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GENETIC TESTS: HOW ARE THEY USED IN PORTUGUESE CLINICAL PRACTICE?

Development and validation of a questionnaire

ANA RITA DA SILVA LOPES

Master Thesis

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Ana Rita da Silva Lopes

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Dissertation Application to the degree of Master in Medicine, submitted to Instituto de Ciências Biomédicas de Abel Salazar, University of Porto

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I acknowledge also my tutor, Dr. Jorge Pinto Basto, for his orientation on this investigation project and all the support during the implementation of this questionnaire. Although this thesis is not coincident with the initial project, I hope to conclude the application of this questionnaire to doctors of all specialties and several institutions, even after presenting this preliminary work, with the aim of comparing how genetic testing is used in the medical practice, in Portugal.

Finally, I acknowledge the main authors of the papers that have previously evaluated the use of genetic testing in clinical practice and who gave their permission to use their questionnaires for development of this study, namely Dr. June Carroll, Dr. Sara Kolb, Dr. Janet Williams, Dr. Robert Klitzman and Prof. Sylvia Metcalfe.

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This study intends to be submitted to *Journal of Community Genetics* (Springer) and was written according to its instructions.

ABSTRACT

Introduction: The application of genetic tests has increased greatly in these previous years, accompanying the progress in molecular genetics and substantially changing the medical practice. Genetic testing may have several applications, including diagnosis of symptomatic patients, pre-symptomatic testing and susceptibility tests, which can have important consequences either for the patient, as also to his relatives.

Objectives: Evaluate knowledge, perceptions and attitudes of Portuguese physicians about genetic testing.

Methodology: A questionnaire addressed to physicians of all medical specialties was developed to characterize how genetic tests have been used in Portuguese clinical practice and their attitudes concerning medical genetics. The validation of the questionnaire was performed with an expert panel of medical geneticists and physicians of other medical specialties.

Results: A total of 11 geneticists and 11 non-geneticists were recruited (response rate of 52.4% and 84.6%, respectively). Besides medical specialty, these physicians differed with statistical significance on graduation year (p=0.046), workplace (p=0.040) and previous experience with genetic testing (p=0.037). The questionnaire was validated according to several parameters evaluated in a 7-point Likert scale, without statistical differences between geneticists and non-geneticists. Preliminary results showed that definition of genetic testing is not consensual and some misconception regarding professional responsabilities, applications of genetic testing and interpretation of results.

Conclusion: This study is the first questionnaire to characterize how genetic testing is used in Portuguese clinical practice and, after its validation, these preliminary results registered must now be confirmed with a larger and more representative sample of physicians.

Keywords: genetic testing, genetic counselling, clinical practice, questionnaire, validation studies

RESUMO

Introdução

Nos últimos anos, tem-se assistido a um grande desenvolvimento dos testes genéticos como resultado dos avanços na investigação do genoma humano. Não existe uma definição consensual do que é um teste genético, podendo este ser realizado com várias finalidades, desde o diagnóstico em doentes sintomáticos, testes de farmacogenética, pré-natais e pré-implantação até à realização de testes pré-sintomáticos, detecção de portadores heterozigóticos e testes de susceptibilidade em indivíduos saudáveis. Por outro lado, verifica-se também um aumento da informação dirigida à população em geral, bem como a disponibilização de exames de genotipagem diretamente ao público.

Além da falta de consenso na definição de teste genético, a sua especificidade requer conhecimentos técnicos que garantam uma seleção fundamentada dos vários testes, assim como uma interpretação correta dos resultados obtidos e que poderá ter consequências não só para o doente, como também para os seus familiares. Neste contexto, têm sido desenvolvidos alguns estudos para avaliar a aplicação dos testes genéticos na prática clínica e este projeto de investigação pretende avaliar a percepção dos médicos portugueses sobre os testes genéticos e sua aplicação na prática clínica.

Objectivos

Avaliar os conhecimentos, percepção e atitudes dos médicos portugueses face à especificidade dos testes genéticos e suas potenciais consequências através do desenvolvimento e validação de um questionário destinado à avaliação da realidade da prática clínica portuguesa na utilização dos testes genéticos.

Metodologia

Com base numa revisão bibliográfica sobre a avaliação da utilização de testes genéticos na prática clínica, foi desenvolvido um questionário adaptado à realidade dos cuidados de saúde em Portugal. O questionário é constituído por 38 perguntas, sendo organizado em quatro grupos: *Grupo I* para recolha de informação demográfica, académica e profissional dos indivíduos inquiridos, incluindo também uma auto-avaliação dos conceitos em genética médica; *Grupo II* para avaliação das atitudes dos médicos relativamente ao aconselhamento genético e responsabilidades profissionais em caso de diagnóstico de uma doença genética; *Grupo III* para caracterização da prática clínica relativamente à discussão de assuntos de genética com os doentes, assim como o conforto e confiança dos médicos ao lidar com questões de genética médica, metodologia para registo da história familiar, requisição de testes genéticos e

experiência prévia na referenciação para consultas de genética médica; *Grupo IV* consiste na avaliação dos conhecimentos médicos sobre definição de testes genéticos, legislação no âmbito da requisição de testes genéticos, interpretação de possíveis resultados e também avaliação da importância de vários parâmetros utilizados na seleção de um teste genético. Sempre que possível, foram utilizadas questões fechadas e alguns parâmetros foram avaliados com uma escala de Likert, embora algumas questões permitissem também respostas abertas.

A validação do questionário foi efectuado com um painel de peritos convidados e usando um sistema de inquérito *on-line*, *Survey Monkey*. Na primeira parte da validação, apenas foram convidados geneticistas (n=21) com o objectivo de verificar se o questionário permitia alcançar os objectivos pretendidos e confirmar que as respostas disponíveis eram corretas e completas; a segunda parte da validação foi realizada com médicos de outras especialidades e com uma vasta experiência clínica (n=13), com o objetivo de verificar se o questionário era também compreendido por não-geneticistas. Para a validação, foi desenvolvido um formulário, em que cada participante classificava o questionário numa escala de Likert com 7 pontos, sendo-lhes também solicitados comentários sobre o questionário.

Antes da inclusão no estudo, todos os participantes eram informados sobre os objectivos do estudo e a sua participação era voluntária, anónima e confidencial, com possibilidade de acesso, rectificação ou eliminação das suas respostas a qualquer momento. Este estudo foi sujeito a notificação à Comissão Nacional de Proteção de Dados e aprovação pela Comissão de Ética do Centro Hospitalar do Porto.

A análise estatística foi realizada com auxílio do programa estatístico SPSS para Mac (versão 21.0). Na estatística descritiva, foram determinadas as percentagens de respostas para cada questão avaliada, considerando apenas as respostas válidas, com cálculo da média com desvio padrão e mediana com intervalo de valores.

A análise estatística foi realizada para comparação dos geneticistas *versus* médicos de outras especialidades, tendo sido realizado o teste *Likelihood ratio* para variáveis nominais e o teste Mann-Whitney *U* para comparação das médias das variáveis quantitativas. Um valor $p<0,05$ foi considerado estatisticamente significativo.

Resultados

Neste estudo, participaram 11 médicos geneticistas e 11 médicos de outras especialidades médicas, correspondendo a uma taxa de resposta de 52,4% e 84,6%, respectivamente. Contudo, na fase de validação do questionário, apenas 7 dos geneticistas responderam ao formulário, enquanto que todos os não-geneticistas

participaram, com inclusão das principais especialidades médicas e que têm maior experiência em testes genéticos, nomeadamente: medicina interna, cirurgia geral, pediatria, neurologia, cardiologia, hematologia clínica, imunohemoterapia e oncologia médica. A caracterização demográfica, académica e profissional dos indivíduos recrutados encontra-se descrita na Tabela I. A participação de todos os indivíduos foi voluntária, confidencial e anónima, de acordo com os requisitos legais e éticos.

Tabela I – Caracterização demográfica, académica e profissional dos geneticistas e médicos de outras especialidades (*p* – valor obtido pelo teste *Likelihood ratio* e Mann-Whitney *U*).

	Geneticistas (n=11)		Outras especialidades médicas (n=11)		*p*
	n	%	n	%	
Idade (anos)					
Média ± Desvio Padrão	39,8 ± 8,4		46,6 ± 8,5		0,059
Mínimo – Máximo	32-59		37-60		
Sexo					
Masculino	5	45,5	5	45,5	1,000
Feminino	6	54,5	6	54,5	
Ano de Formação					
1970 - 1979	1	9,1	2	18,2	0,046
1980 - 1989	1	9,1	4	36,4	
1990 - 1999	2	18,2	4	36,4	
≥ 2000	7	63,6	1	9,1	
Mínimo – Máximo	1977-2006		1978-2000		
Principal Local de Trabalho					
Cuidados de Saúde Primários	0	0,0	0	0,0	0,040
Hospital do SNS	7	63,6	11	100	
Unidade Privada de Saúde	2	18,2	0	0	
Outro	2	18,2	0	0	
Grau de Diferenciação					
Especialista	9	81,8	11	100,0	0,085
Interno de Especialidade	2	18,2	0	0	

Os geneticistas e médicos de outras especialidades também diferem em termos de frequência com que discutem assuntos de genética na sua prática clínica (*p*=0,012), experiência na requisição de testes genéticos (*p*=0,037) e esclarecimentos ao doente antes da sua realização (*p*=0,006), pois 50% dos não-geneticistas apenas explicam sucintamente o teste genético, seus resultados possíveis e sua potenciais implicações. O registo da história familiar é feito de forma parcial pela maior parte dos não-geneticistas (27,3% frequentemente e 54,5% sempre) e geralmente de modo escrito (54,5%), enquanto que os geneticistas elaboram sempre um genograma (100%), com o registo da história familiar completa (30% frequentemente e 70% sempre).

A maior parte dos testes genéticos requisitados nos últimos 12 meses correspondia a testes de citogenética (n=410, 36,4%) ou de genética molecular (n=524, 46,4%), tendo sido realizados com a finalidade de diagnóstico (n=372, 48,4%) ou para detecção do estado de portador (n=268, 34,9%). Estes testes genéticos foram realizados principalmente em contexto de síndromes dismórficos, alterações do desenvolvimento psico-motor e doenças neurológicas. Da análise dos dados registados, salienta-se também que alguns médicos não-geneticistas realizaram estudos para detecção do estado de portador de heterozigotia para doenças recessivas e que nenhum deles requisitou testes genéticos para avaliação da susceptibilidade ou testes de farmacogenética.

Na prática clínica dos médicos não-geneticistas, verifica-se que a colocação de questões sobre genética por iniciativa própria dos doentes não é muito frequente (54,5% dos médicos são questionados, pelo menos, uma vez por mês e 27,3% dos médicos nunca foram questionados pelos seus doentes), sendo estas questões geralmente relacionadas com diagnóstico pré-natal (15,4%), aconselhamento para realização de testes genéticos (38,5%) ou discussão dos seus resultados (38,5%).

A referenciação para consultas especializadas em Genética Médica também não é frequente, pois um dos médicos nunca referenciou (9,1%), três dos médicos referenciaram, pelo menos, uma vez por mês (27,3%) e outros três médicos apenas referenciaram, pelo menos, uma vez por semestre (27,3%). Na maior parte dos casos, a referenciação foi realizada para aconselhamento genético do doente (29,4%) e dos seus familiares saudáveis (35,3%), mas dois dos médicos também mencionaram uma baixa acessibilidade a este serviço especializado.

Verificaram-se diferenças estatisticamente significativas na auto-avaliação de conhecimentos de genética médica entre geneticistas e médicos de outras especialidades, usando uma escala de Likert de 5 pontos: conhecimento global (4,50±0,85 *versus* 2,91±1,04, p=0,003), seleção do teste adequado a cada situação e doente (4,60±0,52 *versus* 3,36±0,81, p=0,002), tipo de amostra para cada teste (4,50±0,71 *versus* 3,00±1,18, p=0,003), técnicas utilizadas (4,40±0,69 *versus* 2,45±1,13, p=0,001), limitação das técnicas (4,50±0,53 *versus* 2,45±1,13, p=0,001) e interpretação dos resultados ou relatórios (4,50±0,53 *versus* 3,27±0,78, p=0,002). Quando questionados sobre o grau de conforto e confiança em assuntos relacionados com genética médica, os médicos não-geneticistas demonstraram maior confiança na colheita de informação genética no âmbito da história clínica e familiar (3,80±0,92), assim como na identificação de potenciais doentes candidatos para referenciação para consulta especializada de aconselhamento genético com base na história familiar

(3,70±0,67), sentindo-se menos confiantes nas restantes tarefas avaliadas, nomeadamente na requisição de testes genéticos.

Relativamente à avaliação das atitudes sobre os direitos dos doentes com patologia genética, apenas se verificaram diferenças estatisticamente significativas sobre a recomendação de aconselhamento genético após diagnóstico de uma doença genética (p=0,018), informação dos doentes sobre risco para desenvolvimento de doenças genéticas (p=0,040) e esclarecimento dos doentes sobre a disponibilidade de todas as alternativas reprodutivas (p=0,039). De facto, a maioria dos não-geneticistas considera-se responsável pela prestação de informação aos doentes relativamente ao diagnóstico, história natural da doença, prognóstico e modo de hereditariedade, mas referindo a necessidade de referenciação para consultas especializadas de genética médica em caso de esclarecimento sobre todas as alternativas reprodutivas disponíveis e diagnóstico pré-natal.

Verificou-se também que a definição de teste genético não é consensual, quer para geneticistas e médicos de outras especialidades, sendo de salientar os seguintes resultados: 55,6% dos geneticistas e 36,4% dos não-geneticistas consideram os testes de paternidade e identificação médico-legal como testes genéticos; 44,4% dos geneticistas incluem as mutações somáticas nos testes genéticos, em comparação com 81,8% dos não-geneticistas; 11,1% dos geneticistas consideram que a análise do exame físico, assim como exames sanguíneos e imagiológicos, deveriam ser incluídos na definição de testes genéticos, em comparação com 27,3 a 36,4% dos médicos não-geneticistas.

Não se verificam diferenças estatisticamente significativas sobre a importância dos diferentes parâmetros utilizados na seleção dos testes genéticos, mas verificaram-se diferenças na identificação de quais as especialidades médicas autorizadas a requisitar testes genéticos de acordo com a sua indicação, assim como na interpretação de possíveis resultados de um teste genético. De facto, nem todos os médicos não-geneticistas consideraram ser responsáveis pela requisição de testes genéticos para diagnóstico de doentes sintomáticos (81,8%) e estudos de farmacogenética (28,6%). Pelo contrário, alguns destes médicos consideram a possibilidade de requisição de testes genéticos para detecção de estado de portador de heterozigotia para doenças recessivas (18,2%), diagnóstico pré-sintomático (10,0%) e testes de susceptibilidade (33,3%).

Relativamente à validação do questionário, a Tabela II apresenta os resultados da apreciação dos geneticistas (n=7) e médicos de outras especialidades (n=11) sobre o

questionário e concretização dos objectivos estabelecidos com este estudo. Apenas um geneticista considerou que algumas questões eram redundantes ou desnecessárias e outros participantes sugeriram a inclusão de mais questões relativamente à responsabilidade clínica perante os familiares saudáveis, realização de testes genéticos em crianças e procedimentos a adoptar após diagnóstico de doença genética.

Tabela II – Resultados da validação do questionário usando uma escala de Likert com 7 pontos (1=pior resultado; 7=melhor resultado; DP – desvio padrão; *p* – valor obtido pelo teste Mann-Whitney *U*).

	Geneticistas (n=7)		Outras especialidades médicas (n=11)		*p*
	Média ± DP	Mediana (Intervalo)	Média ± DP	Mediana (Intervalo)	
Clareza	5,71 ± 0,95	6 (4-7)	5,18 ± 0,75	5 (4-6)	0,175
Aplicabilidade	5,57 ± 1,27	6 (3-7)	5,00 ± 1,09	5 (3-6)	0,175
Poder discriminativo	5,29 ± 0,76	5 (4-6)	4,82 ± 0,75	5 (4-6)	0,207
Conteúdo adequado	5,57 ± 0,98	6 (4-7)	4,91 ± 1,04	5 (3-6)	0,217
Enviesamento	4,29 ± 1,38	4 (3-6)	4,09 ± 1,58	4 (2-7)	0,782
Questões redundantes ou desnecessárias	3,14 ± 2,12	4 (1-6)	2,09 ± 1,70	1 (1-5)	0,318
Concretização dos objectivos	5,71 ± 0,95	6 (4-7)	4,64 ± 1,12	5 (3-6)	0,053

Com base nas respostas obtidas em ambas as fases de validação, o questionário foi reformulado para incluir as respostas abertas nas opções de resposta disponíveis, o que se verificou para a questão 18, relativa à frequência de atualização da história familiar, e questão 25, com inclusão dos representantes legais.

Conclusão

Os resultados obtidos garantem a validação do questionário desenvolvido para avaliar a utilização dos testes genéticos na prática clínica portuguesa, não se tendo verificado diferenças estatisticamente significativas entre os médicos geneticistas e médicos de outras especialidades médicas. No futuro, pretende-se aplicar este questionário a todos os médicos da região Norte de Portugal, com inclusão de todos as especialidades médicas e diferentes áreas de prática clínica, de modo a obter uma amostra representativa e que permita o esclarecimento dos resultados preliminares obtidos com esta validação. Esses dados poderão assim fundamentar ações para a regulamentação dos testes genéticos e do aconselhamento genético em Portugal.

Palavras-Chave: teste genético, aconselhamento genético, prática clínica, questionário, estudos de validação

1. INTRODUCTION

The application of genetic tests has increased greatly in these previous years, accompanying the progress in molecular genetics and substantially changing the medical practice, both in diagnosis and in therapeutics. In a survey performed during 2004, the number of laboratories performing genetic tests in Europe was 751 and, concerning the number of genetic tests performed in the public sector, the global estimative of the total EU activity in 2002 was 735,000 reports (Ibarreta et al. 2004).

Genetic tests may have several applications: diagnostic testing in affected patients, either for confirmation or excluding a clinical diagnosis; presymptomatic/predictive testing for late-onset Mendelian diseases; disease predisposition – susceptibility tests to late-onset complex diseases with multifactorial inheritance; pharmacogenetics to predict response to therapeutic drugs; carrier testing (heterozygote detection) for Mendelian recessive diseases; prenatal diagnosis and preimplantation genetic diagnosis; population (genetic) screening; paternity testing or other family relationships; and identity testing for forensic purposes (Sequeiros et al. 2012).

There is no agreed definition of what a genetic test is: according to the Advisory Committee on Genetic Testing in the UK, genetic testing is defined as testing to detect the presence or absence of, or alteration in, a particular gene, chromosome or gene product; in USA, the Task Force on Genetic Testing defined it as the analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease related genotypes, mutations, phenotypes or karyotypes for clinical purposes (Zimmern 1999). In another definition, the concept of a genetic test should include not only the laboratory analysis itself, but the preliminary preparation and counseling of the patient and subsequent interpretation and support (Harper 1997).

Because other tests may also be helpful in heritable disease diagnosis, Zimmern proposed that the term *genetic testing* should be used to any type of test that indicates that a person is likely to have a genetic or familial disorder, including any clinical, haematological, radiological or biochemical test, and the term *gene testing* refers only to tests confined to the analysis of DNA, RNA or chromosomes (Zimmern 1999).

Despite these several definitions, a common concept is that genetic information is different from other types of health information as it identifies individuals and their relatives that have a genetic disease, have increased risk in pre-symptomatic individuals or susceptibility to a multifactorial disorder, which may cause genetic discrimination (Zimmern 1999). Indeed, genetic tests require particular consideration since these tests may be performed on asymptomatic individuals and results may have relevance to

important lifetime decisions both for the individuals being tested and for their family and children (OECD 2007).

The specificity of genetic testing requires expertise to ensure the correct selection of the various tests, as well as a correct interpretation of the results. On the other hand, there is also an increase in information for the public, as well as providing genotyping tests directly to the public, which needs regulation (Wright et al. 2011). This sets a new reality and physicians from all medical specialties should be able to provide appropriate advice to their patients.

Regarding that genetic testing is a very ambiguous term, a questionnaire concerning its perception by other medical specialties and its applicability in medical practice is justified, which has been already performed in other studies (Hofman et al. 1993; Klitzman et al. 2013). This research project aims to assess the knowledge, perceptions and attitudes of Portuguese physicians considering the specificity of genetic testing and its potential consequences. For this purpose, the development and validation of a questionnaire were performed and also a correlation of the preliminary results was interpreted based on the training and skills of physicians surveyed.

2. MATERIAL AND METHODS

A questionnaire was developed based on previous studies that employed this tool to evaluate genetic testing (Carroll et al. 2009; Flouris et al. 2010; Klitzman et al. 2013; Kolb et al. 1999; Pinto-Basto et al. 2010), and adapted to the context of the Portuguese clinical practice. Written consent to use the previously published questionnaires was obtained from the authors.

2.1 Questionnaire Development

A bibliographic survey was performed to ascertain previous questionnaires about the use of genetic testing in clinical practice, using keywords such as genetic testing and genetic test. After analysis of all studies collected, five questionnaires were selected based in their full-text availability, evaluation of attitudes, practices and knowledge concerning genetic testing in general and not for specific diseases, inclusion of different professional groups in target population and more recent publishing date. Based on these questionnaires, a new questionnaire was developed, adapted to the Portuguese clinical practice and established aims of this work (Annex I).

The questionnaire has 38 questions and it is expected to take about 20 minutes to complete. It is organized in four groups: *Group I* contains demographic, academic and occupational information of the interviewed subjects, as well as self-evaluation of concepts in medical genetics; *Group II* assesses the attitudes of physicians concerning genetic counselling and professional responsibilities when a genetic disease is diagnosed; *Group III* intends to characterize clinical practice concerning discussion of genetic issues with patients and the physicians' comfort and confidence when dealing with these issues, methods used for recording family history, genetic tests ordered and previous experience with referral to medical genetic consultations; *Group IV* is an evaluation of physicians' knowledge concerning definition of genetic tests, legislation regarding professional responsibilities in genetic tests, interpretation of possible results and also an evaluation of parameters used when genetic tests are ordered. As far as it is possible, closed questions are used and some parameters were evaluated with a Likert scale. However, some questions also allow an open answer.

2.2 Questionnaire Validation

The validity of questionnaire was evaluated by an expert panel, invited for this purpose by mail and using an online survey system, Survey MonKey. The selection of the expert panel was made from professional and academic relationships of both investigators. The expert panel included geneticists and non-geneticists, who have an extensive clinical

experience as all of them work in a tertiary hospital, have several years of medicine practice and some of them have specialized consultations that included genetic disorders.

In the first part of validation, only medical geneticists (n=21) were recruited in order to verify if the questionnaire could achieve the proposed aims and to verify if the possible answers were correct and complete; in the second part, physicians of other specialties with an extensive clinical experience (n=13) were recruited to guarantee if the questionnaire was well understood by non-geneticists. Additionally to the questionnaire, a validation form (Annex II) was also sent to all participants, where they were asked to classify the questionnaire in a 7-item Likert scale and also were asked to comment on the document.

Before inclusion in this study, all participants were informed about the aims established and their participation was voluntary, anonymous and confidential, with the right to access, rectify or eliminate their answers at any moment. This study was notified to National Commission for Data Protection and was also approved by Ethics Committee of Porto Hospital Centre.

2.3 Statistical Analysis

Statistical analysis was performed with the statistic software Statistical Package for Social Sciences for Mac - SPSS (version 21.0, SPSS Inc.). For each evaluated item, descriptive statistics were calculated: percentages, considering only the valid answers, means with standard deviations and medians with ranges.

The statistical analysis intended to compare results of geneticists *versus* physicians of other medical specialties. The statistical analysis for categorical variables was performed by Likelihood ratio test and, for comparison of quantitative variables, Mann-Whitney *U* test was used to compare means of both groups. A p value <0.05 was considered statistically significant.

3. RESULTS

3.1 Sample Characterization

In this study, 11 medical geneticists and 11 physicians of other medical specialties answered the questionnaire concerning genetic testing, although only 7 from the 11 medical geneticists participated in the validation phase, for which all the other physicians contributed. The response rate was 52.4% and 84.6% for medical geneticists and other physicians, respectively. The demographic, academic and occupational characteristics of the individuals recruited for this study are described in Table 1. The participation of all individuals was voluntary, confidential and anonymous, in compliance with legal and ethical requirements.

Table 1 - Demographic, academic and occupational characterization of geneticists and physicians for other medical specialties (*p* – value obtained by Likelihood ratio test and Mann-Whitney *U* test).

	Geneticists (n=11)		Other medical specialties (n=11)		*p*
	n	%	n	%	
Age (years)					
Mean ± Standard Deviation	39.8 ± 8.4		46.6 ± 8.5		0.059
Minimum– Maximum	32-59		37-60		
Gender					
Male	5	45.5	5	45.5	1.000
Female	6	54.5	6	54.5	
Graduation Year					
1970 - 1979	1	9.1	2	18.2	0.046
1980 - 1989	1	9.1	4	36.4	
1990 - 1999	2	18.2	4	36.4	
≥ 2000	7	63.6	1	9.1	
Minimum– Maximum	1977-2006		1978-2000		
Main Workplace					
Primary Health Care	0	0.0	0	0.0	0.040
National Hospital	7	63.6	11	100.0	
Private Health Unit	2	18.2	0	0.0	
Other	2	18.2	0	0.0	
Degree of Differentiation					
Specialist	9	81.8	11	100.0	0.085
Intern of Specialty	2	18.2	0	0	

All non-geneticists graduated in University of Porto (45.5% in Faculty of Medicine and 54.5% in Institute of Biomedical Sciences Abel Salazar), while geneticists were from several medical schools, including two subjects that studied in foreign schools, which corresponds to a statistically significant difference (p=0.014). Similar results were obtained regarding the localization of main workplace, as all non-geneticists practice medicine in Porto, in comparison with medical geneticists that work in Porto (54.5%), Coimbra (36.4%) and Lisboa (9.1%).

For second part of validation, physicians from the main medical specialities and with more experience of genetic testing were included, namely from internal medicine, general surgery, paediatrics, neurology, cardiology, clinical haematology, immunohemotherapy and medical oncology.

The results of self-evaluation on the knowledge about medical genetics are summarized in Table 2. All medical geneticists reported post-graduation training, including in their own specialty internship and also participation in courses and conferences, in contrast with doctors from other specialties, in which only one doctor performed a training period in genetics.

Table 2 – Self-evaluation of knowledge about medical genetics using a 5-point Likert scale (1=very insufficient; 5=very good; SD – standard deviation; *p* – value obtained by Mann-Whitney *U* test).

	Geneticists (n=10)		Other medical specialties (n=11)		*p*
	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
Knowledge					
Overall	4.50 ± 0.85	5 (3-5)	2.91 ± 1.04	3 (1-5)	0.003
Test Selection	4.60 ± 0.52	5 (4-5)	3.36 ± 0.81	3 (2-5)	0.002
Sample Type	4.50 ± 0.71	5 (3-5)	3.00 ± 1.18	3 (1-5)	0.003
Techniques used	4.40 ± 0.69	4,5 (3-5)	2.45 ± 1.13	2 (1-5)	0.001
Limitations of techniques	4.50 ± 0.53	4,5 (4-5)	2.45 ± 1.13	2 (1-5)	0.001
Interpretation of results/reports	4.50 ± 0.53	4,5 (4-5)	3.27 ± 0.78	3 (2-5)	0.002

3.2 Attitude Assessment

This section was developed to verify agreement of physicians about rights of patients diagnosed with genetic diseases, which results are showed in Table 3, and also to define if the attending physician or a specialized genetic counselling physician is responsible to perform each task or should delegate in another professional. The results are presented in Table 4.

Table 3 – Attitude assessment about rights of patients diagnosed with a genetic disease and agreement was rated on a 5-point Likert scale (1=I don't agree totally; 5=I agree totally; SD – standard deviation; *p* – value obtained by Mann-Whitney *U* test).

	Geneticists (n=10)		Other medical specialties (n=11)		*p*
Questions	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
Degree of agreement with the statements					
Always receive genetic counselling if a genetic disease is diagnosed	5.00 ± 0.00	5 (5-5)	4.27 ± 1.19	5 (1-5)	0.018
Always be referred to a genetic counselling consultation if a genetic disease is diagnosed	4.60 ± 0.52	5 (4-5)	3.82 ± 1.66	5 (1-5)	0.476
Always be referred to a genetic counselling consultation when a patient wants to know medical information about his genetic disease	3.90 ± 1.20	4 (1-4)	3.27 ± 1.68	4 (1-5)	0.502
Always be referred to a genetic counselling consultation when a patient wants to know inheritance of his genetic disease	4.10 ± 1.29	4,5 (1-4)	3.64 ± 1.57	4 (1-5)	0.500
Always be referred to a genetic counselling consultation if doubts in diagnosis of a genetic disease	4.40 ± 0.97	5 (2-4)	3.55 ± 1.57	4 (1-5)	0.174
Always inform patients who might have risk for a genetic disease	5.00 ± 0.00	5 (5-5)	4.09 ± 1.45	5 (1-5)	0.040
All physicians should be able to identify individuals needing genetic counselling	4.80 ± 0.63	5 (3-5)	4.73 ± 0.47	5 (4-5)	0.410
Always perform family history and pedigree if a genetic disease is suspected	5.00 ± 0.00	5 (5-5)	4.91 ± 0.30	5 (4-5)	0.340
Degree of agreement with the statements when a genetic disease is diagnosed					
Receive an explanation of the diagnosis	4.90 ± 0.32	5 (4-5)	4.91 ± 0.30	5 (4-5)	0.945
Receive an explanation of the natural history / prognosis	5.00 ± 0.00	5 (5-5)	4.82 ± 0.40	5 (4-5)	0.167
Receive an explanation of the inheritance	5.00 ± 0.00	5 (5-5)	4.91 ± 0.30	5 (4-5)	0.340
Receive an explanation of the prenatal diagnosis, if available	5.00 ± 0.00	5 (5-5)	4.55 ± 0.93	5 (2-5)	0.083
Be informed of availability of all reproductive alternatives	5.00 ± 0.00	5 (5-5)	4.64 ± 0.50	5 (4-5)	0.039
Have the opportunity to discuss his feeling with a health professional	4.90 ± 0.32	5 (4-5)	4.82 ± 0.40	5 (4-5)	0.602
Have the opportunity to meet other people with the same or similar disease	4.80 ± 0.42	5 (4-5)	4.09 ± 0.94	4 (3-5)	0.062

Table 4 – Attitude assessment about professional responsibilities to perform patient care when a genetic disorder is diagnosed (*p* – value obtained by Likelihood ratio test).

	My responsibility		Other professional		Genetic Consultation		Don't concern		
	n (%)		n (%)		n (%)		n (%)		
	Geneticists (n=10)	Other medical specialties (n=11)	Geneticists (n=10)	Other medical specialties (n=11)	Geneticists (n=10)	Other medical specialties (n=11)	Geneticists (n=10)	Other medical specialties (n=11)	*p*
Explain diagnosis	7 (70.0)	8 (72.7)	0 (0.0)	0 (0.0)	3 (30.0)	3 (27.3)	0 (0.0)	0 (0.0)	0.890
Explain natural history / prognosis	6 (60.0)	7 (63.6)	0 (0.0)	0 (0.0)	4 (40.0)	4 (36.4)	0 (0.0)	0 (0.0)	0.864
Explain inheritance mode	2 (20.0)	7 (63.6)	0 (0.0)	0 (0.0)	8 (80.0)	4 (36.4)	0 (0.0)	0 (0.0)	0.039
Explain prenatal diagnosis	2 (20.0)	1 (9.1)	0 (0.0)	0 (0.0)	8 (80.0)	10 (90.9)	0 (0.0)	0 (0.0)	0.473
Inform of reproductive alternatives	2 (20.0)	0 (0.0)	0 (0.0)	2 (18.2)	8 (80.0)	9 (81.8)	0 (0.0)	0 (0.0)	0.062
Discuss feeling with a health professional	4 (40.0)	6 (54.5)	2 (20.0)	1 (9.1)	4 (40.0)	4 (36.4)	0 (0.0)	0 (0.0)	0.706
Introduce to other families with same disease	2 (25.0)	2 (18.2)	1 (12.5)	0 (0.0)	5 (62.5)	3 (27.3)	0 (0.0)	6 (54.5)	0.021

3.3 Experience with medical genetics and genetic testing

Table 5 shows the previous experience with genetic issues in clinical practice evaluated by ascertaining the methods of collecting and updating family history, as well as previous experience with request and interpretation of genetic tests. Some questions also verify if patients, themselves are also aware of genetic issues.

Table 5 – Previous experience with genetic issues and genetic testing in clinical practice (*p* – value obtained by Likelihood ratio test).

	Geneticists (n=10)	Other medical specialties (n=11)	*p*
	n (%)	n (%)	
Frequency of genetic issues discussion with patients			
Never	0 (0.0)	0 (0.0)	0.012
Only if the patient has a genetic disease	0 (0.0)	3 (27.3)	
Sometimes, but only if I consider that exist a justified reason for it	0 (0.0)	1 (9.1)	
Frequently, always when it seems appropriate	0 (0.0)	3 (27.3)	
In most cases	3 (30.0)	2 (18.2)	
Always	7 (70.0)	2 (18.2)	
Frequency of partial family history			
Never	3 (33.3)	0 (0.0)	0.053
Rarely	1 (11.1)	0 (0.0)	
Sometimes	0 (0.0)	2 (18.2)	
Frequently	2 (22.2)	3 (27.3)	
Always	3 (33.3)	6 (54.5)	
Frequency of complete family history			
Never	0 (0.0)	0 (0.0)	0.002
Rarely	0 (0.0)	6 (54.5)	
Sometimes	0 (0.0)	2 (18.2)	
Frequently	3 (30.0)	1 (9.1)	
Always	7 (70.0)	2 (18.2)	
Frequency for update family history			
In each consultation	6 (60.0)	4 (40.0)	0.072
Yearly	0 (0.0)	0 (0.0)	
5 Yearly	0 (0.0)	0 (0.0)	
Always when new data	2 (20.0)	6 (60.0)	
Rarely	0 (0.0)	0 (0.0)	
Other frequency (contact of patients or according to each case)	2 (20.0)	0 (0.0)	
Mode of recording family history			
Text	0 (0.0)	6 (54.5)	0.002
Genogram/Pedigree	10 (100.0)	5 (45.4)	
Genetic tests ordered in the last twelve months			
Yes	10 (100.0)	8 (72.7)	0.037
No	0 (0.0)	3 (27.3)	
Attitude before ordering genetic tests			
Explain in detail the test, results and implications	9 (100.0)	4 (50.0)	0.006
Explain briefly the test, results and implications	0 (0.0)	4 (50.0)	

	Geneticists (n=10)	Other medical specialties (n=11)	*p*
	n (%)	n (%)	
Frequency of patients' questions about genetic tests			
Every day	2 (22.2)	0 (0.0)	0.011
At least, once every week	5 (55.6)	1 (9.1)	
At least, once every month	2 (22.2)	6 (54.5)	
At least, once every six months	0 (0.0)	1 (9.1)	
At least, once every year	0 (0.0)	0 (0.0)	
Never	0 (0.0)	3 (27.3)	
I don't remember	0 (0.0)	0 (0.0)	
Reason for patient's questions about genetic tests			
Prenatal testing	4 (22.2)	2 (15.4)	0.418
Perform a genetic test	9 (50.0)	5 (38.5)	
Ask information about genetic tests advertised on Internet	1 (5.6)	0 (0.0)	
Discuss results of genetic test	4 (22.2)	5 (38.5)	
Other reason	0 (0.0)	1 (7.7)	
Sources of information concerning genetic tests			
Books	1 (12.5)	1 (9.1)	0.079
Web sites	5 (62.5)	7 (63.6)	
Medical geneticist	0 (0.0)	3 (27.3)	
Genetic lab technician	2 (25.0)	0 (0.0)	
Sales representative or lab promoter	0 (0.0)	0 (0.0)	

Most genetic tests requested in the previous twelve months were cytogenetics (n=410, 36.4%) or molecular genetics (n=524, 46.4%) tests and were performed for diagnosis (n=372, 48.4%) and carrier testing (n=268, 34.9%). However, it is worth noting that some non-clinical geneticists physicians performed carrier testing and none of them ordered susceptibility or pharmacogenetic testing. Genetic testing was performed mainly for dysmorphic syndromes, psychomotor or mental retardation and neurological diseases. The level of comfort or confidence when dealing with genetic issues in clinical practice were also analysed and are described in Table 6.

Table 6 – Self-evaluation of comfort or confidence when dealing with genetics issues in clinical practice using a 5-point Likert scale (1=very uncomfortable or nothing confident; 5=very comfortable or completely confident; SD – standard deviation; *p* – value obtained by Mann-Whitney *U* test).

	Geneticists (n=10)		Other medical specialties (n=11)		*p*
	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
How confortable you are dealing genetics issues with patients					
	4.60 ± 0.52	5 (4-5)	3.64 ± 0.67	4 (3-5)	0.004
How confident you are when performing each of the following tasks					
Elicit genetic information as part of a clinical and family history	4.70 ± 0.48	5 (4-5)	3.80 ± 0.92	3.5 (3-5)	0.024
Assess risk for hereditary diseases	4.80 ± 0.42	5 (4-5)	3.00 ± 0.82	3 (2-4)	0.000

	Geneticists (n=10)		Other medical specialties (n=11)		*p*
	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
How confident you are when performing each of the following tasks					
Decide which patients are candidates for referral for genetic counselling based on family history	4.78 ± 0.44	5 (4-5)	3.70 ± 0.67	4 (3-5)	0.003
Order genetic tests for hereditary cancer or adult onset disease	4.40 ± 0.70	4.5 (3-5)	3.00 ± 1.15	3 (1-5)	0.007
Discuss prenatal diagnosis options with your patients	4.80 ± 0.42	5 (4-5)	2.30 ± 0.67	2 (1-3)	0.000
Evaluate clinical utility of a genetic test	4.70 ± 0.48	5 (4-5)	3.20 ± 0.79	3 (2-5)	0.001
Discuss the benefits, risks and limitations of genetic tests	4.70 ± 0,48	5 (4-5)	3.10 ± 0.88	3 (2-5)	0.001
Provide counselling to patients that are in decision process to perform or not a genetic test	4.70 ± 0.48	5 (4-5)	3.10 ± 0.74	3 (2-4)	0.000
Offering psychosocial support to patients coping with a genetic test result	4.20 ± 0.92	4.5 (3-5)	2.60 ± 0.84	3 (1-4)	0.002
Provide counselling to patients related to screening, lifestyle changes or surveillance strategies based on a genetic test result	4.20 ± 0.79	4 (3-5)	2.80 ± 0.63	3 (2-4)	0.002
Describe to patients the expectations that they may have about a genetic counselling consultation	4.60 ± 0,70	5 (3-5)	3.00 ± 0.82	3 (2-4)	0.001

Referral for a specialized consultation of Medical Genetic is not frequent as one physician has never referred patients (9.1%), three physicians referred at least once every month (27.3%) and an additional three physicians referred at least once every six months (27.3%). The main reason for referral was genetic counselling of the patient (29.4%) and his healthy relatives (35.3%), but two physicians also mentioned that accessibility to this specialized service is low.

The evaluation of professional responsibilities demonstrated that not all non-geneticists consider their responsibility the request of genetic testing for diagnosis of symptomatic patients (81.8%) and much less so, for pharmacogenetics studies (28.6%). However, some of these physicians from other medical specialties consider that they may order

genetic testing for detection of carrier tests for recessive diseases (18.2%), pre-symptomatic diagnosis (10.0%) and susceptibility testing (33.3%).

Subjects were also asked to rank the parameters used for selection of a genetic testing in terms of importance and, to evaluate their knowledge on the selection of methodology and interpretation of results, and the level of agreement with some possible scenarios was recorded. This is summarized in Table 7.

Table 7 – Level of importance of parameters used for selection of genetic tests and level of agreement with statements for evaluation of knowledge on interpretation of genetic test results using a 5-point Likert scale (1=without importance or disagree totally; 5=very important or agree totally; SD – standard deviation; *p* – value obtained by Mann-Whitney *U* test).

	Geneticists (n=9)		Other medical specialties (n=11)		*p*
	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
Level of importance of parameters used for selection of genetic tests					
Sensibility	4.78 ± 0.44	5 (4-5)	4.82 ± 0.40	5 (4-5)	0.827
Specificity	4.78 ± 0.44	5 (4-5)	4.82 ± 0.40	5 (4-5)	0.827
Clinical utility	4.78 ± 0.44	5 (4-5)	4.82 ± 0.40	5 (4-5)	0.827
Type of methodology used	4.56 ± 0.53	5 (4-5)	4.36 ± 0.67	5 (3-5)	0.549
Number of searched mutations	4.11 ± 0.60	4 (3-5)	4.45 ± 0.69	5 (3-5)	0.206
Participation of laboratory in schemes of external quality control	4.44 ± 0.73	5 (3-5)	4.91 ± 0.30	5 (4-5)	0.070
Laboratory certification	4.33 ± 0.87	5 (3-5)	4.91 ± 0.30	5 (4-5)	0.064
Laboratory accreditation	4.33 ± 0.87	5 (3-5)	4.82 ± 0.40	5 (4-5)	0.157
Previous experience with laboratory	4.56 ± 0.53	5 (4-5)	4.64 ± 0.67	5 (3-5)	0.555
Price	4.33 ± 0.71	4 (3-5)	4.45 ± 0.69	5 (3-5)	0.673
Response time	4.11 ± 0.60	4 (3-5)	4.55 ± 0.52	5 (4-5)	0.110
Possibility of having a interlocutor for results discussion and possible need for other tests	4.56 ± 0.53	5 (4-5)	4.82 ± 0.40	5 (4-5)	0.214
Quality of reports	4.78 ± 0.44	5 (4-5)	5.00 ± 0.00	5 (5-5)	0.108
Availability in institution	4.00 ± 1.22	4 (2-5)	4.36 ± 1.12	5 (2-5)	0.322
Laboratory localization (Portugal or abroad)	3.67 ± 1.32	4 (2-5)	4.27 ± 0.79	4 (3-5)	0.334
Level of agreement with the statements when several mutations of the same gene are described for a specific disease					
Best choice is search only the most frequent mutations	2.78 ± 1.30	3 (1-4)	3.64 ± 0.92	4 (1-4)	0.089
Diagnosis exclusion if the most frequent mutations are not detected	1.11 ± 0.33	1 (1-2)	1.45 ± 0.82	1 (1-3)	0.327
Best choice is gene sequencing	4.33 ± 0.71	4 (3-5)	3.82 ± 0.75	4 (3-5)	0.131
Diagnosis exclusion if no mutations are detected in gene sequencing	2.33 ± 1.32	2 (1-4)	2.27 ± 1.49	2 (1-5)	0.811

3.4 Definition of genetic testing

As the definition of genetic testing is not consensual, participants were asked their opinion on what should be considered a genetic test (Table 8).

Table 8 – Definition of genetic testing.

	Geneticists (n=9)		Other medical specialties (n=11)	
	n	%	n	%
Concerning type of testing				
Diagnostic testing	7	77.8	9	81.8
Pre-symptomatic testing	9	100.0	8	72.7
Disease predisposition testing	8	88.9	7	63.6
Pharmacogenetic	8	88.9	6	54.5
Carrier testing	9	100.0	11	100.0
Prenatal testing	9	100.0	9	81.8
Pre-implantation genetic diagnosis	9	100.0	7	63.6
Population screening	4	44.4	4	36.4
Paternity testing	5	55.6	4	36.4
Forensic/criminal identification	5	55.6	4	36.4
Concerning phenotypes evaluated				
Mendelian diseases	9	100.0	11	100.0
Genetic predisposition	7	77.8	4	36.4
Other polymorphic traits	1	11.1	1	9.1
Concerning mutations types				
Somatic mutations	4	44.4	9	81.8
Germinal mutations	9	100.0	8	72.7
Concerning object / evaluation methodology				
Chromosomes / karyotype	9	100.0	8	72.7
Genes / DNA	9	100.0	11	100.0
Gene products	7	77.8	6	54.5
Clinical blood tests	1	11.1	3	27.3
Imaging / physiologic tests	1	11.1	3	27.3
Physical exam	1	11.1	4	36.4
Family history	3	33.3	3	27.3

3.5 Questionnaire Validation

Table 9 summarizes the opinions of both geneticists (n=7) and physicians of other medical specialties (n=11) about the development and achievement of objectives by the questionnaire. Only one geneticist considered that some questions were redundant or unnecessary and others suggested that other issues should also be included, such as clinical responsibility for healthy relatives, genetic testing in children and procedures to be taken after the diagnosis of a genetic disease.

Based on the answers obtained in both rounds of validation, questions 18 and 25 were altered in order to include the open answers registered in the options available, namely frequency for updating the family history and inclusion of legal representatives for child

patients. Consequently, a new version of the questionnaire was developed and the questions changed are attached in Annex III.

Table 9 – Results of questionnaire validation using a 7-point Likert scale (1=worst result; 7=best result; SD – standard deviation; *p* – value obtained by Mann-Whitney *U* test).

	Geneticists (n=7)		Other medical specialties (n=11)		*p*
	Mean ± SD	Median (Range)	Mean ± SD	Median (Range)	
Clarity	5.71 ± 0.95	6 (4-7)	5.18 ± 0.75	5 (4-6)	0.175
Applicability	5.57 ± 1.27	6 (3-7)	5.00 ± 1.09	5 (3-6)	0.175
Discriminative power	5.29 ± 0.76	5 (4-6)	4.82 ± 0.75	5 (4-6)	0.207
Contents adequate	5.57 ± 0.98	6 (4-7)	4.91 ± 1.04	5 (3-6)	0.217
Biases	4.29 ± 1.38	4 (3-6)	4.09 ± 1.58	4 (2-7)	0.782
Questions redundant or unnecessary	3.14 ± 2.12	4 (1-6)	2.09 ± 1.70	1 (1-5)	0.318
Aims achievement	5.71 ± 0.95	6 (4-7)	4.64 ± 1.12	5 (3-6)	0.053

4. DISCUSSION

The aim of this work was to develop and validate a questionnaire designed to evaluate how genetic tests are used in the Portuguese clinical practice. To our knowledge no previous study on this specific subject has been performed in Portugal. In the first part of the validation phase only geneticists were included, to guarantee that the included answers were complete and accurate. In this round, the results showed, globally, a good evaluation, although some discordance arose about the inclusion of some questions, considered unnecessary and/or redundant.

The second round of the validation aimed at guaranteeing comprehension by non-geneticists and the results obtained were very favorable, although the discordance about unnecessary or redundant questions was again reported. No statistical difference was observed between these two groups, which confirmed the validation of this questionnaire with an expert panel.

Although this questionnaire is directed to physicians from all medical specialties and different work settings, the second round of validation was made with a sample of hospital physicians and some with large experience with genetic testing, as 72.7% ordered genetic tests within the last year, which may bias our results of validation about the comprehension of the questionnaire by physicians not familiarized with genetic testing. In fact, initially, the second round was designed to include physicians representative of all different target specialties, but the individuals recruited did not include obstetricians, neither general practitioners.

In addition to the questionnaire validation, the preliminary results of this survey are also described and were used to compare medical geneticists and non-geneticists physicians. According to the national statistics (Ordem dos Médicos 2009), there are only 49 geneticists in Portugal, many of them not working in clinical genetics as their main activity and, therefore the inclusion of 11 of them can be considered quite representative. Apart from the medical specialty, there were also statistical differences concerning graduation year and workplace, which may also influence results. Specifically, the graduation year, as the teaching of genetics has greatly increased in the last two decades. In fact, it has already been described that the most significant predictors of knowledge in genetics were the more recent year of graduation from medical school and practicing in primary care specialties in which exposure to genetic problems is likely (Hofman et al. 1993). The differences in workplace are not considered important as are inherent to recent changes in Portuguese health care, in which medical genetic has been concentrated in institutes and private health units, that give assistance to several hospitals and physicians as it is a very specialized assistance.

Although the discussion of genetic issues with patients was not statistically different between groups, there were some differences regarding the mode of family history collection, since only 27.3% of non-geneticists use to record a complete family history and most of them do not register this information in a genogram. There were also differences about pre-test procedures, in which 50% of non-geneticists do not explain in detail the implications of genetic testing, which favors the need for implementation of a genetic counseling service to guarantee the provision of the best care. In accordance with prevalence of genetic diseases, patients of non-geneticists ask less frequently information about genetic testing.

Results concerning self-evaluation of knowledge about medical genetics showed statistical difference concerning all the items evaluated. In the geneticists group, the variability of answers may be justified as two of them were still residents and, for non-geneticists, this variability may be justified as some of them have a large experience in genetic testing and, consequently, these results may not be representative of all non-geneticists. The self-evaluation of knowledge in medical genetic testing is in accordance with self-evaluation of comfort and confidence when dealing with genetic issues in clinical practice: statistical differences were verified for all tasks, but non-geneticists seem more confident in collection of family history and referral for genetic counseling in comparison with evaluation of risk for hereditary diseases, ordering genetic tests and counseling patients about genetic testing.

To improve confidence and knowledge, genetic education for non-genetics is a powerful tool as described by other studies (Carroll et al. 2009; Kolb et al. 1999). However, these correlations with confidence and knowledge may be not verified as, in a survey applied to 900 Canadian physicians, that included family physicians, obstetricians, pediatricians and internists, although a majority of them considered their knowledge of genetics to be adequate, only a minority were confident to provide genetic counseling for simple genetic scenarios (Hunter et al. 1998).

The self-evaluation of knowledge may be correlated with questions about level of agreement with statements about methodology choice and results interpretation as seen in Table 7: in this hypothetical situation, in which several mutations of the same gene are described for a specific disease, gene sequencing, including coding regions and flanking intronic regions, should be the best methodology and not detecting a mutation should make this diagnosis very unlikely. However, the results showed that agreement is not verified for both groups, although not statistically different, showing that medical genetics

is a very complex field that requires specialized professional and a multidisciplinary team to guarantee that the best care is provided for both patients and their relatives.

The results also revealed non-compliance with the current Portuguese legislation regarding professional responsibilities for particular genetic tests (Law 12/2005): some non-geneticists physicians consider that they may request genetic tests for carrier detection of heterozygotes for recessive diseases (18.2%), presymptomatic tests (10.0%) and susceptibility tests (33.3%). This is not in accordance with legislation as these specific tests for healthy individuals can only be requested by geneticists after proper genetic counseling and must be clarified near all the physicians as genetic testing may have important implications for individual and familiar health in terms of medical management, genetic discrimination, lifestyle modifications and reproductive options.

When subjects were asked to rank the parameters used for selection of genetic tests, there was agreement between both groups, although it is worth noting that non-geneticists considered the quality of the report and the possibility of having a genetics specialist available to discuss the results and guide further testing, very important.

In the section of attitude assessment about rights of patients diagnosed with genetic diseases, not all non-geneticists agreed with referral for genetic counseling, as many of them also take that responsibility, informing patients about diagnostic criteria, natural history, prognosis and inheritance. This result is in accordance with a survey applied to 89 American physicians, in which 95% of them believed that the doctor, among others, has the responsibility to counsel patients about genetic testing, although only 51% felt that they had the time to perform it (Menasha et al. 2000). In contrast, when reproductive alternatives and prenatal or pre-implantation diagnosis are considered, most of them agreed on referral for a specialized genetic counseling service.

Although much debate have been performed about genetic testing definition, a recent systematic review that compared these definitions in recommendations, guidelines and reports from international institutions, policy makers and professional organizations, but also in documents from other stakeholders in the field, as the pharmaceutical industry, insurers, ethics bodies, patient organizations or human-rights associations, confirmed the extreme variability existing in the concepts and the ambiguous or equivocal use of the term (Sequeiros et al. 2012). Based in this survey, the definitions of genetic testing found covered unequivocally always diagnostic and presymptomatic DNA-based testing for germline mutations, i.e. medical applications in hereditary diseases. In over 80% cases, carrier testing, prenatal diagnosis and preimplantation genetic diagnosis, susceptibility testing for complex diseases and population genetic screening were also

covered. Chromosomes (conventional cytogenetics) and gene products (biochemical genetics) were unequivocally covered in 67–70% of those definitions. The research context and non-medical applications, somatic mutations, pharmacogenetics and forensic genetics testing were included only in 17–30%. Non-human DNA for infectious diseases, physical examination and family history were covered only in 7–10% of the definitions (Sequeiros et al. 2012).

Similar results were obtained when European (and other) legislation and policy instruments were analyzed regarding the definitions of genetic testing (Varga et al. 2012) and in results of a questionnaire sent to all EuroGentest partners, which is a non-profit coordination action funded by European Commission for the harmonization and further improvement of genetic services across Europe (Pinto-Basto et al. 2010).

The misconception on genetic testing definition is also verified in this study as it does not seem to be concordant between geneticists and non-geneticists, neither inside both groups: for example, not all of them considered diagnosis as a genetic testing, although all geneticists agreed that pre-symptomatic testing, carrier testing, prenatal or pre-implantation genetic diagnosis are included in this definition. A great majority of both geneticists and non-geneticists considered paternity testing and medico-legal identification as genetic testing, which is not in accordance with Portuguese regulatory definitions of genetic testing.

Concerning phenotypes evaluated, all of them agreed when genetic testing is used for Mendelian diseases, although only 77.8% of geneticists and 36.4% of non-geneticists included genetic predisposition and less of them considered evaluation of polymorphic traits. These results are in concordance with the EuroGentest survey, in which testing for Mendelian diseases was included in the scope by virtually all, but testing for genetic predisposition was less often so (88.1%) and testing for other polymorphic traits was even less (61.1%) (Pinto-Basto et al. 2010).

The groups differed completely about which mutations should be included in genetic testing definition as most non-geneticists (81.8%) considers also somatic mutations, in contrast with 44.4% of geneticists, and not all non-geneticists consider germinal mutations in this definition. According to national legislation, genetic information only includes hereditary characteristics, excluding somatic mutation but, in a previous survey, 73.0% of geneticists also included somatic mutations in genetic testing definition (Pinto-Basto et al. 2010).

Results concerning object (perceived as the type of source providing genetic information) or evaluation methodology confirmed the misconception about genetic information and genetic testing: all geneticists agreed on inclusion of chromosomes and genes/DNA in the definition and a greater percentage of non-geneticists agreed on inclusion of other clinical tests or just family history and physical exam on definition of genetic testing. A similar result was verified in EuroGentest survey, in which DNA, chromosomes and gene products were almost unanimously seen as within the scope of genetic testing, in comparison with other possible sources of genetic information, that were perceived as covered by almost half of the clinical geneticists and less significantly by the other groups (Pinto-Basto et al. 2010).

Our national legislation states that genetic information may be the result of genetic tests, including cytogenetics and molecular genetics, but can also be derived from biochemical, physiological or imagiological studies or just from analysis of family history (Law 12/2005), and does not define clearly what a genetic testing is, although the applications of genetic testing are well clarified.

In fact, a frequent confusion made is between the terms genetic testing and genetic information: *genetic testing* can be defined as the actual analysis with a particular purpose and using specific methodology, while *genetic information* is the data or content derived from a medical exam, regardless of its type, methods and material used, requiring an interpretation to put it into context (Sequeiros et al. 2012). Due to this dubious distinction between genetic testing and genetic information, an expert panel recommend the inclusion of blood tests (49.2%), family history (48.4%), physical exam (34.9%) or physiological tests/imaging (30.2%) as object of the test, besides chromosomes, genes/DNA or gene products (Pinto-Basto et al. 2010).

In conclusion, this study enabled the development and validation of a questionnaire for the evaluation of genetic testing in the Portuguese clinical practice. This is a novel approach in our country and our future aim is to survey physicians from the North of Portugal, from all medical specialties and different work settings, in order to guarantee a representative sample. With this questionnaire, our objectives include the clarification of regulatory issues regarding application of genetic testing. The results obtained may be a powerful tool to organize genetic counseling and genetic services in our country.

5. REFERENCES

Carroll JC, Rideout AL, Wilson BJ, Allanson JM, Blaine SM, Esplen MJ, Farrell SA, Graham GE, MacKenzie J, Meschino W, Miller F, Prakash P, Shuman C, Summers A, Taylor S (2009) Genetic education for primary care providers: improving attitudes, knowledge, and confidence. Canadian family physician Medecin de famille canadien 55 (12):e92-99

Flouris A, Hawthorne G, Aitken M, Gaff C, Metcalfe SA (2010) Development of a questionnaire for evaluating genetics education in general practice. Journal of community genetics 1 (4):175-183. doi:10.1007/s12687-010-0027-8

Harper PS (1997) What do we mean by genetic testing? Journal of medical genetics 34 (9):749-752

Hofman KJ, Tambor ES, Chase GA, Geller G, Faden RR, Holtzman NA (1993) Physicians' knowledge of genetics and genetic tests. Academic medicine : journal of the Association of American Medical Colleges 68 (8):625-632

Hunter A, Wright P, Cappelli M, Kasaboski A, Surh L (1998) Physician knowledge and attitudes towards molecular genetic (DNA) testing of their patients. Clinical genetics 53 (6):447-455

Ibarreta D, Elles R, Cassiman JJ, Rodriguez-Cerezo E, Dequeker E (2004) Towards quality assurance and harmonization of genetic testing services in the European Union. Nature biotechnology 22 (10):1230-1235. doi:10.1038/nbt1004-1230

Klitzman R, Chung W, Marder K, Shanmugham A, Chin LJ, Stark M, Leu CS, Appelbaum PS (2013) Attitudes and practices among internists concerning genetic testing. Journal of genetic counseling 22 (1):90-100. doi:10.1007/s10897-012-9504-z

Kolb SE, Aguilar MC, Dinenberg M, Kaye CI (1999) Genetics education for primary care providers in community health settings. Journal of community health 24 (1):45-59

Law 12/2005 Personal Genetic Information and Health Information

Menasha JD, Schechter C, Willner J (2000) Genetic testing: a physician's perspective. The Mount Sinai journal of medicine, New York 67 (2):144-151

OECD (2007) Guidelines for quality assurance in molecular genetic testing.

Ordem M (2009) Distribution by Specialty, Age and Gender. http://www.ordemdosmedicos.pt/?lop=stats_medicos&type=1&ano=2009. Accessed 23 May 2013

Pinto-Basto J, Guimaraes B, Rantanen E, Javaher P, Nippert I, Cassiman JJ, Kaariainen H, Kristoffersson U, Schmidtke J, Sequeiros J (2010) Scope of definitions of genetic testing: evidence from a EuroGentest survey. Journal of community genetics 1 (1):29-35. doi:10.1007/s12687-010-0004-2

Sequeiros J, Paneque M, Guimaraes B, Rantanen E, Javaher P, Nippert I, Schmidtke J, Kaariaainen H, Kristoffersson U, Cassiman JJ (2012) The wide variation of definitions of genetic testing in international recommendations, guidelines and reports. Journal of community genetics 3 (2):113-124. doi:10.1007/s12687-012-0084-2

Varga O, Soini S, Kaariainen H, Cassiman JJ, Nippert I, Rogowski W, Nys H, Kristoffersson U, Schmidtke J, Sequeiros J (2012) Definitions of genetic testing in European legal documents. Journal of community genetics 3 (2):125-141. doi:10.1007/s12687-012-0077-1

Wright CF, Hall A, Zimmern RL (2011) Regulating direct-to-consumer genetic tests: what is all the fuss about? Genetics in medicine : official journal of the American College of Medical Genetics 13 (4):295-300. doi:10.1097/GIM.0b013e3181f69dd2

Zimmern RL (1999) Genetic testing: a conceptual exploration. Journal of medical ethics 25 (2):151-156

ANNEX I

Introduction

Dear Doctor,

Genetic tests are a tool increasingly used in current clinical practice, and it has been witnessed to the increase in their supply in recent years due to technological research and development.

I would aprreciate your participation in a study concerning the application of genetic testing in Portugal, which is being developed as part of a Dissertation of the Intergrated Master in Medicine of ICBAS. For this purpose, we thank if you could answer to some questions about your previous experience with genetic testing and about your thinkings concerning its application in clinical practice.

This questionnaire will take approximately 20 minutes and will be done anonymously. The confidentiality of your responses is also guaranted, as well as the right of access, rectification and deletion of your own answers at any time in compliance with applicable legal requirements.

Click here to answer the questionnaire.

Thank you very much for your participation!

Group I – Sample Characterization

1. **Age** _____ years

2. **Gender** ☐ Female ☐ Male

Academic Graduation

3. Graduation year in Medicine or Integrated Master in Medicine: _____

4. Graduation School

   ☐ Faculty of Medicine – Oporto University

   ☐ Institute of Biomedical Sciences Abel Salazar – Oporto University

   ☐ School of Health Sciences School – Minho University

   ☐ Faculty of Medicine – Coimbra University

   ☐ Faculty of Health Sciences - Beira Anterior University

   ☐ Faculty of Medicine – Lisbon University

   ☐ Faculty of Medical Sciences– New University of Lisbon

   ☐ Other: _____

Workplace

5. Check the **main** workplace where you develop your professional activity

   ☐ Primary Health Care

   ☐ Hospital of National Health System

   ☐ Private Health Unit

   ☐ Other: _____

6. Check the localization of your **main** workplace:

   ☐ Aveiro ☐ Beja ☐ Braga

☐ Bragança	☐ Leiria	☐ Viana do Castelo
☐ Castelo Branco	☐ Lisboa	☐ Vila Real
☐ Coimbra	☐ Portalegre	☐ Viseu
☐ Évora	☐ Porto	☐ Madeira
☐ Faro	☐ Santarém	☐ Açores
☐ Guarda	☐ Setúbal	☐ Outside Portugal

Medical Specialty

7. Degree of Differentiation:

☐ Specialist

☐ Intern of Specialty

☐ Intern of Common Year

☐ I don't have any medical specialty

8. If you are Specialist or Intern of Specialty, please check your specialty:

☐ Pathology
☐ Anaesthesiology
☐ Angiology and Vascular Surgery
☐ Cardiology
☐ Paediatric Cardiology
☐ Cardiothoracic Surgery
☐ General Surgery
☐ Maxillofacial Surgery
☐ Paediatric Surgery
☐ Plastic, Reconstructive and Aesthetic Surgery
☐ Dermato-Venereology
☐ Infectious Disease
☐ Endocrinology and Nutrition
☐ Stomatology
☐ Gastroenterology
☐ Medical Genetics
☐ Gynaecology - Obstetrics
☐ Immunoallergology
☐ Immunohemotherapy
☐ Clinical Pharmacology
☐ Clinical Haematology
☐ Sports Medicine
☐ Occupational Medicine

☐ Rehabilitation and Physical Medicine
☐ General and Familiar Medicine
☐ Internal Medicine
☐ Legal Medicine
☐ Nuclear Medicine
☐ Tropical Medicine
☐ Nephrology
☐ Neurosurgery
☐ Neurology
☐ Neuroradiology
☐ Ophthalmology
☐ Medical Oncology
☐ Orthopaedics
☐ Otorhinolaryngology
☐ Clinical Pathology
☐ Paediatrics
☐ Pneumology
☐ Psychiatrics
☐ Childhood and Adolescence Psychiatrics
☐ Radiology
☐ Radiotherapy
☐ Rheumatology
☐ Public Health
☐ Urology

9. Please check your sub-specialty, if applicable to your professional situation:

☐ Paediatrics Intensive Care
☐ Cardiology of Intervention
☐ Cardiac Electrophysiology
☐ Hepatology
☐ EEG/Neurophysiology
☐ Paediatrics Gastroenterology
☐ Intensive Care
□ Paediatrics Nephrology
☐ Neonatology
☐ Neuropediatrics
☐ Reproductive Medicine
☐ Paediatric Oncology
☐ Oncologic Gynecology
☐ Dermatopathology

Post-Graduation Training

10. In this moment, how would you classify your knowledges of medical genetics?

☐ Very insufficient ☐ Insufficient ☐ Reasonable ☐ Good ☐ Very good

11. More concretely, how would you classify your knowledges in this moment of genetic tests concerning:

	Very insufficient	Insufficient	Reasonable	Good	Very good
Selection of test appropriate for each situation/patient					
Type of sample for each test					
Techniques used					
Limitations of techniques					
Interpretation of results/reports					

12. After your academic graduation, have you attended any course where the main topic was genetics? ☐ Yes ☐ No

    If yes, please specify the kind of course(s): _____

    _____

Group II – Attitude Assessment

13. These questions evaluate your degree of agreement or disagreement with the statements. Please, point out the answer that most nearly expresses your own attitude.

	I don't agree totally	I don't agree partially	Indifferent	I agree partially	I agree totally
When a genetic disease is diagnosed, the patient should always receive genetic counselling.					
When a genetic disease is diagnosed, the patient should always be referred to a genetic counselling consultation.					
When a patient with a genetic disease asks for medical information about his disease, should always be referred to a genetic counselling consultation.					
When a patient with a genetic disease asks for information about inheritance of his disease, should always be referred to a genetic counselling consultation.					
When there are doubts if a patient's disorder is of genetic cause, the patient should always be referred to a genetic counselling consultation.					
Any individual, who might be at risk to have a genetic disease, should be informed of that risk.					

	I don't agree totally	I don't agree partially	Indifferent	I agree partially	I agree totally
All physicians should be able to identify individuals who need genetic counselling.					
The family history collection and pedigree elaboration should always be done when a genetic disease is suspected.					

14. When a genetic disease is diagnosed, the patient should always: (please, point out the answer that most nearly expresses your own attitude)

	I don't agree totally	I don't agree partially	Indifferent	I agree partially	I agree totally
Receive an explanation of the diagnosis					
Receive an explanation of the natural history / prognosis of the disease					
Receive an explanation of the inheritance of the disease					
Receive an explanation of the prenatal diagnosis, if available					
Be informed of availability of all reproductive alternatives					

	I don't agree totally	I don't agree partially	Indifferent	I agree partially	I agree totally
Have the opportunity to discuss his feeling with a health professional					
Have the opportunity to meet other people with the same or similar disease					

15. Assuming the following genetic counselling services are available, whether on the health institution or by referral, please indicate who should have the responsibility to provide the following care:

	My responsibility	Other professional of my service or institution, excluding geneticists	Consultation/service of genetic	I don't think that I should have concern with providing
Explain diagnosis				
Explain the natural history / prognosis of the disease				
Explain the inheritance mode of the disease				
Explain the prenatal diagnosis, if available				
Inform of availability of all reproductive				

	My responsibility	Other professional of my service or institution, excluding geneticists	Consultation/service of genetic	I don't think that I should have concern with providing
alternatives				
Discuss feelings with a health professional				
Introduce to other families with the same or similar disease				

Group III – Previous Experience with Genetic Tests

16. In your clinical practice, how often do you discuss genetic issues with your patients (including taking a family history)?

☐ Never; please, explain the reason: _____

☐ Only if the patient has a genetic disease

☐ Sometimes, but only if I consider that exist a justified reason for it

☐ Frequently, always when it seems appropriate

☐ In most cases

☐ Always

17. How often do you complete a **partial** family history (i.e., that includes first degree relatives, such as parents, siblings and children) and **full** family history (i.e., that includes at least three complete generations) for each new patient?

	Never	Rarely	Sometimes	Frequently	Always
Partial Family History	☐	☐	☐	☐	☐
Full Family History	☐	☐	☐	☐	☐

If you answered NEVER for both types of family history, please proceed to question 20.

18. How often do you update family history, either partial or full, of your patients?

☐ In each consultation

☐ Yearly

☐ 5 yearly

☐ Always when the patient communicates me new data from his family history

☐ Rarely update

☐ Other frequency _____

19. How do you record the family history, whether it is on paper or computer?

    ☐ Text

    ☐ Genogram/Pedigree

20. In general, how do you feel when you have to deal with genetics issues with your patients?

    ☐ Very comfortable

    ☐ Comfortable

    ☐ Neither comfortable, nor uncomfortable

    ☐ Uncomfortable

    ☐ Very uncomfortable

21. In your clinical practice, please indicate your **confidence level** when performing each of the following tasks:

	Nothing confident	Little confident	Moderately confident	Very confident	Completely confident
Elicit genetic information as part of a clinical and family history					
Assess risk for hereditary diseases					
Decide which patients are candidates for referral for genetic counselling based on family history					
Order genetic tests for hereditary cancer or adult onset disease					
Discuss prenatal diagnosis options with your patients					
Evaluate clinical utility of a genetic test					
Discuss the benefits, risks					

	Nothing confident	Little confident	Moderately confident	Very confident	Completely confident
and limitations of genetic tests					
Provide counselling to patients that are in decision process to perform or not a genetic test					
Offering psychosocial support to patients coping with a genetic test result					
Provide counselling to patients related to screening, lifestyle changes or surveillance strategies based on a genetic test result					
Describe to patients the expectations that they may have about a genetic counselling consultation					

22. Did you order one or more genetic tests in the last twelve months?

☐ Yes ☐ No

If NO, please proceed to question 26.

23. If YES, refer the approximate number of genetic tests ordered in the last twelve months according to:

No. Tests	**Technique Type**
_____	Cytogenetic (for example, karyotype, FISH and array CGH)
_____	Molecular Genetic (for example, search of mutations by sequencing)
_____	Biochemistry Genetic (for example, enzymatic activity)

	Test Type

_____ Prenatal diagnosis (for example, foetal karyotype)

_____ Confirmation / exclusion of a patient's diagnosis (for example, cystic fibrosis)

_____ Carrier test of heterozygosity for recessive diseases (for example, cystic fibrosis)

_____ Susceptibility testing (for example, HLA-B27 and ApoE)

_____ Pharmacogenetic test

24. Indicate, in descending order, the five main **pathologies / group of pathologies** for which you ordered genetic tests:

1st _____

2nd _____

3rd _____

4th _____

5th _____

25. Before ordering a genetic test: (choose the phrase that best characterizes how you proceed)

□ Explain in detail to the patient the test, its possible results and eventual implications to remaining family

□ Explain briefly to the patient the test, its possible results and eventual implications to remaining family

□ I proceed in the following manner: _____

26. In the last year, how often did your patients asked you about issues concerning genetic tests, by their own initiative?

□ Every day

□ At least, once every week

□ At least, once every month

☐ At least, once every six months

☐ At least, once every year

☐ Never

☐ I don't remember

27. If any of your patients asked you about issues concerning genetic tests by their own initiative, specify the main reason(s):

☐ Prenatal diagnosis

☐ The patient wants to perform a genetic test by familiar history of a genetic pathology

☐ Wants to discuss with you if he should or not perform genetic tests advertised on Internet, for example, for evaluate risk of developing some pathologies

☐ To discuss with you results of a genetic test

☐ Other – please, specify: _____

28. During your professional practice, how often do you refer a patient or his healthy relatives to a specialist consultation of Medical Genetic?

☐ Every day

☐ At least, once every week

☐ At least, once every month

☐ At least, once every six months

☐ At least, once every year

☐ Never

☐ I don't remember

29. If you have ever referred a patient or his healthy relatives to a specialist consultation of Medical Genetic, indicate the reason(s) by which you did it:

☐ Investigation and/or confirmation of a diagnosis of patients

☐ Genetic counselling for a patient

☐ Genetic counselling for healthy relatives

☐ Guidance for requesting a genetic test

☐ Discussion of reproductive options

☐ Other reason – please, specify: _____

30. If you have NEVER referred, indicate the reason(s) by which you did not refer the patient or his relatives:

☐ In my daily practice, I don't have patients with genetic diseases, either suspected or confirmed

☐ I perform genetic counselling by myself to my patients and relatives

☐ The accessibility to Medical Genetic services is low

☐ I don't know how to refer to Medical Genetic services

☐ Other reason – please, specify: _____

31. When you have doubts concerning genetic tests, which is your first information source?

☐ Read a book – If you ticked this option, indicate the books you use:

☐ Books of my specialty

☐ Genetic books

☐ Search on the Internet – If you ticked this option, indicate which sites you visit to get information about genetic tests: _____

☐ Contact a specialist physician of Medical Genetic

☐ Contact a genetic lab technician

☐ Contact a sales representative / promoter of genetic laboratories

☐ Use another source information. Please, specify: _____

Group IV –Assessment of Perception about Genetic Tests

Which of the following do you consider to be a genetic test? [Indicate the option(s) that you consider corrects]

32. **Concerning type of testing:**

☐ Diagnostic testing

☐ Pre-symptomatic testing

☐ Disease predisposition testing

☐ Pharmacogenetics

☐ Carrier testing

☐ Prenatal testing

☐ Pre-implantation genetic diagnosis

☐ Population screening

☐ Paternity testing

☐ Medico-legal identification

33. **Concerning phenotypes evaluated:**

☐ Mendelian / monogenic diseases

☐ Genetic predispositions for common diseases (for example, diabetes)

☐ Other polymorphic traits (for example, IQ, height, etc.)

34. **Concerning mutations types:**

☐ Somatic mutations (present in a specific tissue, such as tumour tissue)

☐ Germinal mutations

35. **Concerning object / evaluation methodology:**

☐ Chromosomes / karyotype

☐ Genes / DNA

☐ Gene products (for example, proteins, mRNA)

☐ Clinical blood tests (for example, blood count)

☐ Imaging / physiologic tests

☐ Physical exam

☐ Family history

36. In each of the following situations, please indicate with a cross if you order a genetic test or refer to a specialist consultation of Medical Genetic:

	Order a genetic test	Refer to consultation of Medical Genetics
Diagnosis of symptomatic individuals		
Pharmacogenetic tests		
Carrier test of heterozygosity for recessive diseases		
Pre-symptomatic diagnosis of health individuals		
Susceptibility tests of healthy individuals		

37. How do you rate the importance of the following parameters in the selection of genetic tests and choice of laboratories for their performance?

	Without importance	Little important	Neither important, nor without importance	Important	Very important
Sensibility					
Specificity					
Clinical utility					
Type of methodology used					
Number of searched mutations					
Participation of laboratory in schemes of external					

	Without importance	Little important	Neither important, nor without importance	Important	Very important
quality control					
Laboratory certification					
Laboratory accreditation					
Previous experience with laboratory					
Price					
Response time					
Possibility of having a interlocutor for results discussion and possible need for other tests					
Quality of reports					
Availability in institution					
Laboratory localization (Portugal or abroad)					

38. Imagine that several mutations of the same gene are described for a specific disease. In this situation, what do you think about the following statements?

	I disagree totally	I disagree partially	Neither agree, nor disagree	I agree partially	I agree totally
The best choice is search only the **most frequent mutations**					
In the anterior situation, a non-detection of mutations equals to diagnosis exclusion					
The best choice is perform the **all gene sequencing** (in other words, codificant regions and flanking intronic regions)					

	I disagree totally	I disagree partially	Neither agree, nor disagree	I agree partially	I agree totally
In the anterior situation, a non-detection of mutations equals to diagnosis exclusion					

ANNEX II

QUESTIONNAIRE VALIDATION

We appreciate if you could classify the questionnaire concerning the following items, considering a Likert scale in which 1 is the worst result and 7 is the best result.

1. How do you classify the questionnaire concerning **clarity** of questions, in other words, if the questions are properly enlightening?
2. Do you consider that the questions are **applicable** to the data they intend to analyse?
3. How do you classify the **discriminative power** of questions, in other words, if the questions allow separating the expected results by categories?
4. The questions and answers of the questionnaire have **enough content** to collect desired data?
5. The form and content of questions can generate **biases** in answers?
6. To what extent, do you consider that there are **redundant or unnecessary** questions in the questionnaire?

   If you checked classification ≥2, please indicate the number of question(s) you considered to be redundant or unnecessary. _____

   _____
7. The questionnaire aims to assess knowledge, perceptions and attitudes of portuguese physicians given the genetic tests specificity and their potential consequences, as well as to check their use in portuguese clinical practice. To what degree, do you consider that these aims are achieved?
8. Do you suggest the inclusion or exclusion of any question? _____

   _____
9. Do you suggest add any option of answer (please, indicate the number of question to which you refer to): _____

   _____

ANNEX III

Number	Question	Changed to:
18	How often do you update family history, either partial or full, of your patients? ☐ In each consultation ☐ Yearly ☐ 5 yearly ☐ Always when the patient communicates me new data from his family history ☐ Rarely update ☐ Other frequency _____	After the first consultation, how often do you question your patients about family history, either partial or full? ☐ In each consultation ☐ Yearly ☐ 5 yearly ☐ Always when the patient communicates me new data from his family history ☐ Rarely ☐ Other frequency _____
25	Before ordering a genetic test: (choose the phrase that best characterizes how you proceed) ☐ Explain in detail to the patient the test, its possible results and eventual implications to remaining family ☐ Explain briefly to the patient the test, its possible results and eventual implications to remaining family ☐ I proceed in the following manner: _____	Before ordering a genetic test: (choose the phrase that best characterizes how you proceed) ☐ Explain in detail to the patient, or its legal representative(s), the test, its possible results and eventual implications to remaining family ☐ Explain briefly to the patient, or its legal representative(s), the test, its possible results and eventual implications to remaining family ☐ I proceed in the following manner: _____