THE EFFECTIVENESS OF REHABILITATION MEDICINE IN THE TREATMENT OF POST-STROKE PATIENTS

Faisal Saghir
Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria,Fsaghir16@gmail.com
Galina Mratskova
Department of Medical Rehabilitation and Ergotherapy, Physical Medicine and Sports, Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria, doc_mratzkova@abv.bg

Abstract: Stroke is a medical condition in which poor blood flow to the brain causes cell death. These can be divided into two main sub-types: ischemic and haemorrhagic. Both of these types lead to a starvation of brain cell's inducing hypoxic-like damage or an increase in intracranial pressure resulting in intracranial hypertension associated with a loss of cognitive function amongst many other complications.
The Purpose of this research article is to provide an informed understanding on the effectiveness of a wide range of rehabilitative methods within medicine and how these methods can be applied in order to improve the status of post-stroke patients.
Materials and methods: A review of the available literature was conducted, including articles on the recovery of patients after stroke and possible physical interventions used in the rehabilitation of these patients, which revealed an impact on symptoms, functional deficits and functional activity. The search for scientific articles is realized in the database of Pub Med. Scientific articles were searched for results defining: stroke, epidemiology, risk factors, symptoms, severity of the disease, post-stroke care, stroke rehabilitation, neurorehabilitation, physiotherapy, robot assisted rehabilitation, robotic technology, assistive technology, exoskeleton, activities of daily living, Brain-computer interface (BCI), Electric stimulation, neuromuscular functional electrical stimulation (NMFES) motor imagery (MI), neurorehabilitation devices, Neuroprosthesis.
Results: In the conducted review of the literature we found articles that contain evidence of the effectiveness of the rehabilitation. The results indicated, from this stroke-suffering patients the symptoms such as headache, visual difficulty and confusion were swiftly corrected through the utilisation of rehabilitative techniques, in comparison to no implementation of any rehabilitation medicine. The duration of treatment was reduced significantly, however, more research needs to be undertaken in order to understand the pathophysiology in regards to the numbness and hemiparesis displayed by stroke patients so can provide a link that rehabilitative techniques do provide a more effective and concise way in which to treat post-stroke patients. The results achieved from this review proved that there does exist, nonetheless a positive relationship between the administration of these rehabilitative devices in the form of treatment and the shortening in recovery time taken for a post-stroke patient from the onset of stroke to the eradication of major and minor clinical signs and symptoms associated with stroke.
Conclusion: Overall, physical and rehabilitation medicine plays an integral and supportive part in the treatment of post-stroke patients. Through the various techniques and devices, we can establish a positive relationship in a shortened duration of recovery a patient suffering from stroke as opposed to stand-alone and conventional methods to treat stroke patients, however, more research needs to be undertook in order to provide innovation and to advance the field of physical and rehabilitative medicine and the role it plays within stroke medicine and related health disciplines.
Keywords: stroke, hemiparesis, rehabilitation, assistive technology, robotic technology, exoskeleton, brain computer interfaces, neuroprosthesis.

1. INTRODUCTION

Stroke is one of the most important and leading causes of morbidity and mortality worldwide (Strilciuc, S. and al. (2021)) and poses a serious problem for health systems (Wafa et al. (2020)). It is a medical condition in which poor blood flow to the brain causes cell death. These can be divided into two main sub-types: ischemic and haemorrhagic. The ischemic stroke is one in which there is a lack of blood flow and conversely the haemorrhagic type of stroke is one in which there is abnormal amounts of bleeding. Either both of these types lead to a starvation of brain cell's inducing hypoxic-like damage or an increase in intracranial pressure resulting in intracranial hypertension associated with a loss of cognitive function amongst many other complications. (Kuriakose, D., & Xiao, Z. (2020)).
The target audience of this review article is for those individuals who have a background in rehabilitative or stroke medicine or for those individuals who have an expressed interest in the medical discipline in itself. The wide range of sources and journals utilised in this article is indeed appropriate and relevant for the purpose established at the start of this article. To inform and have a wider understanding into whether the effectiveness of various

rehabilitative techniques can improve the outcome of patients who have previously suffered from a stroke. Furthermore, we will be providing a detailed insight into the epidemiology, prevalence and clinical signs and symptoms that can be seen from a patient who has previously suffered from a stroke.

Moreover, this review article will be a review of all the sources cited at the end of this article and it will consist of being an empirical view, based upon the clinical findings and observations of various renowned researchers, in conjunction with our own research.

Generally, stroke is regarded as a serious systemic syndrome comprising of many aetiological risk factors which can lead to an increased chance of developing triggers which will lead to a stroke and these include the following; high blood pressure, smoking, diabetes mellitus, obesity, pre-existing cardiac co-morbidity such as defective heart valves and atrial fibrillation, age, family history of previous stroke, gender and race. Consequently, the incidence of stroke is 1 in 6 people will suffer from an ischemic or haemorrhagic stroke. Every 40 seconds an individual suffers from stroke in which every 4 minutes someone dies from stroke with 85% of these deaths due to a thalamic ischemic stroke in origin. All the aforementioned factors mentioned are quite important as they can increase the likelihood of an individual to suffer from a stroke by about 35-50%. Stroke remains the second-leading cause of death and the third-leading cause of death and disability combined in the world as of the year 2022. In addition, the epidemiological status of stroke is of such that the most common cases of stroke occur within parts of the world with the highest prevalence such as Sierra Leone, North Korea, Mongolia followed by Yemen. These countries mass the highest number of stroke-related cases amounting to approximately 700,000 new cases amongst these countries together (Bo Norrving 2013).

At the same time, cost of illness studies involves two different types of costs, which can be classified into two sub-categories namely, direct, and indirect costs. The direct costs relate to all of the goods, services and other resources, which are, utilised in the treatment plan of a specified illness, in this case stroke. Some of these costs include the money spent on hospital and nursing home care, on the services of medical professionals, drugs, appliances and rehabilitation. On the other hand, indirect costs are the productive losses, which are incurred for both the individual and the lay-on effect on the economy. These specifically include the monetary value of the productive losses. Annually, about 5% of all world economies dedicate a sector of their spending to be used in the treatment of post-stroke patients. (Rajisic et al. (2019)).

The costs per capita are indicated to be higher due to each individual containing certain charecteristics, which involve a longer period of medical treatment or due to the health infrastructure and organization within a specific economy. To further this, in the first year after stroke about 76% of stroke costs are dedicated for inpatient treatment, which is then shifted to the treatment of outpatient and long term care costs. Representing the world economies, in European countries like Scotland and Netherlands, we have a smaller part of the total cost, which is spent on outpatient treatment as opposed to countries like America, and Canada with a 2-3% difference in total costs spent on the treatment and resources of stroke patients. (İçağasıoğlu et al. (2017)).

There is a trend which can be established here which includes a general relationship stating those countries that dedicate a lot of their economic resources to inpatient care have a lower spending on their outpatient services which can be used in the treatment of stroke. Average annual costs of stroke range from $7,432 to $146,149. (Rajisic et al. 2019)).

In addition to this, we can identify certain factors, which can influence the costs of stroke, with one of them being the duration of hospitalization. This can influence the financial burden on the government or the individual suffering from stroke as the longer a stroke patient is hospitalized the costs are considerably higher. Furthermore, a negative correlation is found between elderly patients and the total cost of stroke. Whereby, due to the severe cognitive impairment and family neglect, these patients tend to receive less care and this age group tend to suffer from higher mortality rates, which have an effect in which it reduces the total cost of stroke.

2. MATERIALS AND METHODS

A review of the available literature was conducted, including articles on the recovery of patients after stroke and possible physical interventions used in the rehabilitation of these patients, which revealed an impact on symptoms, functional deficits and functional activity. The search for scientific articles is realized in the database of Pub Med. Scientific articles were searched for results defining: stroke, epidemiology, risk factors, symptoms, severity of the disease, post-stroke care, stroke rehabilitation, neurorehabilitation, physiotherapy, robot assisted rehabilitation, robotic technology, assistive technology, exoskeleton, activities of daily living, Brain-computer interface (BCI); Electric stimulation; neuromuscular functional electrical stimulation (NMFES) motor imagery (MI); neurorehabilitation devices, Neuroprosthesis.

We also made an in-depth analysis of the typical rehabilitative-induced factors which can take an effect on the recovery period of stroke-suffering patients, whilst also looking into the up to date technology in the form of robot

assisted devices and whether the benefit outweighs the risk in the implementation and usage of such forms of medical technology.

3. RESULTS

In the conducted review of the literature we found articles that contain evidence of the effectiveness of the rehabilitation. The results indicated, from this stroke-suffering patients the symptoms such as headache, visual difficulty and confusion were swiftly corrected through the utilisation of rehabilitative techniques, in comparison to no implementation of any rehabilitation medicine. The duration of treatment was reduced significantly, however, more research needs to be undertaken in order to understand the pathophysiology in regards to the numbness and hemiparesis displayed by stroke patients so can provide a link that rehabilitative techniques do provide a more effective and concise way in which to treat post-stroke patients. The results achieved from this review proved that there does exist, nonetheless a positive relationship between the administration of these rehabilitative devices in the form of treatment and the shortening in recovery time taken for a post-stroke patient from the onset of stroke to the eradication of major and minor clinical signs and symptoms associated with stroke. Previous studies have shown a positive and promising relationship between the effectiveness of rehabilitative-like strategies in the medical treatment plan of post-stroke suffering patients, however, a definitive link between these two co-existing variables is yet to be established due to the external environmental factors that can have a polymorphic influence on the development of the signs and symptoms that can be seen from a patient who has previously suffered from a stroke.

4. DISCUSSIONS

The process of treatment and recovery of patients after stroke is a slow and long-term process that requires very accurate determination of the clinical condition and the degree of damage to the nervous system. Clinical symptoms must be determined very precisely and the appropriate time to start rehabilitation and the methods and means to be applied to each patient must be selected.

With this, it is very important to identify the different signs and symptoms of stroke as this can heavily influence the type and stage of treatment and resources needed in order to improve the overall condition of the patient. The American national institute of Neurological Disorders and Stroke have included a list of six important signs and symptoms, which can indicate that a patient is suffering from stroke and these include the following:

- Numbness or weakness in the face, arms, legs and especially if it is confined to one side of the body
- Confusion and difficulty speaking or understanding speech
- Visual disturbances in one or both of the eyes
- Dizziness, trouble walking, loss of balance and a loss of coordination
- Severe headache with an idiopathic origin
- Dysphagia or difficulty swallowing

These signs and symptoms, which can be identified in potentially stroke-suffering patient, are influenced by several factors, which can determine the severity of the stroke. These include age, level of education, sex, income level. In addition to this, age is a big factor, which influences the severity of stroke as it is seen that with an older age the likeliness to make a full recovery is unlikely. The second factor is the level of education as the level of information of stroke will be higher in health-care professionals as opposed to those individuals working in the financial sector as a higher level of education is positively correlated to the detection and early intervention in terms of improving the condition of the stroke patient. In terms of gender, there seems to be no overall influence in the early detection of stroke and so it is unclear and this factor requires further research. In addition to this, history of stroke has played a detrimental effect on the early intervention of stroke as if an individual has already suffered from a stroke they are more likely to be able to notice the main early signs and symptoms which can lead them to take quicker and more effective decisions when determining to seek medical advice. (Nicol & Thrift (2005)).

Following specific medical treatment of acute neurological symptoms associated with acute cerebrovascular accident, it is very important to select the appropriate period to begin early rehabilitation. After overcoming the acute phase of the stroke, the process of consistent and prolonged rehabilitation is essential.

In general, one of the main goals of rehabilitation medicine is to increase the functional activity of the upper and lower limbs, to improve gait capacity, postural instability and imbalance in stroke patients, which is likely to improve the quality of life in post-stroke patients associated with increased independence in performing activities of daily living. (Belas Dos Santos et al. (2018)).

In addition to the traditionally used means and techniques for motor recovery, therapeutic exercises and specialized methods of neuromuscular reeducation, today more often in practice methods of assisted rehabilitation are used, which are based on technological progress, such as robotic rehabilitation systems.

To further improvement functional activity and decrease, and reducing motor deficit, there is a wide range of factors involved within the rehabilitation of a post-stroke patient in order to maximise the patient's potential ability to regain neuro-functional and motor-functional status.

Kinesotherapy is an alternative term for movement therapy and it is a term applied to the therapeutic treatment of a disease by passive and active muscular movements and of exercise. (Church et al. (2022)).

Kinesiotherapy can be successfully combined with physical modalities such as neuromuscular functional electrical stimulation (NMFES), which involves eliciting the neuronal innervation of the paretic muscles. NMFES has shown to elicit an improvement in the general status and wellbeing of a patient who has previously suffered from a stroke by modifying neural transmission in the synaptic contacts of the corticospinal tract with spinal motor neurons and thus the overall effect of this method is to improve the motor functional status of the patient. It does this by increasing and recruiting both rapid and slow myelination muscle fibres to act synchronously and elicit a muscular movement with a reduction of any sudden or opposite movements. NMFES is delivered as a waveform of electrical current sequenced in pulsons and characterised by stimulus frequency, intensity, pulse width and the time intervals between pulson deliveries. Frequency of intense muscular depolarization is given in the ranges of 15 – 50 Hz and the therapeutic application involves facilitating upper and lower extremity motor learning, reducing hemiplegic shoulder pain, strengthening muscles, preventing muscular atrophy. During the course of the prospective study, on the third day after admission to the neurological ward the patients were healthy enough to begin physiotherapeutic treatment. During the first 10 days of being hospitalized, the patients were taught how to hold an upright position, sit down, change positions and perform global movements necessary for everyday life. Then from this, the patients were taught proper locomotion, including walking with a hand stick and walking with orthopaedic equipment. The pathophysiological mechanism of NMFES is explained by the fact that it recovers the lack of descending control of spinal circuits in post-stroke patients by the presynaptic inhibition of muscle spindle reflex activity, the influence of the cortical neuroplasticity via the long-loop biofeedback control or the change in the level of the muscle by the increased efficiency of the muscle motor units themselves. In the case of disturbances of neural activity at the cortical level, the frequency of discharges from the level of the lower motor neuron to the effector increases, which evokes increase in muscle tension? Due to this, there is a decrease in ability of muscle motor units to perform proper muscle contractions. Overall, from this type of method employed in the treatment of post-stroke patients, there was a positive correlation by a means of decreased spasticity-related symptoms at rest and an increase in muscle strength correlated with the EMG activity recorded during attempts at maximal amount of muscle contraction on the paretic side (Huber et al. (2022)).

In the recent years, robotic technology has developed with newer and faster computational approaches, as well as greater sophistication of the various electro-mechanical components, which can be used in the therapy of treating stroke patients. Robot can be defined as re-programmable, multi-functional manipulator designed to move material, parts, or specialized devices through variable programmed motions to accomplish a task. These robotic devices can be broadly defined into two categories: Assistive and therapeutic robotic devices. The purpose of assistive robots is compensation and the therapeutic robots provide task-specific training. In specifically, for motor training we have two types of devices: Effector-type devices and exoskeleton-type devices. The end effector devices work by applying mechanical forces to the distal segment of the limbs and they serve the advantage of being easy to set up but suffer from limited control of the proximal joints of the limb, which could result in abnormal patterns (D.Christophe 2019).

Dehem et al. (2019) conducted a study focusing on analyzing the treatment of post-stroke patients using robotic assisted therapy, conducting a single, blinded and controlled randomized trial. They randomly selected patients to meet the following criteria; single first ischemic or haemorrhagic stroke, less than 1 month delay in stroke and each patient being 18 years of age or older, the ability to understand instructions, assessed by the mini-mental state examination method with patients needing to a score of 15 or greater in order to be included in the trial and finally a health status which enables the method of rehabilitative procedures to take place. The study was performed in clinical settings and patients were recruited to an assessment and rehabilitation centre, whereby via computer-generated randomization the subjects were separated into two different groups. Both groups then undertook their rehabilitation sessions during their hospitalization with their regular physical therapists and occupational therapists. The first group, which is the individuals who underwent conventional therapy, focused their treatment on motor rehabilitation dependent on the motor needs of each patient. For the second group, which was the robotic associated therapy, the conventional therapy way of treatment was substituted for RAT therapy for approximately 25% of the total weekly rehabilitation time. Thus, the RAT was substituted with the CT group each week for 4 sessions in total and therefore the RAT group performed 36 RAT-dedicated sessions in total. On the contrary, with the CT group, the RAT group received the same duration of motor rehabilitation each including both RAT and CT targeted treatment.

Finally, if the patients had any additional impairments they each received speech language therapy and/or cognitive rehabilitation, but these therapies were not modified in any way for the duration of the study. (Dehem et al. (2019)).
The exoskeleton-type robotic devices have two planes of axes, which include anatomical axes and robot axes, which are utilised to accurately determine the kinematic configuration of the human joints. These robots provide direct control of individual joints, which can minimize abnormal posture or movement. The efficacy of robotic devices deployed in the treatment of stroke is with limited but beneficial use. In terms of chronic stroke, robotic devices cannot be used solely on its own and in many cases, conventional gait training is the preferred method due to lower costs and improvements of patient's motor functional activity within a shorter period. However, in the treatment of sub-acute stroke and more importantly upper limb paresis, robotic devices in conjunction with conventional gait techniques provide the best outcome for both the patient and the practitioner. (Chang & Kim (2013)).
Within rehabilitation medicine, we can also use brain computer interfaces in which various devices detect brain wave activity base on the patient's intent and this information is translated by a computer into commands or messages for the patient (Iosa et al. (2012)). This is a very good procedure to use in the treatment of stroke patients as it provides the patient with real-time feedback to enable passive monitoring and active manipulation of computer and other related devices. The intended method to measure brain wave activity is electroencephalography and alongside this we have a device called fNRIS which measures the blood oxygenation levels in the brain to determine if this has a direct influence on brain wave activity. Mainly, brain computer interfaces are used in relation with robotic assisted devices to provide optimum environmental conditions for the patient with the intention of providing a speedy recovery and recently brain computer interfaces have been providing support training based on motor imagery to elicit neuro-action potentials which can target in specifically the motor neurons of the brain (Iosa et al. (2012)).
Furthermore, within rehabilitative medicine we also have methods to influence an enhanced or inhibited form of electrical activity produced from the brain itself. There are two techniques which are in current use in the practice which are: Trans cranial magnetic stimulation and Trans cranial direct current stimulation. Generally, this technique involves varying the spontaneous neuronal firing rates without producing action potentials and specifically within a clinical aspect of treating stroke-related patients it can be used to recover motor and cognitive impairments. The preferred target has been the primary motor cortex, brain area in motor execution, memory formation, and consolidation of motor skills. Overall, small-randomized trials have been carried out with signs of positivity but more intensive studies need to be carried out before it can be rolled out in multi-stroke centres to be used on a wide scale. (Iosa, M. et al. (2012))
Neuroprosthesis is a generalized term applied to devices which can both provide input and receive output from the central nervous system. Within this field, the electronical devices may directly stimulate muscles or nerves that should in turn stimulate muscles. To our understanding today, it is based on functional electrical stimulation whereby during locomotion of a stroke patient the neuroprosthesis can be programmed to be in time with the specific movement and to elicit that specific neuro-muscular movement at stronger frequencies which would usually be weak in patient recovering from stroke. FES has been used as of today as a surface or implanted device, in the form of a tilt sensor which records the orientation of the trunk and controlling when to turn in line with the movement of the specific bodily limb. It can also be used as a pressure for example below the foot for the allowing to know if the heel is in contact with the ground or not in order to control ankle joint movements. Overall, neuroprosthesis has provided information that it may improve active movements and strengthen muscles, improving gait velocity and endurance, preventing falls, reducing spasticity and providing better functional recovery. (Iosa, M. et al. (2012)) Müller et al. (2020) conducts a study on the effects of adaptive full-cycle full-leg support FES adaptive neuroprosthesis. In their opinion, this neuroprosthesis can be considered as the next step in the use of neuroporothesis. (Müller, P. et al. (2020)).

5. CONCLUSIONS

Overall, physical and rehabilitative medicine plays an integral and supportive part in the treatment of post-stroke patients. Through the various techniques and devices, we can establish a positive relationship in a shortened duration of recovery a patient suffering from stroke as opposed to stand-alone and conventional methods to treat stroke patients, however, more research needs to be undertook in order to provide innovation and to advance the field of physical and rehabilitative medicine and the role it plays within stroke medicine and related health disciplines.

REFERENCES

Belas Dos Santos, M., Barros de Oliveira, C., Dos Santos, A., Garabello Pires, C., Dylewski, V., & Arida, R. M. (2018). A Comparative Study of Conventional Physiotherapy versus Robot-Assisted Gait Training Associated to Physiotherapy in Individuals with Ataxia after Stroke. Behavioural neurology, 2018, 2892065.

Bindawas, S. M., & Vennu, V. S. (2016). Stroke rehabilitation. A call to action in Saudi Arabia. Neurosciences (Riyadh, Saudi Arabia), 21(4), 297–305.

Chang, W. H., & Kim, Y. H. (2013). Robot-assisted Therapy in Stroke Rehabilitation. Journal of stroke, 15(3), 174–181.

Church, G., Ali, A., Smith, C. L., Broom, D., & Sage, K. (2022). Examining Clinical Practice Guidelines for Exercise and Physical Activity as Part of Rehabilitation for People with Stroke: A Systematic Review. International journal of environmental research and public health, 19(3), 1707.

Clark, W. E., Sivan, M., & O'Connor, R. J. (2019). Evaluating the use of robotic and virtual reality rehabilitation technologies to improve function in stroke survivors: A narrative review. Journal of rehabilitation and assistive technologies engineering, 6, 2055668319863557.

Dehem, S., Gilliaux, M., Stoquart, G., Detrembleur, C., Jacquemin, G., Palumbo, S., Frederick, A., & Lejeune, T. (2019). Effectiveness of upper-limb robotic-assisted therapy in the early rehabilitation phase after stroke: A single-blind, randomised, controlled trial. Annals of physical and rehabilitation medicine, 62(5), 313–320.

Di Carlo, A. (2009). Human and economic burden of stroke. Age and ageing, 38(1), 4–5.

Duret, C., Grosmaire, A. G., & Krebs, H. I. (2019). Robot-Assisted Therapy in Upper Extremity Hemiparesis: Overview of an Evidence-Based Approach. Frontiers in neurology, 10, 412.

Huber, J., Kaczmarek, K., Leszczyńska, K., & Daroszewski, P. (2022). Post-Stroke Treatment with Neuromuscular Functional Electrostimulation of Antagonistic Muscles and Kinesiotherapy Evaluated with Electromyography and Clinical Studies in a Two-Month Follow-Up. International journal of environmental research and public health, 19(2), 964.

İçağasıoğlu, A., Baklacıoğlu, H. Ş., Mesci, E., Yumuşakhuylu, Y., Murat, S., & Mesci, N. (2017). Economic burden of stroke. Turkish journal of physical medicine and rehabilitation, 63(2), 155–159.

Iosa, M., Morone, G., Fusco, A., Bragoni, M., Coiro, P., Multari, M., Venturiero, V., De Angelis, D., Pratesi, L., & Paolucci, S. (2012). Seven capital devices for the future of stroke rehabilitation. Stroke research and treatment, 2012, 187965.

Khan, M. A., Das, R., Iversen, H. K., & Puthusserypady, S. (2020). Review on motor imagery based BCI systems for upper limb post-stroke neurorehabilitation: From designing to application. Computers in biology and medicine, 123, 103843.

Kuriakose, D., & Xiao, Z. (2020). Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. International journal of molecular sciences, 21(20), 7609.

Müller, P., Del Ama, A. J., Moreno, J. C., & Schauer, T. (2020). Adaptive multichannel FES neuroprosthesis with learning control and automatic gait assessment. Journal of neuroengineering and rehabilitation, 17(1), 36. Nicol, M. B., & Thrift, A. G. (2005). Knowledge of risk factors and warning signs of stroke. Vascular health and risk management, 1(2), 137–147.

Norrving, B., & Kissela, B. (2013). The global burden of stroke and need for a continuum of care. Neurology, 80(3 Suppl 2), S5–S12.

Rajsic, S., Gothe, H., Borba, H. H., Sroczynski, G., Vujicic, J., Toell, T., & Siebert, U. (2019). Economic burden of stroke: a systematic review on post-stroke care. The European journal of health economics : HEPAC : health economics in prevention and care, 20(1), 107–134.

Strilciuc, S., Grad, D. A., Radu, C., Chira, D., Stan, A., Ungureanu, M., Gheorghe, A., & Muresanu, F. D. (2021). The economic burden of stroke: a systematic review of cost of illness studies. Journal of medicine and life, 14(5), 606–619.

Wafa, H. A., Wolfe, C., Emmett, E., Roth, G. A., Johnson, C. O., & Wang, Y. (2020). Burden of Stroke in Europe: Thirty-Year Projections of Incidence, Prevalence, Deaths, and Disability-Adjusted Life Years. Stroke, 51(8), 2418–2427.