Universidade de Aveiro Secção Autónoma de Ciências da Saúde
2015

FILIPA ALEXANDRA ANTUNES VENCES DE MATOS PEREIRA

ASSOCIAÇÕES DE DOENTES: DAR VISIBILIDADE ÀS DOENÇAS CRÓNICAS

PATIENT ASSOCIATIONS: RAISING AWARENESS ON CHRONIC DISEASES

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Dissertação apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Biomedicina Farmacêutica, realizada sob a orientação científica do Professor Doutor Bruno Gago, Professor Assistente Convidado da Secção Autónoma de Ciências da Saúde da Universidade de Aveiro.

I dedicate this work to my husband, José, for all the support and encouragement that made this project possible.

I also dedicate this work to my daughter, Alice, for inspiring me during this journey and in my life.

Finally, I dedicate this work to my parents, Graça and João, for their love and support throughout my life.

o júri

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- Dra. Marta Campos, Vogal da Direção Nacional da APIR – Associação Portuguesa de Insuficientes Renais;

- Dra. Filipa Júlio, Vice-Presidente da APDH – Associação Portuguesa de Doentes de Huntington;

- Dra. Ana Margarida Cavaleiro, Diretora do Departamento de Formação e Projetos da Alzheimer Portugal – Associação Portuguesa de Familiares e Amigos dos Doentes de Alzheimer;

- Dra. Alexandra Martins Costa, Técnica Superior de Educação da APDP – Associação Protetora dos Diabéticos de Portugal;

- Dra. Susana Fonseca, Presidente da Direção da MulherEndo – Associação Portuguesa de Apoio a Mulheres com Endometriose.

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palavras-chave

Associações de doentes, doenças crónicas, capacitação de doentes, prestadores de cuidados de saúde, insuficiência renal crónica, doença de Huntington, doença de Alzheimer, diabetes mellitus, endometriose, Portugal.

resumo

As associações de doentes assumem um papel fundamental na representação dos direitos dos pacientes, na divulgação de informação acerca das doenças, no acesso aos recursos disponíveis, no relacionamento com os vários intermediários e nos desafios a enfrentar.
Estas associações prestam não só um grande apoio aos doentes, como também aos seus familiares e amigos, que são na maior parte das vezes os seus cuidadores diretos.
Atualmente, a capacitação de doentes tem vindo a ser bastante discutida.

Este projeto pretende demonstrar em cinco quadros clínicos distintos, quais as motivações presentes, os objetivos, as atividades realizadas, o envolvimento com outros *stakeholders* e os desafios enfrentados pelas respetivas associações de doentes.

O resultado deste trabalho permitiu concluir que a prevalência significativa de doenças crónicas tem introduzido alterações nos sistemas de saúde e nos planos nacionais de doenças. Em simultâneo, a responsabilidade dos pacientes tem vindo a aumentar, contribuindo para um posicionamento cada vez mais participativo junto dos profissionais de saúde e para uma tomada de decisão mais consciente em relação às terapêuticas disponíveis.
As associações de doentes dão voz a estes pacientes e atuam em áreas críticas, tais como, a área social, emocional, clínica, de investigação, de formação, de educação e de defesa e representatividade de direitos e benefícios.

keywords

Patient associations, patient organizations, chronical diseases, patients empowerment, healthcare providers, chronic kidney disease, Huntington's disease, Alzheimer's disease, diabetes mellitus, endometriosis, Portugal.

abstract

The patient associations assume a significant role in representing the patients' rights, sharing information on the diseases, accessing the available resources, maintaining important interactions with other relevant stakeholders and facing challenges.
These organizations provide an important support not only to the patients, but also to their families and friends, who are most of the times their direct caregivers. Currently, the patient empowerment has been highly discussed.

This project aims to demonstrate in five different clinical disorders what are the motivations, the objectives, the activities, the involvement with other stakeholders and the challenges assumed by the correspondent patient associations.

The result of this project allowed to conclude that the significant prevalence of chronic diseases has been introducing changes into the healthcare systems and national disease programmes. Simultaneously, the patients' ownership has been increasing, contributing to a more participated role near the healthcare professionals and to a more conscious decision regarding the available therapeutics.
Patient associations represent these patients and act in critical areas, such as, social, clinical, research, training, education and advocacy.

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LIST OF ABBREVIATIONS

- ACSS – *Administração Central do Sistema de Saúde* - Central Administration of the Health System;
- AD – Alzheimer's Disease;
- ADI - Alzheimer's Disease International;
- APD – Automated Peritoneal Dialysis;
- APDH – *Associação Portuguesa de Doentes de Huntington* - Huntington's Portuguese Association;
- APDP – *Associação Protetora dos Diabéticos de Portugal* – Protective Association of the Diabetics of Portugal;
- APDR – *Associação Portuguesa de Doentes Renais* – Portuguese Association of Renal Patients;
- APIFARMA – *Associação Portuguesa para a Indústria Farmacêutica* - Portuguese Association for the Pharmaceutical Industry;
- APIR – *Associação Portuguesa de Insuficientes* Renais - Portuguese Association of Patients with Renal Failure;
- APN – *Associação Portuguesa de Doentes Neuromusculares* - Portuguese Association of Neuromuscular Disorders;
- APOE - Apolipoprotein E;
- APP - Amyloid Precursor Protein;
- ASRM – American Society for Reproductive Medicine;
- CAG – Cytosine-Adenine-Guanine;
- CAPD – Continuous Ambulatory Peritoneal Dialysis;
- CEAPIR - The European Kidney Patients' Federation;
- CGPP – *Centro de Genética Preditiva e Preventiva* - Centre for Preventive and Predictive Genetics;
- CHDI - Cure Huntington's Disease Initiative;
- CKD – Chronic Kidney Disease;
- CNAD – *Comissão Nacional de Acompanhamento da Diálise* – National Commission of Dialysis;
- CRF – Chronic Renal Failure;
- CT – Computerized Tomography;
- CVS - Chorionic Villus Sampling;
- DESG - Diabetes Education Study Group;
- DGS – *Direção-Geral de Saúde* – Directorate-General of Health;
- EC – European Commission;
- EHA - European Huntington Association;

- EHDN – European Huntington's Disease Network;
- EKPF – European Kidney Patients' Federation;
- EMA - European Medicines Agency;
- EPF – European Patients Forum;
- EPFIA - European Federation of Pharmaceutical Industries and Associations;
- ESRD - End Stage Renal Disease;
- EUPATI - European Patient's Academy on Therapeutic Innovation;
- FEDRA – *Federação Portuguesa de Doenças Raras* – Portuguese Federation of Rare Diseases;
- GFR – Glomerular Filtration Rate;
- GnRH - Gonadotropin-Releasing Hormone;
- GP – General Practitioner;
- HbA1c - Glycated Haemoglobin;
- HD – Huntington's Disease;
- HSG – Huntington Study Group;
- HTA - Health Technology Assessment;
- HTT – Huntingtin Gene;
- Htt – Huntingtin Protein;
- IBMC – *Instituto de Biologia Molecular e Celular* – Institute of Molecular and Cellular Biology;
- IDF – International Diabetes Federation;
- IHA – International Huntington's Association;
- INR – *Instituto Nacional de Reabilitação* - National Institute for Rehabilitation;
- IPSS – *Instituição Privada de Solidariedade Social* - Private Social Solidarity Institution;
- K/DOQI - Kidney Disease Outcomes Quality Initiative;
- LADA - Latent Autoimmune Diabetes in Adults;
- MODY - Maturity-Onset Diabetes of the Young;
- MRI – Magnetic Resonance Image;
- NHP – National Health Plan;
- NHS – National Health System;
- NKF - National Kidney Foundation;
- OECD – Organisation for Economic Co-operation and Development;
- PET - Positron Emission Tomography;
- PSEN-1 - Presenilin 1 Gene;
- PSEN-2 – Presenilin 2 Gene;
- RRT – Renal Replacement Therapy;

- SNRIPD – *Secretariado Nacional para a Reabilitação e Integração das Pessoas com Deficiência* – National Secretary for Rehabilitation and Integration of People with Disability;
- US – United States;
- WFN – World Federation of Neurology;
- WHO – World Health Organization.

1. INTRODUCTION

The present work consists on a dissertation as part of the Master's Degree in Pharmaceutical Biomedicine, by the University of Aveiro.

This document aims to present the key role that patient associations play, namely in the awareness on chronic diseases, as well as in the support and guidance provided to patients, their families and carers.

In this chapter it will be presented an overview of the state of the art of the role of patient associations and patient empowerment.
The following chapter will describe five different chronic diseases, each one with specific characteristics. The description will include information on the aetiology, symptoms, diagnosis, treatment and prevalence of each condition. Then, it will be presented the Portuguese patient associations that represent these diseases, describing their process of creation and main motivation, their objectives, the developed activities to reach their goals, the involvement with other stakeholders and their main challenges.
The discussion chapter will approach the general guidance provided by these associations as well as a summary of the collected data. It will also focus on the importance of patient education, clinical research and on the involvement from the pharmaceutical industry.
Finally, the last chapter will include a conclusion for this dissertation.

1.1 OBJECTIVES

The main learning objectives of this project are:

- To apply the knowledge acquired during my academic education, particularly during the Master in Pharmaceutical Biomedicine, and during my professional career in the pharmaceutical industry;
- To get a better understanding of what motivates the creation of a patient association;
- To detail some of the activities developed by these associations;
- To describe the challenges that these patient associations encounter in the process of representing the rights of patients and carers;
- To demonstrate the need of involvement from several stakeholders in the community, in order to achieve the goals of these associations;

- To reinforce the importance of patient education, namely in the prevention and early detection of diseases that represent a growing health problem in Portugal and worldwide.

1.2 STATE OF THE ART – PATIENTS' RIGHTS

The patients' rights differ according to each country and are usually related to their cultural and social norms. In fact, it is possible to observe different models for the patient-physician relationship, which typically determine the rights that patients are entitled [1]. Simultaneously, these models also suggest the professional obligations of the physicians toward the patients.

While there are several discussions on how the best patient-physician relationship model should be, there is an increased consensus on patients' fundamental rights, namely in what concerns the right to privacy, confidentiality, consent or refusal of treatment and information on benefits and risks of medical procedures [1].

In 1948, the "Universal Declaration of Human Rights" recognized the inherent dignity and the equal and inalienable rights of all members of the human family [2]. This statement has contributed to the premise of patients' rights.

In 1994, the "European Consultation on the Rights of Patients" [3] took place in Amsterdam, under the coordination of the World Health Organization (WHO) Regional Office for Europe. This event had the participation of several member states. Its main purpose was to define the principles and strategies in promoting the rights of patients, within the context of the healthcare reforms in most of the European countries.
One of the outcomes was to improve communication and advocacy skills for both healthcare professionals and patients, in order to have a proper understanding of the perspective and role of all parties.

Since 1997, Portugal has a patient's charter, designated as *"Carta dos Direitos e Deveres dos Doentes"* [4], which covers the rights and obligations of patients in the National Health System (NHS).
According to this document, the patients have the following rights:

- To be treated with respect for the human dignity;
- To be respected for their cultural, philosophical and religious convictions;

- To receive care suitable to their health status, in the scope of preventive, healing, rehabilitation and terminal care;
- To be provided with continuous care;
- To be informed on the existent health services, their competences and level of care;
- To be informed regarding their health condition;
- To obtain a second opinion regarding their health condition;
- To give or refuse their consent before any medical procedure or participation in research or clinical trial;
- To assure the confidentiality of all the clinical information and identifying elements about their selves;
- To access the data registered in their clinical file;
- To have privacy during all and any medical procedure;
- To present suggestions and complaints, for their selves or for whoever represents them.

The patients' obligations are as follows:

- To take care of their health condition;
- To provide the healthcare professional with all the necessary information;
- To respect the rights of other patients;
- To cooperate with the healthcare professionals;
- To respect the operating rules of the health services;
- To make good use of the health services and avoid unnecessary costs.

The role of patient associations and patient empowerment is currently a highly discussed topic, namely in the "patient-centred care" model.

Additionally, the high prevalence of chronic diseases necessarily lead to a change in the format of the healthcare systems, implying more preventive procedures and long term care and support for the patients and families.

1.2.1 THE ROLE OF PATIENT ASSOCIATIONS

The European Medicines Agency (EMA) defines a patient organization as: "*a not-for profit organization which is patient focused, and whereby patients and/or carers represent a majority of members in governing bodies*" [5]. This definition includes the criteria that patient organizations need to fulfil, in order to participate and be involved in EMA's activities.

The sharing of patient's experiences and testimonies in managing a certain health condition has been historically the main motivation for the creation of patient associations. A common cause, in this case a disease, represents a common goal.

The increased importance of these associations is also related to the actual context in the majority of countries, where the health systems are overwhelmed with demands and requirements associated, for instance, to the growth and aging of population, to the high prevalence of certain diseases and to the implementation of health programs to incentive prevention and early detection [6].

In the United States (US) and Europe, there has been recently a significant increase in the number of associations. It is also becoming evident that patient associations that serve as umbrella organizations, integrating counter-parts of several countries, play a major role in creating a common platform of best practices, experiences and negotiations [7].

Some of the most important objectives of patient associations are to:

- Improve the quality of life of patients living with a chronic disease and their families;
- Act as a support group, providing guidance to the patients, families and carers;
- Raise awareness on a disorder, disseminating near the community information on the disease, including prevention, causes, diagnosis and treatment;
- Act as a patient advocate near the official entities, namely in what concerns rights, benefits, policy review and implementation of health plans;
- Present the real needs and concerns of these patients to the healthcare professionals;
- Incentive the research and investigation of the chronic diseases.

In order to elevate their voice, patient associations create a close relationship with several stakeholders, such as healthcare professionals, pharmaceutical industry, other patient organizations, policy makers and official entities.

1.2.2 PATIENT EMPOWERMENT

Empowerment is defined by the WHO as: *"a process through which people gain greater control over decisions and actions affecting their health"* [8]. This should be seen as both an individual and a community process.

In fact, patient empowerment encourages an actively participation of patients and carers in the management and decisions on their diseases. This implies that patient and carers are well educated about all aspects of their condition.

Patient empowerment has been associated to the "patient-centred care" model, where the healthcare system is defined to meet the needs and decisions of the patient and where the latter assumes a more active role, as presented in Figure 1.

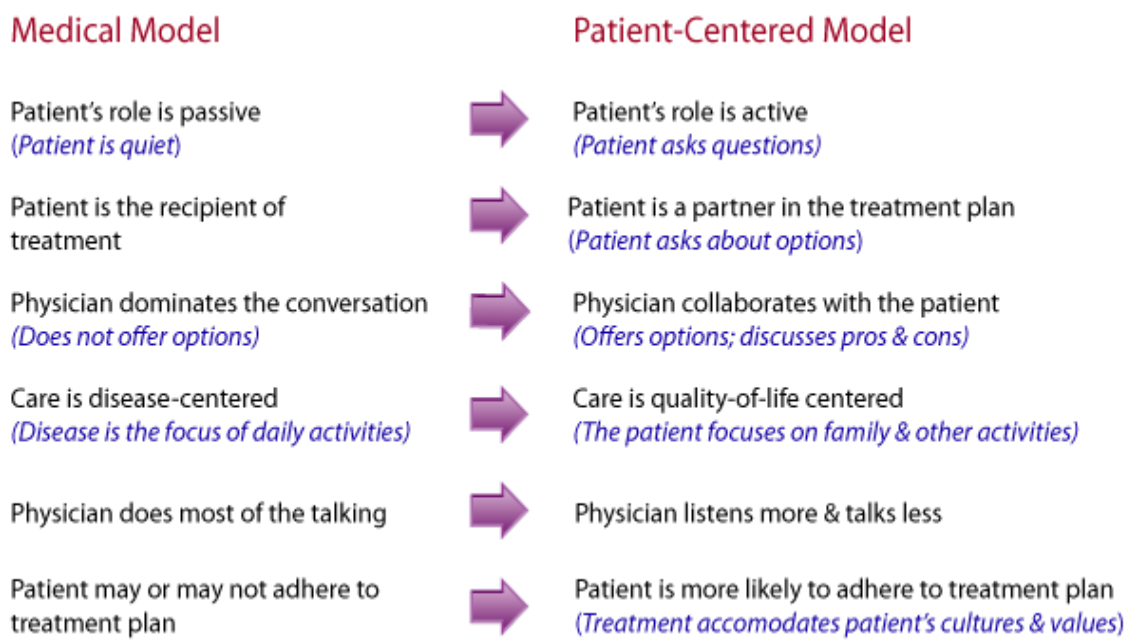

Figure 1 – Traditional medical model *versus* patient-centred model [9].

This has been controversial since, in many countries, the healthcare professionals are educated to assume certain responsibilities and expectations, which ultimately define their professional identity.

The "patient-centred care" model implies that:

- Healthcare professionals and patients change their perspective, focusing on dialogue and co-production;
- Health systems and processes need to be re-design in order to facilitate the integration and perception of patients;
- Healthcare professionals must focus on an open dialogue;

- The clinical information transmitted to the patient should be easily perceived and comprehended;
- Patients should have a self-awareness about their condition in order to take informed decisions about the treatment options;
- Patients should express needs, concerns and expectations toward a treatment programme.

An increased involvement of patient in the healthcare contributes to an overall improvement of healthcare organizations and it is usually associated to better outcomes, namely due to patients' education.

Chronic diseases are the biggest cause of death and disability worldwide, including cardiovascular diseases, cancer, diabetes, obesity and chronic respiratory diseases [1].
The healthcare services and systems have been gradually shifting from a response to acute illnesses to the care and treatment of these chronic diseases.
This change has also an impact in the role of patients, namely in their responsibilities.
This needs to be seen as a process of cooperation, where the healthcare professionals and patients work together on the management and treatment of the disease, involving also the families, direct carers and even the support groups.

In one hand, the patients need to be educated, to be able to take informed decisions. On the other hand, the healthcare professionals need to communicate effectively and listen to the patients [10]. This implies that patients are at the same level as any other member of the healthcare team (Figure 2).

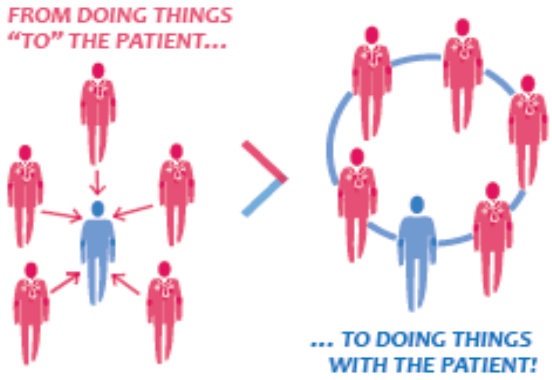

Figure 2 – Empowered patients as part of the healthcare team [11].

In May 2015, the European Patients Forum (EPF), an important umbrella organization that works with patient groups in public health and health advocacy across Europe, launched a campaign on patient empowerment [11]. This campaign intends to promote the patient perspective among policy makers and health stakeholders.

This campaign refers to five "E" of empowerment for sustainable health systems: education, expertise, equality, experience and engagement, as presented in Figure 3.

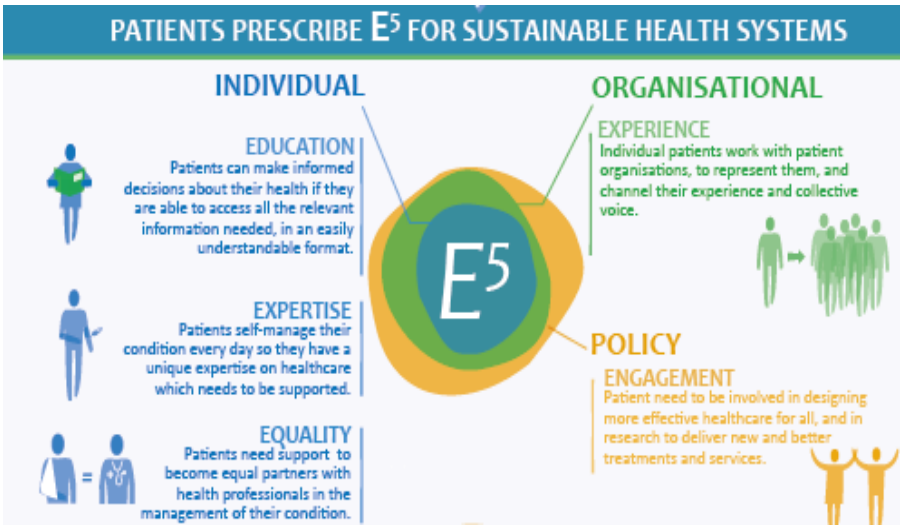

Figure 3 – Patients empowerment in sustainable health systems [11].

2. METHOD

For this project a total of fourteen patient associations, related to different clinical conditions, were contacted with the purpose of conducting an interview.
Six entities agreed to participate in this project. From these, five associations were selected, in order to have a group of diseases with different particularities that lead to different challenges. The association that was not included in this project was APN, the Portuguese Association of Neuromuscular Disorders, due to time constraints. One of the selected patient organizations represents a rare inherited neurodegenerative disease, therefore this project still meets its intended objectives.

The selected patient associations included in this project are the following:

- **APIR – *Associação Portuguesa de Insuficientes Renais***
  Portuguese Association of Patients with Renal Failure:

  Collaboration of: Dr. João Cabete, President of the Association and Dra. Marta Campos, Member of the Association's Direction.
  Disease: Chronic kidney disease.
  Particularity: Considered a silent and highly prevalent disease.

- **APDH – *Associação Portuguesa de Doentes de Huntington***
  Huntington's Portuguese Association:

  Collaboration of: Dra. Filipa Júlio, Vice-President of APHD.
  Disease: Huntington's disease.
  Particularity: Rare disease.

- **Alzheimer Portugal – *Associação Portuguesa de Familiares e Amigos dos Doentes de Alzheimer***
  Portuguese Association of Family and Friends of Patients with Alzheimer:

  Collaboration of: Dra. Ana Margarida Cavaleiro, Responsible for the Division of Training and Projects of Alzheimer Portugal.
  Disease: Alzheimer's disease and other dementia related illnesses.
  Particularity: High support to families and carers.

- **APDP - *Associação Protetora dos Diabéticos de Portugal***
  Protective Association of the Diabetics of Portugal:

  Collaboration of: Dra. Alexandra Costa, Member of the General Assembly of APDP.
  Disease: Diabetes mellitus.
  Particularity: Highly prevalent disease.

- **MulherEndo – *Associação Portuguesa de Apoio a Mulheres com Endometriose***
  Portuguese Association of Support of Women with Endometriosis:

  Collaboration of: Dra. Susana Fonseca, President of the Direction of MulherEndo.
  Disease: Endometriosis.
  Particularity: Underdiagnosed disease.

The questionnaire that guided the interviews consisted in a group of questions that were not validated, intended to collect an opinion from the associations, as well as qualitative data. The set of questions is as follows:

<u>The Patient Association</u>:

- When was the association created?
- What was the main motivation for its creation?
- Who was initially involved in the project?
- What are the association's main objectives?
- What is its actual composition?
- Currently, how many members does the association have?
- Since its creation, how has the number of members evolved?
- How is the association divulged?
- How is the association funded?
- What are the activities implemented by the association?
- Which protocols and partnerships does the association present?

<u>Disease:</u>

- In what consists the condition?
- What is its prevalence in Portugal?
- What is its prevalence in Europe and worldwide?

Detect, treat and control the disease:

- How is performed the diagnosis?
- What are the current available treatments?
- What type of support should be provided to patients?
- What type of involvement has the association in this support?
- Is there any perspective regarding new treatments?
- Does the association have access to information on recent clinical trials, namely in what concerns new therapeutics?

Differentiated Physicians:

- In the last years, how has evolved the number of specialists in the disease?
- Does the association refer or direct the patients to these specialists?

Involvement with other Stakeholders:

- Is there a close relation with other national and international associations related to the disease? If yes, what type of information is exchanged?
- Is there a close relation with the professional healthcare providers, namely with the specialists in the disease?
- Is there a close relation with the pharmaceutical industry, namely in what concerns new available treatments? Is there any sponsorship and support from these entities?
- Is there a close relation with the official public health entities, such as Directorate-General of Health (DGS) or the NHS?

Patient Empowerment:

- In what extend does the association contribute to its patients' empowerment?

Specific question addressed to APDH:

- The Huntington's disease is a rare condition. Based on this, what additional challenges does the association face?

Specific questions addressed to MulherEndo:

- What is the correlation between endometriosis and infertility?
- What type of support does the association provide to women with endometriosis and diagnosed infertility?

- Is there any protocol established between the association and healthcare providers of medical assisted reproduction?
- Is there any available information regarding success rates of pregnancy in women with endometriosis?

3. FIVE CHRONIC DISEASES – FIVE PATIENT ASSOCIATIONS

3.1 CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is a long-term condition characterized by a gradual loss of the kidney's function. CKD may also be referred as chronic renal failure (CRF).
The impaired renal function leads to an accumulation of fluids, waste and toxic substances in the bloodstream. Generally, CKD is detected and diagnosed in an advanced stage.

This condition represents a major health problem worldwide, due to its increasing incidence and high prevalence [12]. The health care costs associated to its treatment are also significantly high.

CKD outcomes include kidney failure, complications related to the decreased kidney function and cardiovascular disease. The early detection and treatment assume a considerable relevance in the prevention and delay of these outcomes [12].

3.1.1 AETIOLOGY

CKD may present several causes, namely:

- Diabetic nephropathies;
- Vascular nephropathies;
- Inherited nephropathies, namely polycystic kidney disease;
- Glomerulonephritis, that leads to the inflammation and damage of the glomerulus;
- Congenital. One example is the occurrence of a narrowing that prevents the normal outflow of urine, causing urine to flow back up to the kidney;
- Diseases that affect the body's immune system, such as lupus.
- Obstructions in the kidneys derived from kidney stones, tumours or an enlarged prostate gland in men.
- Repeated urinary tract infections [13].

The main causes of CKD in Portugal for incident and prevalent patients, reported by the Portuguese Society of Nephrology for 2014, are presented in Table 1:

Table 1 – Aetiology of CKD in Portugal, for incident and prevalent patients in 2014 [14].

	2014	
	Incident patients	**Prevalent patients**
Diabetes	32.2%	27.8%
Indetermined	17.3%	19.8%
Hypertension	14.7%	14.9%
Glomerulonephritis	10.8%	12.4%
Autosomal dominant polycystic disease	4.3%	6.1%
Other	20.6%	19.1%

3.1.2 SYMPTOMS AND SIGNS

In an early stage of CKD, patients are frequently asymptomatic [13]. Usually, the clinical manifestations appear in more advanced stages.

In mild to moderate renal insufficiency, the main symptoms that are observed are the following [15]:

- Nocturia, related to the failure to concentrate the urine;
- Lassitude;
- Fatigue;
- Anorexia;
- Decreased mental acuity.

In a more severe stage of renal failure, the symptoms may include:

- Neuromuscular conditions, like hyperreflexia, muscle cramps and motor neuropathies;
- Anorexia;
- Nausea;
- Vomiting;
- Weight loss;
- Stomatitis and unpleasant taste in the mouth.

More occasionally, it can be observed:

- Uremic frost;
- Pruritus;
- Undernutrition, due to chronic uraemia;

- Change in the skin's appearance.

In an advanced CKD, patients are usually affected with:
- Gastro-intestinal ulceration and bleeding;
- Hypertension;
- Pericarditis;
- Heart failure caused by hypertension or coronary artery disease;
- Edema, caused by the renal retention of sodium and water.

3.1.3 DIAGNOSIS

The diagnosis is usually based on laboratory analyses. An ultrasonography or even a renal biopsy may be performed [13].

It is important to determine in which CKD stage is the patient.
The glomerular filtration rate (GFR) of creatinine is the most accurate test to measure the overall kidney function in health and disease.
The normal level of GFR differs considering the age, gender and body size of the individual. For instance, normal GFR in young adults corresponds nearly to 120 to 130 mL/min per 1.73 m^2. It is expected that this level decreases with age [13].
A GFR level below 60 mL/min per 1.73 m^2 represents loss of half or more of the adult level of normal kidney function, contributing to the prevalence of CKD complications [13].

The classification system for the CKD stages was proposed in 2002, by the Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) **[13]**, an US based association. This classification is as follows:

- Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m^2). In this stage, the kidney function is normal, but there are urine findings or structural abnormalities or genetic trait point to kidney disease;

- Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m^2). At this point, the kidney function is mildly reduced, and other findings point to kidney disease;

- Stage 3: Moderate reduction in GFR (30-59 mL/min/1.73 m^2). The kidney function is moderately reduced;

- Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m^2). The kidney function is severely reduced;

- Stage 5: Kidney failure (GFR < 15 mL/min/1.73 m^2 or dialysis). This last stage is referred to as end stage renal disease (ESRD). At this point, a renal function replacement therapy, such as dialysis or transplantation, is necessary to be in place in order to survive.

3.1.4 TREATMENT

In terms of treatment, the desirable would be having an early diagnosis, a treatment of the underlying cause and the implementation of secondary preventive measures. In fact, this would slow, or even halt, the progression of the disease [13].

The medical care of patients with CKD should focus on:

- Slowing or halting the progression of CKD;
- Treating the pathological manifestations of CKD;
- Planning the possible long-term renal replacement therapy.

The therapeutic options for stage 5 CKD are:

- Haemodialysis: In this case, the patient's blood is filtered through a dialyzer, returning after the procedure to the patient. The blood is pumped along one side of a semipermeable membrane, while a specific solution referred as dialysate is pumped in a different compartment, in an opposite direction. The membrane allows exchanges between the blood and the dialysate, leading to a filtration of waste and toxic components.

  A haemodialysis session takes approximately 4 to 5 hours, and it is performed usually 3 times a week. It might take place at a hospital, private clinic or even at home. There are several options and techniques.

  Haemodialysis is usually done through a surgically created arteriovenous fistula.

- Peritoneal dialysis: This type of dialysis uses the peritoneum as a natural permeable membrane. In this case, the dialysate is instilled through a catheter into the peritoneal cavity. The dialysate is left in the cavity during a period of time to dwell and it is drained after.

Peritoneal dialysis in comparison to haemodialysis allows the patient to have a greater flexibility, once it requires only a peritoneal dialysis catheter, instead of a vascular access. Additionally, peritoneal dialysis can be done at home.

It is important to note that this technique requires a greater patient involvement than an "in-centre" dialysis, due to the assurance of sterile procedures.

There are two kinds of peritoneal dialysis:

- Continuous Ambulatory Peritoneal Dialysis (CAPD) – This technique does not require an equipment and might be performed during the day-to-day activities. This process usually is done 3, 4 or 5 times in a 24-hour period. The exchange takes approximately 30 to 40 minutes.

- Automated Peritoneal Dialysis (APD) – This procedure requires an equipment, named cycler, which delivers and drains the cleansing fluid. Usually this treatment is done overnight.

- Renal transplantation: The kidney transplant is the best treatment whenever possible. The decision to proceed with a kidney transplant implies that the patient is fully aware that:
  - Might need to wait a long time for a compatible organ;
  - Needs to attend a significant number of consultations and perform several exams;
  - Needs to take medication for the rest of his life;
  - Needs to constantly follow medical instructions.

  If a living kidney donor is available, better long-term outcomes occur when a patient receives the transplanted kidney early. Patients who are transplant candidates but have no living donor should receive a cadaveric kidney transplant as early as possible. For both options, a *pre emptive* procedure is preferable.

- Conservative (non-dialytic) management of ESRD: The conservative management is not comparable to the other techniques. In fact, it should be applied in specific cases where the use of renal replacement therapies will not improve the quality of life of the patient, or the disease's prognosis. The selection of this method implies a benefit-risk analysis.

  Usually the conservative management of ESRD is addressed to the very elderly and patients with comorbid diseases.

It includes careful attention to fluid balance, treatment of anaemia, correction of acidosis, hyperkalaemia, management of blood pressure and calcium/phosphorus metabolism [16]. Specific dietary modifications may be helpful in prolonging life and decreasing the CKD symptoms. Finally, individualized symptom management and palliative care are crucial to maximize the quality of life of the patient.

3.1.5 PREVALENCE

CKD is considered a "silent" epidemic, once it is usually diagnosed in an advanced stage. The awareness, however, remains low in many communities and among many physicians. CKD's prevalence worldwide is estimated to be 8 to 16% [17].

According to a recent Kidney Health for Life report [18], which includes the analysis of nineteen countries, the incidence of CKD in Portugal in 2011 was over 6.1%.
The Portuguese Society of Nephrology estimates currently that CKD may affect 800.000 individuals [19] in Portugal.
Portugal also presents one of the highest ESRD prevalence in Europe [20], corresponding to 1.794 cases per million population, in 2014 [21].
As of 2011, Portugal presented also a highest prevalence of diabetes as a risk factor of ESRD, comparatively to the Organisation for Economic Co-operation and Development (OECD) average (12.7% vs. 6.5%, respectively) [18].

The Portuguese Society of Nephrology presents recent data, from 2014, regarding the RRT in Portugal [21]:

- Diabetes is the main cause of ESRD in patients starting RRT;
- The total number of CKD patients in RRT corresponds to 18.703. The majority of these patients belong to the age group above 65 years old;
- Haemodialysis is higher relatively to peritoneal dialysis, in prevalence and incidence, as presented in Table 2:

Table 2 – Prevalence and incidence of RRT in 2014 [21].

2014

	Haemodialysis	Peritoneal dialysis	Transplantation
Prevalence - n. of patients	11,350	735	6,618
Incidence - pmp	214.15	20.71	2.3

3.1.6 APIR – THE PATIENT ASSOCIATION

APIR, the Portuguese Association for Patients with Renal Failure [22], was created in November of 1977 and officially established in October of 1978. Initially, the Association was designated as APDR – Portuguese Association of Renal Patients.

The initiative was assumed by a group of Portuguese patients that were performing haemodialysis in Barcelona, once there were no clinical conditions to perform this treatment in Portugal. This group of patients had the support from other CKD patients, relatives, physicians, nurses and other healthcare providers.

APIR is currently a Private Social Solidarity Institution (IPSS). It has members and representatives in all the country districts. The association presents also representatives in most of dialysis centres and transplant units.

APIR is a non-profit association that is funded by the contribution of its members, by sponsorships from the pharmaceutical industry and healthcare providers, and by specific funds associated to the degree of incapacity of its members.

The majority of the work developed by APIR is performed by volunteers.

According to APIR, the association has approximately 3.500 members. The number of members had its higher increase in the 90's, due to the establishment of benefits and rights of CKD patients.

The association assumes its role before the public official entities, such as:

- The DGS;
- The Inspectorate-General of Health Activities (IGAS);
- The Central Administration of the Health System (ACSS);
- The National Institute for Rehabilitation (INR);
- Other regulatory entities.

3.1.6.1 AIMS AND OBJECTIVES

The main objectives of APIR are as follows:

- Provide support and guidance to the CKD patients and their carers;
- Inform these patients on their rights, interests and benefits;

- Represent the patients near the official entities, healthcare providers and common interest services;
- Promote the right to work, through the professional and social reintegration and rehabilitation;
- Improve the understanding, prevention, detection and management of the renal disease, raising awareness;
- Promote the union and gathering of the CKD patients;
- Defend and assure the access to the best quality health services of CKD patients.

3.1.6.2 ACTIVITIES

APIR's main activities include:

- Participation in national and international conferences, events and forums;
- Meetings with the official public entities;
- Sharing of best practices with counter-part associations;
- Visits to dialysis centres and transplant units;
- Meetings with the association's members. APIR also promotes encounters of members, according to age groups;
- Screening activities;
- Publishing a quarterly magazine, named *"Nefrâmea"*. This magazine summarizes all the actions and plans of the association for each quarter;
- Celebration of specific dates, such as the Worldwide Kidney's Day, the European Day of Donation and Transplantation, the association's anniversary;
- Culinary workshops;
- Holiday camps for young associates;
- Activities addressed to children with CKD;
- Outdoors activities;
- Contacts with other associations, namely related with the pathological causes of the renal insufficiency, in order to promote synergies.

This patient organization has been very active in the vindication of benefits and rights of CKD patients. There are several significant achievements, namely:

- Since 2011, it is mandatory that the CKD patients are duly informed on the available RRT. This is stated and described in detail in the norm 017/2011, from DGS [23]. It is

mandatory to perform a consultation fully dedicated to the available therapies, allowing the patient to take an informed decision.

This consultation is mandatory, even if the patient has initiated an urgent dialysis treatment;

- Some medicines for CKD patients are fully reimbursed by the NHS;
- All the diagnostic exams, routine exams and treatments are fully supported by the NHS;
- Exemption of user fees;
- Concerning the employment, there are specific rights for these patients:
    - Technical and financial incentives granted to companies that recruit and maintain workers with this type incapacity;
    - Reduction in the amount of Social Security contributions related to these workers;
    - Incentive for the CKD patient that creates his own job, through a specific subsidy;
    - Existence of a quota for people with deficiency in the public services that are hiring;
- Existence of benefits in what concerns the acquisition of vehicles and credit loans;
- The majority of dialysis centres belong to the private sector. There is a bundle price determined, which includes dialysis treatments per week, medicines, diagnostic exams and vascular access, to be reimbursed by the NHS;
- Free transportation for the nearest dialysis unit that is accredited by DGS, and in accordance to the referral system.

It is important to refer that the majority of the benefits for the CKD patients are a result of APIR's involvement and effort, for the past 37 years.

3.1.6.3 INVOLVEMENT WITH OTHER STAKEHOLDERS

Other Organizations

APIR is a member of the National Commission of Dialysis (CNAD), which monitors and evaluates the healthcare services provided to the renal patients, namely in what concerns the access and offer of special services, their quality, the safety of the patients, the financing models and results.

It is also a member of CEAPIR, the European Kidney Patients' Federation [24], which defends and promotes the minimum requirements of the healthcare services rendered to the CKD patients in the European countries.

APIR participates actively in national and international forums with counter-part associations, namely *ALCER Federación Nacional* (Spain), *NVN – Nierpatiënten Vereniging Nederland* (the Netherlands) and *OSOD* (Poland). It is frequent to discuss and review legislation and norms, as well as share best practices.

Healthcare Professionals

APIR establishes also a close relation with physicians and healthcare professionals, sharing the existing concerns of CKD patients and renal services.
The association has a permanent medical consultant. It is currently developing a multi-disciplinary commission, in order to give extra support to its members.

Pharmaceutical Industry

This industry sponsors some of the association's activities and provides information on the available therapeutics.

Academia

APIR has a protocol with a University, which comprises services from students that are finishing their degree in Social Assistance.

Directorate-General of Health

The National Health Plan (NHP) covers the non communicable diseases.
A specific strategy for CKD is under preparation.
DGS has a national guideline for referral and management of CKD.
There is no targeted active or passive surveillance system to identify and detect early CKD.

3.1.6.4 MAIN CHALLENGES

One of the most concerning issue is related to the inexistence of specific registries in Portugal, such as pre-dialysis registries, CKD registries that not require RRT, registries for each CKD phase. In fact, this lack of information does not allow to have a traceability of all the CKD patients, and of how the disease is evolving.

The NHS does not present a targeted active or passive surveillance system to identify and detect early CKD stages.

There is also the need to train the general practitioners (GP's) in the early detection of CKD, namely within the high risk population. Additionally, the coordination of care between GP's and specialists needs to be improved, allowing an early detection and response to renal impairment.

Although there is already legislation in force that mandatory requires comprehensive information to the patient, it is still necessary to reinforce it. In fact, the patient needs to be a co-participant in the decision of his/her best suitable treatment.

It is also important to refer that most of CKD patients are elderly, with a low level of education and literacy, which implies a higher effort on the support provided, management and control of the condition.

There is a limited funding from the NHS, with competitive priorities from other diseases (diabetes, cancer and cardiovascular diseases).

The current transportation system of patients in haemodialysis, needs also to be improved, assuring that the schedules of treatments are accomplished.

Overall, the awareness of CKD among healthcare providers, policy makers, patients and general population is still low.

3.2 HUNTINGTON'S DISEASE

Huntington's disease (HD) is an inherited and neurodegenerative disorder that affects movement, cognitive ability and emotional control [25].

HD symptoms are caused by the progressive breakdown of nerve cells in the brain, particularly in the basal ganglia [26]. Usually, symptoms appear gradually in midlife, between the ages of 30 and 50, although the disease may impact young people (Huntington's juvenile form) and the elderly [25].

The disease was named after the Long Island physician George Huntington, in 1872, who first described the illness [25]. In fact, this physician examined the medical history of a family that presented similar symptoms, throughout several generations. He concluded that the symptomatology would be somehow related. Based on this investigation, Huntington presented his first publication, including a detailed and precise definition of the disease, conjointly with the exact description of the autosomal dominant inheritance pattern [27].

The involuntary or abnormal writhing movements belong to the most common symptoms of HD. That is why initially the disease was known as "Huntington's Chorea". In fact, chorea derives from the Greek word for dance – *"chorein"* [28]. Once these are not the only symptoms of the disorder, it was later changed to HD.

3.2.1 AETIOLOGY

In 1993, it was identified the location of the responsible gene for the disease [25]. In fact, HD is caused by an autosomal dominant mutation in a gene called Huntingtin (HTT) on the short arm of chromosome 4. HTT gene provides information for a protein that is referred also as Huntingtin (Htt). The exact function of this protein is still unknown, however it seems to impact the brain nerve cells.

One specific region of the HTT gene contains a DNA segment referred as CAG (cytosine-adenine-guanine) trinucleotide repeat. Individuals with HD present an abnormally high number of CAG trinucleotide repeats, being the inherited mutation that causes HD known as CAG trinucleotide repeat expansion.

Individuals with HD have 36 to more than 120 CAG repeats, while individuals with no gene mutation have normally 10 to 35 CAG repeats. The abnormal CAG repeats seem to disrupt the function of Htt product.

It is important to refer that individuals with 36 to 39 CAG repeats may or may not develop the signs and symptoms of HD, while individuals with 40 or more repeats will most likely develop the disorder [29].

The higher number of CAG repeats leads to an earlier onset of the disease and to a more severe form. Within successive generations, there is the possibility to observe an increased severe phenotype, as well as an earlier onset, phenomenon known as anticipation [30].
An individual with a defective Huntington gene can pass along the defective copy of the gene or the healthy copy, to his descendant. Therefore, there is a fifty percent chance to pass the gene that causes the genetic disorder [31]. HD does not skip generations, so if an individual does not inherits the mutated gene, his descendant(s) will not too.
Nowadays, there is the possibility to perform a genetic test to determine whether or not an individual carries the mutated gene for HD [25].

3.2.2 SYMPTOMS AND SIGNS

The symptoms and signs of HD may vary significantly between individuals, even within the same family. In some cases, involuntary movements are evident in the early stages of the disease. In other cases, emotional and behavioural signs are the first to set in [25].
The most common symptoms and signs of HD are as follows:

- Motor symptoms:

These symptoms consist of changes in coordination, involuntary movements (chorea), fidgeting, restlessness, twitching, muscle spasms, tics, facial grimaces, bradykinesia, rigidity, slow reaction time, general weakness and weight loss [32].
HD affects the ability to walk, speak, swallow and perform other coordinated activities.
Ultimately, the patient loses the capability to take care of himself, becoming dependent on others.

- Emotional and behavioural symptoms:

The main symptoms include depression, irritability, anxiety, apathy, hallucinations, mania, denial, mood swings, disinhibition, repetition and altered sexuality [32].
Some individuals experience depression for a long period, before it is recognised as an early symptom of HD.

- Cognitive and intellectual symptoms:

The cognitive abilities that may be impaired by HD are short-term memory, communication, organization, coping with new situations, awareness and visual spatial capacity [32]. The main cognitive alteration in HD refers to deficits in executive functioning.

According to the progression of symptoms, most patients eventually require professional care through institutionalization.
As mentioned before, symptoms usually appear between the ages of 30 to 50 [25]. These symptoms worsen over a period of 10 to 25 years. Lastly, due to his debilitating status, the patient passes away from other life-threatening medical condition, such as pneumonia, heart failure or other complications.

Around ten percent of HD cases affect children or adolescents. The adult onset of HD is inherited from both parents, while the juvenile form is most likely to be inherited from the male parent [25]. The juvenile HD is commonly designated as Westphal variant [25].
The symptoms associated to this variant are different from the adult onset. In fact, usually there are no involuntary movements or chorea. The initial symptoms include slow, stiff and awkward walking and talking, choking, clumsiness and falls [25]. In terms of cognitive symptoms, the child may start to present a slow response and low performance at school. The juvenile form is usually more rapid in its progression than the adult onset form [25].

3.2.3 DIAGNOSIS

The clinical diagnosis of HD may be performed in individuals that present the typical HD symptoms and have a family history consistent with autosomal dominant inheritance.
Usually, a full neurological and psychological exam, as well as a detailed family history analysis is performed.
Medical imaging, such as magnetic resonance image (MRI) or computerized tomography (CT) are not used alone to diagnose HD. These exams may be performed to identify the existence of an atrophy of the caudate nuclei early on the disease, and often some frontal-predominant cortical atrophy. These exams may also confirm the existence of other medical conditions with similar symptoms.

The diagnosis may be confirmed through genetic testing, that measures the number of CAG repeats. It is important to refer that the genetic testing diagnoses HD at every stage of the disease.
The genetic testing may be performed as follows:

- Pre-implantation testing – The embryos created through the *In Vitro* Fertilization technique may be tested for the presence of the HTT gene.

- Pre-natal testing – The amniocentesis or chorionic villus sampling (CVS) exams allow to confirm the presence of the HTT gene in the gestational period.

- Pre-symptomatic testing – This test is applied in the case of individuals that are at risk of inheriting HD but still don't present any symptom.

- Confirmatory testing – In the presence of symptoms, this test will allow to confirm the presence of HD.

3.2.4 TREATMENT

There is no cure for HD [26]. The treatment consists in controlling the common symptoms of the disease [25].

There are therapeutics to control depression and anxiety. Also the involuntary movements may be relieved. However, significant side effects are often observed.

In this context, the physician should consider a benefit-risk analysis and discuss the situation with the patient, when applicable, and with the family and direct carers, before initiating any treatment.

Also according to the stage of the disease, the effectiveness of the treatment may vary. It is crucial to have a differentiated neurologist, familiar with HD.

Additionally, a multi-disciplinary team should be considered, in order to assist with the several symptoms. This team may include: physiotherapists, occupational therapists, speech therapists, nutritionists and psychologists. The main goal is to improve the quality of life of the patient.

The HD patients, their families and direct carers play a critical role in monitoring and assessing the effectiveness of any care and treatment.

Attending to support groups gives the opportunity to share experiences and knowledge, as well as get the appropriate assistance and guidance.

The research related to HD is being conducted permanently after the discovery of the HTT. Still in 1993, the Huntington Study Group (HSG) [33] was founded. HSG is one of the world leader entities in facilitating high-quality clinical research trials and studies in HD. It has a significant clinical research network of investigators, coordinators, scientists and HD experts.

In 2002, the CHDI (Cure Huntington's Disease Initiative) Foundation [34], a non-profit biomedical research organization, was created with the main purpose to develop therapeutics that will slow the progression of HD, enabling the patients to have a better quality of life. This entity presents a significant portfolio of research projects.
CHDI Foundation is the sponsor of Enroll-HD [35], a worldwide observational study and registry for HD. This study includes participants from North America, Latin America, Europe (including Portugal), Australia, New Zealand and some countries of Asia. It is estimated that this study will comprise more than 20.000 participants.

In 2004, the European Huntington's Disease Network (EHDN) [36] was established by a group of scientists, physicians, healthcare professionals and patient organizations, in order to coordinate work groups with the main objective of finding a cure for HD. EHDN is also a partner of Enroll-HD.

3.2.5 PREVALENCE

HD can affect people from both genders. The disease also reaches people from all ethnic groups, however it is more common among European descendants [36].
The prevalence of HD shows significant geographic differences. According to a systematic review and meta-analysis from *Pringsheim et al*. [37], dated from 2012, the overall prevalence in Europe, North America and Australia corresponds to 5.7 cases per 100.000 individuals. In Asia, the prevalence is lower, pointing out to 0.4 cases per 100.000 individuals.
The Maracaibo region of Venezuela presents the highest concentration of HD. It is important to refer that studies conducted in this region have supported the identification of HTT [38].

There are no official prevalence numbers in Portugal. According to the Portuguese patient organization, it is estimated that the prevalence corresponds to 5-10 cases per 100.000 individuals.

The European Commission (EC) Public Health Programme defines rare diseases as *"life-threatening or chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them* [39]*."* Also according to the EC, a rare disease affects no more than 5 in 10.000 individuals.
In the US, through the Rare Diseases Act of 2002 [40], the rare conditions were defined as diseases that affects not more than 200.000 individuals in the US.

HD is considered a rare disease.

3.2.6 APDH – THE PATIENT ASSOCIATION

The Huntington's Portuguese Association is "APDH – Associação Portuguesa de Doentes de Huntington" [41].
This association was created in 2001, in Algarve, by a group of patients, their families and friends. The main purpose of APDH was, and still is, to provide support and guidance to all the Portuguese families affected by HD.

It is a non-profit organization funded by the contribution of its members and some private donations. Since 2003, APDH was recognized as an IPSS.

APDH currently supports approximately 350 members.
The representatives of the association are all volunteers, mainly relatives and friends of HD patients.
The association has four contact groups, located in different regions of the country. This allows to support associates from different geographic areas.

3.2.6.1 AIMS AND OBJECTIVES

The main objectives of the association are as follows:

- Locate, support and provide guidance to the families with HD;
- Share and provide information on the disease;
- Gather patients, families and involved carers, in order to exchange experiences and mutual support;
- Create and manage regional support centres;
- Encourage research and training of healthcare providers on HD;
- Get a specialized and differentiated support from the public health entities.

3.2.6.2 ACTIVITIES

The association presents a big concern with the psychological and emotional support needed by patients, carers and at risk relatives. Therefore, APDH provides psychological support consultations, for individuals or groups. The topics addressed may include adjustment and coping with HD, family issues and concerns, genetic testing and more. It is important to refer that the HD families and friends may be at increased risk of poor health, depression and isolation.

APDH promotes, organizes and participates in several activities, namely:

- Awareness and clarification sessions on HD and genetic testing;
- Participation in national and international conferences and events;
- Meetings and gatherings with HD families;
- Specific counselling sessions for families and direct carers of HD patients;
- Support groups;
- Art and photography exhibitions, that allow a return of funds in favour of APDH;
- Outdoor activities, such as walking and running to raise HD awareness;
- Promotional materials, such as brochures, flyers and books to supply feasible information to the HD Portuguese community.

3.2.6.3 INVOLVEMENT WITH OTHER STAKEHOLDERS

Other Organizations

APDH maintains a close relation with the International Huntington Association (IHA) [25], European Huntington Association (EHA) [41] and EHDN [36]. These organizations share information on scientific researches and on recent medical data, as well as special recommendations in what concerns, for instance, the genetic testing.
Whenever possible, APDH attends international events and conferences.
The association is a member of the Portuguese Federation of Rare Diseases (FEDRA).

Healthcare Professionals

APDH has a scientific commission, composed by a group of differentiated neurologists in HD, geneticists, social workers, lawyers, nurses and psychologists. This commission is consulted whenever necessary.

Commonly, some physicians refer the association to their patients and families. APDH also provides information on the differentiated neurologists, institutions and other available resources, in accordance to the country region.

The Institute of Molecular and Cellular Biology (IBMC) is an investigational unit from Porto's University. This institute includes the Centre for Preventive and Predictive Genetics (CGPP) that provides molecular genetic testing in patients and in relatives at risk for hereditary conditions, including HD. This entity also provides genetic counselling and other services. APDH informs the HD families on the existence of CGPP.

Pharmaceutical Industry

There were in the past limited sponsorships in promotional activities from the pharmaceutical industry, such as HD family reunions and brochures.

The association makes an effort to be informed on the enrolled clinical trials on HD, as well on the respective results.

Directorate-General of Health

In what concerns HD, there is not a specific NHP.

The WHO and the EC have been raising awareness on the prevention and early diagnose of rare diseases. For this purpose, the EC set an overall strategy to support the Member States in the diagnosis, treatment and caring of patients with these conditions.

In 2008, a "National Plan for Rare Diseases" [43] was approved by the Ministry of Health of Portugal. The objective was to integrate this plan in the consolidated NHP in two phases:

- Implementation phase from 2008 to 2010;
- Consolidation phase for the period of 2010 to 2015.

This plan was mainly focused on the Ministry of Health services. It was recognized that this plan should be replaced by a broader vision and strategy, which would imply the participation of several sectors and ministries.

In 2015, the Portuguese Government, through the Ministries of Health, Education, Science, Solidarity, Employment and Social Security approved an "Integrated Strategy for Rare Diseases" [44], for the period of 2015 to 2020. This strategy is based in the cooperation of several available resources and presents as mains priorities:

- Coordinate the available care services;
- Promote the early diagnose;
- Improve the access to treatment;
- Promote the clinical and epidemiologic information, namely through Orphanet, the European information system on rare diseases;
- Promote the investigation;
- Protect the social inclusion and citizenship.

3.2.6.4 MAIN CHALLENGES

Being HD a rare disease, APDH has a crucial role sharing information on the condition and bringing awareness to the "at risk" population.

As mentioned before, these individuals may perform a genetic test. The decision about whether or not to take the predictive test is a deeply personal one. Some individuals believe the test will provide valid information that will help them manage the future, while others are not comfortable to take it, particularly as there is no effective treatment currently available.
The medical, ethical, legal and social issues associated to the availability of the testing are so relevant, that representatives of the IHA and World Federation of Neurology (WFN) Research Group for HD established specific recommendations [45]. For instance, due to the potential burden of the knowledge that one will develop this chronic disease, it is recommended that children should not be tested until they are at least 18 years of age.
APDH, as the national patient organization, follows the implementation of these recommendations.

Also due to the rareness of the disease, APDH has an extra challenge in finding support in order to manage its work and objectives in an effectively manner.
The activity and programmes from APDH are basically entirely funded by members' contributions and private donations.

During several years, APDH pursued the aim to include HD in the list of diseases covered by the "Special Protection Programme of Disability", from Social Security. Until recently, this programme was based in a list of diseases and conditions.
In June 2015, the Portuguese government announced a change in the format of this programme. Instead of a list of diseases, the coverage will be assessed by the direct impact of the illnesses in the working capabilities of the patients. Since October 2015, the Portuguese HD patients are finally covered by this special protection [46].

Moreover, the recent "Integrated Strategy for Rare Diseases" still didn't produce major practical changes on health and social policies.

3.3 ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is an irreversible, progressive brain disorder that slowly destroys the cognitive capabilities, such as memory, attention, concentration, language, thinking and behavioural skills [46]. It is the most common form of dementia among older adults, affecting up to 70% of all individuals with dementia [47].

AD was first described in 1906, by Dr. Aloysius Alzheimer, a German psychiatrist and neuroanatomist [48].

Dr. Alzheimer detailed the long-term study of a middle-aged woman, Auguste Deter, whom he had observed and investigated at the Frankfurt Psychiatric Hospital, since November 1901. Dr. Alzheimer was particularly interested in the symptomatology, progression and course of the illness of this patient, having documented very precisely the development of her disease from the beginning. Her symptoms included memory loss, language problems, and unpredictable behaviour [48].

After her death in 1906, Dr. Alzheimer was able to examine her brain, morphologically and histologically. He observed histological alterations, later known as amyloid plaques and neurofibrillary tangles [48].

For the next 60 years, AD was considered a rare condition that affected individuals under the age of 65, being observed as a rare form of presenile dementia [49].

In the 70's, Dr. Robert Katzman, an American neurologist, researcher and medical activist, and Dr. Robert Terry, an American neuropathologist, concluded that the majority of the cases termed as senile dementia corresponded in fact to AD, and therefore a disease and not a product of aging. Their work contributed to face AD as a major public health issue [49].

3.3.1 AETIOLOGY

AD may be classified as either:

- Sporadic – This is the most common form of Alzheimer's and does not exhibit autosomal dominant inheritance. It may affect adults at any age, although usually occurs after the age of 65 years old.

  The causes probably include a combination of genetic, environmental, and lifestyle factors. The importance of any one of these factors in increasing or decreasing the risk of developing AD may vary according to the each individual.

There is a complex pattern of inheritance, in the sense that having a relative with sporadic Alzheimer's increases the chances of developing the disease, but not in a predictable form [50].

The gene with the greatest influence on the risk of developing late onset AD is named Apolipoprotein E (APOE). This gene is located in chromosome 19 and is presented in three forms: APOE ε2, APOE ε3 and APOE ε4 [50].

Considering that all individuals have two copies of APOE genes, being the same or different from each other, it is possible to have six combinations (ε2/ ε2, ε2/ ε3, ε2/ ε4, ε3/ ε/3, ε3/ ε4 and ε4/ ε4). The risk of AD seems to increase in individuals with two ε4 alleles and decrease in those who have the ε2 allele.

Until recently, APOE was the only gene to be consistently linked to the risk of AD late onset. Recent scientific developments have been relating new genes to an increased risk of developing this AD most common form.

- Familial – It is a rare genetic condition, caused by a mutation in one of three genes: the amyloid precursor protein (APP) gene, presenilin 1 gene (PSEN-1) or presenilin 2 gene (PSEN-2). This form may affect several generations and presents an early onset. In fact, individuals may develop AD in their 30's and 40's.

  According to the Alzheimer's Society in the UK, the prevalence of the defective versions of these genes is the following [50]:

  - More than eighty known families worldwide have a mutation in the APP gene on chromosome 21, which affects production of the protein amyloid.
  - Approximately four hundred known families worldwide carry a mutation in the PSEN-1 gene, on chromosome 14. In this case, the first symptoms are onset as early as 30 years of age.
  - Only a few dozen known families have a mutation in PSEN-2, on chromosome 1. In this case, the symptoms start slightly later than for PSEN-1.

  An individual with a defective gene can pass along the defective copy of the gene or the healthy copy, to his descendant. Therefore, there is a fifty percent chance to pass the gene that causes the genetic disorder.

  If an individual does not inherits the mutated gene, his descendant(s) will not too.

3.3.2 SYMPTOMS AND SIGNS

Alzheimer's disease is a progressive condition, therefore the symptoms and signs develop gradually and become more severe over the course of several years.
Over time, abnormal deposits of proteins form amyloid plaques and neurofibrillary tangles throughout the brain. The neurons stop functioning correctly and lose connections with other neurons. Ultimately they die.
The symptoms may vary depending on the individuals and affected brain area.

Usually, in the initial phase of AD the symptoms may be very subtle. Some of the most common are as follows [47]:

- Persistent and frequent memory losses, especially associated to recent events;
- Forgetting well-known people or places;
- Difficulty in associating the right words to objects;
- Taking longer to do routine tasks;
- Vagueness during conversation;
- Apparent loss of enthusiasm for previously enjoyed activities;
- Personality changes, appearing to no longer care about those around them;
- Inability to process questions and instructions;
- Deterioration of social skills;
- Emotional unpredictability.

It is important to refer that the capabilities of the individual with AD may fluctuate in different days, and even in the same day. Stress and fatigue contribute to a worsening of these symptoms.

3.3.3 DIAGNOSIS

Currently, there is not a specific test to diagnose AD. In order to identify the disease, the patient needs to attend a thorough clinical evaluation.
The clinical diagnosis may include:

- Detailed medical history;
- Complete physical and neurological examination;
- Test of intellectual function;
- Psychiatric assessment;
- Neuropsychological tests;

- Blood and urine laboratory tests;
- Lumbar puncture for cerebral spinal fluid tests;
- Medical imaging, including MRI and positron emission tomography (PET).

These exams will allow the elimination of other possible causes, which present similar symptoms. It is possible to reach a diagnosis with 80 to 90% of accuracy. The final diagnosis can only be obtained through the examination of the brain tissue.

As soon as the AD is diagnosed, the patients and direct carers should be informed on the therapeutics and specific assistance. It is important that all the options are carefully discussed. This is the crucial moment when patients and families should get support and assistance.

3.3.4 TREATMENT

AD is a chronic disease that has no cure. The available treatments are addressed to improve some of the symptoms and slow the progression of the disease in some individuals:

- Therapeutics that may provide temporary improvement in the cognitive functioning, such as anti-cholinergeric drugs and N-methyl-D-aspartate-receptor antagonist, with mild to moderate AD;
- Therapeutics that may control secondary symptoms, such as depression and anxiety;
- Psychological treatments that may improve cognitive capabilities, such as memory, problem-solving skills and language. This is known as cognitive stimulation;
- Occupational therapy to improve the ability to perform the routine tasks;
- Relaxation therapies that help to reduce the depression, anxiety and agitation;
- Support groups and counselling for patients, relatives and carers.

In a more advanced stage, AD will lead to a complete dependence and ultimately death, caused by another condition. The average survival from the moment of diagnosis is of seven to ten years.

3.3.5 PREVALENCE

Alzheimer's Disease International (ADI) estimates that in 2015 there are 46.8 million of individuals worldwide, living with dementia [51]. This estimate is based on a systematic review of 273 studies and correspondent meta-analysis. According to the same study, the number

of cases will practically double in 20 years. The increase will be mostly observed in the developing countries.

Alzheimer Europe estimates that in Portugal, in 2012, there were approximately 182.500 individuals with dementia [52].

According to a study performed in 2013, the estimated number of Portuguese individuals with dementia, over 60 years old, was 160.287. This corresponds to 5.91% of the population-stratum. Considering that AD represents 50 to 70 % of all dementia cases, the estimated AD patients correspond to 80.144 to 112.201 [53].

3.3.6 ALZHEIMER PORTUGAL – THE PATIENT ASSOCIATION

Alzheimer Portugal, the Portuguese Association of Family and Friends of Patients with Alzheimer, was founded in 1988 [54]. It is currently the only association in Portugal especially conceived to improve the quality of life of patients with dementia, their families and carers.

The initiative was assumed by Professor Carlos Garcia, an important neurologist that dedicated a significant part of his work and life to the area of dementia.

Professor Carlos Garcia was responsible for the change in the scientific approach of dementia in Portugal. He was also responsible for the creation of the first medical consultation of dementia in the country, and one of the first in Europe.

His dedication to the area of dementia and AD, allowed him to realize the devastating effects of these conditions in the life of patients and their families and carers. This was the main reason for the creation of the association.

Alzheimer Portugal is an IPSS. It is funded by the contribution of its members, services rendered, contributions from private and public entities, private donations and funds obtained from the application to specific projects. Also, the Social Security and National Secretary for Rehabilitation and Integration of People with Disability (SNRIPD) have been funding the association's day care centres, in-home care and other services. Through the National Integrated Continued Care Network, entities from the private sector and non-profit organizations establish partnerships with state departments.

The association presents several regional divisions, all over the country. Currently, Alzheimer Portugal has approximately 10.000 members.

A part of the work developed by the association is assumed by volunteers.

3.3.6.1 AIMS AND OBJECTIVES

Alzheimer Portugal presents as main objectives:

- Alert for the urgency of a National Plan for Alzheimer and related dementia illnesses, providing the knowledge and experience of the association in its creation and implementation.
- Raise awareness on the disease in the community, developing national and local campaigns;
- Encourage the research into the prevention, cause, diagnosis, treatment and cure of AD and related conditions;
- Inform on the importance of an early diagnosis;
- Emphasize the GP's key role in the detection of the first signs of dementia and patients referral to differentiated physicians (neurologists and psychiatrists);
- Represent the direct carers, promoting their needs and rights;
- Provide support to the patients, families and caregivers;
- Include the study of dementia in the medical training;
- Provide specific training to the caregivers;
- Create services and model equipment in order to learn and share best practices.

In October 2009, Alzheimer Portugal prepared and delivered a document to the members of the Portuguese parliament, including an action plan for intervention in AD and dementia. This document was based in important measures already applied in some of the European countries. Soon after, two proposals were discussed and approved by the Parliament. Unfortunately, these proposals were never implemented.
Recently, in March 2015, Alzheimer Portugal addressed a letter to the Portuguese Prime Minister, emphasizing the growing problem of dementia in Portugal and worldwide. Once again, the association urged the implementation of a "National Plan for Dementia" and provided support for this process.

3.3.6.2 ACTIVITIES

When the association was created started to provide the following services:

- Training and counselling for families and carers;

- Technical support, lending temporarily accessories and equipment to help with the mobility of patients and improving their quality of life;
- Incontinence help program, important for patients in an advanced stage of the disease and their families;
- Financial support.

Currently the association has a detailed group of services, which are a reference for AD and dementia disorders. The actual services include:

- Day care centres;
- Domiciliary support to patients and carers;
- Nursing homes;
- Residential homes;
- Therapeutic centres;
- Training and project centre;
- Technical support designated as *"Banco de Ajuda Técnica"*;
- Incontinence help program designated as *"Apoio na Incontinência"*;
- Awareness campaigns, such as *"Banco de Memória"*;
- Social and psychological support, namely the programs: *"Cuidar Melhor"* and *"Café Memória"*;
- Helpline – *"Informar +"*;
- Participation in national and international events;
- Protocols with several entities;
- Manuals for the caregivers;
- Outdoor activities, such as *"Passeio da Memória"*;
- Celebration of specific dates, such as the "World Alzheimer's Day";
- Palliative care;
- Legal advice.

3.3.6.3 INVOLVEMENT WITH OTHER STAKEHOLDERS

Other Organizations

Alzheimer Portugal is a member of Alzheimer Europe. This organization intends to raise awareness on dementia and for that purpose creates a common ground for the Alzheimer's counter-part associations all over Europe. This organization also provides information in the latest developments in AD and dementia.

Alzheimer Portugal presents a close relation with Alzheimer's Australia [47], sharing web contents.

The association also integrates the *"Plataforma Saúde em Diálogo"*, a non-profit organization composed by patient associations, healthcare professionals and consumer's protection organizations. This entity aims to work as an active partner in the definition of the health policies, intervening near the competent authorities.

Healthcare Professionals

The association presents a scientific commission, composed by a multi-disciplinary group of neurologists, psychiatrists, jurists, GP's, gerontologist and a nurse.

In case of need, the association provides information to the patients and families on differentiated physicians. However, this is not a common practice.

The association intends to maintain and reinforce the cooperation with the different stakeholders, namely professional associations (such as physicians and nurses), as well as academia, in order to share knowledge and experience in the dementia area.

Pharmaceutical Industry

Alzheimer Portugal receives sponsorships from pharmaceutical companies, related to activities organized by the association.

The association also reinforce the need of feedback on clinical trials and respective results.

Directorate-General of Health

The actual NHP, presented by the DGS was recently extended to 2020 and present as main goals: the reduction to less than 20% of the premature mortality rate (under 70 years old), the increase of 30% in the healthy expected life at 65 years old and the reduction of the risk factors associated to non-transmitted diseases (namely, consume and exposure to cigarette smoke and child obesity). The dementia disorders are not clearly stated in the plan, however they are implicit in some of the goals.

Alzheimer Portugal will continue leading the advocacy on this issue.

3.3.6.4 MAIN CHALLENGES

As already mentioned, Alzheimer Portugal is pressuring the official entities to assure the implementation of a "National Plan for Dementia", with a particular focus on:

- National campaigns to help with the perception of the first symptoms of the disease, as well as to avoid the stigma associated to dementia;
- The quality of life of patients and their carers, requiring the implementation of specific health and social policies. For instance, informal carers face often a significant pressure, being prone to neglect their own health and find themselves in a delicate financial situation;
- The research and investigation on AD, namely on the causes, prevention, diagnosis and collection of epidemiological data;
- The creation of a legal framework, oriented to the rights of people with disabilities, covering care, intervention and research;
- The real needs of patients and carers, identifying the available resources and the alterations that need to be implemented. The support and healthcare network should be clearly defined, considering that the number of people with dementia will double every twenty years.

Additionally, the association requires a high number of differentiated personnel, to support patients and their families, as well as the activities and programs of Alzheimer Portugal. This implies a major effort on the management of resources.

The funding for all programs, activities and patients' support is also a significant challenge for Alzheimer Portugal.

3.4 DIABETES MELLITUS

According to the American Diabetes Association, diabetes mellitus consists in a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia, with disturbances of carbohydrate, fat and protein metabolism, resulting from defects in insulin secretion, insulin action, or both [55].

The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs [55]. In fact, the long–term effects of diabetes mellitus include progressive development of the specific complications of retinopathy with potential blindness, nephropathy that may lead to renal failure, and/or neuropathy with risk of foot ulcers, amputation, Charcot joints, and features of autonomic dysfunction. Patients with diabetes are also at increased risk of cardiovascular, peripheral vascular and cerebrovascular disease.

There are two main categories of diabetes:

- Type 1 – This type of diabetes is usually diagnosed in children and young adults, and was previously known as juvenile diabetes. In this case the patient does not produce insulin. The type 1 diabetes represents less than 10% of the total diabetes cases.

- Type 2 – In this case, the patients have developed a resistance to insulin. This is the most common form of diabetes and usually affects adults.

There is also the gestational diabetes, which affects approximately 1 in 20 women during pregnancy. Usually, it affects women that didn't have diabetes before being pregnant. When the pregnancy reaches its term, the diabetes does not prevail. However, if there are no precautions, later in life these women might develop diabetes type 2.

Not frequently, there are other types of diabetes [56]:

- Type LADA (Latent Autoimmune Diabetes in Adults), also designated as type 1.5 – In this case the patients present features from both type 1 and type 2. LADA can be considered as a slow progression of type 1 diabetes, yet it is often misdiagnosed as type 2.

- Type MODY (Maturity-Onset Diabetes of the Young) – Is a form of diabetes associated to mutations in a number of different genes. MODY is usually diagnosed in late

childhood, adolescence, or early adulthood. However, it has been known to develop in adults as late as their 50's.

- Secondary diabetes – Results as a consequence of another medical condition;
- Double diabetes – When type 1 diabetics develop insulin resistance;
- Type 3 – Close relation to the development of AD;
- Steroid-induced diabetes – When type 2 diabetes is brought on by the extensive use of corticosteroids;
- Brittle diabetes – Corresponds to type 1 diabetes, having the additional challenge of being difficult to manage with insulin;
- Diabetes *Insipidus* – A rare form of diabetes, not associated to diabetes mellitus, that occurs when the level of the antidiuretic hormone is below the normal standard.

Finally, there is an important stage before diabetes called pre-diabetes, also known as impaired glucose tolerance, a condition where the glucose level reaches a high level, but not enough to be considered diabetes.

3.4.1 AETIOLOGY

In Type 1 diabetes the production of insulin is absent, due to the autoimmune pancreatic β-cell destruction, possibly triggered by an environmental exposure in genetically susceptible people [56]. This process elapses over time until β-cell mass decreases to the point where insulin concentrations are no longer adequate to control plasma glucose levels.
As mentioned before, Type 1 diabetes generally develops in childhood or adolescence. Until recently, this was the most common form of diabetes diagnosed before the age of 30 years old.

In Type 2 diabetes the insulin secretion is inadequate, once patients have developed resistance to insulin. This resistance leads to an inability to suppress hepatic glucose production, and peripheral insulin resistance impairs peripheral glucose uptake. This combination gives rise to fasting and postprandial hyperglycaemia [57].
The insulin levels are significantly high, namely early in the disease. Over time, the insulin production may decrease, exacerbating the hyperglycaemia.

Type 2 diabetes generally develops in adults, becoming more common with ageing. However, the Type 2 diabetes is becoming more common among children, mainly due to childhood obesity.
Obesity and weight gain are important determinants of insulin resistance in Type 2 diabetes. It has some genetic determinants but also reflects diet, exercise and lifestyle.

The gestational diabetes is caused by the extra insulin resistance in pregnancy, which affects all women, but only a few develop the disease.

The causes related to the other types of diabetes include:

- Genetic defects that affect the β-cell function, the insulin action and the mitochondrial DNA, as in Type MODY;
- Pancreatic diseases, such as pancreatitis and hemochromatosis;
- Endocrine diseases, like Cushing syndrome;
- Drug-induced diabetes, as glucocorticoids, β-blockers, protease inhibitors and therapeutic doses of niacin.
- Toxins.

3.4.2 SYMPTOMS AND SIGNS

The signs and symptoms of diabetes are related to the level of glucose in the blood. The symptoms of marked hyperglycaemia include [58]:

- Glycosuria, leading to frequent urination;
- Polyuria;
- Polydipsia that may progress to orthostatic hypotension and dehydration. In this case, the patient may feel weak, fatigued and with an altered mental status;
- Polyphagia.

Hyperglycaemia can also cause weight loss, nausea and vomiting, and blurred vision. It can also predispose to bacterial or fungal infections.
The prevalence of symptoms may vary, in accordance to the fluctuation of plasma glucose levels.

Acute forms of hyperglycaemia with ketoacidosis or the non-ketotic hyperosmolar state, may lead to stupor, coma and, in the absence of effective treatment, death [58].

Usually, the symptoms are not severe, or may be absent. This may lead to a late diagnosis. This is typically the case of Type 2 diabetes.

3.4.3 DIAGNOSIS

The presence of diabetes is confirmed by the measurement of plasma glucose [59]:

- Fasting Plasma Glucose – Corresponds to the measurement after 8 to 12 hours fast.
  ⇨ Diabetes is diagnosed at fasting blood glucose of greater than or equal to 126 mg/dl.

- Oral Glucose Tolerance Test – Test perform after the ingestion of a concentrated glucose solution.
  ⇨ Diabetes is diagnosed at 2 hour blood glucose of greater than or equal to 200 mg/dl.

- Glycated Haemoglobin (HbA1c) – This parameter will measure the average blood glucose over long periods (example: past 2-3 months).
  ⇨ Diabetes is diagnosed at an A1C of greater than or equal to 6.5%.

- Random Plasma Glucose Test - This test is performed in the presence of severe diabetes symptoms.
  ⇨ Diabetes is diagnosed at blood glucose greater than or equal to 200 mg/dl.

People that are considered at risk, should be subjected to a diabetes screening. In the case of patients with diabetes, the screening usually occurs in the case of complications.

The complications in diabetes patients may be very severe. These complications arise from poorly or practically inexistence control of hyperglycaemia, during a long period of time. The complications include:

- Microvascular disease [59], that comprises the most common and dramatic complications:

  - Retinopathy - It is characterized initially by retinal capillary micro-aneurysms and later by neovascularization and macular edema.

  - Nephropathy – This is one of the leading causes of CKD worldwide, including Portugal. It is characterized by the thickening of the glomerular basement membrane, mesangial expansion and glomerular sclerosis. These changes cause glomerular hypertension and progressive decline in GFR.

The systemic hypertension may accelerate progression. The disease is usually asymptomatic until the renal failure develops.

- Neuropathy - This is the result of nerve ischemia due to microvascular disease, the direct effects of hyperglycaemia on neurons and the intracellular metabolic changes that impair the nerve function.
  These neuropathies include: symmetric polyneuropathy, autonomic neuropathy, radiculopathies, cranial neuropathies and mono-neuropathies.

The microvascular disease may also impact the skin healing. Minor breaks in the skin may become deep ulcers. This affects particularly the lower extremities. The "diabetic foot" is one of the examples of neuropathies.

- Macrovascular disease [59], which derives from hyperinsulinemia, dyslipidaemias, and hyperglycaemia, causing large-vessel atherosclerosis. The macrovascular disease may lead to:

  - Angina pectoris and myocardial infarction;
  - Transient ischemic attacks and strokes;
  - Peripheral arterial disease.

3.4.4 TREATMENT

Diabetes mellitus has no cure. For patients with diabetes, the treatment corresponds to eliminate the existing symptoms and to prevent or slow the development of complications. The prevention of diabetes consists in:

- Patient education – Informing on causes of diabetes mellitus, diet, exercise, drugs, self-monitoring testing, symptoms and signs of hypoglycaemia and hyperglycaemia, and diabetic complications. Most patients with Type 1 diabetes may also be taught how to adjust their insulin doses. Education should be reinforced at every physician visit and hospitalization.

- Monitoring of glycaemia;

- Medication:
  - Patients with Type 1 diabetes require insulin. This may be administered through injections or pumps (continuous insulin infusion therapy).

- Patients diagnosed with Type 2 diabetes should review and change their lifestyle in terms of diet and exercise. If these changes are not sufficient, an anti-hyperglycaemic drug is prescribed. If needed, more medicines may be added. After this, the insulin therapy is also an option.

- Diet – Change to a healthy diet reducing the ingestion of fat and salt, and increasing fibres. This will help to control the glycaemia, cholesterol, triglycerides, blood pressure and maintain a healthy weight.

- Physical exercise – This will improve the well-being of the patient and contribute to the production of insulin.

3.4.5 PREVALENCE

In 2014, according to the International Diabetes Federation (IDF) [60], the number of individuals with diabetes was 387 million. It is estimated that by 2035, the number will correspond to 592 million.
Around 179 million people have diabetes, but were not diagnosed.
Only in 2014, diabetes caused 4.9 million deaths worldwide.
The individuals with Type 2 diabetes is increasing in every country.

According to a report from the Portuguese Society of Diabetology [61], in 2014 the prevalence of diabetes in Portugal corresponded to 13.1%. This study included the Portuguese population from 20 to 79 years old. From this percentage, it is estimated that approximately 5.7% represents the undiagnosed population.
This study revealed a significant difference within genders: 15.8% of prevalence in men and 10.8% of prevalence in women.
Also, the prevalence of diabetes increases with age. It is estimated that more than a quarter of population from 60 to 79 years old has diabetes.
In 2014, the expenses incurred with diabetes in Portugal corresponded to: 0.7%-0.9% of the Portuguese gross domestic product and to 8-10% of the total health expenditures.

3.4.6 APDP – THE PATIENT ASSOCIATION

APDP, the Protective Association of the Diabetics of Portugal [62], was created in 1926, by Dr. Ernesto Roma.

In 1922, Dr. Ernesto Roma had the opportunity to do an internship in the Massachusetts General Hospital. He also had the chance to visit the Joslin Clinic, where the first insulin doses were being administered. He observed the impact that the insulin had in children, that otherwise would not be able to live.

When Dr. Ernesto Roma returned to Portugal, he started to apply the insulin therapy to his patients. However, he verified that the poor population, with no support, could not afford to be treated. This was the main motivation for the creation of the association.
The association was founded by Dr. Ernesto Roma, friends and patients with diabetes, being initially designated as "Protective Association of the Poor Diabetics".
This was the first patient association of diabetics in the world.

One of the first premises was to educate the patients on their condition and to do a self-monitoring. The association always reinforced the educational needs of patients with chronic diseases.
Due to its valuable accumulated experience, APDP participated in the creation of the Diabetes Education Study Group (DESG), in 1979.
In 2009 it was recognized as the first International Diabetes Centre of Education in the world.
In 2011, was also certified as Centre of Reference for Paediatric Diabetes.

It is funded by the contribution of its members, services rendered, contributions from private and public entities, private donations and funding and co-funding obtained from the application to specific projects.

APDP is a non-profit organization, classified as an IPSS, acting on the healthcare area.
The association has approximately 11.380 members from all the country.

3.4.6.1 AIMS AND OBJECTIVES

The main objectives of APDP are integrated in four main areas:

- Social area:
  - To provide social assistance to patients with diabetes;
  - To represent the patients with diabetes, promoting their rights and benefits;
  - To create a close relation with other associations and national structures, with the aim to vindicate the interests of the diabetics;

- To co-operate with international entities.

- Clinical area:
  - To provide integrated and specialized healthcare services to patients from all over the country, in multi-disciplinary areas.

- Investigation:
  - To promote the development of scientific studies in epidemiology and diabetology;
  - To promote relevant scientific work with other reference entities.

- Training:
  - To educate the patients and carers in diabetes;
  - To educate he healthcare professionals in diabetes.

3.4.6.2 ACTIVITIES

The services and programs of the association are also related to the four areas previously described. They include:

- Social:
  - Therapeutic education;
  - Support groups and counselling for patients and families;
  - Forums;
  - Meetings and events for young patients with diabetes, organized by *"Núcleo Jovem APDP"*;
  - Award "Ernesto Roma", to incentive the investigation and research in diabetes;
  - Scholarships for the education research centre of APDP;
  - Protocols with public and private entities, to promote the quality of life of the patients;
  - Outdoor activities;
  - Holiday camps;
  - Culinary workshops;
  - Social pharmacy;
  - Celebration of special dates, such as the "World Diabetes Day".

- Clinical:
  - Consultations in several areas, such as diabetology, nutrition, ophthalmology, podiatry, cardiology, nephrology, urology, paediatrics, women's health, mental health and diagnostics;
  - Participation in national and international events, congresses and symposiums;
  - Screenings.

- Investigation:
  - Development of clinical studies;
  - Participation in international diabetology network studies;
  - Presentation of investigational work developed by APDP in national and international congresses.

- Training:
  - Training courses in diabetes for healthcare professionals, diabetes educators, professionals and users of communitarian support institutions, university students and professors and patients with diabetes and their families;
  - *"Portal da Diabetes"*, that intends to support and educate the patients and community;
  - Publications.

3.4.6.3 INVOLVEMENT WITH OTHER STAKEHOLDERS

Other Organizations

APDP is a member of IDF [60]. This organization intends to raise awareness on diabetes, influence policy, encourage health improvement, promote the exchange of quality information on diabetes and provide education for patients and carers.

The association also integrates the Portuguese Society of Diabetology.

Healthcare Professionals

APDP integrates a multi-disciplinary team that supports the diabetic patients.
The association also provides training to healthcare professionals.
The association integrates an ethic commission and an advisory committee.

Pharmaceutical Industry

APDP receives sponsorships from pharmaceutical companies, related to activities organized by the association.

The association is permanently aware of the recent achievements in the diabetes area.

Directorate-General of Health / National Health System

APDP provides scientific and technical consultancy in diabetes, and also provides recommendations on policy measures.

APDP has an active participation in the implementation of the "Portuguese National Program for the Prevention and Control of Diabetes" [63]. The main goals of this plan are as follows:

- Integrate management of diabetes;
- Reduce diabetes prevalence;
- Delay the beginning of diabetes related complications and reduce their incidence;
- Reduce diabetes morbidity and mortality.

APDP has a convention with the NHS for the rendered services.

Academia

The association provides training, including a post-graduation on diabetes. For this purpose, there is a protocol with a University.

3.4.6.4 MAIN CHALLENGES

The increasing number of diabetic patients, namely Type 2, is a true challenge and concern. It is therefore important to assure that the strategies of the "National Program for Diabetes" are being followed.

For the prevention and early detection of diabetes, the general population needs to be aware of the risk factors and make the necessary changes in their lifestyles.

The healthcare professionals need to have an appropriate training, namely GP's need to be aware on the early detection of diabetes, namely in high risk population.

Patients with diabetes must be educated and perform a "self-management" of their condition.

3.5 ENDOMETRIOSIS

Endometriosis is a chronic oestrogen-dependent condition characterised by the growth of endometrial tissue outside the endometrial cavity and uterine musculature [64].

This disease usually affects the following sites:

- Pelvic cavity, including the ovaries;
- Uterosacral ligaments;
- Pouch of Douglas;
- Recto-sigmoid colon;
- Bladder;
- Distal ureter.

Not so common, endometriosis may be present in:

- Fallopian tubes;
- Serosal surfaces of the small and large intestines;
- Ureters;
- Vagina;
- Cervix;
- Pleura;
- Pericardium.

The inflammation seems to be triggered by the bleeding from peritoneal implants, followed by fibrin deposition, adhesion formation, and, eventually, scarring, which distorts peritoneal surfaces of organs and pelvic anatomy.
The appearance of endometriosis implants typically has been described as bluish grey, dark brown, or black “powder burn” lesions. The color is attributed to hemolyzed blood from ectopic endometrium that is encapsulated by adhesions or fibrotic tissue [65].
An area affected by endometriosis that is large enough to be described as a tumour, is designated as endometrioma. This is commonly the case of cysts in the ovaries.

Adenomyosis is known as the uterine endometriosis. In this case, the endometrial cells from the lining of the endometrial cavity migrate into the posterior side or back wall of the uterus. Endometriosis is a complex disease that affects women during their reproductive-age.

3.5.1 AETIOLOGY

There are several theories on the cause of endometriosis, although none was yet proven. In fact, the extensive investigations were not able to clearly define the mechanism responsible for the development of endometriosis.

Some of the more discussed theories suggested as possible mechanisms:

- Retrograde menstruation;
- Lymphatic or haematogenous spread;
- Celomic metaplasia.

Currently the consensus is that endometriosis presents a multi-factorial aetiology, including possible genetic, hormonal, immunological and environmental factors.
Endometriosis affects women equally across all racial/ethnic and socioeconomic backgrounds.

3.5.2 SYMPTOMS AND SIGNS

There is a wide variety of endometriosis symptoms. Some symptoms strongly suggest the presence of endometriosis. However there are patients that are asymptomatic.

The most common signs and symptoms that endometriosis patients experience are:

- Pelvic pain – Usually occurs during the menstrual cycle. There are different manifestations of this symptom like backaches, rectal pressure, constant lower abdominal aches, dysmenorrhea and dyspareunia. The presence of endometriomas in the ovaries are frequent.

- Dysfunctional uterine bleeding – This includes for instance spotting. However most cases of bleeding are attributed to coexistent pathology rather than true dysfunctional uterine bleeding.

- Infertility – The adhesions and/or significant anatomic distortion may explain the presence of infertility. The incidence of infertility in endometriosis is still unknown, due to limitations of selection bias. However, the incidence of endometriosis in infertile woman is on average 14% [65].

- Other symptoms – This usually relates to the location of endometriosis foci and adhesions: rectal bleeding or obstruction for bowel implants; suprapubic pain, haematuria and dysuria for bladder implants; urinary tract symptoms for ureteral involvement; pleuritic pain, pleural effusion, haemoptysis or pneumothorax for pulmonary involvement.

3.5.3 DIAGNOSIS

The clinical suspicion of the presence of endometriosis usually occurs after the report of symptoms, clinical history and pelvic examination.
In the presence of endometriosis, the pelvic examination may include a retroverted and fixed uterus, enlarged ovaries, fixed ovarian masses, thickened rectovaginal septum, induration of the cul-de-sac, nodules on the uterosacral ligament and/or adnexal masses. In very rare situations, lesions may be observed on the vulva, cervix, vagina, umbilicus or in surgical scars.

The confirmation of endometriosis requires a direct visualization, through laparoscopy. It is very important that the surgeon is familiar with the condition. A biopsy may be performed in case the surgeon is not certain of the diagnosis.
There are other exams that may be used to complement the diagnosis. This includes the MRI that allows to have information on the extent of the lesions and laboratory tests.

Defining the stage of the disease, provide the possibility to formulate an accurate treatment plan and also evaluate the response to therapy.
The American Society for Reproductive Medicine (ASRM) defined the endometriosis stages according to the number, location and depth of implants, presence and severity of adhesions, and presence of endometriomas.
The classification is as follows:

- Stage I – Minimal;
- Stage II – Mild;
- Stage III – Moderate;
- Stage IV – Severe [66].

It is important that the diagnosis is performed by a doctor that is familiar with the disease. In fact, some of endometriosis symptoms may be incorrectly associated to other conditions. Also the treatments applied may not be the most appropriate. This is in fact, one the major

problems in patients with endometriosis: being diagnosed in an advanced stage, when their infertility and quality of life may be already highly compromised.

3.5.4 TREATMENT

Endometriosis has no cure. The existing treatments are addressed to control the symptomatology and the progression of the disease.

Usually, the immediate approach to control pain starts with nonsteroidal anti-inflammatory drugs.
The next line of treatments is evaluated based on the patient's age, the symptoms, the stage of the disease and the desire to preserve fertility.
The available treatments are:

- Hormonal therapy [64] – Is defined based on the response of existing oestrogen and progesterone receptors on ectopic endometrial tissue to certain hormonal agents.
  This treatment may vary according to the patient, due to the presence of different endometrial lesions. It is important to note that this therapy is suppressive, therefore in case of discontinuation the endometriosis will recur. The usual hormonal therapy applied is:
    - Oral contraceptives - Combine oestrogen and progestin to regulate the hormonal levels and suppress endometrial growth. This treatment may lead to a diminishing of lesions.
    - Gonadotropin-releasing hormone (GnRH) agonists – Suppresses the pituitary hormones, preventing the ovary from producing oestrogen and the patient enters into a menopausal state. This treatment may lead to a diminishing of lesions.
    - Progestins – Keep the oestrogen and progesterone at a low level, preventing ovulation and suppressing endometrial growth.
    - Danazol – Presents some androgen effect and reduces ovarian hormonal production. Most patients will suspend ovulation, leading to a shrinking of endometrial lesions.

  Some of these therapies imply very uncomfortable side effects. Additionally, some therapies may not be used for a long period of time.

- Surgical treatment [64] – The laparoscopic surgery is considered the golden standard for endometriosis treatment. Through the laparoscope the endometrial lesions may be excised. Unfortunately, not all the gynaecologists are experienced with the technique

and the disease. It is very important that the patient is followed by a differentiated gynaecologist.

After the surgery, the patient may be put on a hormonal therapy or be advised to try to conceive. In fact, there is a greater chance for patients to get pregnant in the period of six months that follows the surgery.

All of these treatments are symptomatic. In most of the patients, the disease will reappear, within six months to one year.

The hysterectomy and bilateral salpingo-oophorectomy are not a definitive treatment for endometriosis.

3.5.5 PREVALENCE

According to the World Endometriosis Society and World Research Foundation, it is estimated that 1 in 10 women in their reproductive years (from 15 to 49 years old) are affected by endometriosis. This leads to an estimate of 176 million of women worldwide [67].

In Portugal there are no official figures. According to the Portuguese patient association the estimate corresponds approximately to 10 to 15% of women in their reproductive years.

3.5.6 MULHERENDO – THE PATIENT ASSOCIATION

The Portuguese association of support of women with endometriosis is MulherEndo [68].

This association was formally created in 2013, by a group of patients and families. However, it was already active as a support group since 2011.

The idea for the creation of MulherEndo came from its actual president, Dra. Susana Fonseca that wanted to add credibility to the existing project near the healthcare professionals and general community.

The association is located in Leiria, providing support to patients from all the country. The representatives of the association are all volunteers.

MulherEndo is a non-profit organization and is funded mainly by the contribution of its members, which are 105.

3.5.6.1 AIMS AND OBJECTIVES

The main objectives of the association are:

- Support and promote the medical psychological assistance for the patients of endometriosis in Portugal;
- Prepare and gather information on all topics on endometriosis;
- Clarify the existing doubts from patients and families, through presential support, social networks and phone;
- Raise awareness on the disease near the general community and public and private entities;
- Represent the patients of endometriosis near official public or private entities;
- Promote the public and scientific debate on endometriosis;
- Present workshops and sessions;
- Provide a helpline;
- Cooperate with national and international entities that have similar objectives;
- Celebrate protocols and agreements with private and public entities, in order to improve the access to the treatment of endometriosis and infertility;
- Clarify near the community in general, what are the physical and emotional consequences of living with the disease. Also provide information on the available treatments.

3.5.6.2 ACTIVITIES

MulherEndo promotes, organizes and participates in several activities, namely:

- Congresses;
- Informative events for patients;
- Meetings with patients to share experiences;
- Protocols with several entities. This includes an agreement with an assisted reproduction centre;
- Clarifying sessions within the community, namely schools and universities;
- Invitation of members from international associations to participate in meetings;
- Participation in the endometriosis worldwide walk;
- Participation in TV shows.

3.5.6.3 INVOLVEMENT WITH OTHER STAKEHOLDERS

Other Organizations

MulherEndo maintains a close relation with other international endometriosis associations and support groups, exchanging experiences and ideas.

The association has already organized events together with other organizations.

Healthcare Professionals

The association is permanently in contact with the main specialists in endometriosis. This gynaecologists support the association in the clarification of doubts. They also participate in some of the organizations activities, such as informative events.

In case of need, the association informs the patients on the list of differentiated physicians.

Pharmaceutical Industry

The association does not maintain a relation with the pharmaceutical industry.

Directorate-General of Health

There is not a specific NHP for endometriosis, although the high prevalence of the disease in women.

3.5.6.4 MAIN CHALLENGES

One of the main challenges of this association is to raise awareness on the disease. Endometriosis is still considered an underdiagnosed and complex disease. The number of physicians that are specialized in the disease is still low. The diagnosis and treatment of endometriosis, namely laparoscopic surgery, implies differentiated knowledge.

From the symptom onset until a correct diagnose is performed, several years may pass. Considering that this disease affects women in their reproductive years, the desire to conceive may be seriously compromised. It is important that, in case of need, women are also guided to infertility centres that are familiar with the disease.

The emotional and psychological consequences of the disease imply a constant support to these patients. Also the close relatives need support and information.

MulherEndo is a recently created organization that has a limited structure and is based on volunteer work. Therefore, the management of information requests and clarifications, namely from recently diagnosed patients represents also a significant challenge, as well as the association’s funding.

3.6 RESUME OF PATIENT ASSOCIATIONS' DATA

This project allowed to gather relevant information from the five patient associations. A resume and comparison of the data is presented in Table 3:

Table 3 – Resume of patient associations' data.

	APIR	APDH	Alzheimer Portugal	APDP	MulherEndo
Condition	**Chronic Kidney Disease**	**Huntington's Disease**	**Alzheimer's Disease**	**Diabetes Mellitus**	**Endometriosis**
Particularity	Silent and highly prevalent disease	Rare disease	Support to family and carers	Highly prevalent	Underdiagnosed
Prevalence in Portugal (most recent data)	- 18.703 patients in RRT; - Estimate of 800.000 individuals affected by CKD.	5-10 cases per 100.000 individuals	Approximately 182.500 individuals affected by dementia	13,1% Portuguese population	10%-15% women in reproductive age
Creation date	1977	2001	1988	1926	2013
Approximate members	3.500	350	10.000	11.380	105
Funding support other than members	Yes	Yes, but limited	Yes	Yes	Yes, but limited
Associated to "umbrella" organizations	Yes	Yes	Yes	Yes	Yes
Permanent activities	Yes	Yes	Yes	Yes	Yes
National Health Plan	- Specific strategy for CKD under preparation; - Existence of a national guideline for referral and management of CKD; - Existence of a national guideline to provide comprehensive information on RRT.	- Global for rare diseases (recent integrated strategy).	No	Yes	No
Main challenges	- Awareness on CKD; - Inexistence of registries; - Coordination care between GP's and specialists; - Integrative consultations and information for the patients; - Mostly elder population and low level of literacy; - Transportation of patients to hemaedialysis units; - Limited funds to CKD programs; - Association's funding.	- Awareness near the "at risk population"; - Guidance on genetic testing; - Association's funding.	- Awareness on dementia near the healthcare professionals and general community; - Implementation of a National Plan for Alzheimer and other dementia conditions; - Specialized personnel; - Association's funding.	- Awareness on the prevention and early detection of diabetes; - Healthcare professionals training; - Self-management of the disease that implies education for patients.	- Awareness near the healthcare professionals and general community; - Psychological and emotional support; - Association's funding; - Available time from volunteers.

4. DISCUSSION

This chapter presents a discussion of relevant topics related to the patient associations and patient empowerment, namely: the challenges endured by these associations, the relevance of patient education, the importance of clinical research and the involvement from the pharmaceutical industry.

Based on the performed interviews it was possible to observe that the guidance provided by these entities covers several important aspects, namely:

- Social – Providing all the possible means and resources to improve the quality of life of patients and relatives;
- Emotional – Acting like support groups, promoting meetings and reunions between patients and families, organizing counselling and psychological consultations;
- Clinical – Providing information on specialized physicians when requested, clarifying doubts near scientific commissions, or even providing the clinical services;
- Investigation and research – Being informed on the latest scientific advances and supporting, when possible, research and investigational programs. Also sharing on a permanent basis this information with their members and general community;
- Training – Organizing sessions for patients, families, healthcare professionals and general community;
- Education – Encouraging the patients and families to learn about their diseases and be able to discuss with the physicians the options in terms of diagnosis and treatments, getting information on all the options;
- Advocacy – Representing the patients' rights and benefits near the official entities and demanding changes in health and social policies.

In general, the five patient associations included in this work present similar objectives.

The main differences observed in this group of patient associations are related to the challenges that they endure. In fact, the awareness on the chronic disease near the general community, as well as the existence of a health plan from the official health entities, has a significant impact.

That is why the work developed by these associations is so relevant and important. Moreover, the existence of "umbrella" organizations that represent these associations at a higher level, is of major importance.

Considering the "patient-centred care" model, patients should be able to discuss with healthcare professionals the treatment options, having at the same time a good knowledge of their disease.
This is only possible if the available information for patients and carers is comprehensive, if these healthcare professionals are sensitized with this approach and if the processes and systems in place are "readable".
This is particularly relevant in the case of diseases affecting mostly elderly patients, like the majority of CKD and diabetic patients.

A very interesting example of patients' education is the European Patient's Academy on Therapeutic Innovation (EUPATI) [69] that represents a pan-European Innovative Medicines Initiative project, involving 33 organizations, including patient associations, academia, pharmaceutical companies and non-profit organizations.
The main aim of EUPATI is to assist on patients' education, namely on the research and development process of new medicines. Through an accessible and comprehensive information and training, patients are able to understand areas, such as drug discovery, non-clinical studies, clinical trials and registries, regulatory affairs, pharmacovigilance, benefit-risk assessment and the principles of health technology assessment (HTA).

The patient associations make an effort to follow and be informed on the latest developments in terms of new therapeutics.
According to this project, most of the information gathered from clinical studies and registries are obtained from counter-part associations, at an international level.
In the specific case of APDP, there is a department fully dedicated to clinical investigation.
The clinical research for some chronic diseases is assumed also by study groups, funded by private organizations. This is the case of CHDI and Enroll-HD, previously mentioned.
Based on this work, the patient associations demonstrated an interest on receiving direct feedback from the pharmaceutical companies, namely on the results of studies.

The pharmaceutical industry usually recognizes the important role of patient associations. In fact, an involvement from the industry allows to get information on the concerns, advices and experiences from a patient's perspective, and also on unmet medical needs.

The pharmaceutical industry must comply with the Code of Practice [70] on relationships between the pharmaceutical industry and patient associations established by the European Federation of Pharmaceutical Industries and Associations (EPFIA).
The Portuguese Association for the Pharmaceutical Industry (APIFARMA) transferred these principles to Portugal [71].
These companies may sponsor the patient associations, assuring a full transparency.

One of the strengths of patient associations is related to the fact that the work developed by an organization has a high impact near the community and official public entities. Also the practiced influence to demand changes in health and social policies is more significant.
In terms of weaknesses, the patient associations that do not represent conditions with a high prevalence have more difficulties to exercise pressure near the parties involved, namely official public entities, general community and healthcare providers.
Also, some of the healthcare systems and procedures are not yet prepared for a co-participating role from patients.
Regarding opportunities, these organizations help to raise awareness on chronic diseases and on the needs of patients and caregivers.
This new perspective of the patient role creates the opportunity to assume a higher responsibility and control in the management of the disease, through an accurate patient education.
In different situations, the causes of certain pathologies are related to other onset diseases. There is therefore the opportunity to create synergies between different patient organizations.
Finally, in what concerns threats the funding of patient associations may be quite challenging. Also the management of other resources, such as personnel and available time, is often complex. As already mentioned, a significant part of the work developed by these associations is based on volunteer work.

5. CONCLUSION

The aim of this dissertation has been to discuss the fundamental role of patient associations in raising awareness on chronic diseases and supporting patients and families.

The highly discussed “patient-centred care” model and the high prevalence of chronic diseases, contributed to the relevance and purpose of this project.

Overall, the proposed learning objectives were accomplished, once it was possible to learn about the motivation to create this type of organization, the actual context, the main goals, the developed activities, the important involvement of several parties and general community, and the existing challenges.
It was also possible to conclude that the significant prevalence of chronic diseases has been introducing changes into the healthcare systems and into the national disease programmes. Simultaneously, the patients’ ownership has been increasing, contributing to a more participated role near the healthcare professionals and to a more conscious decision regarding the available therapeutics. Patient associations represent these patients and act in critical areas, such as, social, clinical, research, training, education and advocacy.

The role of these associations implies a continuous dedication and involvement, which may be enabled by the synergies created with other patient associations, namely the “umbrella organizations”, and with the official public entities. Farther, the partnership with other associations related to connected pathologies may also contribute to an increase of the awareness.

This project also intends itself to raise awareness on this topic and provide information to the general academic community.

As part of a future project, it would be interesting to make a follow up on the current faced challenges, on the implemented measures of the national health disease programmes and on the perception of chronic diseases near the general community.

Finally, this project proved to be a gratifying and inspiring experience. Actually, the associations, as well as their representatives, are truly dedicated to the patients and their families. The challenges that they are facing seem to provide an extra incentive to proceed with their cause.

6. APPENDIX

Base inquiry addressed to the patient associations, for interview purpose.

A Associação de Doentes:

- *Quando foi criada a associação?*
- *Qual foi a motivação para a sua criação?*
- *Quem esteve inicialmente envolvido no projeto?*
- *Quais os principais objetivos da associação?*
- *Qual a sua atual constituição?*
- *Qual o presente número de associados da associação?*
- *Desde a sua criação, como tem evoluído o número de associados?*
- *Como é efetuada a divulgação da associação?*
- *Com que apoios conta a associação?*
- *Quais as atividades que tem vindo a implementar?*
- *Que protocolos e parcerias apresenta a associação?*

Doença:

- *Em que consiste a condição?*
- *Qual a sua prevalência em Portugal?*
- *Qual a sua prevalência na Europa e no resto do mundo?*

Detetar, tratar e controlar a doença:

- *Como é efetuado o diagnóstico?*
- *Quais são os tratamentos atualmente disponíveis?*
- *Que tipo de acompanhamento deve ser providenciado aos doentes?*
- *Que tipo de envolvimento tem a associação neste acompanhamento?*
- *Existe alguma perspetiva em relação a novos tratamentos?*
- *A associação tem acesso a informação de ensaios clínicos recentes, no que respeita a novos fármacos/tratamentos?*

Especialistas na doença:

- *Como tem evoluído nos últimos anos o número de especialistas na doença?*

- *A associação referencia os doentes para estes especialistas?*

Envolvimento com outros "Stakeholders":

- *Existe uma relação próxima com outras associações nacionais e internacionais relacionadas com a doença? Em caso afirmativo, que tipo de informação é partilhada?*
- *Existe uma relação próxima da associação com os profissionais de saúde, nomeadamente com os especialistas da doença?*
- *A associação estabelece alguma relação com a indústria farmacêutica, designadamente no que respeita a tratamentos disponíveis? Existe algum apoio desta indústria à Associação?*
- *A associação estabelece alguma relação com as entidades de saúde oficiais públicas, tais como a Direção-Geral da Saúde e o Serviço Nacional de Saúde?*

Capacitação de Doentes:

- *Em que medida a associação contribuiu para a capacitação dos seus doentes?*

Questão específica dirigida à APDH:

- *A doença de Huntington é considerada uma doença rara. Tendo em conta este fato, que desafios adicionais a associação enfrenta?*

Questões específicas dirigidas à MulherEndo:

- *Qual a correlação da endometriose com a infertilidade?*
- *Que tipo de apoio dá a associação a mulheres com endometriose e infertilidade diagnosticada?*
- *Existe alguma informação disponível relativa à taxa de sucesso de gravidez, em mulheres portadoras da doença?*
- *Existe alguma parceria da associação com clínicas de procriação medicamente assistida?*
- *Existe alguma informação disponível relativa à taxa de sucesso de gravidez em mulheres portadoras da doença?*

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