation in trial (yes/no) and loss to follow-up (yes/no) as the dependent variable, were conducted. Independent variables were sex, age, education, BMI, and for loss to follow-up also baseline measures of physical activity level, fat intake, and attitudes towards testing for diabetes. Logistic regression analyses were conducted with study group as dependent variable to examine the similarity of the study groups at baseline. Independent variables for this analysis were sex, age, education, BMI, and follow-up measures of the detailed family history questionnaire. Chi-square tests were used to test for differences on the Diabetes Risk Test result between study groups. Linear regression analyses were conducted to test for follow-up group differences in outcome measures, with the follow-up measurement (3-month for behavioural outcomes and post-test for perceptions) of the outcomes as dependent variable, and study group and the baseline score of the outcome indicator as independent variables. Furthermore, we checked for effect modifiers in the analyses. Effect modification was defined as a significant (p<0.1) interaction term between the study group and variable of interest. In
case of effect modification subgroup analyses were performed on the modifying variable. All analyses were performed as was intended according to the study protocol.

Results
Participants
Of the 1,300 participants randomly selected to participate in the web-based intervention, at 3-month follow-up 1,115 completed the questionnaire (86% response rate) (figure 1). Response analyses showed no differences between participants and those who refused participation. No differences were found between individuals who were lost to follow-up after three months and respondents who completed all three questionnaires. Baseline characteristics of the participants are shown in table 1. In both cohorts of participants (with and without family history) there were no differences between the intervention and control group on these measures, as well as on baseline measures of the behavioural outcomes.

Table 1 – Characteristics of participants

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<tr>
<th></th>
<th>With family history</th>
<th>Without family history</th>
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<tbody>
<tr>
<td></td>
<td>Control n=286</td>
<td>Intervention n=288</td>
</tr>
<tr>
<td></td>
<td>Control n=269</td>
<td>Intervention n=266</td>
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<tr>
<td>Sex (% female)</td>
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<td>55.2</td>
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<td>53.5 ± 5.3</td>
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<td>98.5</td>
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<td>Education* (%)</td>
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<td>low</td>
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<td>high</td>
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<td>BMI (%)</td>
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<td>obese ≥30 kg/m²</td>
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<td></td>
<td>2.2</td>
<td>2.6</td>
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</tbody>
</table>

The number of participants are those who were analyzed for the study.
*Low education refers to people who finished elementary school, lower secondary education or lower vocational education; Middle education refers to higher secondary education or intermediate vocational education; High education refers to university or higher vocational education.
†As assessed with the detailed family history questionnaire, high familial risk for diabetes refers to at least 2 affected first-degree relatives or at least 3 affected maternal or paternal relatives from the same lineage; moderate refers to 1 affected first-degree relative, or 2 affected maternal or paternal second-degree relatives from the same lineage; average refers to all others (Scheuner et al., 1997).
Research question 1: Individuals with family history

Table 2 shows the scores on behavioural outcomes and illness and risk perceptions for baseline and the follow-up measurements for individuals with and without a family history and the outcomes of the regression analyses. Familial risk communication had no effect on saturated fat intake, physical activity level, or attitudes towards testing for diabetes. Education level was an effect modifier for the effect on saturated fat intake, therefore subgroup analyses were performed. A decrease in self-reported saturated fat intake for low-educated individuals in the intervention group when compared to the control group was found (Beta (b) -1.01, 95% confidence interval -2.01 to 0.00), whereas there was no effect for middle (b -0.37 (-0.51 to 1.25) and high educated individuals (b -0.61, -1.66 to 0.44). There was no effect of familial risk communication on causal beliefs, perceived personal control, and risk perception. However, there was a decrease in worries about diabetes risk for individuals in the intervention group (b -0.21, -0.40 to -0.03). Table 3 shows that a significant greater proportion of individuals in the intervention group (96.2%) had a risk of 20 in 100 (highest diabetes risk test result) compared to those in the control group (85.7%) within the cohort of individuals with a family history (p<0.001). Of the 8 items of the Diabetes Risk Test there was only a significant difference between the intervention and control individuals on the family history item, thus it is likely that this higher risk result can be attributed to the detailed family history questionnaire. Also, for individuals without a family history there was an increase of 8%, though not significant (p=0.17), of individuals who had the highest diabetes risk test result in the intervention group compared to the control group (data not shown). This increase could be explained by the identification of second-degree family members.

Research question 2: Individuals without family history

Specifying the impact of familial risk of diabetes had no significant effect of the intervention on self-reported fat intake (b -0.49, -1.00 to 0.05), physical activity (b 0.06, -0.05 to 0.18), or attitudes towards diabetes testing (b -0.03, -0.20 to 0.13) among individuals without a family history. There was also no significant effect on perceived risk of diabetes in this group of participants (b -0.12, -0.29 to 0.04). In the intervention group there were higher scores for the perception that heredity (b 0.19, 0.06 to 0.33) and predisposition (b 0.31, 0.19 to 0.43) are important causes of diabetes. There was no effect of familial risk communication on other illness perceptions.
Table 2 – Outcomes at baseline and follow-up and regression coefficients (β) for regression analyses

<table>
<thead>
<tr>
<th>Illness and risk perceptions</th>
<th>With family history</th>
<th>Without family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causal beliefs (1-5)</td>
<td>Control n=266</td>
<td>Intervention n=267</td>
</tr>
<tr>
<td>Heredity</td>
<td>baseline follow-up†</td>
<td>baseline follow-up†</td>
</tr>
<tr>
<td>4.0 (0.9)</td>
<td>4.0 (0.7)</td>
<td>4.1 (0.8)</td>
</tr>
<tr>
<td>Predisposition</td>
<td>3.7 (0.8)</td>
<td>3.9 (0.7)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>3.7 (0.9)</td>
<td>4.1 (0.7)</td>
</tr>
<tr>
<td>Healthy diet</td>
<td>3.9 (0.8)</td>
<td>4.1 (0.7)</td>
</tr>
<tr>
<td>Overweight</td>
<td>4.2 (0.7)</td>
<td>4.2 (0.6)</td>
</tr>
<tr>
<td>Personal control (1-5)</td>
<td>3.8 (0.6)</td>
<td>3.9 (0.6)</td>
</tr>
<tr>
<td>Perceived risk (1-7)</td>
<td>4.5 (1.1)</td>
<td>4.7 (1.2)</td>
</tr>
<tr>
<td>Diabetes risk worry (1-7)</td>
<td>3.5 (1.4)</td>
<td>3.9 (1.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Behavioural outcomes</th>
<th>Sum score Fat list (0-90)</th>
<th>IPAQ categories§</th>
<th>Days/week physical activity</th>
<th>Attitudes towards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control n=266</td>
<td>15.7 (5.2)</td>
<td>vigorous</td>
<td>43 (2.4)</td>
<td>diabetes testing (1-7)</td>
</tr>
<tr>
<td>Intervention n=267</td>
<td>15.0 (5.3)</td>
<td>medium</td>
<td>25.2</td>
<td>5.3 (1.3)</td>
</tr>
<tr>
<td></td>
<td>15.1 (5.3)</td>
<td>light</td>
<td>10.5</td>
<td>5.2 (1.3)</td>
</tr>
<tr>
<td></td>
<td>14.2 (5.5)</td>
<td>Total</td>
<td>10.3</td>
<td>5.3 (1.3)</td>
</tr>
<tr>
<td></td>
<td>-0.29 (-0.85 to 0.27)</td>
<td></td>
<td>2.8 (2.4)</td>
<td>5.2 (1.3)</td>
</tr>
<tr>
<td></td>
<td>15.6 (5.0)</td>
<td></td>
<td>4.2 (2.4)</td>
<td>-0.07 (-0.23 to 0.09)</td>
</tr>
<tr>
<td></td>
<td>15.3 (5.1)</td>
<td></td>
<td>4.1 (2.4)</td>
<td>4.9 (1.4)</td>
</tr>
<tr>
<td></td>
<td>15.5 (5.2)</td>
<td></td>
<td>4.2 (2.4)</td>
<td>4.9 (1.4)</td>
</tr>
<tr>
<td></td>
<td>14.5 (4.9)</td>
<td></td>
<td>4.2 (2.4)</td>
<td>4.8 (1.4)</td>
</tr>
<tr>
<td></td>
<td>-0.49 (-1.00 to 0.05)</td>
<td></td>
<td>4.2 (2.4)</td>
<td>4.9 (1.3)</td>
</tr>
<tr>
<td></td>
<td>56.5 (5.0)</td>
<td></td>
<td>4.1 (2.5)</td>
<td>-0.03 (-0.20 to 0.13)</td>
</tr>
<tr>
<td></td>
<td>52.0</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>56.1</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50.7 (5.0)</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.08 (-0.05 to 0.18)</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27.3</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11.9</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11.9</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11.9</td>
<td></td>
<td>4.2 (2.4)</td>
<td></td>
</tr>
</tbody>
</table>

Data are means ± SD or percentages.

The numbers are based on the availability of the detailed questionnaire to assess family history.

Follow-up for illness and risk perception is directly post-test. For behavioural outcomes after three months.

The interpretation of the regression coefficient (β) for e.g. the illness perception diabetes risk worry (β) would be that an individual in the intervention group will score 0.21 less on the perception of worries about their diabetes risk compared to an individual in the control group, when baseline values for diabetes risk would be similar.

About 6% of the participants are missing data due to data cleaning according to the IPAQ data processing guideline.
Table 3 – Diabetes risk presented to the participants based on the Diabetes Risk Test

<table>
<thead>
<tr>
<th>Diabetes Risk Test result</th>
<th>With family history</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control n=286 (%)</td>
<td>Intervention n=288 (%)</td>
</tr>
<tr>
<td>2 in 100</td>
<td>3.8</td>
<td>0</td>
</tr>
<tr>
<td>10 in 100</td>
<td>10.5</td>
<td>3.8</td>
</tr>
<tr>
<td>20 in 100</td>
<td>85.7</td>
<td>96.2</td>
</tr>
</tbody>
</table>

$\chi^2$-statistic; p-value$^\dagger$ 21.8; p<0.001

*Indicating people’s risk of getting diabetes within the next five years.
$^\dagger$P-value based on the Chi-square test

Conclusions

Overall, the addition of family history information to the web-based general diabetic risk information did not result in improvements in risk behavior among participants with a diabetes family history. However, there are promising results for low-educated individuals, they were more likely to reduce their saturated fat intake. Also, the information appeared to reduce worry related to diabetic risk among participants with a family history. For individuals without relevant family histories, the emphasis on familial risk information did not result in false reassurance as demonstrated by no significant difference in risk-reducing behavior and diabetes risk perception. Furthermore, a detailed family history assessment resulted in a greater percentage of individuals at familial risk for diabetes compared to a simple enquiry.

Individuals with a family history

In contrast to findings in this study, an observational study and two controlled trials, that examined the impact of informing people about their familial risk for type 2 diabetes, reported increased self-reported risk-reducing behaviour (Pijl et al, 2009a; Qureshi & Kai, 2008; Ruffin et al., 2011). These studies, however, involved a consultation with a health care professional. Perhaps, in that setting, the professional providing the information could verify whether people understood the complex interaction of genetic and behavioural causes and was able to give additional feedback and support. Moreover, individualized messages tailored to specific characteristics and knowledge of individuals about familial risk information personalized the risk, thus may be more persuasive than general healthy lifestyle advice, e.g. eat healthy (Claassen et al., 2010). It has been previously described that computer tailoring, as was performed in this study, lack features to imitate all characteristics of personal contact, since it mostly does not allow direct interaction between the respondent and the education expert (Brug et al., 2003). Further, people might be more familiar with face-to-face contact.

Lower socioeconomic groups often engage more in unhealthy behaviours (Stringhini et al., 2011), whilst interventions to improve health behaviours may result in greater uptake of the message in higher socioeconomic groups, resulting in an rising social inequality in health (Capewell & Graham, 2010). This population-wide study suggests an effect of familial risk information on saturated fat intake for low-educated individuals. This is consistent with other population-wide community-based health education interventions showing an improvement in fat intake among a low-educated population as compared to higher educated individuals (Govil et al., 2009; Wendel-Vos et al., 2009). Further, low-educated individuals were more positive towards tailored dietary fat-feedback in earlier studies as compared to higher educated individuals (Brug & Van Assema, 2000).
The incidental finding that 10% more individuals were classified at high diabetes risk (20 in 100 for getting diabetes within five years) in the intervention arm, suggests that incorporating a detailed family history questionnaire into the web-based assessment tool enhanced identification of individuals at high risk due to more accurate ascertainment of familial risk. This is supported by a related study (Wijdenes-Pijl et al., 2011). Currently the number of (online) self-administered risk assessment tools for common diseases is increasing. These tools often limit family history enquiry to a single question (Alssema et al., 2008; Hippisley-Cox et al., 2009). Integrating a detailed family history questionnaire to these risk assessments might result in a higher number of participants that will be identified as having a high diabetes risk, however this may take more effort.

A high baseline score in individuals with a family history on the questions enquiring about the perception that a cause of diabetes is heredity and predisposition left little room for improvement. This finding might indicate that individuals with a family history are already aware of family history as a risk factor. This is in line with earlier findings, that individuals with a family history indicated a parental history as the most important risk factor for diabetes (Pierce et al., 2001). Conversely, in this study, individuals without a family history were less aware of heredity and predisposition as a cause of diabetes at baseline, but their perception increased post-intervention.

Previous studies indicate that advising participants of their familial risk does not lead to sustained psychological harm (Pierce et al., 2000; Pijl et al., 2009b; Qureshi et al., 2001). In this study, those receiving general information had more worries than those receiving additional information related to familial risk. This suggests that explaining the role of familial risk raises understanding of the risk and moderates worries about diabetes risk.

Individuals without a family history

It has been shown that a (favourable) negative test result on a screening for having type 2 diabetes does not lead to false reassurance, as demonstrated by no decrease in perceived diabetes risk, behavioural intentions, and self-rated health (Paddison et al., 2009). It might be anticipated if participants have no family history of diabetes, giving information about the significance of familial risk will lead to a decline in these participants’ perceived diabetes risk and adherence to risk-reducing behaviour (Marteau et al., 1996). However, there was no such false reassurance in this study, as indicated by no effect on risk perception and risk-reducing behaviour by participants without family history of diabetes.

Strength of this trial was that the participants were not aware of being selected on their diabetic family history, as this attribute was identified before the study. Further, there is no item non-response, since participants are obliged to give an answer to each question in order to complete the web-based questionnaire. A further strength is that the random sample was representative of the Dutch population with respect to sex and education, as these numbers were compared with data about the Dutch population (StatLine, 2011). However, the study population did not represent the ethnic mix of the Dutch population and reflected individuals with a BMI >25, therefore one should be cautious when generalizing these findings to the broader community. As the Diabetes Risk Test, used in this study, did not accurately predict the diabetes risk of non-Caucasian individuals, these minority populations were excluded from the study. Another limitation of the study is that self-reported measures were used for the behavioural outcomes; nevertheless all such measures were validated instruments. Objective measures, such as data from biomarkers or accelerometers were not feasible in this online research panel.

Although there was generally no clear improvement in risk-reducing behavior, the intervention improved dietary fat intake among lower educated participants. Often interventions to improve health behaviors widen the social inequality in health, i.e. low-educated individuals show more unhealthy
behavior (Capewell & Graham, 2010). However, this low-cost diabetes prevention tool with integrated familial risk information did show improved health behavior among the subgroup of individuals at greatest need of preventative care. Conversely, a drawback of using web-based information is that it might lead to a selected utilisation. Younger, high-educated, employed, and healthier people have better access to internet and are more interested in health risk information (Cresci, Yarandi & Morrell, 2010). The challenge is now to get individuals who would benefit the most to complete a diabetes prevention tool on the internet. Reassuringly, the incorporation of familial risk appears to reduce worry related to diabetic risk assessment. This would suggest a benefit from including familial risk identification in chronic disease assessment. Furthermore, there is no evidence that incorporating familial risk identification into a diabetes prevention programme leads to false reassurance in individuals identified without relevant family histories. In terms of identifying individuals at high diabetes risk, a detailed family history questionnaire identifies more individuals at familial risk than a simple enquiry and can contribute to a more correct familial risk identification in chronic disease assessment.
How do users evaluate a web-based diabetic familial risk assessment?

Abstract

Aim
To examine the perceived value among users of a detailed diabetic familial risk assessment compared to a general diabetes risk assessment, and the perceived implications for individuals and families.

Methods
Questionnaires were completed by healthy individuals, 574 with and 535 without a family history, aged 35 – 65 years with a Body Mass Index ≥ 25, which participated in a randomized control trial that examined the impact of web-based diabetic familial risk information.

Results
Overall, the detailed diabetic familial risk information was evaluated valuable. Users regarded it as useful, without being too time-consuming and it resulted in less feelings of worry compared to a general risk assessment. Although few users of both assessments perceived a negative influence on family relations, autonomy, responsibility, or medicalisation, almost half perceived fear for discrimination by insurance companies. Except for the influence of extended familial risk information on feelings of blame, there were no differences for people with and without a diabetes family history,

Conclusions
Users perceive a detailed familial risk assessment as valuable without being too time-consuming and there is no great barrier for addressing the entire population, suggesting that it is feasible to use this tool in a public health approach.
Introduction
A positive family history, reflecting genetic, behavioural and environmental influences, is an independent risk factor for diabetes. Family history is seen as a useful instrument to select high-risk groups and provide them prevention information (Qureshi et al., 2009a). Moreover, it has been shown that family history can be used as a tool to personalize prevention messages and may change preventive behaviour among certain high-risk populations (Ruffin et al., 2011; Pijl et al., 2009; Chapter 6). In order to predict diabetes risk, family history information is often incorporated in diabetes risk assessments in addition to other risk factors, such as age and being overweight. Examples of these self-completed tools are the QDscore (Hippisley-Cox et al., 2009) and the Diabetes Risk Test (Alssema et al., 2008). To actually collect a family history, several methods can be used, ranging from detailed and standardized instruments using a pedigree to simple dichotomous enquiry (presence or absence of disease in any relative) (Qureshi et al., 2009a). It has been shown that a self-reported detailed family history identifies more individuals at familial risk than a simple dichotomous enquiry (Wijdenes-Pijl et al., 2011a; Cohn et al., 2010). However, a detailed family history assessment can be time-consuming and individuals are more inclined to complete a tool that is short (Kalantar & Talley, 1999).

Although it has been shown that the great majority of people consider knowing their family’s health history important to their personal health (CDC, 2004), little is known about how individuals actually perceive the value of familial risk information and consequently receiving tailored feedback on their risk. Do people appreciate it to be informed about their familial risk and do they perceive the information as useful? In particular, how do individuals without a family history perceive the information when familial risk, that does not concern them, is emphasized as is done in a public health approach? Do they perceive the provision of risk information that they did not ask for as a threat to their autonomy, or as a welcome stimulus to take on responsibility for their own health? Other relevant questions concern the possible impact on people’s fear for discrimination by insurers, and the possibility that the use of familial risk information as a public health instrument may falsely make people feel ill (medicalisation).

Besides the effects of familial risk information for the individuals concerned, it may also have an impact on (their) families (Yoon, Scheuner & Khoury, 2003). Communication about genetic health risks is often considered difficult within families, because of complex communication patterns and family structures (Wilson, 2004). It has been suggested that familial risk information may support family relations by promoting the adoption of healthy behaviour as a shared initiative, or distort family relations if relatives do not want to be informed about their risk (Wijdenes-Pijl et al., 2011b). The latter effect may occur especially if a detailed family history questionnaire is used to collect a family history rather than a simple enquiry, as individuals will be more triggered by a detailed assessment to reflect on affected relatives (Cohn, 2010) and may even be more inclined to contact relatives to confirm their disease status. A detailed assessment also reveals more personal information (Wijdenes-Pijl et al., 2011b), and families might feel labelled at risk when familial risk is emphasized (Yoon, Scheuner & Khoury, 2003).

This study is part of a randomized controlled trial (PreDiCT) that was conducted in 2009 and is described in detail elsewhere (Chapter 6). The PreDiCT trial aimed to determine the effect of tailored web-based diabetic familial risk information on risk-reducing behaviour. The trial compared individuals who received general diabetes risk assessment and tailored feedback (simple condition) with individuals who received additional detailed familial risk assessment and tailored familial risk information (extended condition), using two cohorts of individuals with and without a family history of diabetes. The research question of the study presented here is: How do users (with or without family...
history) who complete a web-based general diabetes risk assessment compared to those who complete an extended diabetic familial risk assessment evaluate a diabetes risk assessment with respect to a) the perceived value, and b) the perceived implications on individuals and families concerning autonomy, responsibility, discrimination, and medicalisation?

Methods
Participants in the PreDiCT trial (Chapter 6) were individuals with and without a family history of diabetes aged 35 to 65 years with a Body Mass Index (BMI, kg/m^2) ≥ 25, recruited from an independent certified research agency. Family history was defined as having ≥ 1 first-degree relative with diabetes. Participants were not aware of being selected because of their familial risk. All participants were informed that the study was to determine the best way to advise people about their diabetes risk and thus blinded for study groups. During the trial diabetes risk was assessed with a web-based version of the Diabetes Risk Test (Alsema et al., 2008), including risk factors such as age, BMI, waist circumference, and being physically active. Results were categorized in 3 risk strata (2 in 100, 10 in 100, and 20 in 100) that refer to their risk of getting diabetes within the next 5 years. Each participant received individual risk information based on the risk test, supported by risk-reducing preventive measures. Familial risk was assessed as part of the Diabetes Risk Test, by means of a simple enquiry in the simple condition and by means of a detailed family history questionnaire in the extended condition. Differences between the simple and extended condition and are presented in Figure 1.

Outcome measures
Online questionnaires were administered directly post-test and after 3 months. 
Perceived value. Participants were asked directly after they performed the assessment how they evaluated the Diabetes Risk Test and corresponding information, using a 7-point semantic differential rating scale (pointless [1] – useful [7]; not worrisome [1] – worrisome [7]); hard to understand [1] – easy to understand [7]). Percentage of people who agree with the items was determined by a score of 5 – 7. At 3 months, participants were asked in what way they agreed with two statements about the Diabetes Risk Test using a 5-point semantic differential rating scale (completely disagree [1] – completely agree [5]): 1) I would recommend others to take the test; 2) completing the test takes a lot of time and effort. Percentage of people who agree with these items was determined by a score of 4 or 5.
Perceived implications for individuals and families were assessed at the end of the last questionnaire of the trial at 3 months. Participants were asked in what way they agreed with nine statements about the Diabetes Risk Test and information provided using a 5-point semantic differential rating scale (completely disagree [1] – completely agree [5]). The statements concerned implications for their family and public health, i.e. autonomy, responsibility, medicalisation, and discrimination. The statements are shown in full length in table 3. Percentage of people who agree with these statements was determined by a score of 4 or 5.
Figure 1 – Differences in diabetes risk assessment and feedback information between the simple and extended condition

<table>
<thead>
<tr>
<th>Pre-assessment information</th>
<th>Simple condition</th>
<th>Extended condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>- main risk factors (not including family history)</td>
<td>- main risk factors (including family history)</td>
<td></td>
</tr>
<tr>
<td>- effectiveness of preventive options</td>
<td>- familial risk increases with the number and kinship of affected relatives</td>
<td></td>
</tr>
<tr>
<td>- familial risk increases with the number and kinship of affected relatives</td>
<td>- effectiveness of preventive options</td>
<td></td>
</tr>
</tbody>
</table>

| Family history assessment | Simple enquiry: Participants were asked “Does diabetes occur within your family?” 1) no; 2) yes, with my grandfather, grandmother, uncle, aunt, nephew, niece; 3) yes, with my father, mother, brother, sister, or child.” | Detailed questionnaire: First, participants had to indicate the number of children and siblings, and the number of both paternal or maternal aunts and uncles. Subsequently, they could indicate for each first-degree relative and second-degree relative whether these relatives had been diagnosed with diabetes or whether they did not know this. |

<table>
<thead>
<tr>
<th>Feedback information</th>
<th>- Individual risk based on the risk test</th>
<th>- Individual risk based on the risk test</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Risk-reducing preventive measures</td>
<td>- Information about the total number of affected relatives</td>
<td>- Risk-reducing preventive measures</td>
</tr>
</tbody>
</table>

Statistical analyses
Potential group differences in the baseline characteristics of the study participants (sex, age, ethnicity, education, BMI, and familial risk) were assessed using chi-square tests for proportions and t-tests for means. Logistic regression analyses were conducted to test for differences between users of each condition in perceived value and burden, and perceived implications on families and public health, with the condition (extended/simple) as dependent variable. Furthermore, we checked whether having a diabetic family history was an effect modifier. Effect modification was defined as a significant (p<0.1) interaction term between the study group and variable of interest. In case of effect modification subgroup analyses were performed on individuals with or without a family history.

Results
Participants
Baseline characteristics of the participants are listed in Table 1. No significant differences in sex, age, ethnicity, education, BMI, and familial risk were found between individuals who received the extended condition and those who received the simple condition.

Perceived value
Agreement to statements about the perceived value by users of the extended versus simple condition is presented in Table 2. Most participants perceived the extended condition as useful, understandable and people would recommend it to others. Few participants perceived the burden of the test taking a lot of time and effort, even less so for the extended condition, though not statistically significant. As compared to the simple condition, extended familial risk assessment and feedback resulted in a lower perception that the information was worrisome (22% versus 17%, p<0.05). No further differences were found between both conditions.
Table 1 – Characteristics of participants

<table>
<thead>
<tr>
<th></th>
<th>Extended condition (n=554)</th>
<th>Simple condition (n=555)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (% female)</td>
<td>52.2</td>
<td>49.2</td>
</tr>
<tr>
<td>Age (years, mean ± SD)</td>
<td>53.5 ± 5.8</td>
<td>53.3 ± 5.6</td>
</tr>
<tr>
<td>Ethnicity (% native Dutch origin)</td>
<td>96.9</td>
<td>97.3</td>
</tr>
<tr>
<td>Education* (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>low</td>
<td>29.6</td>
<td>32.1</td>
</tr>
<tr>
<td>medium</td>
<td>44.0</td>
<td>44.3</td>
</tr>
<tr>
<td>high</td>
<td>26.4</td>
<td>23.1</td>
</tr>
<tr>
<td>BMI (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>overweight 25-30 kg/m²</td>
<td>66.2</td>
<td>67.0</td>
</tr>
<tr>
<td>obese ≥30 kg/m²</td>
<td>33.8</td>
<td>33.0</td>
</tr>
<tr>
<td>Familial history of diabetes** (%)</td>
<td>52.0</td>
<td>51.5</td>
</tr>
</tbody>
</table>

Number of participants are those who were analyzed for this study.
*High education refers to university or higher vocational education; Medium education refers to higher secondary education or intermediate vocational education; Low education refers to elementary school, lower secondary education or lower vocational education.
**People with at least one first-degree relative with diabetes were considered to have a family history of diabetes. Detailed family history was assessed during the intervention for the extended condition and at 3 month for the simple condition.

Table 2 – Perceived value and burden for users of the extended versus simple condition

<table>
<thead>
<tr>
<th></th>
<th>Extended condition (n=554)</th>
<th>Simple condition (n=555)</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>The information* was...</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>useful</td>
<td>87.2</td>
<td>87.9</td>
<td>.71</td>
</tr>
<tr>
<td>worrisome</td>
<td>16.6</td>
<td>22.2</td>
<td>.02</td>
</tr>
<tr>
<td>understandable</td>
<td>93.5</td>
<td>93.7</td>
<td>.90</td>
</tr>
<tr>
<td>I would recommend others to take the test</td>
<td>59.6</td>
<td>61.6</td>
<td>.48</td>
</tr>
<tr>
<td>Completing the Diabetes Risk Test takes a lot of time and effort</td>
<td>2.0</td>
<td>2.3</td>
<td>.68</td>
</tr>
</tbody>
</table>

*The information provided along with the Diabetes Risk Test (see figure 1)
** Based on logistic regression analyses

Perceived implications on individuals and families

Table 3 shows that most participants who received the extended condition (74%), perceived a positive influence on family relations and hardly any participants (5%) believed the information can distort family relations. When comparing these participants to those who receive the simple condition there are no differences. With regard to the perceived implications, 73% of the users of the extended condition believe people will take responsibility for their health and some (28%) even think the Diabetes Risk Test can be offered with some insistence. Few individuals (15%) believe the information will make people falsely feel ill. However, 46% have fear for discrimination by insurance companies. There are no differences with regard to perceived implications between users who received the extended or the simple condition. Having a family history of diabetes was an effect modifier for “perceived blame for getting diabetes if someone doesn’t follow the advice of the Diabetes Risk Test”. Figure 2 shows that more users of extended familial risk assessment compared to the simple condition perceived feelings of blame among individuals with no family history and less among individuals with a family history.
Table 3 – Users’ perceived implications for individuals and families of the extended versus simple condition

<table>
<thead>
<tr>
<th>Family implications</th>
<th>Extended condition (n=554) Agree (%)</th>
<th>Simple condition (n=555) Agree (%)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative can support each other by discussing their risk of getting diabetes</td>
<td>74.4</td>
<td>71.0</td>
<td>.21</td>
</tr>
<tr>
<td>Discussing diabetes risk with relatives can distort family relations</td>
<td>5.4</td>
<td>6.7</td>
<td>.38</td>
</tr>
<tr>
<td>People who are at risk of getting diabetes should warn their relatives about their potential risk</td>
<td>70.4</td>
<td>69.2</td>
<td>.66</td>
</tr>
<tr>
<td>Autonomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health is important, therefore the Diabetes Risk Test can be offered with some insistence</td>
<td>27.6</td>
<td>28.8</td>
<td>.65</td>
</tr>
<tr>
<td>Responsibility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>People will take more responsibility for their health, when they know their risk of getting diabetes</td>
<td>73.1</td>
<td>72.1</td>
<td>.70</td>
</tr>
<tr>
<td>If someone does not follow the advice of the Diabetes Risk Test, he is to blame for getting diabetes</td>
<td>22.7</td>
<td>23.2</td>
<td>.84</td>
</tr>
<tr>
<td>Medicalisation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Diabetes Risk Test can falsely make people feel ill</td>
<td>14.6</td>
<td>13.7</td>
<td>.66</td>
</tr>
<tr>
<td>Discrimination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I fear that insurance companies will exclude people based on the results of the Diabetes Risk Test</td>
<td>46.3</td>
<td>42.5</td>
<td>.21</td>
</tr>
</tbody>
</table>

* Based on logistic regression analyses

Figure 2 – Subgroup analyses for having a family history of diabetes (effect modifier) for perceived blame for getting diabetes if someone doesn’t follow the advice of the Diabetes Risk Test.

Of the people with a family history who completed the extended condition 18.8% agree, of the simple 27.3% agree. Differences between the conditions are significant* (p=0.02). Of the people with no family history who completed the extended condition 27.1% agree, of the simple 19.0% agree. Differences between the conditions are significant* (p=0.03).
Discussion
The aim of this paper was to evaluate users' perceptions of a web-based diabetic familial risk assessment based on an extended family history assessment compared to a simple enquiry. The extended diabetic familial risk assessment and tailored feedback was evaluated valuable, as users regarded it as useful, without being too time-consuming and when compared to users of a general diabetes risk assessment it reduced feelings of worry. Furthermore users of both conditions believed the provided information would positively influence family relations and people should warn their family members about the risk. Concerning public health implications, almost half of the users of both conditions had a fear for discrimination by insurance companies based on their results of the risk test, however this perception was not significantly enhanced when familial risk information was emphasized.

Individuals who complete disease risk assessments are considered to be more interested and have more understanding of a tool that is short (Kalantar & Talley, 1999) and simple (Wilson, 2002). In this study, individuals with and without a diabetic family history who completed the detailed family history questionnaire experienced no more time constraints than people who completed the simple enquiry. A possible explanation might be that addressing relatives' diabetes history enhances motivation for personal diabetes risk assessment, since it has been shown that people consider knowledge of family history important to their personal health (CDC, 2004). In this study, individuals who received the simple and the extended condition regarded the tool as equally useful and understandable, which underlines that the extra elaboration of a detailed questionnaire is no drawback. Furthermore, those receiving general diabetes risk information had more worries than those receiving extended familial risk information. This suggests that explaining the role of familial risk moderates worries about diabetes risk.

In this study, users of both conditions believe relatives can support each other to engage in preventive behaviour after receiving Diabetes Risk Test results. It has indeed been shown that family involvement in adopting a healthy lifestyle improves healthy eating habits (Haga, 2009). The contrary was also shown in a cross-sectional study, parental advice about diabetes prevention did not improve having a healthy diet, being physical active or prevent weight gain (Nishigaki, 2008). Moreover, offspring did not see their family as reliable information sources for preventive measures, whereas they did regard medical professionals and mass media as reliable (Nishigaki, 2008).

We did not find support among users for the concern that providing unasked for diabetic risk information would amount to an invasion of personal autonomy. Some participants even stated that diabetes familial risk assessment and information could be offered with some insistence. This is in line with earlier qualitative findings (Wijdenes-Pijl et al., 2011b), in which individuals were not concerned about the voluntariness of a diabetic familial risk assessment and it was even suggested that the assessment should be actively offered to the entire population. Many users of both the extended and the simple condition indicate that they believe that insurance companies might exclude people based on the results of the Diabetes Risk Test. It has been suggested that individuals might have less reason to fear discrimination based on their risk profile for common chronic diseases, because of the preventive options that are available (Janssens & Khoury, 2006). Moreover, in a review on the delivery of genomic medicine for common chronic diseases it was concluded that there are no well-documented cases of health insurers either asking for or using genetic test results for discriminative purposes (Scheuner, Sieverding & Shekelle, 2008). However, this study and others (Hall & Rich, 2000) show that fear of genetic discrimination with regard to testing for diabetes or other adult-onset multifactorial diseases is still considerable.
Some individuals stated that the use of extended familial risk information puts individuals in a position where they can rightly be blamed if they will develop diabetes after ignoring preventive advice. However, the percentage of those holding this view was higher among individuals without a family history. Also when general diabetes risk advice (as opposed to extended familial risk information) was given to those with a family history, the view that blame might be appropriate was given more support. Possibly, individuals who complete the Diabetes Risk Test ground their opinion on their own situation. Therefore individuals with a family history, for example, believe you can not be blamed for getting diabetes when a family history as a risk factor is emphasized, since you cannot change being at familial risk. Individuals without a family history would more likely perceive individuals as being to blame if they get diabetes and haven’t followed the prevention advice. Perhaps since more avoidable risk factors are involved for the (non-)avoidance of which they might hold individuals responsible.

Strength of this study was that the participants in the trial were not aware of being selected on their diabetic family history, as this attribute was being identified before the study. However, it should be noted that the items in the questionnaire refer to the Diabetes Risk Test and not familial risk assessment specifically. The implication items for families and public health concern hypothetical scenarios, thus the findings are possible perceptions (agreement with statements) and do not reflect confirmative outcomes. Generalization of the findings in this study should be done cautiously, since the population did not represent the ethnic mix of the Dutch population and represents only overweight individuals. Also, it should be noted that participants were rewarded with an incentive and were aware of participating in a scientific research. If the detailed family history assessment and information is provided in usual practice individuals might reserve less time for the information.

The findings in this study indicate that the addition of extended familial risk information to diabetes risk assessments seems feasible and acceptable, since the information is perceived as understandable, useful, and users would recommend it to others, without regarding it as too time-consuming. Besides, additional familial risk information reduced feelings of worry among users as compared to users who received general diabetes risk assessment and tailored feedback. Whereas there is no evidence of insurance companies using genetic test results, users of extended familial risk information did have the fear that they would use results of the Diabetes Risk Test. Therefore, it is important to inform individuals who want to complete extended diabetic familial risk assessments that the test results will not be used for other purposes. In addition to the issues addressed here, it should be noted that economical, legal, and organisational aspects, such as accessibility for the target group, are also important aspects for implementation of a family history tool. In this study, diabetes risk assessment was taken as an example to explore the role of family history information in common disease prevention, findings of this study may provide information on how individuals would evaluate extended familial risk information for other common diseases, such as cardiovascular diseases and cancer.
Chapter 8

General discussion
General discussion
Previous literature recognized the use of family history information as a very promising strategy in the prevention of common chronic diseases by improving risk assessment and by motivating positive lifestyle changes (Claassen et al., 2010; Yoon et al., 2003). Since, familial risk is an important and independent risk factor for these diseases (Valdez et al., 2010), over the past ten years, many initiatives have been taken to evaluate the use of family history as a tool for assessing risk for common diseases and influencing early detection and prevention strategies. For example, in 2004, the Centers for Disease Control and Prevention (CDC) developed the Family Healthware™ (Yoon et al., 2009), a tool to assess a person’s familial risk for six diseases, feeding back a personalised prevention plan. However, evidence for effective familial risk assessment and the effect of familial risk information on positive lifestyle changes has been scarce thus far (Heideman et al., 2011; Qureshi et al., 2009). Also, there was little attention in the literature for illness and risk perceptions of people at familial risk for these diseases and their perceptions about the need for the use of family history information as a tool in common disease prevention. In this thesis these knowledge gaps were addressed by using several study designs, which are presented in the main findings section, followed by a discussion of the findings, methodological reflections, and the implications for future research and practice. Diabetes type 2 was used as an example as this disease reflects the environmental (behavioural) and genetic factors that define common chronic diseases. Moreover, it is a highly prevalent disease in the Netherlands, and there is ample expertise of diabetes prevention at the EMGO Institute of Health and Care Research (www.emgo.nl), where this thesis was done.

Main findings
First a brief summary of the results related to each research question is provided.
1. What are causal beliefs, perceived risk, and perceptions of control among individuals at familial risk for diabetes and do these differ from perceptions of individuals without a family history?
   Studies performed in this thesis suggest that individuals use causal beliefs to construct their perceptions of risk and control (Chapter 2). However, people often have difficulty understanding the complex interaction between genetic and behavioural causes of diabetes and have limited concerns about getting the disease. As their perceptions do not always correspond with the epidemiological evidence, future diabetes prevention strategies would benefit from giving more attention to individual perceptions. In the context of family history this can be done by explaining the multifactorial character of diabetes and highlighting effective ways to reduce the risk.

2. How do people perceive diabetic risk assessment based on family history assessment?
   a. What issues related to predictive testing based on family history assessment in diabetes prevention do lay individuals perceive?
      Most laypeople, including patients, believed that a family history assessment could be used to identify people at risk for diabetes and to motivate preventive behaviour (Chapter 3). However, a diabetes family history assessment was not considered useful by some, since there are also other risk factors involved and not everyone has a diabetes family history or knows their family history. Respect for the autonomy of individuals was not perceived to be an issue. Furthermore, psychological harm, discrimination, and privacy were only briefly mentioned as issues of concern if family history were to be used in the context of diabetes prevention.
   b. Do these issues differ from the issues with regard to DNA testing?
      Different reasons underlying motivation to change behaviour were considered when laypeople compared DNA test results and a family history risk assessment. Moreover, a perceived drawback of
DNA testing only was that diabetes was considered not severe enough for this type of risk assessment. Respect for the autonomy of individuals was emphasized more with regard to DNA testing than a family history assessment (Chapter 3).

c. What is the perceived value of diabetic familial risk assessment and information for users and what are the perceived implications for individuals and families?

Users of a diabetic risk assessment with detailed family history questionnaire perceived the information equally valuable compared to users of a simple enquiry (i.e. a single question on family history), without being more time-consuming (Chapter 7). Although many individuals perceived fear for discrimination by insurance companies on the basis of their test results, few users of both assessments perceived a negative influence on family relations, autonomy, responsibility, and medicalisation. These results suggest that, at least according to the users themselves, there is no major barrier for addressing the entire population. Apart from these aspects, economic, legal, and organisational aspects such as accessibility for the target group have to be considered before further implementation.

3. What is the additional value of using a detailed diabetic family history questionnaire compared to a simple enquiry for diabetes risk identification?

Compared with a detailed questionnaire, a simple enquiry correctly identified the majority of individuals classified as having no significant family history, but missed a significant proportion of individuals with a positive family history (Chapter 4). Furthermore, a detailed family history questionnaire results in a higher percentage of individuals reporting familial risk, and thus in a higher number of people that will be identified as having a high diabetes risk (Chapter 6). Consequently, integrating a detailed family history questionnaire into disease risk assessments might result in a higher number of participants that will be identified as having a high risk of getting the disease.

4. What is the effect on people of assessing and communicating diabetic familial risk?

a. What is the impact of communicating familial risk of diabetes in a personal consultation on illness and risk perceptions and self-reported behavioural outcomes of people with a family history of diabetes?

Compared with individuals receiving general risk information, those receiving familial risk information perceived heredity to be a more important cause of diabetes in a personal consultation. Communicating familial risk also increased personal control over preventing diabetes and, thus, did not result in fatalism. Although the intervention did not influence intentions to change behaviour, there was some evidence to suggest it increases healthy behaviour since people reported having eaten more healthily (Chapter 5).

b. What is the impact of web-based familial risk information on illness and risk perceptions and risk-reducing behaviour of people with a family history of diabetes?

Web-based diabetic familial risk information appeared to reduce worry related to diabetes risk. Moreover, among low socioeconomic groups, web-based diabetic familial risk information decreased dietary fat intake, although it did not improve risk-reducing behaviour in the total population (Chapter 6).

c. Does an intervention that emphasizes familial risk information result in false reassurance among people without a family history of diabetes?

Emphasis on familial risk did not significantly reduce risk-reducing behaviour and risk perception among individuals without a diabetic family history (Chapter 6). Thus, there is no evidence that the information leads to false reassurance in people who do not have a family history of diabetes.
Discussion of the findings

The need to address individuals at familial risk

It has been shown that the majority (94%) of first-degree relatives of patients with diabetes would like to be informed about possibilities on reducing their risk (Whitford et al., 2009). To design effective targeted prevention strategies, more in-depth information about the perceptions of individuals with a family history of diabetes is needed, as was explained in the introduction of this thesis. The results of the qualitative study as described in Chapter 2 further suggests that individuals use causal beliefs to construct their perceptions of risk and control: e.g. when people perceive genetic causes for diabetes, they tend to have a higher perception of their risk and lower perception of control over getting diabetes. As individuals may have incorrect or incoherent causal beliefs, prevention programmes should promote correct understanding of the multifactorial causes of type 2 diabetes among individuals at high risk due to their family history, which might have a positive effect on their perceptions of risk and control and, directly or indirectly, on preventive behaviours. Perceptions of risk and control in turn are motivating factors for preventive health behaviours (Rippetoe & Rogers, 1987). In this thesis the effect of familial risk information on the separate elements of the conceptual model (causal beliefs, risk perception, perceived personal control, and behaviour change) were investigated. However, the chapters in this thesis provide no modelling of the relationships between these concepts.

Requirements for assessing diabetic family history

In order to target individuals at familial risk, it is essential to adequately assess family history. In the introduction of this thesis it was hypothesized that a systematic way of assessing familial risk would increase the accuracy of the reporting by people of their family history and also increase their risk awareness. The findings in this thesis show that 10% more individuals were classified at high diabetes risk (20 in 100 for getting diabetes within 5 years) when familial risk was assessed with a detailed web-based family history questionnaire as compared to a simple enquiry. This tool enhanced identification of individuals at high risk probably due to a more accurate ascertainment of familial risk. Currently the number of self-administered multifactorial risk assessment tools for common diseases on the Internet is increasing (e.g. www.kijkopdiabetes.nl and the QDScore) (Alssema, 2008; Hippisley-Cox, 2009). These tools often limit family history enquiry to a single question. Integrating a detailed family history questionnaire into these risk assessments might result in a higher number of participants that will be identified as having a high disease risk. Moreover, studies performed in this thesis show that the addition of a detailed familial risk assessment to a general diabetes risk assessment is evaluated as equally time-consuming as a simple enquiry by individuals with a family history. A possible explanation might be that addressing relatives’ diabetes history enhances motivation for personal diabetes risk assessment, since it has been shown that people consider knowledge of family history important to their personal health (Centers for Disease Control and Prevention, 2004).

Effect of familial risk information on illness and risk perceptions

Chapter 5 showed that individuals who received familial risk information as compared to those receiving general risk information had a higher increase in the perception that heredity or diabetes running in the family is a cause of diabetes. The information was provided in a personal consultation. However, the study described in Chapter 6 showed an increase in the perception that family history is a cause of diabetes among people without familial risk and no change among individuals at familial risk. This suggests that individuals at diabetic familial risk were already aware of family history as a risk factor. The latter is in line with earlier findings showing that individuals with a family history indicated a parental history as the most important risk factor for diabetes (Pierce et al., 2001).
the means of the perception that family history is a cause of diabetes were similar at baseline in both studies, the differences in findings between the trial in Chapter 5 and Chapter 6 might be explained by the difference in ways of communicating the risk: a personal consultation versus web-based information. It is likely that the information is retained better when communicated in a personal consultation, as has been shown in Chapter 5.

Several studies show that people at familial risk for diabetes perceive a higher risk of getting the disease than people without a family history, but that it is often still an underestimation of their actual diabetes risk (Acheson et al., 2010; Adriaanse et al., 2003; Hariri et al., 2006). As the most important risk factor in explaining perceived risk to diabetes was shown to be the number of affected first-degree relatives (Claassen et al., 2011), it can be expected that raising awareness by providing familial risk information will increase people’s risk perception. However, this thesis shows that explicitly informing individuals about their familial risk did not change their perception of being at risk for diabetes when compared to general risk information. A possible explanation for the remaining underestimation of their risk is that people show an optimistic bias when considering their own health risk (Weinstein, 1987), even when their familial risk is emphasized. Another explanation might be that familial risk information does not provide new information about the height of the risk, but rather about the multi-causality of diabetes and thus does not influence people’s risk perception.

A drawback of communicating familial risk might be that it has a potential for fatalism, i.e. the feeling that one has no control over the risk of getting diabetes (Shiloh et al., 2002). This thesis showed that familial risk information increased perceived control over preventing diabetes in a face-to-face consultation (Chapter 5) and resulted in equal perceptions about control as compared to general diabetes risk information in the web-based trial (Chapter 6), and thus does not result in fatalism. A systematic review, which investigates whether personalized genetic risk information may lead to fatalism and uses data of this thesis, among others, supports this conclusion (Collins et al., 2010). Thus, diabetic familial risk information does not result in fatalism, i.e. does not decrease feelings of control over getting diabetes.

**Effect of familial risk information on behaviour change**

It has been suggested that family history can play an important role in risk assessment and prevention of common chronic diseases (Yoon et al., 2003; Claassen et al., 2010). In this thesis diabetes was taken as an example for other common diseases. Chapter 5 shows that participants of an intervention in which familial risk of diabetes is communicated in a face-to-face consultation and resulted in equal perceptions about control as compared to general diabetes risk information in the web-based trial (Chapter 6), and thus does not result in fatalism. A systematic review, which investigates whether personalized genetic risk information may lead to fatalism and uses data of this thesis, among others, supports this conclusion (Collins et al., 2010). Thus, diabetic familial risk information does not result in fatalism, i.e. does not decrease feelings of control over getting diabetes.

**Adverse effects of diabetic familial risk information**

Individuals with a strong family history of diabetes were five times more likely to be worried about developing diabetes than were people without familial risk, when they were asked “How worried are you that you will get diabetes in the future?” (Zlot et al., 2009). However, this thesis showed that worries about their risk for getting diabetes were lower when individuals with a family history received
specific familial risk information as compared to these individuals who only received general diabetes risk information. This might be because the importance of risk-reducing measures was emphasized in the intervention group. As the aim of the intervention was to make individuals at familial risk more aware of their risk, it is important to note that their risk perception (which is not the same as risk worries) did not change. Furthermore, Chapter 5 showed that familial risk information does not result in psychological harm, as represented by anxiety at the time of measurement, or change in mood state. This finding has been confirmed by other studies (Qureshi, et al., 2001; Pierce et al., 2000).

When a public health approach is used, also people without a family history of diabetes will be confronted with familial risk information of diabetes. A potential drawback of the emphasis on familial risk might be that this group without a family history will be falsely reassured about their risk (Marteau et al., 1996). They might believe they are not at risk for diabetes, while they may have other risk factors such as being overweight. As a result, they will adopt or maintain an unhealthy lifestyle. However, there was no difference on risk-reducing behaviour or the perception of their risk between individuals who received general risk information only compared to individuals who received familial risk information, as was shown in Chapter 6. Thus, there was no evidence of false reassurance when diabetic familial risk information is provided to individuals without a family history. Although there is no other data available to confirm this finding, in a stepwise screening programme a negative test result at diabetes screening did not seem to promote false reassurance either (Paddison et al., 2009), as represented by no lower perceived risk, lower intentions for health-related behavioural change, or higher self-rated health.

The qualitative data in Chapter 3 proposed that familial risk information might have a negative influence on family relations. Individuals argued that some family members do not want to be informed, or the patient might be blamed for putting the family at risk. More quantitative findings presented in Chapter 7, however, showed that hardly any participant receiving familial risk information believed that this information could distort family relations. Also, Van Esch et al. (2011) showed that Dutch diabetes patients were positive about their ability to disseminate risk- and preventive messages in the family. This suggests that providing familial risk information can be considered an accepted strategy in diabetes prevention, which may even enhance family communication.

Methodological reflections
Some methodological issues of this thesis should be noted.

Strengths
The step-by-step methodology, both quantitative and qualitative, that were used in this thesis ensured the development of a well-informed intervention strategy to target people with a diabetic familial risk and provide them with relevant family history information and suggest preventive measures. To gain an understanding of underlying reasons and motivations of the effect of familial risk information on motivation to engage in preventive behaviour, perceptions of risk and illness of people at diabetic familial risk (Chapter 2) were explored. These perceptions were used to design an intervention that explains the role of family history in diabetes risk to promote healthy behaviour. Consequently, the potential effectiveness of this intervention was evaluated in a first study (Chapter 5), showing promising results. After consulting the target group again by using focus group interviews (Chapter 3), the intervention was improved further and its effectiveness was evaluated in a randomized controlled trial with a relatively large study population (PreDiCT trial) (Chapter 6). This method, a randomized controlled trial, is the preferred design for investigating causal relations between determinants and outcomes. Furthermore, in both randomized controlled trials, people were not aware that they were selected because of being a familial risk for diabetes. Knowledge about this selection criterion might
otherwise have biased the perceptions of the participants as the effect of familial risk information was compared to the effect of general diabetes risk information. Both trials conducted in this thesis had fairly high response rates (80% and 86%). Also in the PreDiCT trial response analyses showed that there were no differences between participants and those who refused participation and no differences were found between individuals who were lost to follow-up after three months and respondents who completed all questionnaires.

**Limitations**

One should be cautious when generalizing these findings to the broader community. The samples used in this thesis did not represent the ethnic mix of the Dutch population, there was an age limit of 35 – 75 years and the populations reflected individuals with a Body Mass Index ≥ 25 (Chapter 6) or a high score on the symptom risk questionnaire (Chapter 5) (Ruige et al., 1997). While the intervention was designed to target overweight people at familial risk, some people with a healthy weight are also at risk for developing diabetes, some of them having a relatively rare monogenic form of diabetes (e.g. Maturity-Onset Diabetes of the Young, MODY). It is also important to provide this group with adequate information, since preventive measures given in the interventions in this thesis are of less relevance for this group (except for the fact that they can be motivated to maintain their healthy lifestyle). No golden standard (e.g. medical records) has been used to validate the accuracy of the detailed family history questionnaire. This limits confirming evidence regarding whether the higher number of individuals at increased risk of diabetes identified with the detailed questionnaire as compared to a simple enquiry is correct. Furthermore, the increase of blended or reconstituted families may weaken the use of family history as a tool in diabetes prevention (Yoon et al., 2003). Also, because families are getting smaller, having no positive family history will be less informative, whereas a positive family history increases the value of the information (Yang et al., 1998). For the web-based PreDiCT trial, described in Chapter 6, it should be noted that participants were rewarded with an incentive and were aware of participating in scientific research. If the detailed family history assessment and information is provided in usual practice individuals might reserve less time for the information. Another limitation of the studies presented in this thesis is that self-reported measures were used for the behavioural outcomes. Nevertheless, for all such measures in the PreDiCT trial validated instruments were used. Objective measures, such as data from biomarkers or accelerometers were not feasible, since time and resources were limited and in the PreDiCT trial an online research panel was used that restricted the possibility of performing physical measurements. Nonetheless, if over- and underreporting occurred, this would probably have been true for both groups. A final limitation that should be noted is the possible measurement errors of some of the illness and risk perception measures used in either trial, since validity and reliability has not been tested for all. However, the measures were optimized in the PreDiCT trial (Chapter 6) by using data of the first trial (Chapter 5).

**Implications of the findings**

**Implications for practice**

Today, risk assessment instruments for many common chronic diseases are increasingly offered via the Internet or in primary care in order to indicate individuals at risk and to be able to give the appropriate lifestyle advice or refer them to specialised care. An example in the Netherlands is the ‘ PreventieConsult’ (Dekker et al., 2011), using a health risk assessment tool to be completed at home, followed by preventive measures for diabetes, cardiovascular disease, and renal diseases in high-risk groups. Another example is the Diabetes Risk Test (Alssema, 2008), the instrument that was used in Chapter 6 (www.kijkopdiabetes.nl). A more systematic and detailed way of assessing diabetic familial
risk might improve the risk assessment of these instruments. The PreDiCT study showed that an important gain of using a detailed diabetic familial risk assessment is that 10% more individuals at familial risk will be identified. Individuals are more likely to report having a family history when using this type of assessment than with a simple enquiry. Furthermore, this thesis shows that familial risk information may lead to improved self-reported risk-reducing behaviour, especially among those having the greatest need of preventive measures, i.e. lower socioeconomic groups. These findings show that it is preferable to use detailed familial risk information in addition to general disease risk information as a public health approach (i.e. universal prevention), since more people at risk will be identified. In this way family history information can be considered as a population-wide screening tool, a similar approach to that intended with Family Healthcare™ (Yoon et al., 2009). Additionally, individual care (i.e. indicated prevention) remains of importance, as studies performed in this thesis show an effect of familial risk information on preventive behaviour when communicated during a personal consultation. As diabetes was used as an example for other common chronic diseases (e.g. heart diseases), a detailed familial risk assessment of other common diseases might enhance identification of people at risk and familial risk information might increase risk awareness and motivate preventive behaviour. In conclusion, the findings of this thesis suggest that detailed familial risk assessment and information is used in a public health approach to identify people at risk for diabetes, and familial risk information within individual care is important for diabetes prevention.

**Implications for future research**

Findings of this thesis show the effect of diabetic familial risk information on overweight individuals of 35 – 75 years of age. Further studies are needed to determine whether the findings can be extrapolated to the general population, including normal-weight individuals, and individuals of a wider age range. Whereas diabetes is used as an example for other multifactorial diseases, it remains to be seen whether people respond in the same way when other diseases are considered, such as cardiovascular disease or cancer. Chapter 6 showed an effect of familial risk information on saturated fat intake among lower socioeconomic groups. Within this study this effect could not be explained by less knowledge of risk factors or more saturated fat intake among this subgroup, which are often-used explanations of an effect among lower socioeconomic groups (Govil et al., 2009). Therefore, further research is needed among this subgroup. Findings in Chapter 6 showed that the addition of a detailed familial risk questionnaire to a diabetes risk assessment is preferred, at least in a public health setting, since this method results in a better reporting of the family history and consequently improves risk identification. Further research can examine whether this method also improves diabetes risk identification within the primary care setting or workplace setting. The proposed relations shown in the conceptual model in figure 1 in the introduction section have not been tested, but these concepts have only been explored by using qualitative data. It would be interesting to confirm the relations between the concepts and health behaviour, by using Structural Equation Modelling for example.

As new susceptibility genes for common chronic diseases are being discovered every day and individuals can today be tested for a large number of genetic conditions, varying in seriousness and controllability, genetic risk information (based on DNA test results) might become more important in the future. The question arises whether findings of studies performed in this thesis about familial risk information can be translated to genetic risk information. Genetic risk information solely reflects the genetic predisposition, whereas family history information reflects both the genetic predisposition and the shared behavioural and environmental factors. Chapter 3 of this thesis show that different reasons underlying motivation were considered when comparing DNA test results and a family history risk assessment in this thesis and a study of Markowitz et al. (2011) supports this finding. These results
suggest that the impact of family history information as described here cannot be translated one-on-one to the future impact of DNA test results, as differences in perceptions are expected. More comparative trials of DNA test results versus family history-based disease risk assessment are needed to confirm these findings. In addition, even if a sufficient number of susceptibility genes are discovered to predict common chronic diseases, family history will still remain an important information source as it reflects more than merely a genetic predisposition (Burke et al., 2011).

Key messages from this thesis
Most common chronic diseases are the result of interactions of multiple genes and environmental influences. Although these interactions are complex, almost every individual has access to a free, well-proven, personalized ‘genomic’ tool that captures many of these interactions and can serve as the cornerstone for individualized disease prevention: their family history (Guttmacher et al., 2004). This thesis examined the potential use of family history assessment and information for the prevention of common chronic diseases, and used type 2 diabetes as an example. Three key messages can be drawn from this thesis that could be considered when developing individualized prevention strategies for diabetes or other common disorders that make use of family history information:

1. **A detailed familial risk assessment improves diabetes risk identification, without being evaluated as time-consuming.**

   This thesis shows that incorporating a detailed family history questionnaire into a web-based diabetes risk assessment tool enhances identification of individuals at high risk due to more accurate ascertainment of familial risk. Also, it shows that individuals who complete the detailed family history questionnaire regard the tool as taking equal time and effort compared with those who complete a simple enquiry.

2. **Familial risk information may lead to improved self-reported risk-reducing behaviour, especially among lower socioeconomic groups.**

   The findings show that participants of an intervention in which familial risk of diabetes is communicated in a face-to-face consultation reported having eaten more healthily. This intervention was performed among a relatively low-educated, older and overweight Dutch population. In a larger randomized controlled trial the addition of family history information to general web-based diabetic risk information did not result in improvements in risk behaviour among the total population with a family history of diabetes, however, low-educated individuals were more likely to reduce their saturated fat intake.

3. **Familial risk information used in a public health approach does not result in negative effects (i.e. no psychological harm, fatalism, or false reassurance).**

   For people with a family history, findings of two randomized trials show that familial risk information does not result in psychological harm. Also, it was shown that worries about their risk for getting diabetes are less than when these individuals receive general risk information about diabetes. Explaining both the familial risk and the lifestyle risk factors of diabetes in a face-to-face consultation led to increased perceived control over preventing diabetes, and thus familial risk information does not result in fatalism. Furthermore it was shown that individuals without a family history of diabetes who received web-based familial risk information showed no difference in their risk-reducing behaviour or perception of their risk when compared to people who received general diabetes risk information only. Thus there was no evidence of false reassurance.
References
References


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