Familial hypercholesterolemia screening in the Netherlands: psychological and social consequences
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With the emerging knowledge of genetics, predictive testing for an increasing number of genetically mediated risk factors will be likely to be more broadly available, the testing often being organised within screening programmes [1]. Before implementing such a screening programme, one has to consider the pros (e.g. health benefits) and cons. Even if the empirical evidence of beneficial health effects of the screening is convincing, the broader psychological and societal consequences may require a limited or at least carefully guided implementation [2,3].

Familial hypercholesterolemia (FH) is a genetic disorder, predisposing for coronary artery disease, with an estimated frequency of 1 in 500 persons in Western countries [4]. In 1994 the ‘Foundation for tracing hereditary hypercholesterolemia’ (Dutch acronym: StOEH) was founded in the Netherlands to perform genetic cascade-screening for FH. Within this screening programme, relatives of genetically confirmed FH patients are tested for FH [5,6].

The aim of this thesis was to evaluate the acceptability and feasibility of the implementation of this preliminary FH screening programme to support national decision-making on a future screening programme.

To evaluate the individual consequences of the screening programme a longitudinal study design was used following a large unselected cohort of screenees, screened between March and September 1998. Data for this evaluation of psychological consequences were collected by means of four self-administered questionnaires (T0: at screening, before knowing the test result; T1: 3 days after receiving the test result; T2: 7 months after the test result; T3: 1.5 years after the test result). The first questionnaire was handed out at screening and filled out at home. The other questionnaires were send by mail. All participants of the evaluation study were 18 years or older. Non-participants of the screening programme were interviewed by phone.

To evaluate the possible social consequences of the screening, 350 individuals aged 20 to 60 years with known test results, and who were screened between 1st of January 1994 and 31st of December 1997, were selected from the StOEH registry. We chose to select this second sample of screenees different from those participating in the evaluation of psychological consequences, because due to the longer time span after testing, more people would have acquired life insurance and/or a mortgage (technically spoken, exposure was insufficient in the first sample). Again data collection was by means of a self-administered postal questionnaire.

The overall response rate of the evaluation of psychological consequences was 76% (see figure 1); 677 screenees agreed with participating in the evaluation study, 647 send back the first, 603 the second, 556 the third and 513 the fourth questionnaire. The response rate of the evaluation of the social consequences was 61%.

In chapter 2 the screenees’ views on, and the psychological impact of the family-based genetic screening programme for familial hypercholesterolemia (FH) were assessed and non-participation was evaluated. Less than 5% of the screenees were critical of the approach and of the information provided. Of all screenees, 20% expressed some degree of social pressure. Furthermore, effects on mood were minimal to absent, as were ‘quality of life’ (QoL) effects in general. In this chapter it was concluded that screening for FH is highly acceptable to screenees, although some degree of social pressure is prevalent. Only 2% of the people approached for screening declined the screening offer.
While chapter 2 described only short-term effects of the screening offer on QoL, chapter 3 focussed on the long-term QoL effects. The QoL in FH-screenees remained essentially unchanged during FH-screening. No differences between FH-positive and FH-negative screenees were found. Some known small effects of age and gender on QoL-levels were confirmed, as well as an initial effect on QoL in some of the screenees. Furthermore, the more one experienced a feeling of social pressure, and the higher one perceived the chance of having a heart attack later in life, the lower the QoL; all these significant effects, however, were small to negligible relative to the scale. Combining the results from chapter 2 and 3, no adverse effects both on short- and long-term QoL were shown and the set-up of the screening programme seemed adequate. Only a low percentage approached people declined the screening offer.

In chapter 4 the perceived control and preventive behaviour of the screenees was assessed by using the Multi-Dimensional Health Locus of Control scale, and by a question on ‘fatalism’ in FH-positive and ‘false reassurance’ in FH-negative screenees. Of the FH-positive screenees, 54% were labelled as ‘fatalistic’ and 23% of the FH-negative screenees as ‘falsely reassured’. Being ‘fatalistic’ or ‘falsely reassured’ was inversely related to clinical outcome quality. Almost all FH-positive screenees planned to have a cholesterol check in the future. However, the ‘falsely reassured’ FH-negative screenees planned this less often than other FH-negative screenees. Furthermore, both ‘fatalistic’ and ‘falsely reassured’ screenees externalise the locus of control of their cholesterol level more than those who were not. Overall, in people screened for FH, ‘fatalism’ and ‘false reassurance’ seem to be associated with worse clinical outcome quality and thus more effort should be put into preventing ‘fatalism’ and ‘false reassurance’ in the screening set-up.

In chapter 5 the accuracy and determinants of the screenees’ risk perception were described. Furthermore, it was tested whether a predicted influence of risk perception on subsequent preventive behaviour could be observed. On average, the screenees underestimated their numeric risk of having FH and getting a
myocardial infarction (MI). FH-positive screenees perceived being at higher risk of MI than FH-negative screenees, risk perception being measured prior to disclosure of FH status. Furthermore, screenees with the highest actual risk more often used medication, perceived a greater risk and opted more often for future gene therapy. Risk perception of having FH was influenced by cholesterol level, while MI risk perception was affected by age, education, cholesterol level, and cardiovascular disease (CVD) in the family. The conclusion was that FH-positive screenees 'correctly' perceived a higher risk of getting a heart attack than FH-negative screenees. Screenees did not believe that MI was inevitable and risk perception was associated with both medication use and the intention to opt for gene therapy, but not with other preventive measures, like quitting smoking. Thus, genetic risk notification seemed to be acceptable and did not lead to aversion to preventive behaviour, despite inaccurate quantitative risk estimates.

To judge the performance of the screening programme, in chapter 6 the entire chain of detection, treatment process and clinical outcome quality in FH-positive screenees were assessed. Treatment process quality was measured by the number of people treated according to the key recommendations of the Dutch guidelines on hypercholesterolemia [7,8] at 7 months after screening; clinical outcome quality was measured by achieved cholesterol level, body mass index and smoking status at 18 months after screening. Although quality generally improved substantially, screen-positives as a group – 25% newly identified cases and 75% patients already known to be clinically hypercholesterolemic – ultimately did not receive optimal care. Treatment process quality was still unsatisfactory in 21% (new: 40% versus already known patients: 14%) and clinical outcome quality was insufficient in 47% (new: 48% versus already known patients: 46%) of the cases. Insufficiencies were observed for all predefined quality aspects and were unrelated to setting or patient. In conclusion, to justify screening, current treatment performance in screen-positives must be improved. This may be achieved by improved physician education, explicit treatment process monitoring and change of the programme's follow-up procedure for screen-positives.

In the last chapter (chapter 7) the presence of negative social consequences of the screening programme was evaluated, specifically the presence of unduly limited access to insurance. In spite of detailed guidelines and legislation on the use of genetic test information, screenees encountered unanticipated insurance problems. It is not clear why these problems occur: do insurance companies ask unjustified questions regarding genetic testing or questions that can be read as such, or do individuals themselves provide more information than strictly asked for. We concluded that guidelines and legislation on genetic information are but a prerequisite, that education of all involved is equally important, and that still actual risk and insurance behaviour are difficult to reconcile.

Having arrived at the end of the chapter by chapter summary of the results, we proceed with the ultimate goal of the evaluation study: the support of national decision-making on the future of the screening programme. As apparent from table 1, our research filled out the gaps in the table of key factors for screening evaluation (see also the introduction of this thesis).
Table 1 Known and unknown factors for the assessment of FH screening

1. Knowledge of population and FH
   a. Disease burden: In Western countries 1 in 500 persons has FH [4]
   b. Target population: Family members of clinically diagnosed and genetically confirmed patients
   c. Level of risk: Patients with a clinical diagnosis have an excess mortality from CVD, in particular at a young age [4,9-11]
   d. Pre-clinical phase: Present [4]
   e. Natural course of FH: Known [4], however in clinically diagnosed patients only, not in genetically identified patients without clinical signs of FH. The natural course of FH in genetically diagnosed patients was estimated in the evaluation study of the Dutch FH-screening programme using the Framingham function [12], assuming that the extra CVD risk in FH patients is caused completely by the raised serum cholesterol level [13]

2. Feasibility of screening procedures
   a. Test: Feasibility of the mutation analyses within the Dutch screening programme is evaluated within the evaluation study of the Dutch FH-screening programme [13]
   b. Acceptability of screening procedure to screened population: Screening procedure is well accepted by the screenees [Chapter 1 of this thesis]
   c. Screening process: Screening process is feasible [Chapter 2, 3 & 6 of this thesis]

3. Interventions and follow up
   a. Physical effects: the screening has a positive health effect [13]
   b. Psychological effects: no adverse effects both on short and long term QoL were shown; ‘fatalism’ and ‘false reassurance’ need more attention; genetic risk notification seemed to be acceptable and did not lead to aversion to preventive behaviour [Chapters 2 to 5 of this thesis]
   c. Social effects: no adverse effects on the social sub-scales of the QoL questionnaires was shown [Chapter 2 & 3 of this thesis]
   d. Follow-up: Quality of treatment generally improved substantially after screening, although 21% (treatment process) and 47% (clinical outcome quality) of the screenees ultimately did not receive optimal care. [Chapter 6 of this thesis]
   e. Consensus on management for those with FH: Present (cholesterol consensus) [7,8]

4. Societal and health system issues
   a. Economic and medical costs: the screening is ‘border-line’ cost-effective with costs per saved person year between €25.000,- and €32.000,- [13]
   b. Psychological costs: no adverse effects both on short and long term QoL were shown; ‘fatalism’ and ‘false reassurance’ need more attention; genetic risk notification seemed to be acceptable and did not lead to aversion to preventive behaviour [Chapters 2 to 5 of this thesis]
   c. Societal costs: Although guidelines and legislation on the use of genetic test information exist, screenees still may encounter unanticipated insurance problems [Chapter 7 of this thesis]
   d. Appropriate screening services accessible to entire population: Insufficiencies were observed for all predefined quality aspects and were unrelated to setting or patient [Chapter 6 of this thesis]
   e. Confidentiality procedures and anti-discrimination provisions: Although guidelines and legislation on the use of genetic test information exist, screenees still may encounter unanticipated insurance problems. Guidelines and legislation on genetic information are but a prerequisite and that education of all involved is equally important [Chapter 7 of this thesis]
The results described in this thesis, combined with the results from the overall report of the evaluation of the screening programme [13], including a cost-effectiveness analysis [14], allow for the following recommendations:

- Evidence so far warrants introduction of the screening for FH. However, follow up of this recommendation requires a political judgement whether the feasibility and cost-effectiveness is sufficient to cover expenses for screening for FH.
- Information provision has to be improved; this concerns information to clients (both screenees who test positive and negative), to general practitioners (on FH in general and on follow-up) and to insurance companies.
- Compliance with the Medical Examinations Act (MEA) concerning the interpretation of information on FH has to be ensured.
- Screening has to follow an explicit protocol, with concerning both the diagnostic and therapeutic pathway, especially after a positive test result. In the diagnostic pathway, a simultaneous DNA-test and cholesterol measurement should be considered. Regarding the clinical follow-up, the Dutch guidelines on hypercholesterolemia [7,8] should be more closely followed with extra attention to compliance.
- Once implemented, the screening programme should be (continuously) monitored, and its effectiveness and efficiency under practice circumstances should be re-estimated [15]. This evaluation should be conform a detailed description of the screenees, including their relation to the index patient, the presence of other CVD risk factors, and has to cover a relevant follow-up where on an individual basis process and outcome are observed. In general, a continuous evaluation of the screening process (including the DNA testing) should be implemented combining expertise of the executive organisation and relevant national organisations (e.g. the Dutch Heart Foundation, Foundation for Clinical Genetics in the Netherlands, National Health Board, Dutch Institute for Health Care, Health Care Insurance Board and academic research institutes).

Apart from the above direct recommendations, our investigations showed the utility and feasibility of systematic, quantitative research on the process effects of medical screening. As these process effects are relevant to all genetic screening programmes and their measurement is a returning challenge in screening evaluations, the methodological yields of this thesis are now summarised.

A general methodological achievement was the measurement of the quality of the first stage of the screening programme. With this first stage the invitation is meant, the background of participation and non-participation, the role of provided information and social processes, and the degree to which this vital part of any screening programme is in accordance with generally accepted ethical performance criteria. The successful operationalisation of the (adapted) Wilson and Jungner criteria, relevant to these issues, justifies in our view further application in the evaluation of future screening programmes.

A second general achievement of the study was the demonstration that a formal empirical analysis of insurance consequences was possible and showed facts crucial for societal decision making (see below). This analysis should be, in our view, a regular explicit part of any evaluation study.

It is regrettable that insurance companies and their representatives so far were inaccessible to provide information on the guidelines – if present – they use for decisions on acceptation and the
height of premiums. In a sense, our test is one-sided, as we have to rely on patient's experience only. However, our data suggested irrational behaviour of insurance companies. In the best case, insurance companies are not unwilling but ill-informed and base decisions on unreliable risk tables.

A third general achievement was the successful application of pre-specified models to describe and explain attitudes and behaviour of screenees in the various stages of the programme. We used standard QoL tools in a repeated measures design to describe QoL effects and adapted previously defined thresholds to define 'abnormal' or 'adverse', being aware that multi-item questionnaires need external reference to define a threshold of 'relevance'. However, the wide experience with the measures chosen supported this application. The framework of 'false reassurance' and 'fatalism' was particularly successful to explain procedural adherence of the screenees. The addition of 'locus of control' as an explanatory concept has not only proved a valuable concept to explain variance in attitude, but also as a concept to individualise counselling. We intended to describe outcome in terms of preventive behaviour and medical follow-up undertaken to improve cardiovascular risk (rather than hypercholesterolemia alone), and in terms of more distal parameters of cardiovascular disease. Although follow-up was too short to be able to observe cardiovascular manifestations like myocardial infarction, still, the used outcome measures demonstrated an interesting discrepancy between actions undertaken and effects achieved. From a clinical point of view our results imply a warning to those process quality measures of screening and treatment alone: only distal measures can teach us the benefits of screening programmes. From a methodological point of view, this combination of effect measures may prove useful in any context with a long chain of events connecting primary events and final benefit.

Finally a remark should be made to the use of cost-effectiveness models, although the results are not a regular part of this thesis. From the cost-effectiveness analysis performed by Marang-van de Mheen et al. [14] it is clear that the cost of life long statin therapy, not the screening process itself, is the single most important determinant of the costs. These costs, combined with the life years gained, determine the cost-effectiveness ratio. Another study (performed by the StOEH in collaboration with the London School of Hygiene and Tropical Medicine) estimated considerably lower costs [16] (approximately 8.700 Euros compared to the 25.000 to 32.000 Euros per life year gained estimated in our evaluation study). In the analysis performed by Marang-van de Mheen et al., methods to avoid overestimation of the effectiveness of the FH screening programme were used. As the assumption was made that the increased CVD risk in FH patients is carried through the elevated cholesterol level [14], it is justifiable to use the Framingham risk function [12]. Although this may have underestimated the CVD risks in FH, the alternative _ using risks as found in the Simon Broome register [9] _ may not apply to this screening cohort, as many FH positive screenees in the Dutch screening programme did not comply with the clinical criteria of FH [4] (no overt CVD (this thesis) or hypercholesterolemia [17]). Moreover, the effectiveness as estimated in the analysis performed by Marang-van de Mheen et al. may even be lower because the compliance assumptions of 100% follow-up, treatment and treatment compliance were probably too generous [13, 18]. However, debate about the assumptions made for cost-effectiveness studies will always exist [19] and one can conclude that, at present, the cost-effectiveness as estimated by Wonderling et al. [16] will represent the lower limit and the estimate by Marang-van de Mheen et al. [14] the upper limit.

Another article on the evaluation of the implementation of the FH screening programme is
published recently [20]. In this study of Umans-Eckenhause et al. less screenees were treated with statins before screening than in the current study (39% versus 57%). This difference might be due to a slight difference in study population, concerning age and inclusion period.

The implementation of the FH screening programme is both evaluated by the StOEH itself [16] and an external evaluation study (results partly reported in this thesis) [13]. We think that this external evaluation certainly has an additional value due to the conceptual approach using a systematic evaluation by the criteria of Wilson and Jungner.

**Policy implications**

After assessing the pros and cons of the screening as described in the independent evaluation study, the next logical step is to give a provisional analysis of what health policy actions actually were undertaken since our report appeared in September 2000 [13].

The policy judgement on the feasibility of the FH screening programme was positive and in July 2002 the Dutch minister of Health, Welfare and Sports endorsed the recommendations on the Dutch screening programme for FH as given in the evaluation study [21].

Furthermore, as the committee of the Health Council of the Netherlands concluded that FH is a treatable disease [17], the act does not limit the right of insurers to ask questions and carry out investigations in respect of FH, but asking questions about (the results of) genetic testing is not permitted below the 'question limit' (see chapter 7).

However, problems with access to important insurance policies for FH positive screenees were seen as a major obstacle to the implementation of the screening programme. The solution of these problems was put forward as a prerequisite and only if the insurers will have a suitable answer to the possible problems concerning the accessibility to insurance policies, the ministry will effectuate its decision to fund the genetic screening programme for FH.

The solution as seen by the committee of the Health Council of the Netherlands [22] were both more detailed rules on the permissibility of certain questions and the obligation for insurers to make clear to applicants what information he or she is required to give. Also improvements should be made in public publicity on this matter. Furthermore, insurers should base their assessment of risk on accepted medical understanding.

Attractive as this method of political pressure may seem, many involved in the screening programme fear discontinuation of the programme, given the long time involved in changing rules and perhaps even legislation. More effective on the short term would be better patient education, so patients can decide better both on whether they want to participate in the screening and, if they decided on participating and apply for an insurance, what to answer to the questions in the application.

**Future genetic screening programmes**

The genetic knowledge expands rapidly and it has been suggested that new technologies like DNA microarrays (or the so-called DNA chip) will be routinely used for disease diagnosis within the decade [23]. These new diagnostic tests will make large-scale genetic testing for various genetic risk factors feasible. Using these new techniques, more genetic screening programmes will become available in the future. When those programmes will become available, the cost-
effectiveness of those programmes should be assessed for every programme independently. Foreseeing this, what can we learn from the FH experience?

This thesis proves that a broad evaluation using a conceptual approach based on the criteria of Wilson and Jungner [2], independent of the screening set-up, is a good way to evaluate screening programmes, although it has to be seen whether this is applicable to other than Caucasian ethnic groups. An important part of this evaluation is a cost-effectiveness analysis, using fixed criteria [15]. Furthermore, persons who participate in a screening should not have unduly limited access to insurance. And lastly, the evaluation should support health policy decisions on the screening programme under evaluation.

Research implications

After this comprehensive evaluation study a few questions on FH and the screening for this condition remain to be unanswered. Most of these questions can only be answered by following a cohort of screenees over time. For justification of the screening programme in the future, it is e.g. important to know what the natural course of FH is when it is treated with statins from adolescence, and what the CVD risk is for FH-positive screenees without hypercholesterolemia. Thus a detailed description of the screenees, including relation to the index patient, other CVD risk factors, and during a follow-up period a description of therapy, hypercholesterolemia, and CVD events is needed. This should be done as a part of a continuous evaluation process of the screening programme.

Samenvatting

Met het groeien van de kennis over genetica zullen er steeds meer genetische risicofactoren ontdekt worden. De volgende stap is dat mensen, vóórdat ziekte is opgetreden, op deze genetische risicofactoren getest kunnen worden. Steeds meer van deze testen zullen beschikbaar komen en waarschijnlijk georganiseerd worden binnen screeningsprogramma's.

Voordat een screeningsprogramma op grote schaal ingevoerd kan worden, moeten een aantal factoren afgewogen worden. Het is belangrijk om te weten wat de positieve effecten van een screeningsprogramma zijn (bijvoorbeeld gezondheidswinst), maar het is net zo belangrijk om te weten of er niet te veel negatieve effecten zullen optreden. Dus, zelfs als er genoeg bewijs is voor de positieve effecten, verdienen de bredere psychosociale en maatschappelijke gevolgen aandacht voordat een screeningsprogramma kan worden ingevoerd.

Familiair Hypercholesterolemie (FH) is een genetische aandoenig die hart- en vaatziekten kan veroorzaken. In Westerse landen wordt geschat dat 1 op de 500 mensen drager is van deze aandoening [4]. In Nederland worden familieleden van mensen met een genetische diagnose FH op deze aandoening getest binnen een genetisch screeningsprogramma.

Het doel van dit proefschrift was om de aanvaardbaarheid en de haalbaarheid van de invoering van het voorlopige screeningsprogramma op FH te onderzoeken. Dit ter ondersteuning van beleidsvorming op het gebied van toekomstige screening.

Wij evaluerden de mogelijke gevolgen van het screeningsprogramma door middel van een longitudinaal vragenlijstonderzoek. De deelnemers aan het onderzoek kregen vier vragenlijsten (bij screening, voordat het testresultaat bekend was (T0), en vervolgens 3 dagen (T1), 7 maanden (T2) en 1,5 jaar (T3) na het ontvangen van het testresultaat). De eerste vragenlijst kregen de deelnemers bij bloedafname, zij konden deze vervolgens thuis invullen. De overige drie vragenlijsten werden per post naar de deelnemers opgestuurd. De mensen die niet wilden deelnemen aan het screeningsprogramma werden per telefoon geïnterviewd.

Om te onderzoeken wat de mogelijke sociale gevolgen van de screening zouden kunnen zijn, werden 350 mensen benaderd. Deze mensen waren getest tussen 1 januari 1994 en 31 december 1997, waren tussen de 20 en 60 jaar, en hun testresultaat was bekend. We kozen ervoor om andere mensen te benaderen dan de deelnemers aan het psychologische deelonderzoek, omdat na verwachting niet voldoende mensen een verzekering of hypotheek zouden hebben afgesloten in slechts anderhalf jaar na het krijgen van de testuitslag. Ook dit deelonderzoek werd verricht door middel van een vragenlijst.

De totale respons van de psychologische evaluatie was 76% (zie figuur 1); 677 gescreenden stemden in met deelname aan de studie, van wie 647 de eerste, 603 de tweede, 566 de derde vragenlijst en 513 alle vier de vragenlijsten terugstuurden. De respons van de evaluatie studie van de mogelijke sociale consequenties was 61%.
In hoofdstuk 2 hebben we zowel de mening van de gescreende over het screeningsprogramma, de psychologische gevolgen van de benadering voor het screeningsprogramma, als de non-participatie van het screeningsonderzoek onderzocht.

Van de mensen die benaderd werden voor de screening, stemde 2% van de mensen niet in met deelname. Deze 2% was niet geïnteresseerd, al klinisch gediagnostiseerd met FH, of bang voor problemen met het afsluiten van verzekeringen.

Minder dan 5% van de gescreende was niet tevredee over de benadering en de informatievoorziening. Van alle gescreende, zei 20% sociale druk tot deelname gevoeld te hebben. Verder was er geen tot weinig invloed op stemming en algemene 'kwaliteit van leven' (KvL).

In dit hoofdstuk concludeerden we dat screening op FH zeer aanvaardbaar is voor de gescreende, hoewel sociale druk aanwezig is. Verder besloot slechts een klein deel van de benaderde mensen om niet deel te nemen aan de screening.

Terwijl hoofdstuk 2 slechts de korte termijn effecten op de KvL beschrijft, gaat hoofdstuk 3 dieper in op de KvL effecten op langere termijn. De KvL van de op FH gescreende mensen veranderde vrijwel niet gedurende de screening en de periode daarna. Er werden geen verschillen in KvL aangetoond tussen mensen met en mensen zonder FH. Een aantal kleine bekende effecten van leeftijd en geslacht op de KvL werden in dit onderzoek bevestigd. Ook was er bij een aantal gescreende een kortdurend effect op de KvL. Verder werd een slechtere KvL gerapporteerd door de mensen die een hogere sociale druk voelden en hun kans op een hartinfarct hoger inschatten. Al deze effecten waren wel statistisch significant, maar slechts klein of zelfs verwaarloosbaar. In dit hoofdstuk concludeerden we dat zowel op korte als op langere termijn geen effecten op de KvL van de gescreende mensen aantoonbaar was. De opzet van het screeningsprogramma lijkt op dit gebied dus adequaat.

In hoofdstuk 4 beschreven we de invloed die gescreende denken te hebben op hun cholesterolgehalte en het preventieve gedrag dat gescreende ondernemen na het horen van de
testuitslag. De ervaren invloed op het cholesterolgehalte werd geëvalueerd met behulp van de 'Multi-Dimensional Health Locus of Control' vragenlijst en met een vraag naar 'fatalisme' of 'onterechte geruststelling', al naar gelang de testuitslag. Aan de gescreenden met FH werd gevraagd of, nu zij FH blijken te hebben, hun cholesterolgehalte ooit normaal kan zijn en aan gescreenden zonder FH werd gevraagd of, nu zij geen FH blijken te hebben, hun cholesterolgehalte ooit te hoog kan worden.

54% van de gescreenden met FH werden als 'fatalistisch' aangemerkt en 23% van de gescreenden zonder FH als 'onterecht gerustgesteld'. 'Fatalisme' en 'onterechte geruststelling' waren negatief gerelateerd aan klinische uitkomstmaten. Bijna alle gescreenden met FH waren van plan onder controle te blijven (of gaan) voor hun cholesterolgehalte. De gescreenden die 'onterecht gerustgesteld' waren, waren minder vaak van plan hun cholesterolgehalte in de toekomst te laten controleren. Verder legden zowel de 'fatalistische' als de 'onterecht gerustgestelde' gescreenden de controle over hun cholesterolgehalte vaker buiten zichzelf dan de overige gescreenden.

Over het algemeen leek 'fatalisme' en 'onterechte geruststelling' negatief geassocieerd te zijn met klinische uitkomstmaten. Expliciete aandacht binnen het screeningsprogramma voor 'fatalisme' en 'onterechte geruststelling' lijkt dus aangewezen.

In hoofdstuk 5 beschreven wij de risicoinschatting van de gescreenden en de factoren die samenhangen met deze risicoinschatting. Ook testten wij of de voorspelde invloed van risicoinschatting op preventief gedrag kon worden aangetoond.

Over het algemeen onderschatten de gescreenden hun numerieke kans op het hebben van FH en het krijgen van een hartinfarct. Mensen met FH schatten hun kans op het krijgen van een hartinfarct hoger in dan mensen die geen FH hadden, ook voordat zij wisten of zij FH hadden of niet. Verder gebruikten de gescreenden die feitelijk het hoogste risico hadden ook vaker medicijnen, schatten zij hun kans op een hartinfarct hoger in en zeiden zij vaker dat zij gentherapie zouden overwegen wanneer dit in de toekomst beschikbaar zou zijn.

Hoe hoog de gescreenden hun kans inschatten op het hebben van FH werd beïnvloed door hun cholesterolgehalte, terwijl het inschatten van de kans op het krijgen van een hartinfarct werd beïnvloed door leeftijd, opleiding, cholesterolgehalte en hart- en vaatziekten in de familie.

Mensen met FH schatten hun kans op het krijgen van een hartaanval terecht hoger in dan mensen zonder FH. Verder dachten gescreenden niet dat een hartaanval onvermijdelijk was als men FH had en was de risicoinschatting geassocieerd met zowel medicijngewoon als het overwegen van het ondergaan van gentherapie. Risicoperceptie was niet geassocieerd met andere preventieve maatregelen, zoals het stoppen met roken.

We kunnen dus concluderen dat het geven van een genetische diagnose acceptabel leek voor de gescreenden en dat het niet leidde tot aversie tegen preventieve maatregelen, ondanks een inaccurate risicoinschatting.

Om in te kunnen schatten of het screeningsprogramma effectief was, analyseerden we in hoofdstuk 6 de gehele keten van het opsporen van FH, de behandeling en de kwaliteit van de klinische uitkomst in gescreenden met FH.

De kwaliteit van de behandeling werd afgemeten aan het aantal mensen dat behandeld werd volgens de Nederlandse consensus voor hypercholesterolemie, 7 maanden na het krijgen van de testuitslag. De klinische uitkomstkwaliteit werd 18 maanden na het krijgen van de testuitslag gemeten met behulp van het cholesterolgehalte, 'body mass index' en of de gescreende rookte of niet.
Hoewel de uitkomstkwaliteit over het algemeen substantieel verbeterde, kregen de mensen met FH als groep (25% nieuw gediagnostiseerd en 75% mensen die al klinisch gediagnostiseerd waren met een te hoog cholesterolgehalte) uiteindelijk geen optimale zorg. De kwaliteit van de zorg was onvoldoende in 21% (nieuw: 40% versus al bekende patiënten: 14%) en klinische uitkomstkwaliteit was onvoldoende in 47% (nieuw: 48% versus al bekende patiënten: 46%) van de gescreende met FH.

Tekortkomingen werden gesignaleerd in alle vooraf gedefinieerde kwaliteitsaspecten en waren niet gerelateerd aan setting of patiënt.

Geconcludeerd kan worden dat, om screening te rechtvaardigen, het huidige behandeltraject moet worden verbeterd. Dit kan worden bereikt door het beter voorlichten van de dokters, en door het aanpassen en vervolgens continu monitoren van het behandeltraject voor gescreende met FH.

In hoofdstuk 7 beschrijven we het bestaan van eventuele negatieve maatschappelijke gevolgen. Een van de maatschappelijke gevolgen van genetische screening zouden problemen met het afsluiten van levensverzekeringen, ziektekostenverzekeringen of arbeidsongeschiktheidsverzekeringen kunnen zijn. In Nederland bestaat hierover sinds 1990 een moratorium tussen verzekeraars en overheid waarbij spelregels zijn afgesproken over het omgaan met informatie uit genetische screening. In de Wet Medische Keuringen, welke in 1998 van kracht is geworden, zijn hierover ook wettelijke regels vastgesteld. In het kader van een evaluatie van de genetische screening op Familiaire Hypercholesterolemie (FH) in Nederland is gebleken dat er ondanks afspraken in die periode toch problemen met het afsluiten van verzekeringen zijn voorgekomen. Het hebben van de aandoening FH lijkt hierbij eerder de aanleiding voor de problemen dan een te hoog cholesterolgehalte. Goede voorlichting aan zowel personen die zich willen laten screenen als aan verzekeraars, alsmede waakzaamheid bij het naleven van de gemaakte afspraken lijkt geboden.