

## **LESIONS AND PATHOLOGIES OF THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM: EPIDEMIOLOGY AND RELATED SOCIO-ECONOMIC COSTS**

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### *Abstract*

Every year, nervous system injuries and disorders affect millions of people worldwide, causing a significant and, unfortunately, rising incidence of social and health costs among all the countries. The present contribution is focused on the analysis of the data concerning the predominance and the incidence of severe injuries affecting the nervous system caused by accidents, car crashes and by the main pathologies affecting the nervous system. Finally, there will be provided data regarding the burden that countries have to carry, which concern both social and health costs that are steadily increasing in recent years and are expected to rise in the next decade.

### **1. Introduction**

This research is focused both on the analysis of the nervous system injuries and disorders and on the consequences they have in terms of social and health costs arising from treatments and therapies. Moreover, these costs have grown significantly in recent years, they are increasingly piling on public budgets and are expected to further soar in the next decade.

Chronic-degenerative diseases, whose incidence is alarmingly spreading worldwide, determine a significant commitment of financial resources, due to the continuous need for assistance which often lasts for long periods of time and requires a strong synergy between health and social services, as well as adequate residential and territorial services.

According to recent studies, around 70-80% of health resources are spent globally on the management of chronic and degenerative diseases. These data become increasingly alarming, considering that epidemiological projections report in 2020 that individuals affected worldwide by these pathologies will be the 4/5 of sick people.

For over a decade, the European Union has been launching a number of initiatives in order to develop actions of contrast to neurodegenerative diseases - such as Alzheimer and Parkinson diseases - so as to allow the Member States to deal with these emergencies in a more efficient and effective manner, especially by sharing research activities, useful to avoid unnecessary duplication of work. Furthermore, these initiatives focus on increasing investments in research, on the interaction between the

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European government bodies and those of the Member States, on promoting the comparison between the scientific and industrial worlds and, finally, on prevention and on the promptness of therapies.

At a national level, noteworthy initiatives include the adoption of the National Chronicity Plan (NCP), approved in Italy by the State Regions Conference in September 2016: the NCP was born from the need to harmonize interventions in the field of chronic diseases and aims both at identifying standard approaches used in care and assistance measures and at guaranteeing a better organization of services offered to patients, in order not only to contribute considerably to the improvement of the protection and the quality of life of patients suffering from chronic diseases, but also to relieve, to the extent possible, the burden on sick people, their family members and society.

## **2. Lesions and trauma to the central and peripheral nervous system: causes and epidemiological aspects**

According to the data released by the Società di Medicina e Fisica Riabilitativa (Society of Medicine and Rehabilitation Medicine), every year 250,000 to 500,000 people suffer from spinal cord injuries (SIMFER, 2013). Traumatic injuries to the central nervous system show worldwide an incidence of 200 cases per 100,000 inhabitants with a mortality rate of 10%. Although there is full awareness of both the causes and the social and economic consequences of the traumas affecting the nervous system, their incidence remains very high worldwide and continues to rise in developing countries. Spinal cord injuries are particularly significant due to the consequences that they entail; moreover, their incidence has a variability range between 14.5 and 57.8 cases per million inhabitants (Ackery et al., 2004). Mortality rates are bimodal and particularly afflict individuals under 25 and over 65.

The incidence of traumatic spinal cord injury exhibits a broader range worldwide: the cases vary from a minimum of 3.6 to a maximum of 195.4 per million inhabitants, indeed (Jazayeri et al., 2015). This type of lesion affects almost 10-20 people out of a million in Finland, Norway, France, Australia and Turkey; 20-30 people out of a million in Spain and Romania; 30-50 people out of a million in the United States, up to peaks of 80 in Alaska (Singh et al., 2014).

According to the National Spinal Cord Injury Statistical Center data, in 2017 the number of individuals, living in the United States, that present a spinal cord injury is between 250,000 and 350,000, while every year about 17,500 new cases with an incidence of about 54 cases out of a million individuals are observed.

The Federazione Associazioni Italiane Paraplegici (Federation of Italian Paraplegic Associations) (FAIP) estimates that in Italy in 2016 people with spinal cord injury were 90,000, with an annual increase of about 3,000 with an incidence of 50 cases out of a million. According to a recent research undertaken within the GISEM (Gruppo Italiano Studio Epidemiologico Mielolesioni) – which involves the 37 major specialist centers of spinal cord injuries – over a period of 2 years 1014 new cases of spinal cord injuries were found, with an age range that in the 80% cases is between 10 and 40 years. Most cases are of traumatic causes (67.5%), even if those of non-traumatic causes are continuously increasing (Figure 1 and Figure 2).

### traumatic etiology

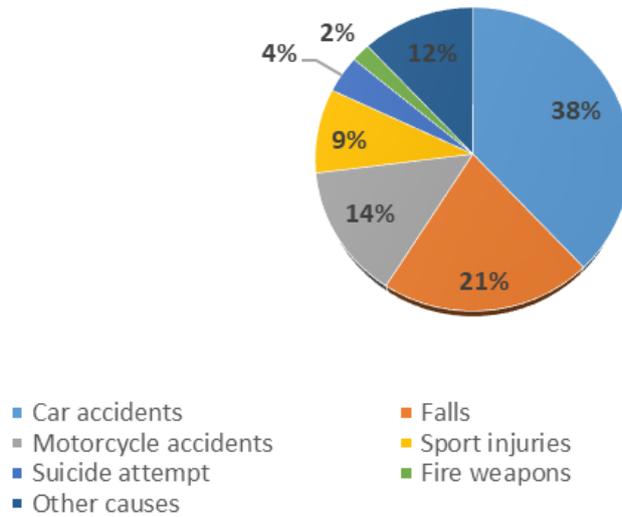


Figure 1: Traumatic etiology; our elaboration on traumatic etiology of spinal cord injuries in Italy. Source: Studio GISEM.

### non-traumatic etiology

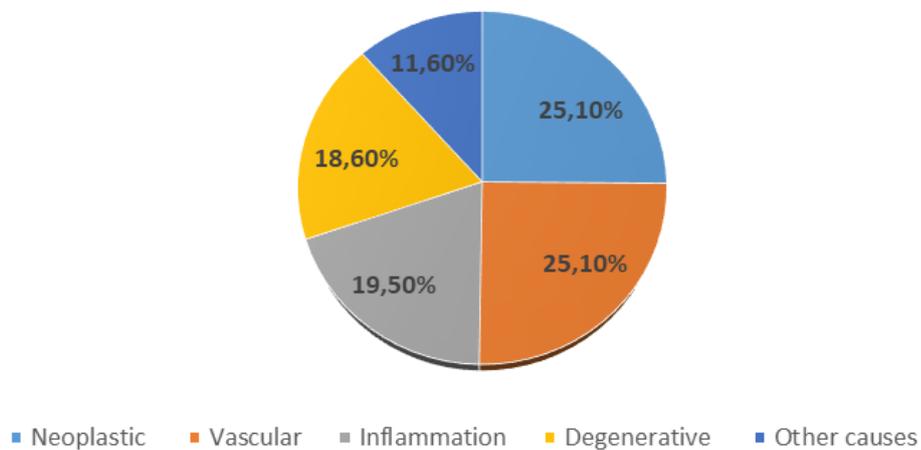


Figure 2: Non-traumatic etiology; our elaboration on non-traumatic etiology of spinal cord injuries in Italy. Source: Studio GISEM.

Patients with traumatic injury are on average younger than those with non-traumatic injury (34 versus 58 years); a general prevalence of male subjects (F:M = 1:3) is found and it is even more clear within the traumatized group.

In both patients groups, a prevalence of paraplegic patients is found: they represent the 56.6% of patients with traumatic injury and the 76.4% of those with non-traumatic injury. Furthermore, more cases with complete injury are found within the traumatic etiology group: the 51.5% suffer a complete injury compared with the 24.2% of the non-traumatic injuries. In Italy, compared to the rest of Europe, there is still a lack of

a suitable number of Spinal Units, the specialized and adequately equipped centers for the care and assistance of people suffering from spinal cord injuries: the total number of beds reaches 350 compared to over 800 in Germany. A census of healthcare facilities identified the presence of 22 Spinal Units across the Italian territory, 9 of which are Unipolar, offering in a highly specialized manner a care pathway for people with spinal cord injury. First, there is a substantial inhomogeneity between the central-northern regions, where more than 90% of the centers are gathered, and the southern ones, where only 4 spinal units have been fully operational (Ospedali Riuniti of Ancona, Policlinico of Bari, Ospedale Cannizzaro of Catania and Villa delle Ginestre of Palermo) (FAIP, 2019). In 2009, Marini and Reale carried out a research regarding the subjects that provide assistance to the patient (caregiver). These subjects are predominantly female gender: this datum finds evidence of studies conducted under the Fondazione ISTUD and those reported in literature, which show that the percentage of women taking care of loved ones is close to 80%.

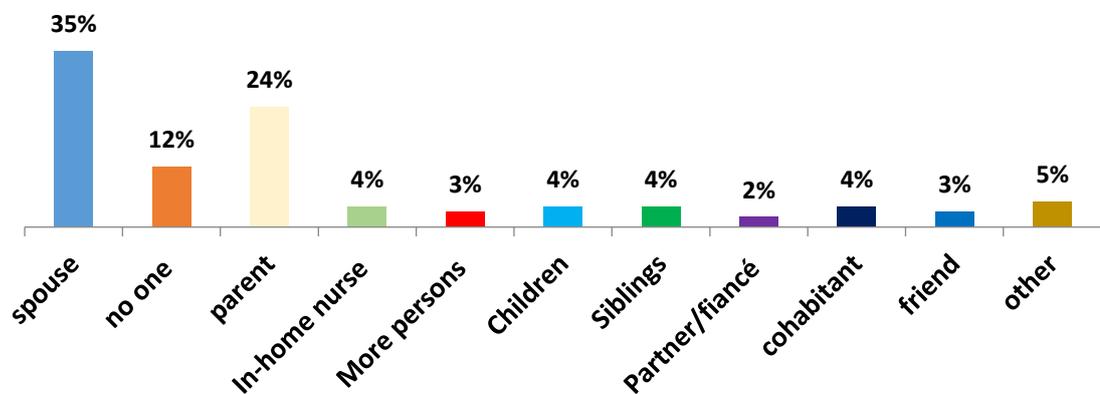


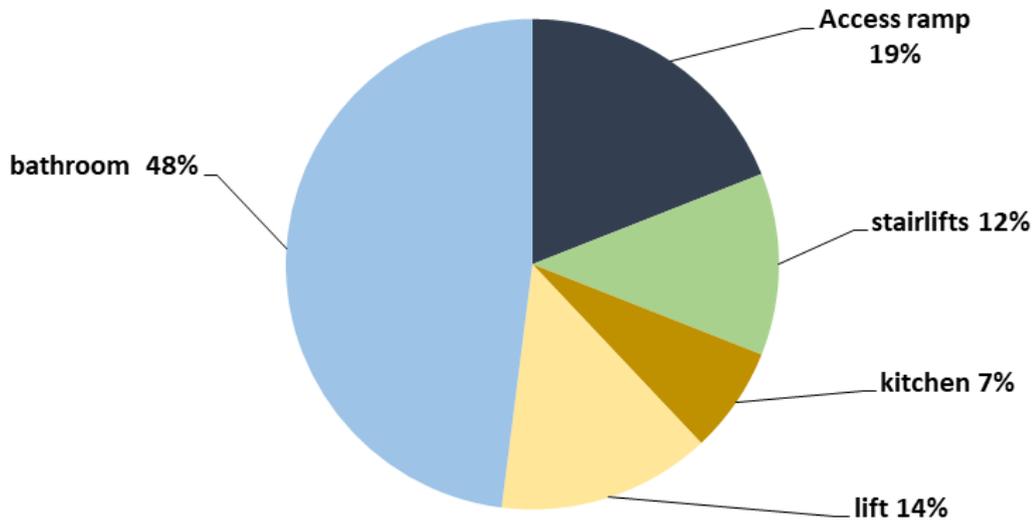
Figure 3: Main caregivers of the patient suffering from spinal cord injury.

The average age is 45, a lower value than other studies already mentioned that report a datum equal to 55: this gap can be ascribable to the fact that people suffering from spinal cord injury in the 80% of cases are between 18 and 40-year-old, as argued above. Accordingly, caregivers are mainly parents or young partners unlike other pathologies where the average age of patients is significantly higher and in most cases the spouse is the main assistant.

The “cost” section would deserve a separate discussion: in the USA it has been estimated that the expenses for intensive medical and rehabilitation treatments in the first year for subjects suffering from spinal cord injuries amounted to over 1000 million dollars in 2017, a figure far higher than that necessary for tumors, heart attacks and strokes (American Spinal Injury Association). Furthermore, according Health Department of the United States the research expenses on spinal cord injuries amounted to about 71 million of dollars. In Italy, according to the study conducted by Martini and Reale as well, the average yearly expense amounts to about 15,000 euros per patient fully charged to the family.

The management of spinal cord injury entails costs that can overturn the family’s economic and social balance in the various stages of the disease: in this regard, significant costs are incurred to make the house accessible to the patient. In the first year alone, the costs can amount to 27,000 euros fully charged to the family; the

estimated costs to modify the housing patterns fluctuate considerably, as shown in Figure 4: the 62% of people suffering from spinal cord injury spends less than 20,000 euros, while the remaining 38% bears higher costs.



*Figure 4: Percentages of costs per home.*

Despite the awareness of the causes and the human and economic costs of trauma affecting the nervous system, the rate remains severely high worldwide and keeps rising in developing countries. In 2017, according to the World Health Organization (WHO), the estimated road fatalities were 1.35 million, while subjects suffering a serious injury for the same reason can amount to 50,000 million. Car crashes are the main cause of both spinal cord injuries and road trauma and between 30% and 40% of these accidents cause injuries to the nervous system (Ackery et al., 2004).

The datum relating to the mortality rate in the EU in 2017, equal to 49.7%, shows significant variations and trends between the various Member States: in Sweden and in the United Kingdom, the rates of road deaths are lower – the 25.3 % in the former and the 27.1% in the latter per million inhabitants – while in Romania and Bulgaria the rates raise to 99.3% and 96% per million inhabitants (Fig. 5). The 90% of the patients going in a hospital center in the United Kingdom has minor injuries, the 5% moderate ones while the 5% are serious. The majority of patients suffering from minor injuries fully recuperates but many suffer after-effects and disabling symptoms. According to a research carried out by Thornill, in 2000 minor injuries present posthumous symptoms in a rate of 51% while moderate ones in a rate of 54%. Specifically, with regard to minor injuries, those are identified with persistent headache among the 79% of the population and with memory loss in the 59%.

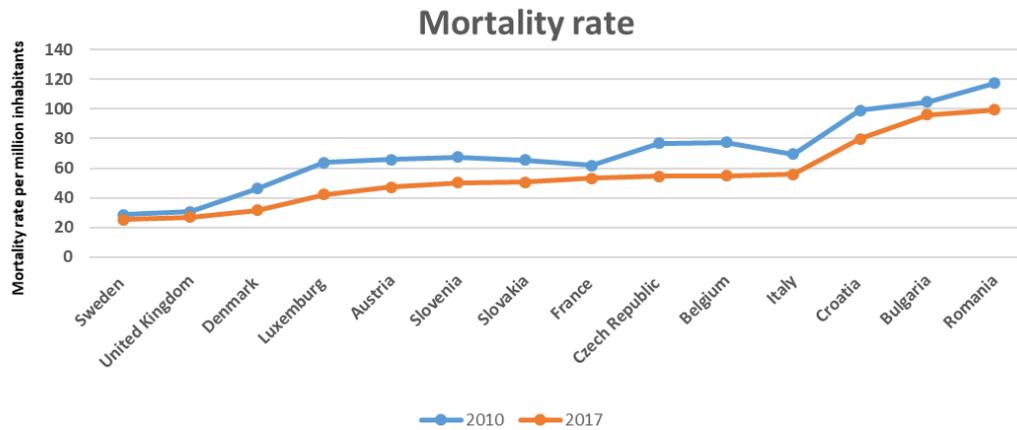


Figure 5: Our elaboration of road accident mortality rate in Europe. Source: ISTAT.

With regard to Italy, the rate (55.8%) is slightly higher than the EU average, but it has significantly reduced if compared with 2010 when it was 69.4%. Lastly, with regard to seriously injured in car accidents, in 2017 in Italy there were 17,309 cases with a ratio of 5 out of 1 death (report from ISTAT regarding car accidents) (Fig. 6).

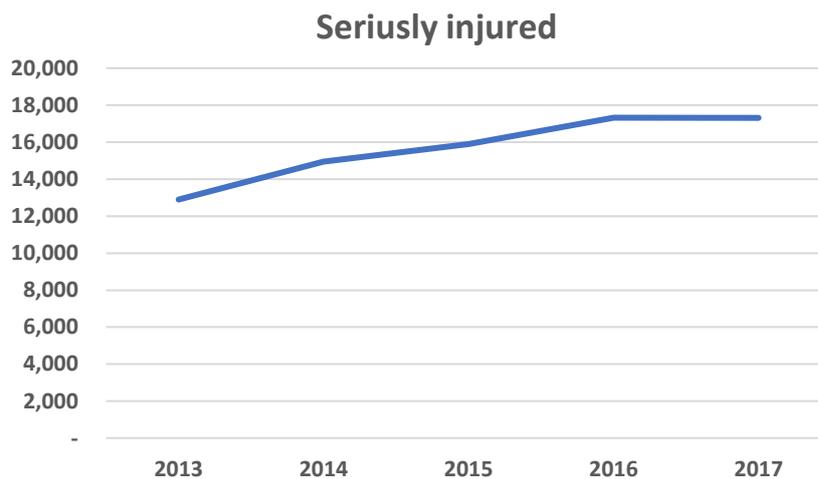
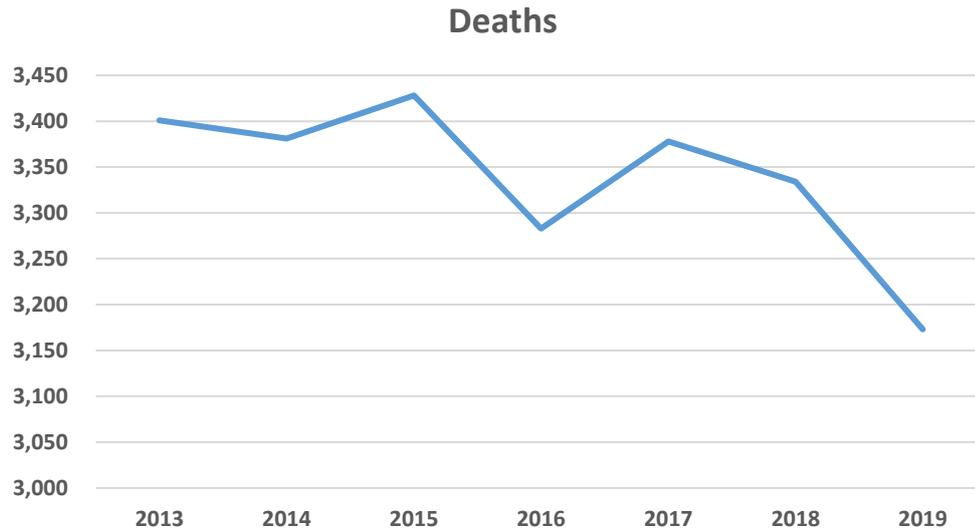


Figure 6: Our elaboration of seriously injured in car accidents in Italy. Source ISTAT.



*Figure 7:* Our elaboration of deaths in car accidents in Italy. Source: ISTAT.

In Italy, the main cause for spinal cord injury of traumatic origin are car accidents: in greater detail, car accidents represent the 45% of the incidence of this trauma, followed by accidents at work that represent the 20%, sport injuries that represent the 10% and those owing to other causes, for example fire gun accidents that are the 25%. In Italy, 75,000 inhabitants are estimated to suffer a spinal cord injury, whose 80% is between 10 and 40 years old; this situation has consequently a very high social cost (Federazione Associazioni Italiane Paraplegici, 2019).

The definition of costs is a key issue to evaluate the prevention and treatment policies of the phenomenon. In our country, this analysis hasn't been provided, but reference can be made to the one developed at European level. A research carried out by Olesen and partners in 2010 shows that in Europe more than 64,054 million euros are spent to minister to 8.2 million subjects suffering trauma. The expenditure is subdivided in 42,353 million euros for direct patient care, 16,769 million euros for direct non-health care and finally 4,932 million euros for indirect costs.

Traumatic brain injury (TBI) represents an extremely frequent occurrence in today's reality and rests on high social costs because affects mainly young people; TBI is one of the major health problems due to its frequency and use of resources. The estimated TBI rate in all industrialized countries is of around 300 cases per 100,000 inhabitants per year. In Europe, cases are slightly below the world average, 262 per 100,000 people (Peeters et al., 2015).

It is difficult to acquire accurate epidemiological data, in Italy at least, due to the dispersion of the health system and the typology of the hospitals recovering patients suffering TBI. According to a quite recent and detailed study carried out in Lombardy region, 35,000 new cases are registered per year, with a ratio of 410 cases every 100,000 inhabitants. Comparing this data to the domestic population, an incidence of around 5% is obtained: considerably higher is the male rate which reaches 70%, the most affected age group is between 15 and 40 years old.

However, for some time now, a progressive decrease in mortality due to traumatic brain injury has been recorded; the decrease is ascribable to the development of

vehicles that are much safer if compared to the past<sup>1</sup>. Finally, the ever more widespread presence of emergency services, which allows faster intervention of vehicles and dedicated personnel directly at the accident site, contributes significantly to the reduction in the mortality due to TBI.

In recent years, Italian first aid units have gained more efficiency even thanks to increasingly widespread presence of neuroradiological departments and intensive care. The mortality rates inferred from the literature data are rather discordant because they are clearly linked to the patient's selection criteria: when considering all the patients suffering TBI, the mortality rate is roughly between 2% and 6%, while the mortality rate is roughly between 30% and 45% if considering coma patients caused by cranial trauma with brain injury.

Peripheral nerve injury represents the most prevalent cause for trauma, registering more than 300,000 cases per year only in Europe, while in developing countries those trauma are estimated to affect 13-23 people per 100,000 inhabitants every year (Ruijun et al., 2014). Injuries to the peripheral nervous system originate mainly from road accidents, fire guns, incisions due to different type of surgery (Kouyoumdijan et al., 2017). Today, vehicle accidents are the first cause of injuries to the peripheral nervous system in the world (Eser et al., 2009) and according to the data released by the World Health Organization, 3,200,000 people suffer disabilities due to this type of trauma every year (Gin-Shaw and Jorden, 2002).

Lesions to peripheral nerves can be combined with traumas to the central nervous system, so that it might be problematic to identify the lesion to the peripheral nerve, worsening the degree of disability: about the 60% of patients with peripheral nerve lesions suffers cerebral trauma, indeed; for these reasons, a peripheral nerve lesion can be classified in the context of trauma to the central nervous system.

Lesions by severing peripheral nerves, for instance caused by glass and blade weapons are less widespread than compression lesions and they are often combined with lesions to adjacent structures (for example to tendons). Although nerve injuries represent only the 3% of traumas affecting hands – this type of accident has a range that varies from 7-37 cases per 100 inhabitants per year in Europe (Dahlin and Wiberg, 2017) – the total cost impacting on society of a worker suffering a lesion of the median nerve of the forearm might amount to 50,000 euros, particularly linked to the productivity loss (Rosberg et al., 2008).

The most common accident injury affects the digital nerve: it can be total or partial (incidence: 6.2/100,000 inhabitants/year) and it mainly affects men (75%) of productive age (Dahlin, 2008).

A research carried out in Sweden has analyzed the factors affecting the costs of median and ulnar nerve injuries: it has quantified both the sanitarian costs and those related to the productivity loss on a sample of about 70 patients with results equal to 51,238 euros for injuries affecting the median nerve and 31,186 euros for ulnar ones, of which slightly less than 90% due to the productivity loss (Rosberg et al., 2008).

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<sup>1</sup> Monocoque, greater diffusion of airbags and therefore more and more passengers deemed to have belts; the obligatory nature of the helmet certainly guarantees greater safety while driving two-wheeled vehicles.

### **3. Pathologies of the central and peripheral nervous system: the Parkinson and Alzheimer diseases and Multiple Sclerosis (MS)**

The Parkinson's disease (PD) is classified as a primary degenerative disease affecting the nervous system which implicates a process of programmed cell death, in particular the nerve cells. The incidence of PD within forty-years-old people is equal to about 41 subjects per 100,000 individuals, rising to more than 1,900 cases per 100,000 among elderly subjects over the age of eighty (Cacabelos, 2017). These rates identify the PD as one of the biggest age-related health problems (Zou et al., 2015; Hirsch et al., 2016; Savica et al., 2016). Considering people who are under 50 years of age, the Parkinson's disease affects men less frequently than women (ratio M/F <1.2%), while this disease occurs 1.6 more times among men than among women, considering people who are over 80 years of age (Moisan et al., 2016).

According to a study carried out by Pringsheim, a close correlation between the distribution of the disease and some specific geographical areas is observed: in North America, Australia and Europe 1,601 cases out of 100,000 are registered, while in Asia a huge decrease has been recorded with a rate of 346 cases out of 100,000. According to other researches, in the 15 most populated countries in the world, which represent the 2/3 of the global population, the number of people suffering from PD varies between 4.1 and 4.2 million. This rate is expected to rise in the coming years, reaching values between 8.7 and 9.3 million in 2030, registering peaks in China where rates are evaluated to rise from 2 to 5 million by 2030. (Dorsey et al., 2007).

In Italy, despite the lack of recent data regarding people affected by the Parkinson's disease, 230,000 patients are estimated to suffer this pathology today. The average age of onset of the Parkinson's disease is 60 years old: in 5-10% of subjects this disease occurs before the age of 50 and, in some cases, before the age of 40 (juvenile onset). The incidence of the PD fluctuates from 5 to 10 new cases out of 100,000 inhabitants per year, but the Italian data may be underestimated. Recent studies carried out by Valent and partners show an incidence rate in the Friuli Venezia Giulia region of 389 cases out of 100,000 people, with a rise of 28 new cases per year; those data are data far superior compared to the European ones, where incidences of 15-20 out of 100,000 inhabitants per year are recorded (Valent et al., 2018; Campenhausen et al., 2005).

People affected by PD experience particular difficulties entering and remaining active in the labor market and represent lower revenue capacity than general population. Welfare to PD patients generates significant costs for healthcare services: on the one hand, Britain's National Health Service spends more than 383 million pounds per year; on the other, in Italy, according to data of a research conducted in five of the Italian regions, the average annual cost per PD patient charged to the National Health Service fluctuates between 3,500 and 4,800 euros while that charged to the patient fluctuates between 1,500 and 2,700 euros; finally, the average annual cost per patient for the community varies between 10,000 and 11,000 euros. These rates let us understand the importance of monitoring the costs related to the disease, since it may be possible to reach suitable choices in identifying the care priority thanks to precise analysis.

The total costs are estimated to rise in the coming years due to the progressing aging of the population. Infact, it is assumed that in the next few years the Italian population residing above 50 will increase from about 21 million (2001) to about 30 million (2030) and that PD registered cases will increase from today's 5,800 to 8,000 per year, causing an increase of annual expenditure from the current 2,344,700,000 to 3,199,200,000 euros.

The Alzheimer disease is the most common cause of dementia and consists in a degenerative process that slowly and progressively destroys brain cells: this disease affects memory and mental functions (e.g. the thinking and speaking capabilities), but might also cause confusion, emotional changes and spatial and temporal disorientation. According to the World Alzheimer Report of 2018 drafted by the Alzheimer Disease International, the total number of people that lives with this disease reaches slightly less than 50 million: the Alzheimer disease affects a new person every 3 seconds; those data are expected to rise in the coming years reaching about 82 million cases by 2030 and 152 million by 2050. The data referring to the worldwide distribution of Alzheimer's patients, deduced from the 2015 report, shows a particular concentration in Asia: there less than half of the patients are gathered (about 23 million), the remaining are equally distributed among Europe (10.5 million) and Americas (9.4 million), while in Africa are estimated to be about 4 million cases. In Italy, according to a research carried out by the CENSIS in collaboration with AIMA (Associazione Italiana Malati di Alzheimer) (Italian Association for Alzheimer Patients) in 2015, patients suffering the Alzheimer disease were about 600,000, 2/3 of which are women.

Today in Italy 800 thousand people are estimated to be affected by dementia and every year there are about 120 thousand new cases, 3.2% of which are old people between 70 and 79 years old while the 10.8% are over 80 years old. The treatments and cares intended for Alzheimer patients entail high direct and indirect healthcare costs: again, according to the World Alzheimer Report (2018) approximately 1 trillion dollars is estimated to have been spent globally and this amount is expected to double in 2030. In Italy, the recorded incidence per capita related to the annual costs for treatments and cares of Alzheimer patients is about 70,600 euros, 19,000 euros of which are direct costs charged on the National Health Service while 51,600 euros are direct costs fully charged on families (data recorded by CENSIS).

The disease indirectly affects those who assist the patient on a daily basis, mainly members of the family nucleus, the so-called caregivers: given that about the 80% of the patients receive assistance at home, caregivers suffer depressive symptoms, insomnia, psychophysical stress and increase their consumption of medical products (about the 30% begins taking medicine after the disease onset). The 60% of caregivers experience the worsening of the quality of life while the 25% has a direct impact on working life (Bianchetti et al., 2002).

Multiple sclerosis (MS) is a central nervous system disorder that results in damage and loss of myelin in different areas of the central nervous system: the causes of the onset of the disease are attributed to a single triggering event but often the disease affects genetically predisposed individuals as a result of environmental exposure. Considering that genes are necessary for the onset of the disease, the prevalent role of the environment in determining the risk of Multiple Sclerosis and in particular of latitude cannot be ignored. Some data concerning the geographical distribution of the disease can be explained with ethnicity and genetic factors, but latitude represents the highest risk factor after ethnicity. In fact, in regions with a temperate climate, the incidence and prevalence of the disease increases with latitude (Kurtzke et al., 1980): in this regard, the case of Australia can provide a clear example of this effect if we consider that the prevalence of MS in Hobart (south Australia) is 75.6 per 100,000 compared to a prevalence of 11 per 100,000 in northern Queensland (Hammond et al., 1988). However, the geographical distribution of the disease is sometimes connected to other

causes: in Norway, for example, the risk for the occurrence of MS does not increase due to latitude but seems to be closely connected to the coastal areas dedicated to fishing and to the consumption of fishery products (Kampman et al., 2008). Recent studies show that the prevalence of MS among low-risk regions in areas closest to the equator is in the Americas.

According to the data contained in the Atlas file regarding the MS and published by the Multiple Sclerosis International Federation (MSSIF) and the World Health Organization in 2008 (data updated in 2013), the number of patients suffering MS in the world would be about 2,300,000: 600,000 are located in Europe; as regards the distribution in Europe, the higher incidence rate are recorded in Denmark (227 cases for every 100 thousand inhabitants), Sweden (189), Hungary (176) and United Kingdom (164), while in France, Spain, Portugal and Western European countries MS prevalence data are lower than average.

In Italy patients suffering MS are estimated to be between 68,000 and 75,000 with 1800-2000 new cases every year (Istituto Superiore di Sanità, 2018; Totaro et al., 2000): the situation seems particularly worrying in Sardinia where, according to studies published by the Associazione Italiana Sclerosi Multipla (AIMS) (Multiple Sclerosis Italian Association), the incidence reaches the value of 299 new cases per 100,000 inhabitants per year.

The WHO recognizes the MS among the diseases with the higher social costs: among the neurological disorders it has a higher incidence compared to Alzheimer's disease and stroke, firstly since it mainly affects the working-age population, secondly as it reveals itself with disabilities of various degree and, above all, progressive, finally due to the expectation of life of the patient, which can reach up to 40 years after its onset. In 2001, in Europe about 15 billion euros were expended compared to the 2 billion estimated to be spent in Italy: the average social cost per patient is 38,000 euros per year, with a range that varies between a minimum of 23,000 euros up to a maximum of 63,000 euros, depending on the severity of the disease.

#### **4. Conclusions**

On the basis of the above, it is clear that the social cost of diseases affecting the central nervous system has become a significant component of the nation budgets: according to a research on European social-economic costs, in 2010 just under 800 billion euros were spent (the average cost per inhabitant is 5,550 euros), risen compared to the data previously recorded; approximately the 37% is spent on direct costs in healthcare, the 23% on non-medical direct costs and the 40% on indirect costs.

As regards to the costs of the Multiple Sclerosis and the Parkinson's disease, they amount for the former to 14.6 billion euros 5.3 billion of which represent the direct costs for the patient's care, 4.6 billion the non-medical direct costs and 4.7 billion the indirect costs – and to 13.9 billion euros for the latter (7 billion of which represent the direct costs for the patient's care, 5.5 billion the non-medical direct costs and 1.4 billion the indirect costs) (Olesen et al., 2012).

According to the World Alzheimer Report 2018, the social and economic costs related to this disease were 604 billion dollars in the world, representing the 1% of the global GDP, while in Europe the cost deriving from this disease was about 175 billion euros. Almost ten years later, the worldwide cost of the disease has been estimated to increase from 1,000 billion dollars in 2018 to two thousand billion dollars in 2030 (World Alzheimer Report, 2018).

Focusing on Italy, it is possible to highlight an increasing trend of pathological incidences and related costs: specifically, the National Health Service spends 2 billion euros for multiple sclerosis, 2.4 million euros for the Parkinson's disease and 1.8 million for the Alzheimer's disease.

Finally, it is considered appropriate to reiterate that only through targeted prevention measures and a continuous and constant synergy between the various institutional subjects involved will it be possible to achieve the dual objective of containing social and health costs and improving the quality of life of people suffering from chronic degenerative diseases.

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