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## Review article

# Current status of stroke epidemiology in Greece: A panorama

Angelo V. Vasiliadis <sup>a,\*</sup>, Milorad Zikić <sup>b</sup><sup>a</sup> School of Physical Education and Sports Science in Serres, Aristotle University of Thessaloniki, Greece<sup>b</sup> Private praxis Novi Sad, Serbia

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## ABSTRACT

Although strokes have been documented since about 3 millennia, they remain today as one of the leading causes of mortality, as well as of subsequent serious long-term physical and mental morbidity, among patients in many different countries all over the world. Greece presents an increase in mortality rates according to World Health Organization, and this fact underlines the need for early diagnosis and treatment, as well as, the need to implement effective prevention strategies for strokes. This review makes an effort to describe the current status of stroke epidemiological features, as well as to present the risk factors prevalent in Greece. The incidence rate is 261–319/100,000 based on the recent population based registry. Stroke appears to be more prevalent in men than in women, and the mean age of stroke onset in Greece is at 70 years of age. Hypertension, atrial fibrillation, dyslipidaemia and diabetes mellitus are the major risk factors of stroke in the Greek population, while smoking is the most commonly documented modifiable risk factor in young adults with ischemic stroke. Similar to other parts of the world, ischemic stroke is the most common stroke type. The 28-day case fatality rate for men and women was 26.5%. The mean in-hospital cost per stroke patient was 3624.9 € and the mean rehabilitation cost of outpatients with stroke was 5553.3 €, while the cost proportion of hemorrhagic stroke is higher when compared to ischemic stroke. Stroke is a devastating condition with recognized challenges in identifying effective prevention programs. In Greece, limited data exists regarding the epidemiology of strokes. As a result, the need to conduct new studies and researches across the country is well documented.

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## 1. Introduction

Stroke incidences and familial stroke occurrence have been reported as early as 2700 years ago, in ancient Mesopotamia

and Persia [1]. Hippocrates (460–370 BC) was the first person to provide detailed accounts of strokes, referred to as apoplexy, from the Greek word *ἀποπληξία*, meaning 'struck down with violence', and describing the incidences as resulting in a sudden collapse, a loss of consciousness and paralysis. From

\* Corresponding author at: School of Physical Education and Sports Science in Serres, Laboratory of Exercise Physiology and Biochemistry, Aristotle University of Thessaloniki, Greece. Tel.: +30 6948402828; fax: +30 2310541610.

E-mail addresses: [vasiliadisvangelo@hotmail.com](mailto:vasiliadisvangelo@hotmail.com) (A.V. Vasiliadis), [milorad.zikic@gmail.com](mailto:milorad.zikic@gmail.com) (M. Zikić).

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**Fig. 1 – Map of Greece showing the different places where stroke studies have been conducted.**

the late 14th to the late 19th century the word 'apoplexy' was also used to describe any sudden death which began with a sudden loss of consciousness, as well as to describe the symptom of a sudden loss of consciousness which immediately preceded death [2]. Little was known back then about the cause of strokes, and the only established therapy was to feed and care for the patient until the attack ran its course [3].

Nowadays, a stroke, or "brain attack" is recognized as the third most common cause of death in many developed countries, following coronary heart diseases, and all cancer types combined [4,5]. Annually, statistics show that fifteen million people worldwide suffer a stroke episode. Of these, nearly five million die and another five million are permanently disabled, experiencing loss of vision and/or speech, muscle weakness and confusion [6,7]. Although stroke can affect all ages, the chance of having a stroke approximately doubles for each decade of life over the age of 50, while it appears uncommon in people below 40 years of age [8]. Stroke is so common [9] that it should not come as a surprise that most people know of someone who has suffered a stroke, or have a close family member who has faced a stroke episode.

Europe occupies a large geographical area, in which about one million of the stroke incidences occur each year [10]. Data on strokes vary and show large differences across countries, and even across geographical areas within the same country

[11]. Geographic comparisons of stroke incidences within countries are valuable, in order to help identify high risk populations as well as to define preventive and effective intervention programs [12,13]. However, comparability of stroke studies might be hampered by several methodological differences in data collection, leading to limitations in their findings [13,14]. In Greece, a typical Mediterranean country, there is lack of epidemiological studies of strokes and these studies present a geographical inequality and a wide variation among data [15,16].

Thus, the objective of the study in question has been to provide an overview analysis of the epidemiological context of strokes (incidence rates, mortality rates, risk factors), as well as to outline recent trends in treatment patterns and finally present the economic aspects of stroke treatment. These data will be used in order to estimate the total stroke burden in Greece (Fig. 1).

## **2. Epidemiological context**

### **2.1. Incidence rates**

Incidence information relates to the number of new cases of strokes for a given year per 100,000 inhabitants. The estimated

annual incidence rate for strokes among Christian and Muslim populations in Thrace was 261.1/100,000 residents, who had suffered their first documented stroke episode in the period between 1998 to 2002 [15]. A second study was established in the Arcadia province of Southern Greece, which mentioned an overall standardized incidence rate of 319.4/100,000 in both genders in the period starting from November 1993 till October 1995 [16]. These crude annual incidence rates are quite similar to the incidence rates from studies in other countries such as in the Balkan area (Croatia, 344.6/100,000 from 1996 to 2005) [17] and the Iberian Peninsula (Portugal, 305/100,000 from 1998 to 2000) [18]. In contrast, lower incidence rates were reported in Zabrze, in Southern Poland, 131/100,000 (from 2005 to 2006) [69], in Spain, 141/100,000 (1 year period, 2005) [19] and in the Sicilian Aeolian Archipelago in Italy, 154/100,000 (from 1999 to 2002) [20].

Also, one of the most recent studies, a population-based study in the Evros province in Greece, determined only subarachnoid hemorrhage incidences over a 5-year period (2001–2005). The annual incidence was 7.9/100,000 for the totality of the area's population [21], which is very similar to the incidence rates reported in the Arcadia province, 7.2/100,000 [16] and to other European standardized rates in South London, 8/100,000 (from 1995 to 2004) [22] and Aosta, 10/100,000 (1 year period, 1989) [23]. In contrast, lower incidence rates were reported in Dijon – France, 4/100,000 (1 year period, 1985) [24] and in Belluno – Italy, 4/100,000 (from 1992 to 1993) [25].

## 2.2. Mean age of first-ever stroke incidence and gender issues

Despite the fact that stroke can occur at any age, it seems that the elderly population is at a much greater risk [26]. The mean age of stroke patients was 70.14 years of age (in detail, Christian population: 71.43; Muslim population: 67.26), with a little more than half (52.1%) of strokes occurring in males, in the Xanthi region, a mainly rural and remote area in Northern Greece [15]. In the Arcadia area in Southern Greece, research also found a male predominance (55.7%) in strokes and a mean age of first-ever stroke incidence (with an age range from 18 to ≥85) at 75.1 and 76.1 for men and women, respectively [16]. In a most recent research, referred to as the Athens Stroke Registry (a computerized, prospective, observational databank), consisting of 1448 patients with a first-ever stroke, the mean age of stroke was at 69.9 and again the results confirmed male

predominance (61.5%) [27]. Moreover, during an 8-year period (1992–2000), 1418 stroke patients were identified (60% of them men), in a study in Athens (Stroke database of the University Department of Clinical Therapeutics, “Alexandra” Hospital, Athens), with the mean age of stroke incidence at 70 years of age [28]. The EVRO-SAH (The Evros Registry of Subarachnoid Hemorrhage), a population-based computerized registry, recorded 51 cases (54.9% of them men) of subarachnoid hemorrhage incidences, with a mean age of 59, in a range of 25–92 years of age, during a 5-year period [21]. (Table 1)

Stroke has traditionally been considered a disease of old age [8] and this fact appears to be in accordance with the selected provinces over the Greek territory [15,16,27,28]. Epidemiological studies from Southern Europe have shown that stroke is more common in women than in men, with this predominance ranging from 50.5 to 62.1% for women [29], while data based on Western European surveys show a stroke ratio of 1.41, meaning that stroke episodes were 41% more common among the male population [30]. Although Greece extends over a peninsula located on the South-Eastern side of Europe, Greek studies have found a slight male predominance in stroke incidence, which appears to match the results and findings of studies in Northern Europe [31,32].

## 2.3. Types of strokes

In two prospective studies, 86.6 and 80.5% of recorded patients had suffered ischemic strokes in the Xanthi and Arcadia provinces, respectively. The pathological diagnoses for the first-ever hemorrhagic strokes were as follows: the 12.6% of cases has an intracerebral hemorrhage and only the 1.7% of cases has a subarachnoid hemorrhage in the Xanthi region [15]. Slightly higher figures are reported in the Arcadia region with intracerebral hemorrhages comprising 13.9% of the total, and subarachnoid hemorrhages 2.5% [16]. In a hospital-based study, a diagnosis of an ischemic stroke was reported in 84% of patients, while 13% of patients presented stroke symptoms resulting from an intracerebral hemorrhage, and finally 3% of patients were identified with subarachnoid hemorrhage occurrence [27]. The same results, with ischemic strokes comprising of over 80% of all strokes, with strokes caused by intracerebral hemorrhage and subarachnoid hemorrhage making up the rest, also appear in studies in Thessaloniki and Patra [33,34] (Fig. 2). It appears therefore, that a stroke is a heterogeneous disorder, and at a global level, ischemic strokes, resulting from occlusion of one or more arteries, account for

**Table 1 – Registry studies on Greek stroke patients.**

Study [references]	Years	Location	Patients	Patients number	Mean age (years)	Male/female (%)
Vemmos et al. [16]	1993–1995	Arcadia province	Strokes (IS & HS)	555	75(m)–76(f)	55.7/44.3
Stergiou et al. [28]	1990–2000	Athens	Strokes (U)	1418	70	60/40
Papadopoulos et al. [15]	1998–2002	Xanthi	Strokes (IS & HS)	530	70.1	49.5/50.5
Gioldasis et al. [34]	2001–2002	Patra	Strokes (IS & PICH)	429	68.9	58/42
Spengos et al. [27]	1992–2003	Athens	Strokes (IS & PICH)	1448	69.9	61.5/38.5
Vadikolias et al. [21]	2001–2005	Evros province	Strokes (SAH)	51	59	54.9/45.1
Vasiliadis [33]	2008–2010	Thessaloniki	Strokes (IS & HS)	18	58.8	50/50

IS = ischemic stroke; HS = hemorrhagic stroke; U = undetermined; PICH = primary intracerebral hemorrhage; SAH = subarachnoid hemorrhage; m = male; f = female.

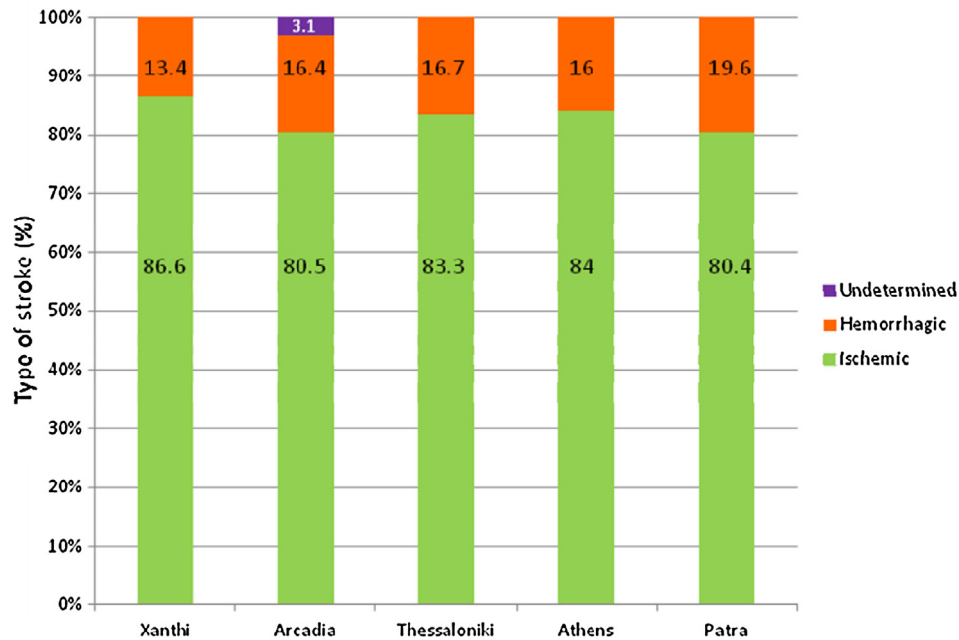


Fig. 2 – Distribution of stroke subtypes in various territories in Greece.

about 80% of the instances, while 15% are caused by intracerebral hemorrhage (bleeding within the brain tissue) and 5% are due to subarachnoid hemorrhage (bleeding into the subarachnoid space) [35].

#### 2.4. Stroke severity

Neurological assessment is one of the most important tools in clinical neurology, which helps identify and assess stroke severity. The Scandinavian Stroke Scale (SSS) or the National Institute of Health and Stroke Scale Score (NIHSS) are commonly applied for assessing the neurological severity of strokes [36,37]. In Greece, only one study from the University Hospital of Patras has indicated stroke severity. Along with functional disability examination (based on the modified Oxford Handicap scale), patients were also evaluated on the SS Scale for assessment of the severity of the stroke, on admission to the hospital. Three hundred and seventy-five patients were divided into 4 groups: (i) scores ranging between 0 and 18 were defined as 'very severe strokes' (17.1% of patients), (ii) scores ranging between 19 and 32 were defined as 'severe strokes' (27.7% of patients), (iii) scores ranging between 33 and 44 were defined as 'moderate strokes' (33.9% of patients), and finally (iv) scores ranging between 45 and 58 were defined as 'mild strokes' (21.3% of patients). As has been noted in the research, lower scores indicate more severe strokes. The research identified that stroke severity was highly correlated with the length of stay, which is directly related to the costs of bed facilities and staff resources. Also, it emerged that the length of stay, as well as the stroke severity were predictors of the total in-hospital costs. In this study, the cost of more severe strokes was higher because of the

increased length of stay as well as of the increased intensity of care [34].

#### 2.5. Case mortality/fatality

According to a clinical research based on information provided through the electronic databases of the World Health Organization (WHO), and which represent national vital statistics from 1990 until 2006, from 39 countries in Europe and Central Asia, the stroke mortality rate in Greece was 143.9 and 194.6 deaths per 100,000 inhabitants for men and women, respectively [38]. It is worth noting that despite the high rates of stroke mortality in the baseline year (1990), Greece related statistics have shown a continuous decline. Also, it should be noted that in Greece, the high rate of stroke mortality coexists with a prevalence of coronary heart disease [16]. This can be explained in the high prevalence of specific risk factors, such as hypertension, which we will refer to further on [38].

In detail, out of the 555 patients in a prospective population based study, of acute first ever stroke incidences, during a 1-year period, 204 (36.8%) patients died. The 28-day case fatality rate accounted for 26.5% of the patients, without significant differences in the fatality rate between men and women. Also, the case fatality rate appears to increase with age, and was higher for intracerebral hemorrhage than for cerebral infarction [16,39]. The 28-day case fatality rate documented from the Arcadia based registry study, was similar to the ones documented in Tartu – Estonia, 26–30% [40], L'Aquila – Italy, 29% [41] and the Sicilian Aeolia Archipelago – Italy, 24.4% [20]. On the other hand, substantially higher case fatality rate has been reported in Bulgaria, 35% [42], while in Krakow and Zabrze – Poland, the documented case fatality rates were

significantly lower, 17.8% and 16.6%, respectively [43,69]. In Prague – Czech Republic, the case fatality rate was reduced even more, to 10.7% [44]. In the former SFR Yugoslavia, and in particular in the Community of Novi Sad, annual mortality rate amounted to 42.2% [45].

In the Evros Registry – SAH Study [21], the 28-day case fatality rate was 36 and 35% for men and women, respectively. These findings tend to be lower when compared to the Arcadia Registry Study [16], in which the percentage amounted to 45% and included both intracerebral and subarachnoid hemorrhage incidents. Thus, it is difficult to interpret and compare the results between these studies. On the other hand, the case fatality rate reported in the Evros Registry study, is not significantly different from Scandinavian studies. Findings from Tromsø – Norway [46] and Sweden [47] report 36 and 31.7% case fatality rates, respectively.

### 2.6. Risk factors

Risk factors may be distinguished in two categories: (i) modifiable factors, on which any intervention may potentially alter the results, and (ii) non-modifiable factors, which including age, gender, race, ethnicity, and heredity issues [48]. It should be noted that the impact of the risk factors may exhibit different proportional levels in a comparison between the elder and the younger populations [49]. Given that age is one of the most substantiated risk factors for strokes, the aging of the world population implies a growing number of persons at risk of a stroke [50]. However, a stroke episode can affect anyone, no matter their age, gender, or race.

For a Mediterranean country like Greece, hypertension (47.2–84.6%) appears to be the leading modifiable risk factor for stroke occurrence, with atrial fibrillation (17–38.3%) and diabetes mellitus (24.3–32.57%) ranking in second place of the most important modifiable risk factors of stroke [6,27,39,51–53]. Also, risk modifiable factors such as alcohol consumption, cigarette smoking and metabolic syndrome have been documented and occupy an important place in the culture and life of the Greek people [6,52,53]. The results here are similar to those of Croatian and Italian stroke patients [20,54]. However, the most commonly documented risk factors, in young adults with ischemic strokes at an age up to 45 years, were smoking (59.3%) and dyslipidemia (41.1%) [55]. Regarding risk factors and comparing them to other studies, only in the younger Korean population (aged  $\leq 49$  years) it has been found that smoking and dyslipidemia occurred at significantly higher rates of 48.5 and 39.8%, respectively [56].

### 2.7. Costs of strokes

Recent studies have reinforced the fact that stroke is associated with considerable social and economic costs for individuals as well as societies in total [57,58]. Over the last decade, there have been several studies which have estimated the direct and indirect clinical costs of strokes [59,60]. Direct costs include all the costs that are directly associated to the provision of health care (e.g. in-hospital treatment, medication, rehabilitation, nursing home), whereas indirect costs encompass the costs of lost productivity, due to morbidity or mortality [61]. The differences which appear in results

between different studies can be attributed to the differences in data collection, population size, observation period and definition of cost components [62].

Several studies have estimated the economic cost of strokes in developed countries [60,63], as well as in developing countries [64,65]. As an example, the healthcare and societal costs of strokes in Italy, have been found to have amounted to 11,747 € and 19,953 € per year, per stroke survivor, respectively [57]. On the contrary, data available on the cost of strokes in Greece are limited. Data from two research studies show that the direct in-hospital costs for stroke cases amounted to 331.9 € per day, per patient [34], while rehabilitation costs for outpatients with strokes accounted toward 591.5 € per month [33]. The absence of data concerning the indirect related costs of strokes in Greece is remarkable.

## 3. Discussion

Strokes pose as a significant health problem, existing for more than 2700 years, with a worldwide occurrence. In order to provide a national view on the status of stroke epidemiology nowadays, the present study enrolled a sample of studies conducted in Greece. In addition, this study has attempted to compare these results to relevant international literature sources and background data. The annual incidence of strokes in Greece is 261 incidents and 319/100,000, in an observation period between 1998–2002 and 1993–1995 for the Xanthi and Arcadia provinces, respectively. These results are similar with observations appearing from other rural regions. In a population-based registry in Northern Portugal, which took place over a 2-year period, from October 1998 to September 2000, the crude annual incidence rate of first-ever stroke incidence was 305/100,000 [18]. On the contrary, the incidence of first-ever strokes during 1 year, from May 2000 to April 2001, is nearly three and four times over in the rural populations of North-East Bulgaria, in detail 909/100,000 for men and 667/100,000 for women [42].

If we want to summarize the results from these two studies, we would conclude that the incidence of strokes has continued to decline by almost 20%, in the period between 1993 and 2002 [15,16]. This comes into contrast with the projections on stroke incidence as a direct result of the economic crisis, including the dramatic rise of unemployment, the closure of thousands of local businesses and the inability of Greek citizens to pay bills and new taxes. In general, it is believed that the rise in unemployment, despair and frustration will contribute decisively in the rapid increase of new stroke episodes on the Greek population, as many patients are expected to delay visiting their doctor, because they cannot respond to the costs of medical care and medication. The lack of clinical studies from the last decade, as well as, the absence of studies conducted in urban areas, present limitations for a stronger determination and a better view of incidence rates. The need to conduct more epidemiological studies as additional techniques of scientific investigation, aiming to determine the change patterns in the incidence of stroke episodes, shall help in establishing a better understanding on the topic.

As previously mentioned, there are two types of risk factors for stroke: (i) modifiable and (ii) non-modifiable factors. Age is

the single most important risk factor and the strongest determinant of stroke. Anyone can have a stroke no matter their age, race or gender, but literature suggests that it is mainly a disease of the elderly. According to the relevant studies conducted in Greece, the mean age of patients at the onset of a stroke episode is approximately 71 years old. This age is similar to findings from previous reports of other countries around the world [18,66]. Previous Greek epidemiological studies suggested that stroke incidence rates increase with age, and presented a mean age of 75 and 76 years for men and women, respectively [16]. However, the onset of stroke in the Greek population appears earlier and below 70 years, according to more recently published data [27,33,34]. It seems therefore, that the incidence of a stroke in people aged below 65 years has increased. Also, stroke episodes are increasingly affecting younger people, with the number of young people facing a new stroke potentially doubling over the next years. This may be due to the lack of medical screening examinations, because of financial problems and the general economic, social, political effects of the crisis in Greece. Secondly, a rise in risk factors such as poor diet, diabetes, obesity, hypercholesterolemia and the lack of exercise in younger populations may lead to the development of several vascular diseases.

The majority of risk factors for strokes are modifiable. In other words, strokes appear to be a risk that can be changed and/or controlled. Hypertension is the most common risk factor, as it is a well established risk factor in most studies. With the economic crisis, the Greek lifestyle has rapidly changed over the past 10 years. A result of the crisis is the physical stress, as well as the mental stress inflicted on the Greek population. General stress is often referred to as one of the factors that predispose to hypertension. On the other hand, it is a common belief that competitive and anxious people have a high probability of developing hypertension. In Greece, among the modifiable risk factors, hypertension remains to be the most important and frequent risk factor for all types of strokes [16,27]. Although we should note that risk factors, such as smoking and dyslipidemia, document leading percentages among risk factors for ischemic strokes [55]. At present, changes in stroke risk factors have been observed in Greece in the last 2 decades. The risk from major stroke risk factors, including obesity, hypercholesterolemia and metabolic syndrome, has substantially increased. This may be due to the adoption of the western lifestyle, which includes the prevalence of smoking, poor diet and a lack of physical activity.

It is commonly accepted that by following a Mediterranean diet plan, individuals can lead to longer life expectancy. The main reason behind this lays in the characteristics of the traditional Mediterranean diet, i.e. a diet which primarily revolves around the consumption of olive oil, cereals, vegetables, fruits and less on high-fat foods, fried foods, meats and sugars. But altering the behavior of individuals toward nutritional habits, requires first of all the education of individuals on the specific subject, and also on the importance of adopting and sustaining healthy eating patterns. This can be done through a genuine and systematic education of the population on nutritional issues. Nutrition and health educational programs should primarily be aimed to inform the general population on the association of diet and health

benefits. On the other hand, educational campaigns should be aimed at groups with particular characteristics. Additionally, integrating nutrition educational programs in the school curriculum provides the advantage of information and cultivation of a significant age category. Finally, these can help form correct attitudes and health behaviors toward food, and provide particular nutrition habits to the most vulnerable members of the population. In any case, it is necessary to educate specialists who will be charged with the specific responsibility, while the role of teachers in the whole effort is considered crucial.

In addition, the health benefits of regular exercise and physical activity are hard to ignore. It is generally accepted that regular exercise helps the brain work more efficiently. Another benefit of having exercise is that it provides an effective way to prevent or even reduce the risk of heart attack, stroke and diabetes, as well as other chronic diseases. The organization of exercise programs is of primary importance. In this direction, the awareness of health professionals, information on the benefits of exercise on the same patient and the priority of health providers to organize exercise programs in order to promote health, will play an important and crucial role. Moreover, exercise programs should be developed massively within all municipalities and should be addressed to all citizens without significant financial burden. In general, health educational programs and policies are of great importance to be applied at school level and in the wider municipality community by experts.

Case fatality refers to the proportion of patients who having suffered a stroke episode have died after a specific period of the illness having occurred. Typically, this rate is expressed as a percentage of deceased patients in a 28-day period [67]. Only one study from Greece, a prospective population-based study in the Arcadia province was conducted from 1993 to 1995. This study extracted data from the General Arcadia Hospital, which served as a referral hospital for stroke patients. The findings show and adverse outcome with 26.5% of the patients dying during the first 28-days, and the 36.8% by the end of the follow up period. The overall case fatality rate was 26.6%, which appeared increased with age and without differences noted between the gender affiliations [16,39]. One year mortality from stroke is similar to that of other industrialized countries [20,41].

Knowing the risk factors for stroke is the first step we can take to help prevent them. There are known risk factors that contribute to chances of having a stroke episode. Also, it is obvious that there are a number of non-modifiable risk factors such as age, gender, race, ethnicity and heredity. These risk factors cannot be changed. However, people in these high risk categories should have regular checkups with their doctors. There are important modifiable risk factors that can be modified through changes in lifestyle or by the proper medical intervention and treatment. The systemic control of high blood pressure and cholesterol as provided by maintaining a Mediterranean diet, the introduction of exercise, as well as pharmacological treatment is of great importance. Also, the acceptance of doctors' recommendations for the keeping of safe limits in alcohol consumption is essential in order to help reduce the risks of suffering a stroke. Furthermore, a successful program through which the general population

can be helped in quit smoking, is beneficial to avoid strokes and promote at the same time overall health, at any age. Finally, the importance of achieving and maintaining a healthy weight, is equally important in order to help people in avoiding strokes.

After a stroke episode, rehabilitation for stroke patients has been shown to improve functional ability and independence among stroke survivors [33], with the rehabilitation therapy being a continuous process for many stroke patients after they are discharged from hospital. The need of well-structured rehabilitation departments in order to provide comprehensive stroke rehabilitation is an important issue. As result, the next big step after prevention strategies for strokes is the organization of early inpatient rehabilitation therapies as well as outpatients' services, home care and community support services [70]. Quality improvement of stroke services and the organization of the continuous education of the medical staff are also necessary in order to perform a step toward true rehabilitation [71].

In Greece, the National Insurance System is currently in short of funds and is facing major problems during the economic crisis. The recession has led to a higher incidence of ill-health and widening inequalities. Thus, the poorer social classes are increasingly affected by health problems. It is generally accepted that the poorer social class is significantly affected by chronic cardiovascular diseases, such as stroke, due to the inability to afford the high costs associated with treatment and rehabilitation services [68]. Nowadays stroke is a primary topic of investigation and of great importance worldwide. Although there is a lack of epidemiological data on stroke episodes, where these few data exist, they appear to be out of date in Greece. Thus, efforts should be made to create a region-wide database for stroke epidemiology. Creating a stroke registry is an ideal opportunity to initiate an efficient service and develop strategies to prevent and better care for stroke patients.

#### 4. Conclusions

The annual incidence of strokes in Greece were high, at 261 and 319/100,000, in the observation period between 1998–2002 and 1993–1995 for the Xanthi and Arcadia province respectively, with a 26.5% mortality rate for the first 28-days, and 36.8% by the end of the follow up period. According to clinical research based on information provided in the electronic databases of the WHO, which represent national vital statistics from 1990 to 2006, the stroke mortality rate in Greece was 143.9 and 194.6/100,000 for both genders.

#### Conflict of interest

None declared.

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#### Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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