Technical Feasibility Market Study of Mobile Arm Supports for Patients with Muscle Weakness in Spain

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To my parents, my sister and my friends.

My main aim and reward are to help people with muscle weakness, in special mention to Duchenne and Becker, in order to improve their quality of life.
ACKNOWLEDGMENTS

The work presented in this thesis would not have been possible without the help of many people. I would like to thank all who directly or indirectly contributed to this work.

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On the other hand, give thanks to Marc, Oriol, Gerri, Alberto, Núria, Irene, Clàudia, Mar, Nerea and Àngels among other classmates, it has been a pleasure to share these four years with you, none of this would have been possible without you.

Last but not least, thanks to my parents, Mª Consol and Gaspar for your infinite support in my life. And… moltes gràcies Nur, because without your support, your recommendations and many other things, this project would not be what it is, and I would not be who I am.
SUMMARY

People with muscle weakness, such as Duchenne muscular dystrophy, can benefit from Mobile Arm Supports (MASs) that assist them to independently perform activities of daily living. Moreover, there is evidence that suggests that the use of MASs can also have a therapeutic effect and delay the functional deterioration of people with muscular dystrophy. While MASs are commercially available and popular in many European countries, they are not known nor commercialized in Spain. With the ultimate goal of making this technology accessible in Spain, this work presents a technical feasibility market study of MASs. This work has been carried out in collaboration with the patient organization Duchenne Parent Project España.

Firstly, this work presents a comprehensive inventory of commercially available MASs categorized in terms of price, manufacturers, suppliers, dimensions, weight and other technical properties. We found that there are over 10 companies from Europe, Canada and USA that are manufacturing a total number of 24 devices. Secondly, we present a demographical study of potential users of MASs. We found that in Spain, there are more than 34,700 patients with muscle weakness that could use MASs to improve their upper limb functionality. We also estimated that every year approximately between 26,500 and 53,000 new cases can appear due to accidental diseases that could benefit from MASs, in Spain. Finally, we present the mechanisms of provision, prescription and distribution for this type of assistive technology in Spain and compare it with the Dutch healthcare system. We found that MASs could be introduced to the Spanish market through medical prescription under the subsidy system managed by the Spanish healthcare system.

In conclusion, this technical feasibility market study provides key information to start negotiating with the institutions of the Spanish healthcare system in order to make MASs available to patients under the medical prescription. Moreover, this study has identified that future work should focus on developing a benchmarking framework for MASs, and carry out longitudinal studies to quantitatively evaluate the effectiveness of MASs in people with muscular weakness.

KEYWORDS

PREFACE

This thesis was developed in collaboration with Duchenne Parent Project España, a foundation whose goal is to help people with Duchenne and Becker muscular dystrophies and their families, with the aim of improving their quality of life by promoting and financing scientific research. Following this topic, Duchenne Parent Project España was interested in carrying out a research project about the feasibility of commercializing a Mobile Arm Support (MAS) for Duchenne patients in Spain. As a result, this thesis was carried out to achieve the aforementioned goal. From an economic point of view, it is relevant to search for other pathologies with similar needs that may also require from upper limb assistive technology. This thesis is organized as follows: firstly, a market inventory of commercially available MAS was developed; secondly, a study of prevalence and potential users of MAS was carried out; and finally, this project presents a study of the mechanisms of provision, prescription and distribution of these devices.
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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ALS</td>
<td>Amyotrophic Lateral Sclerosis</td>
</tr>
<tr>
<td>BMD</td>
<td>Becker Muscular Dystrophy</td>
</tr>
<tr>
<td>CMD</td>
<td>Congenital Muscular Dystrophy</td>
</tr>
<tr>
<td>DD</td>
<td>Distal Muscular Dystrophy</td>
</tr>
<tr>
<td>DMD</td>
<td>Duchenne Muscular Dystrophy</td>
</tr>
<tr>
<td>EDMD</td>
<td>Emery-Dreifuss Muscular Dystrophy</td>
</tr>
<tr>
<td>FSHD</td>
<td>Facioscapulohumeral Muscular Dystrophy</td>
</tr>
<tr>
<td>LGMD</td>
<td>Limb-Girdle Muscular Dystrophy</td>
</tr>
<tr>
<td>MAS</td>
<td>Mobile Arm Support</td>
</tr>
<tr>
<td>MD</td>
<td>Muscular Dystrophy</td>
</tr>
<tr>
<td>MG</td>
<td>Myasthenia Gravis</td>
</tr>
<tr>
<td>MMD</td>
<td>Myotonic Muscular Dystrophy</td>
</tr>
<tr>
<td>MS</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>OPMD</td>
<td>Oculopharyngeal Muscular Dystrophy</td>
</tr>
<tr>
<td>SCI</td>
<td>Spinal Cord Injury</td>
</tr>
<tr>
<td>SMA</td>
<td>Spinal Muscular Atrophy</td>
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</table>
1. INTRODUCTION

1.1. Muscular Dystrophies

The muscular dystrophy (MD) is referred to a group of more than 30 rare genetic pathologies that causes debility and progressive degeneration in the skeletal muscles used to make voluntary movements. The dystrophy is not contagious and cannot be provoked by lesions or activity. The muscular dystrophies as a whole are estimated to affect 250,000 individuals in the United States [1].

Most of the cases of muscular dystrophy occur from spontaneous mutations that are not found in the genes of either parent; this defect can be transmitted to the next generation. Other cases of dystrophy are inherited from the parents and it implies a mutation of gens related to the expression of muscular proteins. There are three ways to inherit the muscular dystrophy [2]:

- Autosomal dominant inheritance: The son receives the altered gen of one of the 22 autosomal chromosome (non-sexual) of the one of the parents.
- Autosomal recessive inheritance: The son receives the altered gen of one of the 22 autosomal chromosome (non-sexual) of both parents.
- Recessive inheritance linked to the X chromosome: Alteration of the X sex chromosome of the mother which is transmitted to the son.

These pathologies vary during the years and can also affect the gastrointestinal system, the endocrine glands, the spine, the eyes and the brain, among others; with these diseases the simplest tasks become difficult, and in the later stages, heart and breathing muscles begin to fail.

There is no specific treatment to stop or reverse any form of muscular dystrophy. Some patients have mild cases that get worse slowly and others suffer a disabling and severe dystrophy. As is said, there is no cure for any muscular dystrophy, but symptoms can be controlled, and complications prevented. Treatment is supportive and may include physical therapy, respiratory therapy, speech therapy, orthopaedic appliances used for support, corrective orthopaedic surgery, and medications including corticosteroids, anticonvulsants, immunosuppressants and antibiotics. Some individuals may need assisted ventilation to treat respiratory muscle weakness or a pacemaker for cardiac abnormalities.
The MD that are analysed in this project are the following: Duchenne Muscular Dystrophy (DMD), Becker Muscular Dystrophy (BMD), Facioscapulohumeral Muscular Dystrophy (FSHD), Oculopharyngeal Muscular Dystrophy (OPMD), Emery-Dreifuss Muscular Dystrophy (EDMD), Limb-Girdle Muscular Dystrophy (LGMD), Congenital Muscular Dystrophy (CMD), Distal Muscular Dystrophy (DD) and Myotonic Muscular Dystrophy (MMD)[3].

1.1.1. Duchenne Muscular Dystrophy

DMD is the most common muscular dystrophy diagnosed during childhood. Duchenne affects approximately 1 out of every 5000 male new-borns in the world [5]. This disorder causes a loss of muscular mass and a debilitation of the muscular function that leads to serious medical problems. Children with DMD may have impairment in the upper limb, an unusual walk, difficulty for running, climbing stairs and getting up from the floor, and eventually both the muscles that help them breathe and the heart will stop working. For these reasons, this pathology significantly limits the autonomy and independence of the patients.

DMD manifests mainly in males because it is inherited in an X-linked recessive pattern (see section 7A for more information). The mutation of the gene is usually transmitted from mother to child; however, it may also occur in people who do not have a family history of Duchenne because spontaneous de-novo mutation can occur in 35% of the cases.

The genetic mutation is located on the DMD locus Xp21 gene, the largest known human gene [3]. This gene provides instructions for making a protein called dystrophin. In skeletal and cardiac muscles, dystrophin is part of a protein complex that work together to strengthen muscle fibres and protect them from injury as muscles contract and relax. Therefore, dystrophin is needed for the muscles to work properly, without it, muscle cells become damaged and weakened (see section 7A for more information).

Until a few years ago, young adults with Duchenne usually died before the age of 30 due to this type of complications, but currently with the appropriate care and treatment can survive up to 40; Corticosteroids are one example of therapy to slow the progression of the disease.

Muscle loss in DMD first starts to be noticed in childhood, with loss of strength, function, and flexibility in the hips, thighs, shoulders, and pelvis. In the teens, these losses begin
progressing to the arms, lower legs, and trunk. Due to the absence of dystrophin in the muscles of the heart and lungs, heart function and breathing are also affected. In addition, some people can have issues with learning and behaviour, resulting from a lack of dystrophin in the brain (see section 7A for more information about Duchenne muscular dystrophy). There are 5 general stages in the progression of the pathology (Table 1):

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical characteristics of DMD patients</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Early ambulatory (childhood) with mild impairment: Gower’s manoeuvre, waddling gait, walking on toes and problems with climbing stairs.</td>
</tr>
<tr>
<td>II</td>
<td>Late ambulatory (adolescent) with high impairment: walking becomes increasingly difficult, more problems climbing stairs and getting up from the floor, and part-time wheelchair use.</td>
</tr>
<tr>
<td>III</td>
<td>Early non-ambulatory (young adult): loss of ambulation, active manual wheelchair use still possible, independent standing, and sitting still possible for some time.</td>
</tr>
<tr>
<td>IV</td>
<td>Late non-ambulatory (adult): independent electric wheelchair use but decline of upper limb function and ability to sit independently.</td>
</tr>
<tr>
<td>V</td>
<td>Non-ambulatory with confinement to bed: loss of independent mobility and hand function preserved on a low level.</td>
</tr>
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Table 1. Patient/parent self-evaluated clinical severity stages. Reproduced and modified from Walter et al. [5].

Orthopaedic devices and assistive technology (e.g., canes, braces and wheelchairs) may become necessary to aid walking and may improve the ability to move and take care of oneself. Children diagnosed with DMD should be monitored regularly for potential heart involvement. An enlarged, weakened heart (dilated cardiomyopathy) may be treated with medications, but in severe cases a heart transplant may be necessary. In some individuals, severe respiratory distress may require the use of ventilators to assist breathing, especially during the night and as the disease progresses [8].

In the following diagram (Figure 1) the progression of the disease and its symptoms are displayed, also the assistive technology and therapies involved in each stage of the life are described. This thesis focuses on mobile arm supports as assistive technology for patients with DMD and other related pathologies.
Figure 1. Disease Progression and Assistive Technology used by people with DMD as function of time. Reproduced and modified from Lobo-Prat. [9].

### 1.1.2. Pathologies that cause muscular weakness

All muscular dystrophies are inherited disorders characterized by variable degrees and distribution of muscle wasting and weakness.

BMD is the less severe form of DMD. It is also caused by a mutation in the dystrophin gene and the muscle wasting and weakness is similar to DMD. BMD also follows X-linked inheritance, so it mostly affects males, but some female carriers are affected too. However, it is less common because its prevalence is three or four times lower than DMD. BMD usually begins in the teens or early twenties but can begin later and symptoms vary greatly between affected individuals. Consequently, the symptoms of these two disorders are similar, but most cases of BMD are less severe.

The main difference between DMD and neurological disorders (such as stroke or spinal cord injury) is that the neural pathways of DMD are intact, and the motor disorder is present only on the muscles. Nevertheless, some symptoms of DMD are similar to neurological disorders because of the deterioration of the muscles, such as contractures, fatigue, and coordination or postural problems.

From an economic point of view, it is very relevant to also look to other pathologies with similar needs that may also require from upper limb assistive technology. For this reason,
not only muscular dystrophies are analysed, but also other pathologies can be the target of assistive technology to increase the autonomy and independence of the patients; said pathologies are the following: Spinal Muscular Atrophy (SMA), Amyotrophic Lateral Sclerosis (ALS), Myasthenia Gravis (MG), Multiple Sclerosis (MS), Spinal Cord Injury (SCI) and stroke.

1.2. Mobile Arm Supports

People with muscle weakness need assistive technology to improve their autonomy and independence. When the muscle problems are located on the upper limb, MASs can be used to improve the mobility of the arms in order to carry out the daily activities like eat, brush their teeth, carry the backpack or wallet or simply raise their finger to ask something to the teacher. But their usage not only increases the autonomy of the patients, it improves the rehabilitation of the upper limb tissues.

Without these devices the tissues became less used, generating inactivity and in consequence secondary effects like the formation of skeletal deformities or contractures in the arm joints (shoulders, elbows or wrists). There is evidence that suggests that the use of MASs can also have a therapeutic effect and delay the functional deterioration of people with muscular dystrophy. This evidence is supported by Jansen et al. [10], which shows that the use of assistive technology may decline the deterioration of the muscle due to their disuse; this study involves cycling exercises for arms and legs. Also, the increase of the patient activity can translate to a less dedication time for the family, helpers, rehabilitators and in consequence a decrease of the burden cost of the therapies and treatments involved on the pathologies.

MASs can be classified in three subcategories: passive arm supports (also known as body-powered devices), actively adjustable passive arm supports, and active arm supports (also known as robotic arm supports). Also, can be mounted in a table or in a wheelchair. Three examples of MASs are shown in Figure 2. These devices are described in more detail in the results section where an inventory of commercially available MASs (Table 2) is showed.

From the commercially regulatory point of view, MASs are under the old Regulation described in Council Directives 93/42/EEC (regarding medical devices) and 90/385/EEC (regarding active implantable medical devices). Nowadays, this regulation is changing, and the new Regulation 2017/745 will be completely implemented on 2020. Actually, in Spain,
the Real Decreto 1591/2009 is in force, so it is currently regulating medical devices under the old Regulation, but a new Real Decreto will be introduced according to the new Regulation 2017/745. This regulation should be accomplished to obtain the CE marking to make devices marketable around the European Union members. This information will be explained in more detail in the Results section 3.3.1.

![Examples of commercially available mobile arm supports. (a) Passive: Jaeco WREX (Jaeco Orthopaedics, USA) (b) Actively Adjustable: Armon Elemento (Armon Products, Netherlands), and (c) Active: MyoPro (MyoMo, USA).](image)

**Figure 2.** Examples of commercially available mobile arm supports. (a) Passive: Jaeco WREX (Jaeco Orthopaedics, USA) (b) Actively Adjustable: Armon Elemento (Armon Products, Netherlands), and (c) Active: MyoPro (MyoMo, USA).

### 1.3. Problem definition & Objectives

Patients with muscle weakness in the upper limb need arm orthoses (i.e. MAS devices) to allow the performing of daily life activities, in the case of DMD this type of technology is needed at the age of twelve-thirteen. A relevant point to take into account is the help in form of subventions of governments to make these devices accessible to the patients with these diseases, due to the expensive cost of aforementioned technology.

After a preliminary research is known that in Spain there are no commercially accessible MASs for patients with muscle weakness and these devices are not found in the catalogue of assistive technology prescribed by the National Health System. Otherwise, there are other countries (e.g. Netherlands, Germany, United Kingdom and USA among others) that present several companies working on the commercialization and distribution of this type of devices,
and in consequence, the government of these countries facilitates the access of these devices to patients with muscular dystrophy or similar pathologies through a medical prescription under public subventions.

The aim of this thesis is to carry out a technical feasibility market study of mobile arm supports for patients with muscle weakness in Spain. The investigations towards this goal led to the formulation of the following question/objectives:

<table>
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<th>Research questions and objectives</th>
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<td>III</td>
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<td>IV</td>
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To start with the project a questionnaire for patients and experts on the field was developed to have a quick review of the current field situation (see section 7D). The main conclusion of the questionnaire was that MASs are not known nor commercialized in Spain.

2. METHODOLOGY

This project is divided into three parts and to carry out them an extensive bibliographic research was developed, also obtaining information from different sources explained in further sections. To carry out the project and achieve the defined objectives, the following materials and methodology are applied:

2.1. Inventory of commercially available Mobile Arm Supports

The objective of the first part of the thesis was to develop an inventory of commercially available MASs that are under development or in the market including an analysis of the characteristics and relevant features of those devices; a comparison of these features was carried out to determine which are the more optimum devices to be tested and examined in patients. The studied characteristics are the following: manufacturing location, countries of
distribution, dimensions, weight, weight compensation, price, limitations, specific features and technology involved in the device functionality (passive, semi-active or active devices).

To do the preliminary search of the current devices an internet search was performed in order to obtain the direct contact (i.e. email or phone) of manufacturing companies of the assistive devices, the results of the search involve the medical companies or developers described in Table 6 (see section 7B). The rest of the information of the current MASs was retrieved from the following sources: websites of companies and distributors, scientific papers about reviews and effectiveness studies, research centres, distributors of assistive technology, rehabilitation institutions, orthopaedics, developing and manufacturing companies, experts on the field and patients suffering from the target pathologies. Table 6 (see section 7B) also presents the sources of information used to obtain the required information for the following parts of the project.

2.2. Analysis of prevalence of the pathologies and potential users

The second part of the thesis had the objective to develop an analysis of the epidemiology (i.e. incidence and/or prevalence) of the pathologies the patients of which can be the target of MASs; following the obtained results of the analysis a market size study was developed to determine the potential users of the devices in Spain. The implemented methodology for this part is described below.

2.2.1. Data search

The data of the prevalence and incidence was retrieved by searching on state-of-the-art studies and reviews as is described before, also searching on scientific data, world diseases registries (treat-NMD) and, contacting associations and foundations for patients (e.g. Duchenne Parent Project España). Hand searches of reference lists of identified articles were also conducted. The searched sources present a wide variation in the methodology applied to determine the prevalence and incidence of the pathologies; all of the information is verified and cited in other articles. It is important to take into account the likely variation in prevalence by country, so the affected population of each disease can vary depending on the city. Therefore, the values showed in this study can be diverted depending on the situation. When the data was different from different sources, the research impact of publications was assessed, also we considered the number of citations, and we compared authors, countries, and research institutions, to select the proper and more reasonable data.
The keywords used to search in databases in order to obtain the values of prevalence and incidence are defined below and were combined during the search to improve the results:

- **Pathologies:** Duchenne, Becker, Limb-Girdle, Facioscapulohumeral, Emery-Dreifuss, Limb-Girdle, congenital, distal, myotonic, muscular dystrophy, spinal muscular atrophy, amyotrophic lateral sclerosis, myasthenia gravis, multiple sclerosis, spinal cord injury, stroke and neuromuscular disorders.

- **Keywords:** Prevalence, incidence, burden cost, epidemiology, literature review, literature analysis, systematic review, bibliometric study, potential users, affected individuals, meta-analysis, upper limb, upper extremity and muscle weakness.

### 2.2.2. Inclusion criteria

The values of prevalence (i.e. number of affected people per population) and incidence (i.e. number of affected individuals per year) were searched for Spain and World context. The Figure 3 shows the flow chart followed to include or excluded the retrieved bibliographic data used to carry out the analysis of affected people with muscle weakness.

![Figure 3: Flow chart of study inclusion of retrieved data from the bibliographic research.](image)

When specific Spanish data was not available, it was considered the information for studies about European countries with similar situation as Spain, in terms of total population, ethnicity and social similarities. European countries with these characteristics are United Kingdom, Netherlands, Italy and France. These countries were also selected because are involved on the market of assistive technology like MASs, in terms of manufacturing or distribution. Also, patient registries were studied if they met the inclusion criteria.
The identified data present studies published between 2005 and 2019. Studies were excluded if they were published prior to 2005. Nevertheless, in cases were no data was found with publications between 2005 and 2019, the selected data was recovered from reasonable studies with a high impact index and feasible values; this last incorporated data were retrieved from studies between 1991 and 2005.

Titles and abstracts for all citations were assessed for possible inclusion in the review. Full articles or full website information were obtained and analysed for the selected sources. Publications reporting similar data were compared and merged.

### 2.2.3. Estimation of affected people

To calculate the number of affected individuals by the analysed pathologies, and in consequence the number of potential users of the MASs, mathematical approximations based on the bibliography were implemented (Equation 1). Other mathematical processes were elaborated in collaboration with of Dr. Roberto Elosua (epidemiologist of Institut Hospital del Mar d’Investigacions Mèdiques -IMIM-).

The following formula (Equation 1) was implemented in order to calculate the number of affected individuals for each pathology, that depends on the population considered for each value of prevalence or incidence:

\[
\text{Affected Individuals} = \frac{\text{Population} \cdot \text{Prevalence}}{100,000}
\]

**Equation 1.** Number of people affected by a pathology taking into account the total population of the epidemiology location and the prevalence per 100,000 of said pathology.

The total population of Spain was fixed on 46,500,000 people (approximated and rounded mean of the last 5 years population values), being 50.6% females (23,529,000 people) and 49.4% males (22,971,000 people); according to the WorldBank of the United Nations [14].

In the calculus of the people suffering from Duchenne we used the following parameters: The prevalence value of DMD in Spain is 1:4,000 or 25:100,000 males between 0 and 30 years. Considering that this epidemiology value does not consider the whole Spanish population, to calculate the Spanish affected individuals by DMD, the parameter population was fixed on 7,711,387 (approximated mean of the last 20 years, according to the Demographic DataBase of the Instituto Nacional de Estadística de España [15]), that are the number of Spanish males between 0 and 30 years. All other calculations for the different
pathologies are determined in terms of Spain’s total population. All other calculations follow the parameters mentioned before Duchenne.

Due to the non-exactitude of the prevalence and incidence values, in cases where there are different values for the same pathology, we fixed ranges of the retrieved values (i.e. minimum and maximum recovered values) in order to avoid deviations and to adjust approximations of the affected individuals by a pathology.

In cases (DMD and MS) where we obtained data from disease foundation registries (Duchenne Parent Project and Treat-NMD), the calculated value of the affected individuals was compared with the registry data to certificate the results.

2.2.4. Analysis and estimation of potential users

After implementing the methodology explained above and calculating all values of affected people, we carried out an analysis of the data. The comparison of the whole MDs values was implemented, because some studies show that considering the whole group of pathologies, the epidemiology study should be more significant that considering each pathology by itself.

Regarding MDs, SMA, ALS, all affected individuals can be considered as potential users, but for MG, MS, SCI and stroke pathologies, only a percentage of the affected individuals can be considered as potential users, because not all patients with these pathologies suffer from muscle weakness in the upper limb and cannot be considered potential users of MASs. For the cases of MG, MS, SCI and stroke, we searched the percentage of patients that suffer muscle weakness on the upper limb to include the resulting values on the study.

2.3. Mechanisms of distribution to access Mobile Arm Supports

This chapter presents an investigation of the mechanisms and processes involved to make these devices accessible to the patients in Spain. Firstly, we conducted an investigation of the regulatory affairs that assistive technologies need to be introduced in the market in the European Union. Secondly, we studied the process of prescription, distribution and subvention of the devices and their associated requirements involved to be accessible in Spain. Thirdly, a comparison of the Spanish and Dutch System (from an economic-social point of view) was developed to determine the reasons of the lack of MASs in the Spanish health system, and why MASs are accessible in Netherlands. Finally, we investigated the
burden cost, and economic and social factors that are generated with the progression of the
diseases, in order to assure that MASs would be a good start point to increase savings on the
burden and which are the methods to analyse and quantify the burden cost. To carry out this
part of the thesis, networking is developed by contacting state and health institutions, health
and governmental leaders, distribution and fabrication companies, rehabilitation and
research centres, also searching on institutional directives and legal documentation. The
sources of information are described in Table 6 in Section 7B.

3. RESULTS

In this section the results of the thesis are exposed by following the organization in parts and
subsections described on the methodology section and are discussed further in section 4.

3.1. Inventory of commercially available Mobile Arm Supports

In order to analyse the commercially available MASs an inventory was generated by carrying
out a systematic literature analysis. After the bibliographic search the following sources were
analysed; also, we contacted with 12 manufacturing companies.

- 18 scientific papers about effectiveness or feasibility of MASs
- 26 product brochures with characteristics of MASs
- 50 websites of the manufacturing and distributing companies of MASs

This study had been able to identify that a total number of 10 companies: Companies from
Netherlands are manufacturing a total number of 15 MASs, 6 devices are manufactured in
United States of America (USA), 2 in Canada and 3 in United Kingdom (2 of them also in
USA). In result there are a total number of 24 MASs available in the market, located as is
shown in Figure 4.

![Figure 4](image)

**Figure 4.** Number of MASs depending on the location of their manufacturing company.
The results of this investigation are analysed and described in the inventory showed in Table 2. The resulting devices are shown in Figure 10 (see section 7C). Figure 5 shows the analysed MASs, their price and manufacturing location; Figure 6 also shows the type of the involved technology in each device depending on their price. The price of the devices is approximated and considers only the cost of the device per se, because the final cost for patients or entities depends on the installation, maintenance, travel taxes and electronic integration.

**Figure 5.** Graph comparison of the prices in Euros of existing mobile arm supports depending on the location of the manufacturing company.

**Figure 6.** Graph comparison of the prices in Euros of existing mobile arm supports depending on the location of the manufacturing company and the involved technology in each device.
<table>
<thead>
<tr>
<th>Mobile Arm Support</th>
<th>Company</th>
<th>Weight (Kg)</th>
<th>Price (£)</th>
<th>Location</th>
<th>Distribution</th>
<th>Mounting</th>
<th>Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edero</td>
<td>Armon Products</td>
<td>3.4</td>
<td>3100</td>
<td>NL</td>
<td>AU, NZ, EU, Asia, South America</td>
<td>table</td>
<td>passive</td>
</tr>
<tr>
<td>Pura</td>
<td>Armon Products</td>
<td>6.1</td>
<td>5300</td>
<td>NL</td>
<td>AU, NZ, EU, Asia, South America</td>
<td>wheelchair</td>
<td>passive</td>
</tr>
<tr>
<td>Elemento</td>
<td>Armon Products</td>
<td>6.1</td>
<td>8100</td>
<td>NL</td>
<td>AU, NZ, EU, Asia, South America</td>
<td>wheelchair</td>
<td>actively adjustable</td>
</tr>
<tr>
<td>Ayura</td>
<td>Armon Products</td>
<td>6.4</td>
<td>15800</td>
<td>NL</td>
<td>AU, NZ, EU, Asia, South America</td>
<td>wheelchair</td>
<td>actively adjustable</td>
</tr>
<tr>
<td>iFloat Arm Support</td>
<td>Assistive Innovations</td>
<td>~3.5</td>
<td>3000</td>
<td>NL</td>
<td>USA, EU</td>
<td>wheelchair – table</td>
<td>passive</td>
</tr>
<tr>
<td>iFloat Powered Assist</td>
<td>Assistive Innovations</td>
<td>~3.5</td>
<td>5500</td>
<td>NL</td>
<td>USA, EU</td>
<td>wheelchair – table</td>
<td>actively adjustable</td>
</tr>
<tr>
<td>iFloat NG Dynamic</td>
<td>Assistive Innovations</td>
<td>no data</td>
<td>under development ~8000</td>
<td>NL</td>
<td>USA, EU</td>
<td>wheelchair – table</td>
<td>actively adjustable</td>
</tr>
<tr>
<td>X-Ar</td>
<td>Equipois</td>
<td>2.5</td>
<td>2500</td>
<td>USA</td>
<td>North EU</td>
<td>chair</td>
<td>passive</td>
</tr>
<tr>
<td>Dynamic Arm Support</td>
<td>Exact Dynamics</td>
<td>2</td>
<td>1000 – 1500</td>
<td>NL</td>
<td>USA, EU, Asia</td>
<td>wheelchair – table</td>
<td>passive</td>
</tr>
<tr>
<td>Downing</td>
<td>Focal Meditech</td>
<td>~3.5</td>
<td>3000</td>
<td>NL</td>
<td>USA, NZ, AU, CA, EU</td>
<td>table</td>
<td>passive</td>
</tr>
<tr>
<td>Top/Help</td>
<td>Focal Meditech</td>
<td>~3.5</td>
<td>5000</td>
<td>NL</td>
<td>USA, NZ, AU, CA, EU</td>
<td>wheelchair</td>
<td>actively adjustable</td>
</tr>
<tr>
<td>Sling &amp; Balancer</td>
<td>Focal Meditech</td>
<td>no data</td>
<td>6000 – 8000</td>
<td>NL</td>
<td>USA, NZ, AU, CA, EU</td>
<td>wheelchair</td>
<td>passive</td>
</tr>
<tr>
<td>Gowing &amp; Darwing</td>
<td>Focal Meditech</td>
<td>6.8</td>
<td>13000 – 15000</td>
<td>NL</td>
<td>USA, NZ, AU, CA, EU</td>
<td>wheelchair</td>
<td>actively adjustable</td>
</tr>
<tr>
<td>Exo Arm</td>
<td>Focal Meditech</td>
<td>7 – 8</td>
<td>under development ~30000 – 40000</td>
<td>NL</td>
<td>USA, NZ, AU, CA, EU</td>
<td>wheelchair</td>
<td>active</td>
</tr>
<tr>
<td>Jaeco WREX</td>
<td>Jaeco</td>
<td>2</td>
<td>2000 – 2800</td>
<td>USA</td>
<td>USA</td>
<td>wheelchair</td>
<td>passive</td>
</tr>
<tr>
<td>MultiLink DAS</td>
<td>Jaeco</td>
<td>2</td>
<td>1000 – 2000</td>
<td>USA</td>
<td>NZ, AU, USA, Asia</td>
<td>wheelchair – table</td>
<td>passive</td>
</tr>
<tr>
<td>DAS O110</td>
<td>Kinova Robotics</td>
<td>3.4</td>
<td>~3000</td>
<td>CA</td>
<td>CA, USA, EU, Asia</td>
<td>table</td>
<td>passive</td>
</tr>
<tr>
<td>DAS O540</td>
<td>Kinova Robotics</td>
<td>6.1</td>
<td>~5000</td>
<td>CA</td>
<td>CA, USA, EU, Asia</td>
<td>wheelchair</td>
<td>passive</td>
</tr>
<tr>
<td>Neater Arm Support</td>
<td>Neater Solutions</td>
<td>3</td>
<td>3200</td>
<td>UK</td>
<td>North EU</td>
<td>wheelchair</td>
<td>actively adjustable</td>
</tr>
<tr>
<td>MyoPro</td>
<td>MyoMo</td>
<td>2.5 – 3</td>
<td>30000 – 40000</td>
<td>USA</td>
<td>AU, NZ, EU, South America</td>
<td>arm wearable</td>
<td>active</td>
</tr>
<tr>
<td>Saebo Mass</td>
<td>Saebo</td>
<td>5</td>
<td>3800 – 7200</td>
<td>USA – UK</td>
<td>USA, EU</td>
<td>table</td>
<td>passive</td>
</tr>
<tr>
<td>Saebo Mass Mini</td>
<td>Saebo</td>
<td>3.5</td>
<td>2300 – 3600</td>
<td>USA – UK</td>
<td>USA, EU</td>
<td>table</td>
<td>passive</td>
</tr>
</tbody>
</table>

Table 2. Inventory of mobile arm supports in the market or under development: distribution location, manufacturing location, weight, price, type of mounting and type of mechanics (i.e., technology). WREX: Wilmington Robotic Exoskeleton Arm; DAS: Dynamic Arm Support. CA: Canada, AU: Australia, NZ: New Zealand, USA: United States of America; UK: United Kingdom, EU: Europe, NL: Netherlands.
3.2. Analysis of prevalence of the pathologies and potential users

As is shown in Figure 3, the search strategy used to retrieve the data of the prevalence and incidence of the pathologies mentioned in section 2.2.1 resulted in a total of 105 sources of information from scientific papers or websites making reference to scientific articles and 5 national patient registries. After applying the inclusion criteria described in section 2.2.2, we analysed 25 relevant scientific papers and 2 registries, which meet the inclusion criteria, and we excluded 81 scientific sources and 3 patient registries because they do not meet the inclusion criteria. The resulting included sources are exposed in Table 3 as key references.

The number of affected people in Spain for each pathology was calculated by following the methodology explained in section 2.2.3.

To summarize the results of the study, Table 3 shows the number of affected individuals, considering all the pathologies explained in previous sections. Also, Table 3 shows the selected prevalence or incidence range of values, from Spain, England, Italy, Ireland, France or Finland studies, including the minimum and maximum values of the range.

3.2.1. Muscular dystrophies

LGMD, FSHD and MMD turn out to be the most prevalent MDs, affecting between 7,808 and 17,685 people approximately. The rest of MDs affect between 1,578 and 6,648 people approximately. Analysing the affected people for the whole MDs, the result is approximately between 9,386 and 24,333 people; on the other hand, considering the prevalence value extracted from an English study which is between 19.8 and 25.1 per 100,000 people, the expected people to be affected by MDs is approximately between 9,207 and 11,671. In conclusion, taking into account all MDs, the value of the expected and calculated affected individuals is at least 9,000, and looking at the results of the maximum possible values, a total of approximately 24,000 individuals may be affected by MDs in Spain.

3.2.2. Spinal Muscular Atrophy and Amyotrophic Lateral Sclerosis

In spite that the patients with SMA and ALS could suffer from different degree of muscle weakness, in some point of their life, these patients will need the support of arm orthoses, so all of them could be considered as potential users of MASs. As a result, summing both
On the other hand, not all patients with MG, MS, SCI and stroke are susceptible to have muscle weakness in the upper limb, so a more specific study is required.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Prevalence per 100,000 in European countries</th>
<th>Prevalence per 100,000 in the World</th>
<th>Affected people in Spain</th>
<th>Key references</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMD</td>
<td>Spain 25 b</td>
<td>20 – 28.57 c</td>
<td>600 e – 1928</td>
<td>[21,22]</td>
</tr>
<tr>
<td>BMD</td>
<td>–</td>
<td>1.53 a 3.33 e</td>
<td>351 - 376</td>
<td>[23,24]</td>
</tr>
<tr>
<td>LGMD</td>
<td>England 2.27 Spain</td>
<td>0.9 – 2.3 2.22 – 6.89</td>
<td>1056 – 3209</td>
<td>[25,26,27]</td>
</tr>
<tr>
<td>FSHD</td>
<td>England 3.95 Italy Netherlands 3.2 – 4.6</td>
<td></td>
<td>1837 – 2139</td>
<td>[26,28,29]</td>
</tr>
<tr>
<td>OFMD</td>
<td>England 0.13 France 0.13</td>
<td>–</td>
<td>60 – 465</td>
<td>[26]</td>
</tr>
<tr>
<td>EDMD</td>
<td>England 0.13 Ireland 0.13</td>
<td>1-2</td>
<td>60 – 205</td>
<td>[26,30]</td>
</tr>
<tr>
<td>MMD</td>
<td>England 10.57 Spain 26.53</td>
<td>12.5</td>
<td>4915 – 12337</td>
<td>[25,32]</td>
</tr>
<tr>
<td>CMD</td>
<td>England 0.76 – 0.9</td>
<td>–</td>
<td>353 – 419</td>
<td>[25,26]</td>
</tr>
<tr>
<td>DD</td>
<td>England 0.33 Finland 0.33</td>
<td>–</td>
<td>154 – 3255</td>
<td>[25,31]</td>
</tr>
<tr>
<td>SUM of MD</td>
<td>–</td>
<td>–</td>
<td>9386 – 24333</td>
<td>–</td>
</tr>
<tr>
<td>MD</td>
<td>England 19.8 – 25.1</td>
<td>–</td>
<td>9207 – 11671</td>
<td>[29]</td>
</tr>
<tr>
<td>SMA</td>
<td>England 1.87</td>
<td>1 – 2 10 – 16.67 d</td>
<td>465 – 930</td>
<td>[25,33,34]</td>
</tr>
<tr>
<td>ALS</td>
<td>Europe 1.7 – 2.3 d Spai 1.1 – 8.2 2.08 – 2.2 d</td>
<td>1628 – 3720</td>
<td></td>
<td>[35,36,37,47]</td>
</tr>
<tr>
<td>MG</td>
<td>Italy 12.96 – 24 Spain 7 – 20</td>
<td></td>
<td>9300 – 15293</td>
<td>[38,39,40,47]</td>
</tr>
<tr>
<td>MS</td>
<td>Europe &gt;100 102</td>
<td>100 – 200 5 – 6 d</td>
<td>42900 e – 46500</td>
<td>[41,42]</td>
</tr>
<tr>
<td>SCI</td>
<td>Spain 2.17 – 2.35 py</td>
<td>–</td>
<td>1009 – 1093 py</td>
<td>[48,49]</td>
</tr>
<tr>
<td>STROKE</td>
<td>Spain 112 – 141 py</td>
<td>–</td>
<td>52080 – 65565 py</td>
<td>[50,51]</td>
</tr>
</tbody>
</table>

a. males ; b. males (0-30 years) ; c. male births per year ; d. live births per year ; e. data from registries ; py. per year ; -. no data

Table 3. Prevalence of pathologies that cause muscle weakness per 100,000 individuals, from studies or registries, reporting epidemiology for the population of countries in Europe and in the World, and affected people of those pathologies in Spain.
3.2.3. Myasthenia Gravis, Multiple Sclerosis, Stroke and Spinal Cord Injury

The main symptom of MG is a progressive deterioration of the muscles, being the face the main affected region, in spite of this, 20% of patients with MG could have muscle weakness in the upper extremities during their life [66], so, the number of potential users of MASs affected by MG could be between 1,860 and 3,059.

In a study conducted by Holper et al. [57] abnormal findings in muscle power, involving upper extremity structures, were found in more than 50% of people suffering MS. These patients had loss of fine motor movements (67%), difficulty in lifting and transporting objects (59%) and decrease in writing ability (56%), among others [67]. On the other hand, two other studies reflect that 66% of the MS population have upper limb dysfunctions and disability that dramatically affect the level of independence of many daily living activities, like eating, dressing and grooming [68,69].

Being 42,900 – 46,500 the range of affected people by MS in Spain and considering the three studies commented above which show that 50% – 66% is the percentage of patients with upper limb muscle disability, the estimated number of potential users of MASs with MS is between 21,450 and 30,690.

Reduced upper extremity function is one of the most common impairments after stroke, since in some studies was reported that approximately 70-80% of patients in the acute stage presents muscle weakness in the upper limb [45]. Other studies exposed that the prevalence of upper extremity disability is present in about 50% to 70% of the individuals who have suffered a stroke in the acute phase and remains in about 50% after three months [43,44]. Finally, another study exposed that muscle force of upper limb a short time after stroke involves a 39% decrease of the function of the arms, generating muscle weakness [46].

Regarding that between 50% and 80% of the people that suffer stroke present reduced upper extremity function, it can be considered that every year a number between 26,040 and 52,452 individuals could be potential users of MASs. Nevertheless, people suffering from stroke only have muscular dysfunction in one side of the body, being the other side of the brain the reason of the dysfunctionality; therefore, these people can use the opposite arm and hand to do daily activities, so in this case, not all estimated individuals would use arm orthoses.

SCI is damage to the spinal cord that causes temporary or permanent disfunction. Symptoms can include muscle weakness in the parts of the body served by the level of the spinal cord
affected by the injury. The symptoms depend on the location and severity of the lesion, resulting in numbness, paralysis or incontinence. Complications can include muscle atrophy.

It is difficult to determine the exact percentage of people that would suffer muscle weakness in the upper limb due to its accidental causes but studies reported that 50% of SCI cases are cervical, generating some impairment on the arm and hand, being C5 the commonest injury level [55]. Also, levels C6 and C7 are related with upper limb affectation [56].

As a result, some people suffering from SCI could suffer from muscle weakness in the upper extremities, so they could become users of MASs. It was estimated that there would be between 1,009 and 1,093 new cases of SCI each year in Spain; considering the approximation of 50% upper limb affectations, the number of potential users would be 505 – 547.

Also, we can consider that people with mobility problems of the upper limb after breast surgery, patients with general back and shoulder pain or patients with Rheumatism would also use MASs as rehabilitation technology in the short term.

The commented results are described in Table 4, where we show the number of affected people in Spain for each type of pathology, the percentage of people suffering muscle weakness in the upper limb for each pathology, the potential users of MASs and the key resources used to obtain the results.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Affected people in Spain</th>
<th>% with muscle weakness in the upper limb</th>
<th>Potential users</th>
<th>Key resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD</td>
<td>9386 – 24333</td>
<td>100</td>
<td>9386 – 24333</td>
<td>–</td>
</tr>
<tr>
<td>SMA</td>
<td>465 – 930</td>
<td>100</td>
<td>465 – 930</td>
<td>–</td>
</tr>
<tr>
<td>ALS</td>
<td>1628 – 3720</td>
<td>100</td>
<td>1628 – 3720</td>
<td>–</td>
</tr>
<tr>
<td>MG</td>
<td>9300 – 15293</td>
<td>20</td>
<td>1860 – 3059</td>
<td>[66]</td>
</tr>
<tr>
<td>MS</td>
<td>42900 – 46500</td>
<td>50 – 66</td>
<td>21450 – 30690</td>
<td>[67,68,69]</td>
</tr>
<tr>
<td>TOTAL</td>
<td>–</td>
<td>–</td>
<td>34789 – 62732</td>
<td>–</td>
</tr>
<tr>
<td>SCI</td>
<td>1009 – 1093</td>
<td>50</td>
<td>505 – 547 py</td>
<td>[55,56]</td>
</tr>
<tr>
<td>STROKE</td>
<td>52080 - 65565</td>
<td>50 – 80</td>
<td>26040 – 52452 py</td>
<td>[43,44,45]</td>
</tr>
<tr>
<td>TOTAL PY</td>
<td>–</td>
<td>–</td>
<td>26545 – 52999 py</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 4. Potential users of MASs in Spain. Calculations considering the percentage of individuals suffering muscle weakness in the upper limb; –. no data; py. per year.
As is shown in Table 4, we found that summing the values of the approximations discussed above without involving the results of SCI and stroke, between 34,789 and 62,732 patients would be potential users of MASs in Spain. On the other hand, considering the incidence of SCI and stroke, every year between 26,545 and 52,999 new users of MASs can appear.

Finally, some of the studied pathologies remain undiagnosed. Also, the tendency in the last years shows that the number of individuals suffering some of the aforementioned pathologies has appeared to increase. As a result, the number of potential users will increase in the short term.

3.3. Mechanisms of distribution to access Mobile Arm Supports

3.3.1. Regulatory affairs in the European Union

Medical devices are regulated by a harmonized health regulation in the European Union. Nowadays, this regulation is changing, and the new documentation will be implemented on 2020. The new regulations represent a major change in the sector which will require new and stricter obligations for all market operators in order to achieve increased transparency and traceability guarantees in the market.

Entering on detail, in May 2017, the new Regulation 2017/745 [70] of the European Parliament and of the Council of 5 April 2017 on medical devices was published, amending Directive 2001/83/CE, Regulation (CE) No 178/2002 and Regulation (CE) No 1223/2009 and repealing Council Directives 90/385/EEC (regarding active implantable medical devices) and 93/42/EEC (regarding medical devices), which will apply on 26 May 2020, ending the transitional period. In the transitional period from 26 May 2017 to 26 May 2020 both regulatory frameworks may coexist, and certificates may be issued in accordance with the provisions of the new Regulation or the old Directives 90/385/EEC and 93/42/EEC. In the latter case, the certificates will have a maximum validity of 5 years and will be considered null and void as from 27 May 2024. In any case, any product placed on the market in accordance with the requirements of the old Directives may only continue to be placed on the market or put into service until 27 May 2025. Nowadays, in Spain, the Real Decreto 1591/2009 [71] of 16 October 2009 is in force, so it is currently regulating medical devices, but a new Real Decreto will be introduced before the transition period finishes, according to the new Regulation 2017/745.
In terms of the modification, the new Regulation presents a concretion and new definition of medical devices, including computer programs, implants or reagents, and establishes the need for the manufacturer to have foreseen a specific medical purpose, admitting new purposes such as the "prediction or prognosis of diseases or the investigation, substitution or modification of a physiological or pathological state". In addition, the new Regulation involves the creation of the European Database on Medical Devices (EUDAMED), a product register in which all medical devices will be described in detail.

One of the major news of the new Regulation is the inclusion of some products without medical aim: aesthetic products (contact lenses or facial fillers), equipment emitting high intensity electromagnetic radiation and equipment for brain stimulation.

Finally, the new Regulation presents a reinforced system of guarantees. For example, the post-marketing guarantees with the establishment of an electronic surveillance system which requires notification of serious incidents and corrective actions; the obligation for manufacturers to have an adequate post-marketing monitoring system for each product to improve the determination of the benefit-risk ratio; risk management; updating of information on design, manufacture, instructions for use; detection of preventive measures and detection of trends, and the obligation to issue a post-marketing monitoring report.

CE marking is a regulatory affair implemented in the European Union for which any product could be commercialized in all countries of the European Union without further evaluation. This marking declares that the product meets the essential requirements (health, safety and environmental protection) of the Directives that apply to it in the European Union through the old Directives 90/385/EEC and 93/42/EEC or the new Regulation 2017/745. The conformity assessment of a product for CE marking (European Conformity) varies according to the risk class of the medical device (I, IIa, IIb and III). For medical devices all Class IIa, IIb and III devices as well as some specific Class I devices, require the intervention of a notified body; so, the manufacturer who wants to market one of these medical devices in Europe, must contact a notified body. In Spain, the only body designated by the Ministerio de Sanidad, Consumo y Bienestar Social to evaluate medical devices is the Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) itself, notified body number 0318 [72].

To obtain the CE marking, companies must present documentation on the design, manufacturing processes, performance tests, clinical trials, packaging materials, the technical
standards they comply with and the information accompanying the product. The notified body evaluates this documentation in addition to carrying out an audit in the facilities where the product is manufactured. If the result of the checks is favourable, it issues a certificate of conformity which allows the notified body number to be affixed together with the CE mark on the product, indicating that it complies with the requirements of the regulation.

The process of certification is organized as follows: a) Determination of the class of the device; b) Verification of essential requirements; c) Compile technical information files; d) Interaction with notified body (if needed); e) Quality management procedure; f) Declaration of conformity; and finally, g) Affixing CE marking.

Referring to MASs, they are considered Class I Medical Device, or in other words a medical device with minimal risk, and their currently required certification is under the directive 93/42/EEC for passive arm supports and also 90/385/EEC for actively adjustable or active arm supports, due to their electrical features, according to the old Regulation. However, as it is mentioned before, the certificates will have a maximum validity of 5 years and will be considered null and void as from 27 May 2024. In any case, any product placed on the market in accordance with the requirements of the old Directives may only continue to be placed on the market or put into service until 27 May 2025, so after these dates, MASs should be certified according to the new Regulation 2017/745. These devices would need the Declaration of Conformity of the European Union (according to Annex IV) and the Technical Documentation (according to Annexes II & III).

**Figure 7.** CE marking and mechanisms of regulation of MASs as Class I Medical Device under the European Union health regulation by certificating the device via AEMPS as notified body 0318 of the Ministerio de Sanidad, Consumo y Bienestar Social of the Spanish Government. Considering the transition stage from Real Decreto 1591/2009 to the next Real Decreto adjusted to the EU Regulation 2017/745 of medical devices.
If a medical device has already obtained the CE marking and aims to be distributed in other countries of the European Union, the distributing company only needs to have access to the aforementioned certified documentation if any national institution of the target country requires it.

3.3.2. Prescription and provision in Spain

To understand the mechanisms of prescription and provision of arm supports, it is important to know that these devices are considered orthoprosthetics as assistive technology.

In Spain, the provision of orthoprosthetics is included and described in Annex VI of Real Decreto 1030/2006, of 15 September [73], which establishes the portfolio of common services of the Sistema Nacional de Salud (SNS) and the procedure for updating it, which is described further on. Orthoprosthetic provision is understood as the prescription for the use of medical devices, implantable or not, and it has the purpose of replacing totally or partially a body structure, or to modify, correct or facilitate its function. This provision could be facilitated by the health services or in other cases, and in accordance with the regulations established by the competent health administrations in Spain, which gives rise to economic grants. Orthoprosthetic services include surgical implants, external prostheses, wheelchairs, orthoses and special orthoprostheses. In this last group there are similar assistive technologies like different types of arm braces, but not technical aids of the type of product as MASs, so for the moment, MASs would not be included in the provision of the SNS.

In Spain, the service portfolio is known as Catálogo General de Material Ortoprotésico [74]; referring to the health system in Catalonia, the prescribed items are described in the Catàleg de Prestacions Ortoprotètiques del Servei Català de la Salut [75]; both portfolios show the monetary quantity that can be financed by the health system to cover the cost of the medical device. Most of the devices included in the portfolios are full covered by the SNS. As an example, the subsidy of an electric wheelchair for patients with impairment in the legs is financed with a quantity between 3,100€ and 3,800€, being full covered for its purchase in most cases.

In order to introduce a new product into the service portfolio it is required to follow a process of evaluation and certification of the new technology. This process is carried out by the Ministerio de Sanidad through the Agencia de Evaluación de Tecnologías Sanitarias del Instituto de Salud Carlos III (AETS-ISCIII) in collaboration with other assessment bodies
proposed by the autonomous communities (e.g. CatSalut in Catalonia). This evaluation process takes into account the cost, efficacy, efficiency, effectiveness, safety and health utility of the technology, such as evaluation reports, expert judgement, evaluation records, supervised uses or others.

The devices that aim to be introduced in the service portfolio must contemplate one of the following requirements: a) Represent a substantially new contribution to prevention, diagnosis, therapeutics, rehabilitation, the improvement of life expectancy or the elimination of pain and suffering; b) Be new indications for existing equipment or products; c) Require new specific equipment for its application; d) Significantly modify organizational forms or systems of patient care; e) Affect broad sectors of the population or groups at risk; f) Imply a significant economic impact on the National Health System; and always, g) Meet safety and effectiveness requirements [73].

After the request and if it is favourable, the Ministerio de Sanidad, Consumo y Bienestar Social must publish an order in agreement with the Consejo Interterritorial of the SNS to the proposals for updating formulated by the common benefits, insurance and financing commission of the SNS; being the devices fully or partially financed. In consequence, the patients will be able to apply to obtain the reimbursement through a request document, that is specific for each autonomic community; in this line, the patients need to transact the required documentation (i.e. facultative report provided by the physician or health expert) [76] to their autonomic institution, in order to prove that they need the specific device.

![Figure 8. Mechanisms for the medical prescription of MASs under the National Health System regulation described in Annex VI of Real Decreto 1030/2006, that requires the evaluation by the AETS-ISCHIII and the conformity of an agreement between the SNS and the Ministerio de Sanidad, Consumo y Bienestar Social.](image)
3.3.3. Mechanisms of distribution in Netherlands

Findings of section 2.1 shows that MASs are very common in the Netherlands and there are 16 commercially available MASs in the market, being accessible for patients that need thereof. On the other hand, there is evidence that suggests that those devices are provided under medical prescription and the Dutch health system presents a provision system that gives patients the possibility to acquiring MASs through full grants, being the orthoses freely accessible under health agent prescription.

The health system is organized in such a way that patients pay for compulsory basic health insurance, approximately 100€/month. When patients need some technology, they must be examined by a health agent that evaluates whether the patient meets the requirements under a public established regulation. In favourable case, the expert agent prescribes the device that best suits the need of the patient, and finally, the insurance covers the whole cost of the device if it overcomes an effectiveness evaluation and meets the specific requirements of the patient. In Spain, the assistive technology needs to be prescribed by a health agent after a functional deterioration evaluation. In favourable case, the assistive devices acquired by patients would be covered by subsidies provided by the SNS which are quantified and described in the aforementioned portfolio.

In comparison with Spain, in Netherlands the service portfolio does not present an inventory of specific devices as in the Spanish portfolio. The Dutch portfolio presents a description of the functionality that would be covered by a device, not the specific required device, in such a way that after the medical evaluation, a specific device is selected following the characteristics that are described in the functional guideline of the portfolio. After this, the device is acquired by the patient under the medical prescription and the patient is able to obtain a subsidy to cover the whole costs of the device.

The economic indicators from Netherlands should be considered in order to be compared with the Spanish economy to investigate the main differences and determine if there is a lack in the Spanish health care system to provide assistive technology to patients that need thereof. They are defined in Table 5.
<table>
<thead>
<tr>
<th>Country</th>
<th>Public Health Expenditure</th>
<th>% of the Total Public Expenditure</th>
<th>% of the GDP</th>
<th>Expenditure per capita</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>72,812.9M€</td>
<td>15.14%</td>
<td>6.26%</td>
<td>1,565€</td>
</tr>
<tr>
<td>Netherlands</td>
<td>60,443.6M€</td>
<td>19.31%</td>
<td>8.24%</td>
<td>3,539€</td>
</tr>
</tbody>
</table>

Table 5. Economic indicators of the Health System from Spain and Netherlands in 2017: Expenditure of the Health System; percentage of the total public expenditure by the Health System; percentage of the Gross Domestic Product (GDP) by the Health System; and expenditure per capita for the Health System [79].

3.3.4. Burden cost, social and economic factors

Referring to the evaluation and burden cost of patients, there is a system named Quality-Adjusted Life-Year (QALY) that measures the disease burden, including the quality and the quantity of life lived. In economic terms, is a health evaluation performed at an early stage of development of health technologies, with the objective to inform manufacturers on their potential cost-effectiveness in order to maximize the efficiency of health care research and development. It is also used to estimate the maximum reimbursable price of a specific device.

Muscular dystrophy, compared with other health conditions shows a high negative impact in terms of QALYs in children, as reported by Craig et al. [77], it is the third in terms of higher average QALY loss, after mental disability and cerebral palsy.

One example of the usage of QALY is to determine the possible dedicated cost for each patient considering its pathology characteristics; the incremental cost-effectiveness ratio (ICER) stipulated by the Care Institute of Netherlands is 80,000 €/QALY for patients with DMD or 50,000 €/QALY for pathologies with lower burden cost [80].

Looking at the burden cost of muscular dystrophies, Landfelt et al. [64] shows that the mean per-patient annual direct cost of illness was estimated at between 20,000€ and 50,000€ approximately, 7 to 16 times higher than the mean per-capita health expenditure in the analysed European countries. The total social burden was estimated at between 70,000€ and 107,000€ approximately per patient and annum and increased markedly with disease progression. The corresponding household burden was estimated approximately between 52,000€ and 63,500€. On another study [65], is exposed that lifetime direct medical costs ranged approximately between 245,000€ and 320,000€, total costs between 702,000€ and 802,500€, and total number of QALY between 5.96 and 7.17. See Table 7 in section 7E for more information about the annual cost of patients with DMD in European countries.
All aforementioned reports have the same conclusion: Economic evaluation should be iterative in order to generate progressively firmer estimates of cost-effectiveness and help to maximise the efficiency of health care R&D; also, in order to generate and quantify savings in the health burden of patients suffering muscle weakness.

4. DISCUSSION

4.1. Technical feasibility market study of Mobile Arm Supports for patients with muscle weakness in Spain

The aim of this thesis was to investigate commercially available MASs to determine if these devices are feasible to be introduced in the Spanish market, in order to help people with muscle weakness in the upper limb.

The discussion of the results is organized by referring to the research questions and objectives described in section 1.3:

I Which mobile arm supports are currently in the market or under development in Spain and other countries around the World?

The results of the first part of the study show that there are 24 available devices in the world; the price of these devices vary depending on the implemented technology: the passive devices cost between 1,500€ and 5,500€, the actively adjustable devices can cost up to 15,000€ and the active devices soar to 30,000€ due to their electronic integrated technology. The price is not exact because it can vary due to the travel taxes, the electronic integration and the maintenance, among others. Looking at the location of the manufacturing companies, most of them are from Netherlands, and there are also, some companies distributing devices in USA, but these ones are not selling in Europe in general, probably because the European market is dominated by Dutch companies. These findings are clearly stated in Figures 4, 5 and 6.

Another finding is that in Spain there are no distributors of these devices, whereas, in countries like France, Germany, Belgium or United Kingdom there exist. Another important aspect is that patients with muscle weakness suffer from specific symptoms and the progression and severity of the muscle deterioration changes among patients; as a result, and considering the changes on the functionality of the upper limb muscles, these devices should
not be used by a single patient to be optimally exploited during their life usage. For this reason, it could be useful to incorporate a renting methodology to sell these devices to patients and allow patients to use different MASs during their life depending on their needs and disease characteristics.

The conclusion of the first part of the thesis related with the inventory of commercially available MASs and thinking in future projects, is that there is a large number of commercially devices with different characteristics (i.e. passive, semi-active or active, also table or wheelchair mounting) located in USA and north Europe, that are able to be tested on patients in order to determine if these devices improve their autonomy, generates a decrease in the burden cost and implies a therapeutic effect.

II Which are the target groups that can be helped with these assistive devices in Spain?

Referring to the second part of the project about the study of potential users of MASs in Spain, the results show that more than 34,700 patients with any type of pathology studied in this project can use a MAS to improve their upper limb functionality. Looking at the highest estimated value, a total number of 62,732 individuals could became users of MASs, but this number can be higher if we consider that every year approximately between 26,500 and 53,000 new cases of SCI and stroke patients can appear, and they can become users of MASs. On the other hand, people with mobility problems on the upper limb after breast surgery, patients with general back and shoulder pain or patients with Rheumatism can also use a MAS in some stages. Finally, it is important to consider that the tendency in the last years shows that the number of individuals suffering some of the aforementioned pathologies has appeared to increase. Therefore, the number of potential users will increase in the short term.

III How are these assistive devices introduced to the market in European countries?

The third chapter shows the mechanisms of distribution and prescription that MASs need to follow to be introduced in the market and be accessible for patients under national grants.

Looking at the requirements to be distributed around Europe, MASs are classified as Class I Medical Device under the old Directives 90/385/EEC and 93/42/EEC. As it was previously commented, the regulation of medical devices is changing and nowadays it is in a transition stage between the old Regulation described in the Real Decreto 1591/2009 and the new
Regulation 2017/745 that will be fully implemented in 2020. This regulation is required for products which will be affixed with the CE marking to be distributed around the members of the European Union. Following this line, MASs that are currently CE affixed and are not complying the new Regulation need to be updated and adjusted to the new requirements before 2024 and can only be commercially available until 2025 with the old Directives. On the other hand, new products need to be certified following the new Regulation to obtain the Class I as medical device and the CE marking to be distributed around the European Union members. In conclusion, the studied MASs can be freely distributed in Spain without passing any new evaluation until 2025, and any distribution agreement with manufacturing companies would be the solution to introduce these devices in the Spanish market through medical companies, rehabilitation institutions, orthopaedics or similar health institutions.

IV How does the prescription and provision of these devices work in Spain and other European countries to become accessible to patients with muscle weakness?

Referring to the mechanisms of prescription in Spain, MASs are not currently prescribed by physicians or health agents due to their inexistence in the market and their unknowledge in the society. Also, MASs are not currently covered by any subvention of the SNS (i.e. are not included in the Catálogo General de Material Ortoprotésico [74]).

However, taking into account the requirements of medical devices to be introduced in the subsidies portfolio, MASs could be incorporated in the portfolio because they accomplish the respective point requirements (a, d, e, f and g) described in Annex VI of Real Decreto 1030/2006 [33]: a) Represent a substantially new contribution to prevention, therapeutics or rehabilitation, and also, the improvement of life expectancy or the elimination of pain and suffering, because the introduction of arm supports in the daily life of patients would imply an increase of the activity and the autonomy of patients, also, a delay in the deterioration of the muscle functionality; d) Significantly modify organizational forms or systems of patient care, because the use of MASs would imply a greater degree of freedom of patients and their support therapies, carried out by familiars or rehabilitation agents, and they would be less necessary; e) Affect broad sectors of the population or groups at risk, because as it has been analysed in this thesis, a large number of people could become users of MASs, considering also the new cases per year due to the presence of SCI and stroke pathologies, approximately more than 34,700 individuals could use MASs and probably more than 26,545 new cases would appear every year; f) Imply a significant economic impact on the National Health
System, because as it has been explained before, the introduction of arm supports in the daily life would imply a decrease on the help and care of patients and would generate savings in the health burden cost; and finally, g) Meets safety and effectiveness requirements.

Looking at the comparison analysis of the SNS in Spain and other health systems in Europe, in Netherlands thanks to the distribution of MASs by different companies, like Focal Meditech or Armon Products, and thanks to the prescription by the health system agents or physicians and the provision of these devices due to the mechanisms of subventions provided by the National Health System based on insurances, MASs are currently accessible by patients. In consequence, there is a healthy competition between developer companies of orthoses that provides a large number of different arms supports, resulting in a good stock to provide the optimum device to each patient. In economic terms, these companies have the freedom to impose favourable prices for their products, resulting in a positive point for both, companies and patients who have access to these devices.

Another economic aspect that differs between Spain and Netherlands is the health expenditure: considering economic indicators of 2017 (Table 5), the Dutch total population was 2.73 points lower than the Spanish total population, in contrast, the Dutch health expenditure was only 1.2 points lower than the Spanish health expenditure, these numbers indicate that the Health System in Netherlands has more relevancy than in Spain. Another indicator that certifies these grounds is the GDP dedicated to the Health System that in Netherlands is 2% higher than in Spain; as a result, these aspects induce an expenditure per capita of 3,539€ in Netherlands and 1,565€ in Spain, being the Dutch people better positioned in terms of health services. In conclusion, companies are not disposed to incorporate MASs in the Spanish market because they are not good supported by the healthcare system and the devices result very expensive to patients that are under an ongoing high burden cost.

From another point of view, there is evidence that show that the burden cost of pathologies causing muscle weakness (e.g. Duchenne muscular dystrophy) are beyond the limits that families can afford. It is exposed that lifetime direct medical costs ranged approximately between 245,000€ and 320,000€, total costs between 702,000€ and 802,500€. On the other hand, some studies reported that using assistive technology like MASs there would be huge savings in the direct and indirect care cost (i.e. pharmacology, rehabilitation agents, help and support by familiars and caregivers). For these reasons, it should be interesting to try to develop one study to establish the economic factors needed to develop a new MASs to be
introduced in the Spanish market. Also, these proposes can be used to determine the cost that would be saved by incorporating MASs in the life of patients with muscle weakness, assuming a possible increase in the quality of life of patients and caregivers as a consequence of the use of the technology. These arguments would be confirmed by the publication of quality of life studies related to the use of the mentioned devices and the resulting reduction of the burden cost.

Lastly, the discussed results show that the current thesis would be a starting point for future projects; in more detail, an increase of studies related to assistive technology for upper extremities is required to have a better knowledge of the mentioned devices in the clinical field, considering physicians, health institutions and the society of patients with muscle weakness. For these reasons, and to improve the relevancy of the thesis, two possible future projects are exposed in section 4.2.

4.2. Future Project Approaches

4.2.1. Selection Guideline and Benchmarking Study

| I | How can these devices be selected depending on the requirements and specific needs of each patient? |

The aim of the proposed project is to develop a Selection Guideline, based on a benchmarking study of the characteristics of the current MASs, in order to have a clearer mechanism to select the proper device for each patient, depending on their requirements and necessities. The main idea of the process is that the patient with muscle weakness would only need to go to the physician or health agent, in order to obtain the prescription following the directives of the mentioned Selection Guideline, which would enable him to have access to the more appropriate assistive arm support for his pathology given the doctor’s criteria.

The first stage for the prescription of the device would be an evaluation of the needs and requirements of the patients. For this, a functional evaluation would be performed, containing an analysis of the customary environment where they complete goals and activities; this evaluation contains a test to determine the level of performance on specific tasks. Furthermore, the specific characteristics of the patients would be necessary to determine the proper device, being the main required information the following: age of the patient, dimensions of the patient (height and weight), stage/degree of progression of the
pathology, affected arm parts, tasks that are difficult to do; also, environmental and personal factors would be considered.

The second stage would be related to the specific features of the devices; in this line, the benchmarking study would be implemented with the objective of analysing the technical and functional features of the MASs and differentiate these features to stablish a portfolio which would describe the developed Selection Guideline.

The considered characteristics of the assistive devices would be the following:

a) Dimensions: height, width, depth; b) Maximum Weight Compensation; c) Workspace: required space by the device during its usage and the space that arms need to achieve; d) Mounting: table or wheelchair; e) Required technology: mechanical or electrical, and/or active, actively adjusted or passive technology.

The cases where the feature cannot be an exact number or condition, ranges with extreme limits would be used, for example for the dimensions.

As a complementary exploration, tests of muscle functionality would be implemented to determine the degree of progression and the location of the muscle weakness: trunk, shoulder, elbow, forearm, wrist and hand, among others.

Finally, after the selection of the specific device and its testing by the patient, the experience of the users would be used to improve the assessment of the Selection Guideline.

4.2.2. Experimental Protocol for Usability and Effectiveness Study

II Are MAS devices really effective? Do they have a positive impact on social-economic aspects?

The aim of the proposed project is to stablish an experimental protocol to quantify the usability and effectiveness of MASs. The hypotheses of this project are:

I) Mobile Arm Supports will decrease the progression of the disease (i.e. involve a delay functional deterioration as is explained in Jansen et al. [10]); they will improve the activity of the arms considering that without the usage of the assistive technology the upper limb suffers a progressive inactivity of the extremities, resulting in an increase of the muscle weakness.
II) Mobile Arm Supports will increase the autonomy and independence of the patients being able to carry out the daily-life activities like eating, brushing their teeth or raising their hands, among others. Therefore, they will improve the quality of life of those patients.

III) Mobile Arm Supports will imply a positive economic impact in terms of healthcare: they will involve a decrease of the constant support of the familiaris and caregivers of the patients, generating some economic and social savings.

The protocol would consider two aspects: the functionality of the extremities of the patient and their requirements, and the functionality of the selected devices. The protocol would include Quality Indicators for Assistive Technologies (QIAT), and it would be revised and validated by professionals of the MedTech field. QIAT would be implemented to determine the feasibility and effectiveness of the studied devices. The protocol would follow the stages explained below: a) Consideration of the need of a MAS during the patient-expert (i.e. physician or medical agent) meeting; b) Evaluation of the requirements of the patient and determination of the proper device depending on its functionality features; c) Implementation of the previously defined use of the device; d) Evaluation of the effectiveness following the technical protocol stages; e) Extraction and analysis of the results; f) Validation and certification of the hypotheses; and finally, g) Proposal of new designs by customizing or fitting the device since that some current devices are uncomfortable and bulky, being too much conspicuous.

The study would be implemented to compare the functionality and activity of the patient with and without the previously selected arm support device. It will be required for the patient to have a clear case of muscle weakness to have a good contrast, but he or she should be able to carry out the involved activities without the support of the assistive device.

The functionality and impact of the devices would be analysed and quantified in three ways: a) Patients would answer some questionnaires after using and testing the devices; which would present questions about the improving of carrying out the daily-life activities of the patient and about the comfort of using MASs, among others. Not only patients would be asked to answer the mentioned questionnaire, but also caregivers and family members, referring to economic and social impacts. b) Wearable sensors would be used and implemented to quantify different variables: Kinematic parameters like position, velocities, reachable workspace, movement smoothness, symmetry between arms and also the
quantification of muscle impairment using the Fugl-Meyer Assessment (FMA). c) Simple quantification of tasks that patients are not able to do without the MAS.

As a result, this project would be a good method to determine the feasibility of studied devices and their effectiveness and impact in the quality of life of patients and the social-economic view.

5. CONCLUSION

The main conclusion of the thesis is that it is possible and necessary to introduce Mobile Arm Supports in the Spanish market so that they become accessible to patients with muscle weakness. These patients require assistive technology in order to increase their autonomy enabling them to carry out daily life activities without the help of third people, such as familiairs, friends or caregivers. The studied devices would be easily introduced to the market through distribution companies like medical companies, orthopaedics, health institutions or rehabilitation centres. On the other hand, these devices could be introduced in the welfare system managed by the health ministry, because they accomplish with the involved requirements: a large number of people would be helped with arm supports, they would imply an improvement of the life expectancy of patients and a significant impact on the economy of the health system; and as a result, those devices could be freely acquired by patients through public subsidies.

In conclusion, after the work carried out in this project, the community of patients with muscle weakness in Spain is closer to be helped by foundations and healthcare companies through the collaboration with the healthcare system by incorporating MASs in the market under medical prescription.

Lastly, the results of this project might be useful for collaborative research between disease foundations and healthcare companies, and also with pharma companies to study future combinations between MASs and pharmaceutics, to prove if together the life quality of the patients can be improved. Future studies of epidemiology of muscular dystrophies and muscle weakness diseases should take the aforementioned results into account. Also, the inventory of MASs developed in this thesis can be considered for future studies of testing of MASs. Finally, future researches should focus on the economic and quality of life impact that would imply the introduction of MASs in the Spanish population.
6. BIBLIOGRAPHY


[80] Confidential Documentation from Yumen Bionics. (2019)


7. APPENDICES

A. Duchenne Muscular Dystrophy

DMD manifests mainly in males because it is inherited in an X-linked recessive pattern. The mutation of the gene is usually transmitted from mother to child; however, it may also occur by spontaneous de-novo mutations. The genetic mutation is located on the DMD locus Xp21 gene, the largest known human gene [3]. This gene provides instructions for making a protein called dystrophin.

The dystrophin complex acts as an anchor, connecting the structural framework (cytoskeleton) of each muscle with the lattice of proteins and other molecules outside the cell (extracellular matrix), and it has an important role in maintaining the membrane (sarcolemma) of the muscle cells. Dystrophin is needed for the muscles to work properly, without it, muscle cells become damaged and weakened. Also, in children with Duchenne, the lack of dystrophin is believed to affect the ability of certain brain cells, the neurons, to connect properly and share information; this can lead to challenges with important brain functions such as attention, memory, learning, speech, and intellectual ability. Due to this lack, patients with Duchenne are more likely to have such conditions as attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorders (ASD), learning disorders such as dyslexia, and obsessive-compulsive disorder (OCD) [6].

1) Diagnosis:

A diagnosis of DMD is made based upon a thorough clinical evaluation, a detailed patient history, and a variety of specialized tests including molecular genetic tests (identifying genetic mutations including deletions, duplications or single point mutations), blood tests (studying elevated levels of the creatine kinase -CK-) and immunoreaction tests using antibodies (studying the level of dystrophin protein).

Molecular genetic tests involve the examination of deoxyribonucleic acid (DNA) to identify a specific genetic mutation including deletions, duplications or single point mutations. Samples of blood or muscles cells may be tested. These techniques can also be used to diagnosis DMD before birth (prenatally).

Blood tests may reveal elevated levels of the creatine kinase (CK), an enzyme that is found in abnormally high levels when muscle is damaged. The detection of elevated CK levels
(usually in the thousands range) can confirm that muscle is damaged or inflamed but cannot confirm a diagnosis of DMD.

Immunoreaction tests are based on the use of antibodies that react to certain proteins such as dystrophin. Tissue samples from muscle biopsies are exposed to these antibodies and the results can determine whether a specific muscle protein is present in the cells and in what quantity or what size.

2) Symptoms:

Young children with Duchenne may be behind in achieving their developmental milestones (for example, walking, crawling, talking) but will usually, eventually catch up to them. Some children are only late on some milestones, like the speech, and some other are not late at all. This confusion may lead to a diagnosis later in childhood, therefore the time from initial symptoms to diagnosis is 2.5 years. The diagnosis changes depending on the patient due to the variation of the symptoms of each patient, and in consequence the pathology is diagnosticated between 3 and 9 years old.

- Early ambulatory (Childhood)

Children in this stage seem awkward and can fall to the floor frequently; also, they will have problems to stand up, climbing stairs and running or jumping, and sometimes they will have delays with the speech and language, having more difficulties than other children of the same age. Some of their muscles (twins and calf particularly) may seem enlarged or overdeveloped. This occurs because the muscle cells are being replaced by fibrous and adipose tissue. This process can cause the child to be less flexible and lose elasticity in the joints, known as contractures. Since the presentation of the first symptoms may be difficult to recognize, it may be difficult for parents to accept or believe that the diagnosis is DMD. Sometimes a child may seem to improve, however their muscles are, in fact, deteriorating.

During this stage, the child will lose the equilibrium while walking, due to this difficulty, the child will walk on the fingers, presenting a quirky walk gait. Their gait is insecure and wiggles and can easily fall to the floor. To try to maintain their balance, they pull out their belly and push their shoulders back.

Children at this stage often have large calf and will use the Gower’s Manoeuvre (needing help getting up from the floor or putting their hands up their legs) to rise from the floor to
standing. Muscle weakness is usually noticeable by 3 or 4 years of age and begins in the hips, pelvic area, upper legs, and shoulders.

On the other hand, the creatine kinase level (CK) is often extremely elevated and liver enzymes (AST, ALT) are elevated [6].

- **Late ambulatory (Childhood-Adolescent)**

At this stage, there is often fatigue while walking long distances. A manual wheelchair may be needed to help decrease this fatigue. Teens with DMD also have difficulty raising their arms and the activities that involve the arms, legs or superior member require mechanic support. Almost DMD patients stop walking between 7 and 12 years and needs a wheelchair to move.

Heart and respiratory muscle problems begin in the teen years and lead to serious, life threatening complications. So, monitoring breathing, heart, bone health and puberty become increasingly important.

- **Early non-ambulatory (Adolescent-Young adult)**

In this stage, the use of mechanic support become more common and the fatigue increases. More than the 90% of the patients moves using a manual wheelchair. Due to the sitting for long times they begin to develop symptoms of scoliosis. Scoliosis, as well as muscle cramps, can sometimes result in some physical discomfort.

When the evolution of the disease progresses, respiratory and cardiac conditions that threaten life become more prevalent. Major symptoms of heart and lung complications include shortness of breath, fluid in the lungs, swelling or edemas in the feet and lower legs. Continued monitoring of heart function, breathing, bone health, puberty, digestive, and urinary systems, as well as continued stretching and maintaining good body alignment and positioning, should continue.

- **Late non-ambulatory (Adult)**

Adults with Duchenne have more trouble using their hands and maintaining good posture. Weakness continues during the adult phase. However, many young adults with Duchenne can maintain some function of their fingers well into the adult stage. It is important to plan
for an adult life that maintains as many elements of independence as possible, within a supportive care environment.

The cardiac muscle of adults become weak and not pump blood properly, for this reason they may have problems with heart rate or rhythm.

The diaphragm and breathing muscles will become weaker with age, and in result, many people with Duchenne will have difficulty taking deep breaths. Adults may also have trouble coughing and require assistance.

3) Treatment and Therapies:

There is no specific treatment that can stop or reverse the evolution of any form of muscular dystrophy. All forms of muscular dystrophy are genetic and cannot be prevented. The treatment is aimed to keep the patient independent for as long as possible to increase the life expectancy and to avoid the complications resulting from weakness, decreased mobility, and cardiac and respiratory difficulties. Treatment may involve a combination of approaches, including drug therapy, surgery and physical therapy. On the other hand, programs of nutrition and alimentation, speech therapy and social interaction, and hydrotherapy could be helpful for patients, to improve their capacities.

Corticosteroids are used as standard of care to treat individuals with DMD. These drugs slow the progression of muscle weakness in affected individuals and delay the loss of ambulation by 2-3 years, also could improve the lung function.

Prednisone is one of the drugs used to treat individuals with DMD, it can slow the rate of muscle deterioration and help children retain strength and prolong independent walking for several years. This drug has the possible side effects of weight gain, high blood pressure, behaviour changes, and delayed growth. Oxandrolone, a medication used in a research study, also has similar benefits to prednisone but with fewer side effects. The U.S. Food and Drug
Administration (FDA) approved, in 2016, *Exondys 51 (eteplirsen)* injection to treat people with DMD who have a change in the *DMD* gene that will allow a shortened form of dystrophin to be made if exon 51 is skipped. An exon is the part of the gene that actually codes for the protein. The *DMD* gene has 79 exons. About 13% of those with DMD may be helped by *Exondys 51*. In 2017, *Emflaza (deflazacort)* was FDA approved to treat patients age 5 years and older with DMD. *Deflazacort* is believed to have fewer side effects than *Prednisone* [3].

The good news is that new gene-based therapies have recently emerged with noted advances in using conventional gene replacement strategies, RNA-based technology, and pharmacological approaches. In particular, antisense-mediated exon skipping has shown encouraging results and holds promise for the treatment of dystrophic muscle.

Physical therapy may be helpful to maintain muscle strength and function. Passive stretching can increase joint flexibility and prevent contractures that restrict movement and cause loss of function. On the other hand, postural correction is used to counteract the vertebral irregularities that force patients with dystrophy to awkward positions. Also, people with weakened diaphragms can learn to cough and deep breathing exercises that are designed to keep the lungs fully expanded [13].
## B. Sources of Information

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</thead>
<tbody>
<tr>
<td>Developers &amp; Companies</td>
<td>Focal Meditech (Netherlands), Armon Products (Netherlands), Assistive Innovations (Netherlands), Kinova Robotics (Canada), Neater Solutions (United Kingdom), Jaeco Orthopaedics (USA), MyoMo (USA), Saebo (United Kingdom), Medifab (New Zealand), Equipois (USA), University of Twente (Netherlands), Yumen Bionics (Netherlands).</td>
</tr>
<tr>
<td>Federations</td>
<td>Federación Española de Ortosistas y Protesistas, Fenin, Federación ASEM.</td>
</tr>
<tr>
<td>Foundations</td>
<td>Duchenne Parent Project España, Duchenne Parent Project Netherlands, Parent Project Muscular Dystrophy, World Duchenne Organization.</td>
</tr>
<tr>
<td>Orthopaedics</td>
<td>Gracare, GrauSoler, Ortoibérica.</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td></td>
</tr>
<tr>
<td>Institutions</td>
<td>Institut Guttmann.</td>
</tr>
</tbody>
</table>

*Table 6. Contacted institutions as sources of information (hyperlink clicking in the names).*
C. Commercially Available Mobile Arm Supports

Passive Arm Supports

(a) Sling (Focal Meditech)  
(b) Balancer (Focal Meditech)

(c) WREX (Jaeco Orthopaedics)  
(d) Dynamic Arm Support (Exact Dynamics)

(e) DAS O110 (Kinova Robotics)  
(f) DAS O540 (Kinova Robotics)
(g) Edero (Armon Products)

(h) Pura (Armon Products)

(i) iFloat Arm Support (Assistive Technologies)

(j) Dowing (Focal Meditech)

(k) Multi Link Dynamic Arm Support (JAECO)

(l) X-Ar (Equipois)

(m) Saebo Mass (Saebo)

(n) Saebo Mass Mini (Saebo)
Actively Adjustable Passive Arm Supports

(o) Top/Help (Focal Meditech)

(p) Neater Arm Support (Neater)

(q) Gowing (Focal Meditech)

(r) Darwing (Focal Meditech)

(s) iFloat Powered Arm Support

(t) iFloat NG Arm Support

(u) Armon Elemento (Armon Products)

(v) Armon Ayura (Armon Products)
Active Arm Supports

Figure 10. Mobile Arm Supports classified by technologies: Passive, Actively Adjustable and Active.
D. Questionnaires for Patients with Duchenne Muscular Dystrophy

To obtain a first vision about the situation and knowledge about MASs and personal opinion of DMD patients a questionnaire was developed. The poll was sent to 53 patients, 52 with Duchenne Muscular Dystrophy and 1 with Becker Muscular Dystrophy (BMD) which was excluded from the results to make a homogeneous analysis and because their age deviates from the range.

![Pie chart showing the distribution of ages of the 52 questioned patients with Duchenne.](Figure 11)

**Figure 11.** Distribution of ages of the 52 questioned patients with Duchenne.

![Pie chart showing the geographical origin of the 52 questioned patients with Duchenne.](Figure 12)

**Figure 12.** Geographical origin of the 52 questioned patients with Duchenne.
The 52 patients have between 0 and 30 years, being 30-40 their lifespan (Figure 11). 19.2% of the patients are from Andalucia, 19.2% from Catalonia, 11.5% from Madrid, 9.6% from Galicia and the rest are from other location around Spain (Figure 12).

On the other hand, 53.8% of the patients need a wheelchair nowadays to travel. It is important to expose that 5 of these patients are younger than 10 years, and the average age when the patients need a wheelchair is 12; those patients are losing in a premature way the whole leg function. On the other hand, only 3 patients of the resting 46.2% that don’t need a wheelchair, are older than 11 years; those patients are having a good muscle condition in the legs to avoid the usage of the wheelchair after the 11 years.

76.9% of the patients can bring the hand from the knee to the mouth, without the help of the other hand, the resting 23.1% cannot carry out this action. Most of cases that cannot do it, are older than 15 years, so at the age of 15 the upper limb function decreases progressively.

The rest of the questionnaire was dedicated to show to the patients a mobile arm support under development [9], named passive A-gear. (Figure 13).

![Duchenne patient using A-Gear arm support to carry out the daily life activities.](image)

Relating to the knowledge of MASs, only a 7.7% of the patients know something about upper limb orthoses. In contrast, all 52 patients are interested in know and test MASs to improve their autonomy to carry out daily life activities: write, eat, work with a computer, scratch and wash their face, wash their teeth, raise the arms, be able to sustain things with the hands and be able to push buttons for example of an elevator, among other tasks.
Looking at Figure 14, 63.5% of the patients are able to expend less than 1,500€ to purchase for a mobile arm support, 30.8% up to 3,000€ and a 5.8% can dedicate between 5,000 and 10,000€ to buy the support device. On the other hand, 42.3% of the patients receive less than 1,500€ from their community health system to buy a wheelchair, a 25% receive between 1,500 and 3,000€ and only a 32.7% receive more than 3,000€ from their community system.

Figure 14. Percentage of patients that can dedicate a specific monetary quantity in Euros to buy a MAS.

Figure 15. Monetary quantity which patients receive from their corresponding Autonomic Communities for the wheelchair purchase and the percentage of patients for each cost value.
### Table 7. Average annual cost per patient with DMD, considering children, adult and all patients, in European countries: Spain, Italy, France and United Kingdom (2012, €). Figure reproduced from Cavazza et al. 2016 [83].

<table>
<thead>
<tr>
<th>Costs (€ 2012)</th>
<th>Spain Children</th>
<th>Spain Adult</th>
<th>Spain All</th>
<th>Italy Children</th>
<th>Italy Adult</th>
<th>Italy All</th>
<th>France Children</th>
<th>France Adult</th>
<th>France All</th>
<th>United Kingdom Children</th>
<th>United Kingdom Adult</th>
<th>United Kingdom All</th>
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</thead>
<tbody>
<tr>
<td>Direct non-healthcare costs</td>
<td>1848</td>
<td>4011</td>
<td>5859</td>
<td>18,708</td>
<td>18,626</td>
<td>27,334</td>
<td>18,708</td>
<td>18,626</td>
<td>27,334</td>
<td>18,708</td>
<td>18,626</td>
<td>27,334</td>
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<tr>
<td>Other informal carer</td>
<td>8570</td>
<td>14,429</td>
<td>23,300</td>
<td>18,708</td>
<td>18,626</td>
<td>27,334</td>
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<td>18,626</td>
<td>27,334</td>
<td>18,708</td>
<td>18,626</td>
<td>27,334</td>
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<tr>
<td>Direct non-healthcare informal costs</td>
<td>27,278</td>
<td>33,055</td>
<td>60,333</td>
<td>27,278</td>
<td>33,055</td>
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<td>60,333</td>
<td>27,278</td>
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<td>Early retirement</td>
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<td>6612</td>
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E. Average Annual Cost per Patient with Duchenne