Twenty Years of a Pre-Symptomatic Testing Protocol for Late-Onset Neurological Diseases in Portugal

Vinte Anos de um Protocolo de Teste Pré-Sintomático para Doenças Neurológicas de Início Tardio em Portugal

ARTIGO ORIGINAL

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ABSTRACT

Introduction: The national protocol of genetic counselling and pre-symptomatic testing for late-onset neurological diseases began in Portugal in 1995. Initially, it was accessible only to adults at-risk for Machado-Joseph disease, but was later extended to other hereditary ataxias, to Huntington's disease and to familial amyloid polyneuropathy caused by Val30Met mutation at the transthyretin gene. The aim of this study was to describe the profile of the population seeking pre-symptomatic testing, while also reflecting on the experience of conducting the protocol of multidisciplinary sessions since 1996.

Material and Methods: We conducted a retrospective study and collected data from clinical records of consultands who requested pre-symptomatic testing at our centre in Porto (Portugal) during the first twenty years of practice (1996 - 2015).

Results: A total of 1446 records were reviewed. The most common reason for testing was to reduce uncertainty (41.7%). The rate of withdrawals before results disclosure was lower (16%) than reported in other international experiences with pre-symptomatic testing, while 45% of the consultands dropped out the protocol after learning the test results (73.5% of them were non-carriers). As far as the mutation carriers were concerned, 29.6% adhered to the protocol a year after test disclosure. Consultands that had learned about pre-symptomatic testing through healthcare professionals tended to adhere more to pre-symptomatic testing consultations.

Discussion: The profile of Portuguese consultands at risk for late-onset neurological diseases is similar to those reported in other international programs. The largest group in this data set was the one comprising the subjects at risk for familial amyloid polyneuropathy caused by Val30Met mutation at the transthyretin gene, and it is likely that therapeutic options for this condition may have influenced this result. Adherence to pre-symptomatic testing may change in the future since effective therapies are available (or given the fact that people think effective treatments are imminent).

Conclusion: This study reflects the first comprehensive description of a Portuguese experience with pre-symptomatic testing for late-onset neurological diseases. The development of innovative approaches to improve the consultands' experience with pre-symptomatic testing and their engagement in genetic departments is still a challenge in Portuguese genetics healthcare departments. A better coordination among primary care and genetics healthcare services is needed.

Keywords: Genetic Counseling; Genetic Testing; Neurodegenerative Diseases; Portugal; Quality of Health Care

RESUMO

Introdução: Em 1995 foi iniciado em Portugal um protocolo nacional para o aconselhamento genético e teste pré-sintomático de doenças neurológicas de início tardio. Inicialmente, foi disponibilizado para indivíduos adultos em risco para a doença de Machado-Joseph e posteriormente estendido a outras ataxias hereditárias, doença de Huntington e polineuropatia amiloidótica familiar ATTR Val30Met. O objetivo deste estudo é descrever o perfil dos consultandos envolvidos no teste pré-sintomático desde 1996, e refletir no protocolo de sessões multidisciplinares.

Material e Métodos: Realizámos um estudo retrospetivo com recolha de dados dos processos clínicos dos utentes que solicitaram teste pré-sintomático ao longo dos primeiros 20 anos do Centro de Genética Preditiva e Preventiva (1996 - 2015), localizado no Porto, Portugal.

Resultados: Analisámos um total de 1446 processos clínicos; a principal motivação para a realização do teste pré-sintomático foi o alívio da incerteza (41,7%). A taxa de abandono do protocolo antes da comunicação dos resultados do pré-sintomático (16% dos casos) foi mais baixa do que em outras experiências internacionais; 45% dos consultandos abandonaram o protocolo depois de saberem o resultado do teste pré-sintomático (73,5% dos quais eram não-portadores). 29,6% de consultandos portadores continuaram envolvidos no protocolo um ano após saberem o resultado do teste pré-sintomático. Os consultandos encaminhados para o protocolo através de outros profissionais de saúde revelaram maior adesão ao protocolo.

Discussão: O perfil sociodemográfico dos consultandos no Centro de Genética Preditiva e Preventiva é similar ao reportado noutras experiências internacionais. Os consultandos em risco para polineuropatia amiloidótica familiar ATTR Val30Met representaram o maior grupo nos nossos dados, sendo provável que as opções terapêuticas disponíveis para esta doença tenham influenciado este resultado. A adesão ao teste pré-sintomático poderá alterar-se no futuro quando terapias eficazes estiverem disponíveis (ou as pessoas as percepcionem como estando iminentes).

Conclusão: Este trabalho constitui a descrição mais completa até ao momento publicada acerca da realização de teste pré-sintomático em Portugal. O desenvolvimento de abordagens com vista à melhoria da experiência dos consultandos com os testes pré-sintomáticos e ao seu envolvimento nos serviços de genética é um desafio atual, assim como a melhor articulação dos mesmos com os cuidados de saúde primários.

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Palavras-chave: Aconselhamento Genético; Doenças Neurodegenerativas; Portugal; Qualidade de Cuidados de Saúde; Testes Genéticos

INTRODUCTION

Predictive testing, also known as presymptomatic testing (PST), is a type of genetic test used to determine the genetic status of at 50%-risk subjects in order to predict their possibilities of developing a given disease in the future. Predictive testing for late-onset neurological diseases (LONDs) was first offered in 1983 when linkage analysis made it possible to identify subjects at increased risk for Huntington's disease (HD).[1,2] In 1993, PST by direct mutation analysis was first possible for HD, expanding to other dominantly inherited neurological diseases a few years later. Then in 1997, the protocol of genetic counselling and psychosocial support for PST proposed for HD became the model used worldwide for those diseases.[3]

In Portugal, PST was first available for transthyretin (TTR)-related familial amyloid polyneuropathy (FAP) in 1986 through biochemical testing,[4] and years later, by molecular analysis. Val30Met is by far the most common disease-related mutation.[5] PST for Machado-Joseph disease (MJD, also known as spinocerebellar ataxia type 3, SCA3) was first offered in 1995.[6] A national protocol of multidisciplinary sessions was then implemented at five genetics departments in Portugal and made accessible to all adults at risk for LONDs. The implementation followed a comprehensive protocol of genetic counselling and psychosocial evaluation and support, first aimed at MJD/SCA3 and other SCAs, and later extended to HD and FAP ATTR Val30Met, among others.[6] All of these diseases are dominantly inherited, progressive, highly incapacitating and have no effective cure. Some therapeutic measures are available for FAP. For example, liver transplantation has been possible for over 20 years now[7] and more recently, Tafamidis,[8] was released as a new drug used to delay loss of peripheral nerve function.

In Portugal, some areas present the world's highest frequency for MJD/SCA3 (national prevalence of 3.1 : 100 000, but 835.2 in Flores, 27.1 in the Azorean island of São Miguel, and 14.4 in the central region of mainland Portugal).[9] Huntington disease has a more uniform prevalence, estimated at 5 – 10: 100 000,[11,12] similar to what is found in most of other European countries. Particularly, FAP has a prevalence of 163.1: 100 000 in the region of Póvoa de Varzim/Vila do Conde, just north of Porto where FAP was initially detected and one of the major clusters of patients worldwide is found.[10] Therefore, these disorders represent a public health problem in these high prevalence clusters.

Due to the high incidence of these disorders in some regions of Portugal, early detection is essential to improve patients' prognosis and management. Consequently, it is extremely important to offer proper genetic counselling and PST to at-risk relatives after the identification of the genetic defect in a single family.[13]

The international guidelines established for PST highlight the relevance of establishing a respectful relationship between counsellor and consultand, the communication of test-related information, and the availability of pre and post-test counselling, including psychosocial support.[14,15] Our experience in Portugal shows that genetic testing for LONDs calls for special attention from genetic counsellors, clinical psychologists and other health professionals.[16-20] Longitudinal studies of 10 years after PST demonstrated that, prior to PST, participants had higher levels of psychopathology than a year after receiving their test results, regardless of that result.[19] Also, the time of contact with the disease in the family and the gender of the affected parent had an impact on the psychological outcome of PST.[20] Evidence has also been collected acknowledging the influence of the counsellor's skills and the quality of the counsellor-consultand relationship based on the perceived satisfaction of consultands.[21,22]

Similarly to recently published studies on national experiences with related programs,[23-28] we describe in this study the experience gained at our centre in conducting PST in Portugal. We aim to characterize the profile of the population seeking PST at the Centre for Predictive and Preventive Genetics (CGPP) outpatient clinic, while also reflecting on the experience of conducting a PST program since 1996.

MATERIAL AND METHODS

The Portuguese PST protocol

The PST protocol has been implemented for over 20 years at an outpatient clinic in Porto (Centre for Predictive and Preventive Genetics CGPP-IBMC), mostly covering the northern region of the country, but not restricted to it. The protocol for genetic counselling in the context of PST (Fig. 1) has been published elsewhere.[6,19] In general, this procedure follows the guidelines produced by the International Huntington Association and the World Federation of Neurology (WFN) Research Group on Huntington's Chorea;[29] it includes (1) a pre-test neurological examination, a psychosocial assessment, and at least two genetic counselling sessions; (2) a session for disclosure of results; and (3) a psychosocial follow-up at 3 weeks, at 6 months, and a year after the results. In addition, it is possible to undergo further genetic counselling sessions and/or psychological, social service or psychiatric intervention, whenever appropriate.[6]

Subjects

From 1996 to 2015, 1498 persons sought PST at CGPP. Of these, 1230 received their genetic test results (Fig. 2); 28 were excluded from the PST protocol after the first visit (2 due to psychiatric problems, which was incompatible at the time with PST); 20 were found not to be at risk for a LOND (usually at 25% risk before a parent was tested and proved to be non-carrier), and 6 were excluded because they were still minors (younger than 18 years). Another 240 subjects withdrew from the protocol in one of the pre-test sessions, before the disclosure of results.

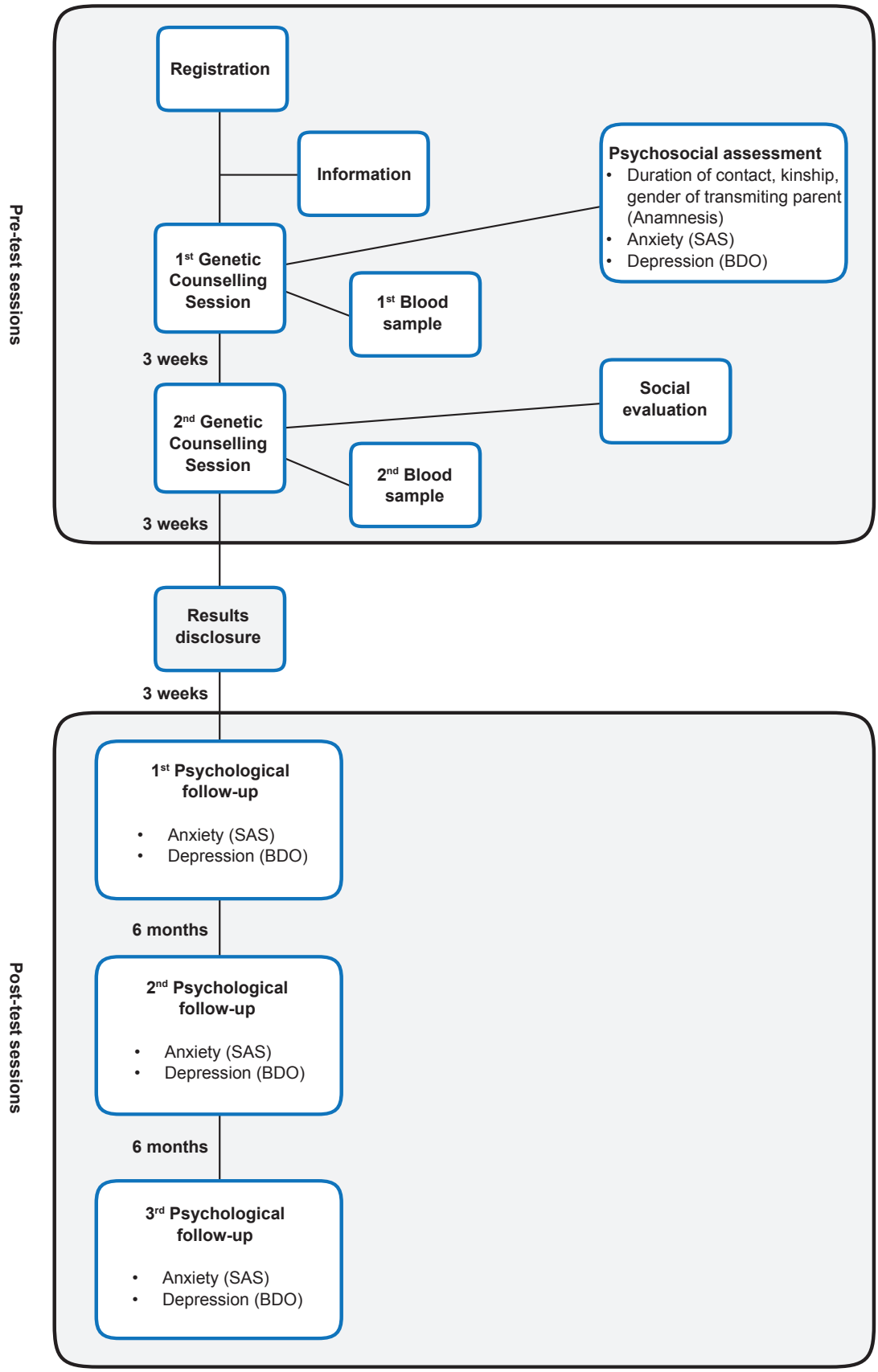

Figure 1 – General protocol of pre-symptomatic testing in use at our centre

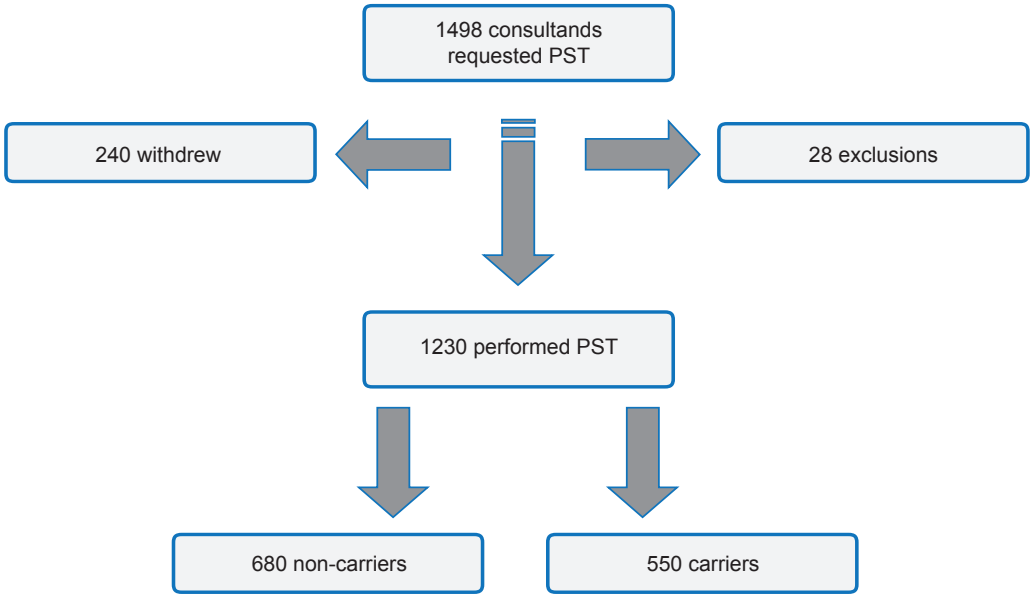

Figure 2 – Flowchart of the outcome of the pre-symptomatic testing and its results

Procedure

We reviewed the registration forms and all written documentation of the genetic counselling sessions from 1498 clinical records. We carried out a retrospective descriptive study of consultands' profile, looking at social and demographic variables (gender, age, marital status, number of offspring, education and family history).

The PST protocol includes two pre-test genetic counselling sessions. An essential point of these sessions is the exploration of psychosocial and motivational issues related to the test request, which are usually explored using open questions. The technique is used to explore the motivations for testing, the anticipated impact of possible results, and the sources of knowledge about the disease and PST. Also, the information on the perceived satisfaction of the consultands with the PST protocol, and if they would recommend it to other persons as well as their general suggestions, are questioned. All this information is expected to be clearly registered in the consultands' clinical file. However, because the information is obtained via open questions, it is common to find that consultands referred more than one answer for each explored theme.

According to the disease at risk, requests were clustered in four groups: (1) FAP ATTR Val30Met; (2) HD; (3) MJD; and (4) other LONDs, such as CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), SCA2 and SCA7 (spinocerebellar ataxia types 2 and 7) and DRPLA (dentatorubral-pallidoluysian atrophy).

When consultands registered in the protocol, during their first visit to the centre, written consent for electronic registry of their data is requested as required by national legislation, and for respective analysis. During the first genetic counselling session, all consultands were informed about

Table 1 - Uptake of pre-symptomatic testing

Disease	Nº records	Pre-test withdrawals			Exclusions	Results of the genetic test	
		Before the 1st session	Before the 2nd session	Before the results session		Carrier	Non-carrier
FAP	1,174 (78.4%)	100 (8.5%)	38 (3.2%)	35 (3.0%)	19 (1.6%)	439 (44.7%)	543 (55.3%)
HD	230 (15.3%)	21 (9.1%)	19 (8.3%)	10 (4.3%)	6 (2.6%)	75 (43.1%)	99 (56.9%)
MJD	55 (3.7%)	4 (7.3%)	6 (10.9%)	0 (0%)	1 (1.8%)	20 (45.5%)	24 (54.6%)
Other LONDs*	39 (2.6%)	3 (3.5%)	2 (5.1%)	2 (5.1%)	2 (5.1%)	16 (53.3%)	14 (46.7%)
Sub-total		128 (8.5%)	65 (4.3%)	47 (3.1%)		550 (44.7%)	680 (55.3%)
Totals	**1498 (100%)**		**240 (16.0%)**		**28 (1.9%)**	**1,230 (82.1%)**	

* Other late-onset neurological diseases: SCA2, SCA7, CADASIL & DRPLA

the PST procedures. The PST protocol was also explained in detail. The consultands had the opportunity to raise questions, doubts or concerns (this opportunity was reiterated in the second session and special emphasis was placed on any questions or doubts arising).

Data analysis

Descriptive statistics and categorical variables were analysed using the chi-square test. The Kruskal-Wallis non-parametric test was used to determine if there were significant differences between the disease groups regarding quantitative variables. Significance was set at $\alpha \leq 0.05$. Statistical analyses were performed using the Statistical Program for Social Sciences (SPSS), version 20.0 for Windows. The Statistical procedures adopted are those approaches commonly used to evaluate these types of variables.

RESULTS

Socio-demographic profile and disease-related features

Between 1996 and 2015, 1498 people requested PST at CGPP clinical facilities. Of these, 28 (1.9%) were not eligible for PST and 240 (16.0%) withdrew from the protocol before the disclosure of test results (Table 1). The reasons for withdrawal are unknown as they were not explored by the clinical team for ethical reasons. However, according to what has been recorded in the clinical files, professional notes from genetic counselling and psychological pre-test sessions, withdrawal might be related to consultands' gains of new perspectives, such as being at a higher risk than their previous subjective perception. On the other hand, it may be due to inaccurate understanding of the disease, including myths and beliefs. All clarifications along pre-test sessions may have prompted a different awareness and further reflection on the implications of the test and sometimes fears of being unable to cope with an unfavourable result. We found that written documentation of consultands-reported experience was not uniformly registered by the professionals. Therefore, registration of the information in the clinical files is inconsistent.

The mean-age at the time of testing was 30.7 years (range 14 - 95 years, SD 12.8 years) (Table 2). The number of PST performed per year according to the at-risk disease is illustrated in Fig. 3. Persons at-risk for FAP ATTR Val-30Met (which has an earlier onset - mean of 33 years in the Portuguese population) had a significantly lower mean-age (28.8 years; $p < 0.001$) than those for the other diseases. Female consultands represented 56.0% of the sample, in a male/female ratio of 1 : 1.27 ($p < 0.001$); females predominated for all disease groups (FAP: $p = 0.005$; HD: $p < 0.001$ and MJD: $p = 0.001$), except for the other LONDs ($p = 0.853$); 47.8% were married or in a relationship; 60.9% did not have offspring; those at risk for FAP ATTR Val30Met (younger, on average) had fewer offspring than the others (34.3%; $p < 0.001$).

The educational level was significantly different among consultands ($p < 0.001$). Those at risk for other LONDs had higher education (39.4% had a university degree), while 55.9% of the consultands at risk for FAP ATTR Val30Met had not completed more than secondary education). A maternal family history of the disease was predominant among consultands at risk for FAP ATTR Val30Met (55.8%), MJD (51.0%), and other LONDs (72.4%), while persons at risk for HD presented only 45.4% of maternal family background (Table 2).

Reasons for testing, anticipated changes after testing, and source of knowledge of PST

The consultands-reported reasons for testing, anticipated changes, and source of knowledge of PST were not recorded uniformly. The reasons for PST were recorded for 1215 individuals (82%). The most common reasons for undertaking PST were "to relieve uncertainty" (41.7%), "to

Follow-up withdrawals						Protocol concluded – after 3rd psychology appointment (12 months)	
After results communication		After 1st psychology appointment (3 weeks)		After 2nd psychology appointment (6 months)			
Carrier	Non-carrier	Carrier	Non-carrier	Carrier	Non-carrier	Carrier	Non-carrier
120 (27.3%)	348 (64.1%)	117 (26.7%)	121 (22.3%)	78 (17.8%)	53 (9.8%)	124 (28.2%)	21 (3.8%)
23 (30.7%)	49 (49.5%)	12 (16.0%)	19 (19.2%)	14 (18.7%)	7 (7.1%)	26 (34.6%)	24 (24.2%)
4 (20.0%)	6 (25.0%)	6 (30.0%)	7 (29.1%)	0 (0%)	1 (4.2%)	10 (50.0%)	10 (41.7%)
2 (12.5%)	10 (71.4%)	9 (56.3%)	2 (14.28%)	2 (12.5%)	0 (0%)	3 (18.7%)	2 (14.3%)
149 (26.5%)	413 (73.5%)	144 (49.2%)	149 (50.8%)	94 (60.6%)	61 (39.4%)	163 (74.1%)	57 (25.9%)
562 (45.7%)		**293 (23.8%)**		**155 (12.6%)**		**220 (17.9%)**	

Table 2 - Social and demographic data of subjects who underwent pre-symptomatic testing (PST), 1996 - 2015 (showing valid percentage)

Disease	Gender		Age	Marital status			
	Female	Male		Single	Married	Divorced	Widow/er
FAP (n = 1174)	635 (53.4%)	539 (46.6%)	28.8	577 (51.6%)	469 (45.2%)	21 (1.8%)	15 (1.4%)
HD (n = 230)	146 (64.3%)	84 (35.7%)	37.0	63 (29.7%)	131 (63.2%)	10 (5.4%)	4 (1.7%)
MJD (n = 55)	37 (72.9%)	18 (27.1%)	40.7	9 (15.0%)	30 (72.5%)	4 (2.5%)	4 (10.0%)
Other LONDs* (n = 39)	21 (51.7%)	18 (48.3%)	37.7	10 (20.7%)	28 (75.9%)	1 (3.4%)	0 (0%)
Total	839 (56.0%)	659 (44.0%)	30.7	659 (47.9%)	658 (47.8%)	36 (2.6%)	23 (1.7%)

* Other late-onset neurological diseases: SCA2, SCA7, CADASIL & DRPLA

prepare for disease onset" (23.2%), "family planning" (23.2%) and "to inform the offspring" (18.0%).

The anticipated changes after testing results were recorded for 902 individuals (63%). As changes anticipated in response to a potential carrier result, 32.4% of consultands referred emotional instability, among which five people (1.7%) expressed suicidal ideation; four of them (2 females, 2 males) were at risk for FAP ATTR Val30Met and one (female) for HD. Additionally, 21.6% of the consultands anticipated changes in family planning, while 23.5% said they would look for therapeutic options (even if these did not exist) and seek medical care; and 22.5% expressed that nothing would change in their lives. On the other hand, under a scenario of a non-carrier result, 41.6% denied any future potential changes; while 37.4% mentioned they would be happy and relieved, 16.9% anticipated some positive change in their lives, and 4.1% expressed their desire of having more children.

The source of knowledge about the availability of PST was recorded from 922 individuals (64.6%). Consultands

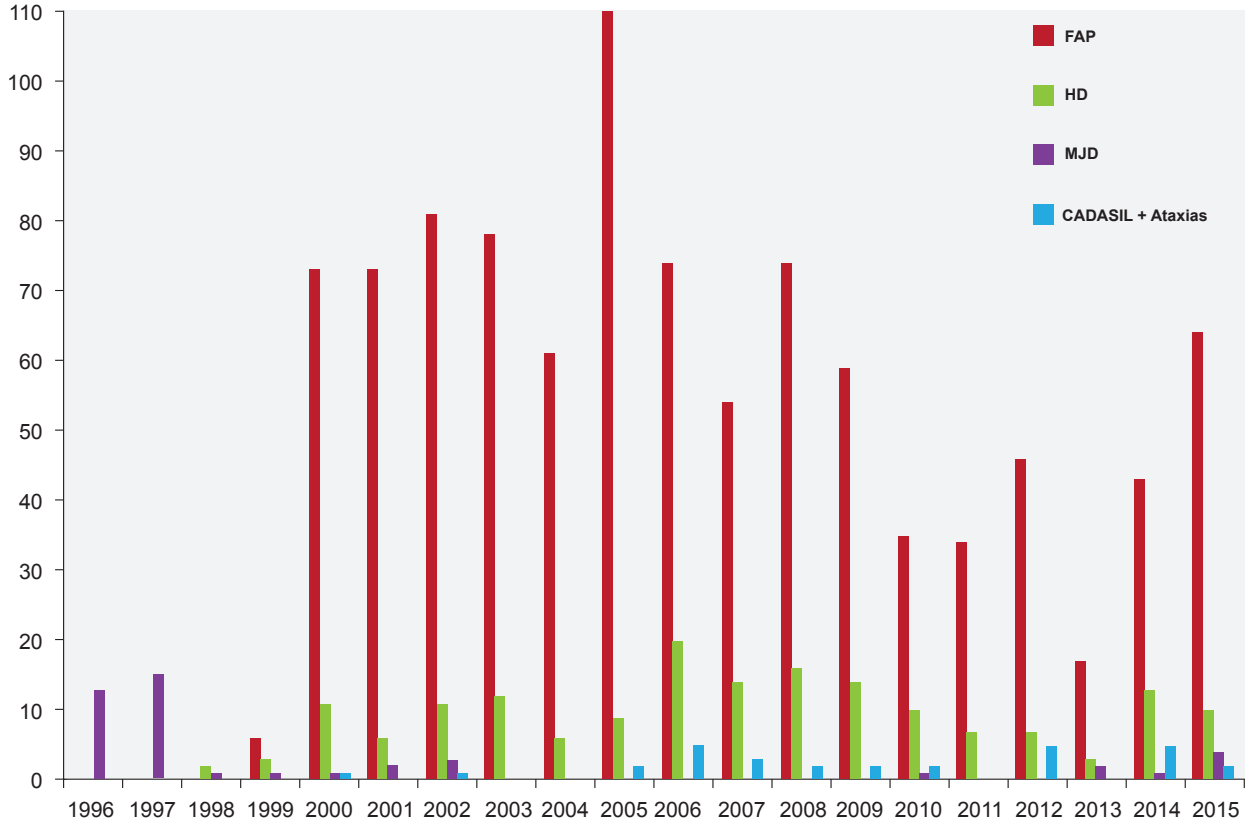

Figure 3 – Number of PST performed per year according to the at-risk disease

Consultands who had offspring	Education				Family history	
	Illiterate-4th year	5th - 9th year	10th - 12th year	Higher education	Maternal	Paternal
362 (34.3%)	88 (9.2%)	430 (44.7%)	328 (34.1%)	115 (12.0%)	603 (55.8%)	477 (44.2%)
107 (53.8%)	25 (14.4%)	49 (28.1%)	64 (36.8%)	36 (20.7%)	89 (45.4%)	107 (54.6%)
34 (72.3%)	11 (26.2%)	11 (26.2%)	11 (26.2%)	9 (21.4%)	25 (50.0%)	25 (50.0%)
21 (53.8%)	4 (12.1%)	10 (30.3%)	6 (18.2%)	13 (39.4%)	21 (72.4%)	8 (27.6%)
524 (39.1%)	128 (10.6%)	500 (41.3%)	409 (33.8%)	173 (14.3%)	738 (54.5%)	616 (45.5%)

learned about PST through health professionals (59.7%); through relatives, friends, or colleagues (30.1%); or via the Internet (10.2%). In FAP ATTR Val30Met, the predominant source of knowledge about PST was the family or individual search ($p < 0.001$), which was higher than for the other diseases.

Test outcomes, follow-up adherence, evaluation of the PST protocol, and potential endorsement

Of the 1230 subjects who received the test results (81.1%), 55.3% were reported as non-carriers (n = 680) and 44.7% were reported as carriers (n = 550) ($p < 0.001$) (Table 1). On the other hand, almost half (45.7%) of the subjects dropped out of the psychosocial follow-up offered regardless of test result (n = 562), of which 73.5% were non-carriers. One year after the communication of results, 220 subjects (17.9%) were still involved in the long-term psychological follow-up session of the protocol. The higher percentage of those who completed one-year of follow-up were pre-symptomatic carriers (74.1%) ($p < 0.001$). Nevertheless, they represent 29.6% of subjects informed as carriers at test disclosure.

We found that 23% of the 551 consultands that had learned about PST through healthcare professionals tended more to complete the PST protocol ($p < 0.001$), when compared to 12.4% of the 371 subjects that reported no previous medical advice.

The evaluation of the PST protocol sessions was recorded for 293 individuals. The PST protocol followed was evaluated positively by 87.7% of consultands. The reasons included its structure of pre- and post-test sessions and the multidisciplinary approach (35.8%), the personalized attention provided by the professional team (20.1%), the existence of psychosocial support (14.7%), the support offered while preparing for potential results (10.0%), and the fact that the information provided resulted in feelings of relief (7.0%). The remaining 12.3% of the individuals reported negative aspects, namely the time lapse between blood collection and the results disclosure (28.8%), the duration of the whole PST protocol (23.3%), the difficulties to access the centre premises (13.7%) and the perception of the psychology consultations as uncomfortable - due to the length of the psychometric evaluation (11.0%), or the negative feelings prompted in the consultation (12.3%) -, and the information provided perceived as complex (10.9%).

The potential endorsement of the PST protocol was recorded for 339 consultands, of which 96.8% would recommend it to relatives and other at-risk persons. The reasons for recommendation were mainly the access to health information provided by the protocol (46.7%), the professional follow-up (12.2%), the relief of uncertainty (11.6%), the implicit benefits of the information (9.3%), the ability to prepare for the future (7.7%), the consideration of reproductive options (6.5%), and the benefits from psychosocial support and counselling prior to results (6.0%). The other 3.2% considered that undertaking PST is a personal decision that depends on the psychological readiness and the experience of each subject.

DISCUSSION

The data presented here reflects the first comprehensive description of the Portuguese experience with a protocol for PST in LONDs, covering 20 years of experience (1996 - 2015). This study adds to a previous body of research conducted by researchers of the CGPP multidisciplinary team.[12,16-22] The results allowed the characterization of the consultands who requested PST at the CGPP facilities as well as some insights on how we could improve our practice.

The profile of the Portuguese consultands at risk for LONDs is similar to that accounted in other international reports.[23-28] For example, motivations for taking a PST and the higher rate of the test uptake in women (56%) are consistent with the findings from Cuba, the United Kingdom and Brazil.[23-28] This may be explained by the role typically ascribed to women as gatekeepers in the management of health-related issues in general and of genetic risks in particular,[30] and also by the fact that women are more

frequently driven by the concern of transmission to offspring.[31] Reasons for uptake are also similar to those given when PST first became available.[2,3,16]

Particularly, individuals at-risk for FAP ATTR Val30Met are the youngest and the largest group requesting PST at our centre. This is largely explained by the earlier age-of-onset of this disease, but also by the more recent therapeutic alternatives available. Although, FAP ATTR Val30Met is globally considered to be a rare disease, it has its historical cluster along the northern coast of Portugal[10,11] with a long-standing national patients association that plays an important role in the advocacy and information provision among affected families.[32] Furthermore, it may be expected that the same higher adherence to PST will occur for other LONDs after the introduction of new therapeutic options such as the use of antisense oligonucleotides-based strategies that might have a dramatic effect on the treatment of many neurological conditions in the near future.[33]

Additionally, the predominance of non-carriers in the studied sample is in accordance to what has been previously described in other PST programs.[23-28] In fact, several persons at risk wait until they are older to come forward for PST, when their actual genetic risk is lower than the a priori risk of 50%. Also, some consultands come at a 25% risk, when their potentially transmitting parent died from other causes.

This retrospective look at the protocol we have conducted for PST showed a lower rate of withdrawal before the disclosure of results compared to other reports.[23-28,34] On the other hand, about 45% of the consultands have dropped the protocol right after knowing the test results. At that time, the proportion of drop-out cases was one carrier per three non-carriers, while at one-year follow-up those who concluded the protocol were mainly presymptomatic carriers, perhaps due to the medical consultation for neurological assessment/check-up that is appointed at the term of the protocol. This suggests that the consultands value knowing their genetics status but after that, they may not need any further clinical contacts. Several reasons might explain this, such as: the lack of support from employers, fear of breach of privacy and discrimination at work, stigmatisation issues,[35] or transportation costs and geographical distance from the centre, the time lapse between consultations and loss of work hours. Another important fact is that after finishing the protocol many presymptomatic carriers often begin to be followed at neurology departments outside the CGPP clinical facilities.

It is an interesting fact that after the communication of results withdrawals were considerably lower among carriers (26.5%) since they may experience a greater need for psychosocial support and have the greatest potential benefits. Other reports have indicated this drop-out rate to be as low as 5% over two years of follow-up, but up to 69% over 10 years;[34] and contrarily to our results, those withdrawals were higher among carriers, described as having higher scores for hopelessness, intrusion and avoidance.[36] Again, this difference may be explained in our sample by the fact that the majority of the consultands came from FAP ATTR Val30Met families, where there are therapeutic interventions available, as opposed to most other LONDs.

We would like to comment particularly on the relevant role played by family physicians in Primary Care Genetics. The results of this study showed how consultands that had learned about PST through healthcare professionals tended to adhere more to PST consultations. This indicates that providing information in advance to perform genetic tests seems to influence the decision-making process. The tendency may also be justified by the fact that these are well-established referral procedures followed by family physicians, which has contributed to a better management of the disease and to health education within affected communities. The latter aspect is even more relevant considering the prevalence of limited health literacy in the Portuguese population.[37]

The potential for collaboration between primary healthcare professionals and specialists from Genetics departments has already been described.[38] The current model does not meet the needs of the current situation. Both specialties should develop better coordination to face the Genetics challenges and the possibilities of preventing and managing many of the conditions in which genetics play a key role.

Limitations of the study and implications for practice

Because our PST protocol was carried out by different professionals along the years, models of practice and procedures of documentation of consultands-reported experience were neither standardised nor uniformly recorded. Therefore, perhaps the major limitation of this report lies in the discrepancies found in the registration of the information in the clinical files. This is a reminder of the relevance of keeping digital records consistent and updated along the protocol. The current data does not allow us to assess a reliable uptake of our PST protocol. As there are more centres conducting PST now, even in our region, it is not possible to estimate the number of the at-risk population for those genetic conditions in our country. Additionally, there are regional differences in terms of prevalence of the conditions, while the area covered by our centre is not clearly defined and there are referrals frequently coming from other regions.

Moreover, the specific clinical features of the different LONDs influenced the results, particularly in view of the high predominance of consultands for FAP ATTR Val30Met. Thus, the statistical data must be interpreted cautiously.

CONCLUSION

We believe the relevance of this retrospective study lies in being the first comprehensive view of PST in Portugal. No other studies have been reported so far. We also consider that two major contributions were made: the call for the national harmonization of practice and discussion of the genetic counselling guidelines for PST that are followed in other Portuguese centres; and the demonstration

of the major role that family physicians can have in genetics healthcare.

In particular, national genetic services would benefit from evidence based research on the practice of genetic counselling. Namely, 1) how professional skills influence the process and potential outcomes of genetic counselling; 2) the efficacy of different genetic counselling interventions and models; and 3) how recently developed tools for quality assessment can be further used at a national level for the improvement of practice.

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PROTECTION OF HUMAN AND ANIMAL SUBJECTS

The authors declare that the research procedures were performed according to the regulations of the institution's ethics committee and the Code of Ethics of the World Medical Association (Declaration of Helsinki).

CONFIDENTIALITY OF DATA

The authors declare that they have followed the protocols of their work centre regarding the publication of data from patients.

CONFLICT OF INTEREST

The authors declare no conflict of interests.

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