Genetic insights, clinical efficacy and practical implications of genetic screening for familial hypercholesterolemia
Umans-Eckenhausen, M.A.W.

Citation for published version (APA):
Chapter 9

Genetic screening in the Netherlands: Practical issues and implications for health policy

Marina A.W. Umans-Eckenhuisen\textsuperscript{1,2}, John J.P. Kastelein\textsuperscript{1,2}, and Robert L.J.M. Scheerder\textsuperscript{1}

1. Foundation for the Identification of Persons with Inherited Hypercholesterolemia (StOEH), Paasheuvelweg 15, 1105 BE Amsterdam, The Netherlands

2. Department of Vascular Medicine, Academic Medical Center at the University of Amsterdam PO Box 22700, 1100 DE Amsterdam, The Netherlands

*Tijdschr v Gezondheidswetenschappen* 2001:79(5); 314-16
Abstract

The Foundation for the Identification of Persons with Inherited Hypercholesterolemia (StOEH), in close collaboration with the Academic Medical Centre (AMC) in Amsterdam, executes the national screening programme for Familial Hypercholesterolemia (FH). It is expected that in the near future similar predictive genetic screening programmes will be developed. In anticipation of these future developments, it is important to evaluate all aspects of the current FH screening programme. With respect to the following issues, knowledge and experience has been gathered by the screening organisation itself that can be useful for the development of similar, genetic screening programmes.

- Procedures of a genetic screening programme
- Information to patients
- The legislative structure
- Costs and finance
- Quality assurance and auditing

In conclusion, it is clear that in the field of genetic screening in the Netherlands much has been achieved. Still, there are a number of bottlenecks such as: the lack of structural financing of genetic screening programmes and the lack of quality assurance and auditing of genetic population screening. Furthermore, it must be noted that, as a result of genetic screening, individuals do experience problems with insurances. Here lays an important task to resolve these bottlenecks currently impairing the execution of genetic screening programmes.
Practical issues and implications

Introduction

Due to the growing knowledge of the human genome and the scientific progress in the field of DNA technology, genetic screening for a number of inheritable diseases has become an option. In the Netherlands most of these programmes are executed on a rather limited scale. Inherent to the method of genetic testing and the presymptomatic diagnosis, various societal issues can arise. The Dutch Health Council addressed these issues in a number of reports.\textsuperscript{1,2,3}

In the Netherlands, experience was obtained in the last few years with a presymptomatic genetic screening programme. The Foundation for the Identification of Persons with Inherited Hypercholesterolemia (StOEH), in close collaboration with the Academic Medical Centre (AMC) in Amsterdam, executes the national screening programme for Familial Hypercholesterolemia (FH). The aim of this programme is to identify FH patients in the presymptomatic stage of the disorder, in order to offer them therapy. The ultimate goal is a timely and effective lipid lowering treatment to reduce the cardiovascular burden of FH patients. The basis of the screening programme consists of DNA analysis in combination with pedigree based family investigation.

This innovative screening programme can serve as an example for genetic screening for other disorders in the population at large. It is expected that in the near future similar predictive genetic screening programmes will be developed. In anticipation of these future developments, it is important to evaluate all aspects of the current FH screening programme. Important issues in this respect are: psychological and social effects (employment and insurance), cost-benefit analyses, ethical and juridical dilemmas and finally health benefits for the individual as well as for the population. The department of Social Medicine of the AMC performed an evaluation study addressing the societal and psychological aspects. Also a cost effectiveness analysis was part of that study. Moreover, substantial knowledge and experience has been gathered by the screening organisation itself that can be useful for the development of similar screening programmes.

Especially the bottlenecks, experienced throughout the years, are valuable and can serve as a teaching base for those that are engaged in prevention, patient care, or insurance and from a general policy perspective. As a responsibility towards society, the FH screening organization wishes to share its knowledge and experience, and hopes to stimulate the public discussion on these topics.
Chapter 9

Procedure of the screening programme

In the Netherlands approximately 35,000-40,000 individuals suffer from FH. The disorder is characterised by elevated serum cholesterol levels, leading to atherosclerosis and premature death due to cardiovascular disease. Many are not aware of having FH and are therefore not receiving the available effective medication. Through the screening programme large numbers of young and untreated FH patients in the presymptomatic phase of the disorder are identified. Preventative treatment is then possible and useful. The StOEH executes the programme in collaboration with a network of Lipid Clinics in the Netherlands. Internists and cardiologists at these clinics send blood samples to the DNA laboratory of the AMC in Amsterdam for characterization of the gene defect of those patients in whom FH was diagnosed on clinical grounds. DNA analysis requires a complex diagnostic procedure that takes a long time and is expensive. In the Netherlands more than 130 FH causing mutations have been identified. After a mutation is established in such a FH patient, now referred to as an index case, this person is contacted for family investigation. The family members are offered the possibility of testing for the FH gene mutation that was identified in the index case. On average 90% of the approached family members gave consent to such testing. The reasons for the refusals (10%) were: anxiety for the social repercussions of genetic testing; advice of the family practitioner, not interested and the absence of offspring.

In case of a mutation which confirms the diagnosis FH, the examined person receives additional information including a letter with the test result, a letter for the family practitioner and a letter for the a specialist at a Lipid Clinic. The patient is encouraged to visit the family practitioner and a Lipid Clinic for further evaluation and treatment. Each identified FH patient is contacted after 2 years in the frame of a long-term follow-up investigation. The aims of this follow-up investigation are: to analyse the results of screening and to obtain information on the experience of the clients who were examined in the programme. With these results, the screening institution is able to adapt and if necessary improve the procedures. Finally, by this means the patient also has the possibility to obtain additional information regarding family screening, FH treatment, insurance issues etc. The StOEH strongly takes a position as a screening organisation and refers patients to Lipid Clinics for diagnostic and therapeutic assessment as well as treatment counselling.
Information

Voluntary participation on the basis of well understood information is an absolute prerequisite for genetic screening. The information needs to be balanced, and both the risks of the disease and the benefits of a timely diagnosis and treatment need to be discussed without any pressure towards the client. This pertains to all information, verbal and written. The StOEH has developed a protocol for this information stream. In this document the information and the way of contacting the index case and the family members are described in detail. The information brochures and the informed consent form have been edited throughout time on the basis of advice of clients and various experts. In the information brochure attention is paid towards the potential disadvantages of genetic testing with regard to future employment and insurance. After screening, few FH patients encounter problems with insurances, notwithstanding adequate treatment. The genetic testing is offered to first and second degree relatives of the index case when they are older then 16 years. Testing of children below the age of 16 year is performed only on specific request from both parents and child, often after consultation of a medical specialist. In a study on parental attitude towards genetic testing of children, parents expressed the need for more specific information on FH in childhood, treatment possibilities and impossibilities, diet and lifestyle. Also, more explanation was required with regard to the current age criterion for genetic testing for FH. Because of the complexity of feelings of guilt, risk perception and potential anxieties of the parent, family investigation requires much attention also for those who are not tested.

The legislative structure

The legal framework for these screening activities is formed by various acts in the field of health care and health policy. Important issues regulated in these acts are: the quality assurance of population screening programmes, rights and privileges of patients and health care practitioners, the protection of privacy of patients, quality assurance of health care practitioners and finally the guarantees for an adequate reaction in case of complaints from patients. The genetic screening programme for FH in the Netherlands falls under the ‘Population Screening Act’ directed at the quality assurance of population screening programmes. However, since FH constitutes a treatable disorder, no formal
license is needed. Therefore the possibilities for testing and controlling the screening programme by the health authorities are non-existent. Until today, there is no other form of quality control. The StOEH acts according to the rules of the Act on the Medical Treatment Agreement (WGBO). Even though, formally speaking, neither the screening programme nor the institution falls under this act. According to the Persons Registration Act (WPR), the StOEH has developed a privacy regulation. This registration was submitted to the Dutch Registration Bureau. On short notice, this act will be changed into the new “Act on the Protection of Personal Information (WBP)”. Then the StOEH will no longer be required to have such a regulation. Another privacy aspect concerns the storage and further use of human biological material (DNA). This is also suitable for other studies than the initial DNA diagnostic test for FH. At this moment a clear legal regulation is lacking and organisations have to develop their own policy and regulations. It will take some time before an ”Act Control over Body Material (WZL)” will be instituted. Therefore, the StOEH has taken the initiative to draw up adequate regulations based on one of the articles of the Medical Treatment Agreement (WGBO). (Article 7:467 BW) and the codes associated with it, such as the “Code Appropriate Use” of the Federation of Medical Scientific Associations (FMWV).17 According to the “Act Professionals Individual Health Care (BIG)” registered nurses are allowed, under certain circumstances, to perform a venapuncture without direct supervision of a physician. The genetic field workers of the StOEH, not all of them being registered nurses, visit clients at home and perform the venapuncture at the home address. In close collaboration with the” Inspection for Public Health Care” a protocol has been developed for venapuncture as well as are written proficiency reports, and specific training programmes.

Costs and finance

The yearly budget of the Foundation can be divided in two separate budget components; one consists of the budget for the exploitation of the organisation and a second component is allocated for the DNA diagnostics. The DNA budget was awarded in 1996 after the budgeting system for DNA diagnostics was changed by the Dutch Ministry of Health. As a result of this change the former subsidy by the Health Insurance Council was ended. The DNA diagnostic procedure at that time became part of the regular health care system
and a special tariff was determined for it. In 1996 the Dutch “National Health Tariffs Authority (COTG)” set an undifferentiated rate at approximately € 568,- for the DNA test. Because of this new policy the clients and the insurance companies were suddenly charged with the costs for the DNA test for FH. Moreover, due to these financial regulations, the family investigations were limited to a maximum number of DNA tests per year. For the screening programme of the StOEH only a simple singular DNA test is required. Through the index patient the mutation is known and only this specific mutation has to be tested in the family members. This test is much cheaper (€ 126,-). Finally, together with the funding partners, a comprehensive financing system of the total screening programme could be achieved. Again, the family investigation could be offered without costs for the participants. In various contracts between the AMC, the Foundation for Clinical Genetics Amsterdam and the StOEH, the conditions for the DNA tests were agreed upon.

Quality assurance and auditing

It is because of the sincere intentions and integrity of those involved in the StOEH organisation that the genetic screening programme has been executed with care and in accordance with all rules and within the framework of the Dutch public health policy and the professional standards. Specific regulations and quality assurance for genetic screenings programmes seem mandatory. Apart from that, as far as the StOEH is concerned, there is a form of indirect quality assurance and audit by the public authorities through the grants en through the licensing procedures for DNA diagnostics. The whole screening programme was previously reviewed and approved by the Dutch Ministry of Health Care and the Dutch Insurance Health Council. With respect to financing the programme, the Foundation is almost completely dependent on these public authorities.

In conclusion, it is clear that in the field of genetic screening in the Netherlands much has been achieved. Still, there are a number of bottlenecks such as: the lack of structural financing of genetic screening programmes, the lack of quality assurance and auditing of genetic population screening. Furthermore, it must be noted that, as a result of genetic screening, individuals do experience problems with insurances. Here lays an important task to resolve these bottlenecks currently impairing the execution of genetic screening programmes.
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