

**TITLE PAGE**  
**- Food and Life-**  
**Upload this completed form to website with submission**

<b>ARTICLE INFORMATION</b>	<b>Fill in information in each box below</b>
<b>Article Type</b>	Review
<b>Article Title (English)</b>	The Mediterranean Diet's Effect on Stroke Risk
<b>Article Title (Korean)</b> English papers can be omitted	
<b>Running Title (English, within 10 words)</b>	The Mediterranean Diet's Effect on Stroke Risk
<b>Author (English)</b>	Zain Qureshi* 1, Dolores Becker RD LDN, Umar Farooq MD
<b>Affiliation (English)</b>	1 Penn State Health Milton S. Hershey Medical Center
<b>Author (Korean)</b> English papers can be omitted	
<b>Affiliation (Korean)</b> English papers can be omitted	
<b>Special remarks – if authors have additional information to inform the editorial office</b>	
<b>ORCID and Position(All authors must have ORCID) (English)</b> <a href="https://orcid.org">https://orcid.org</a>	Zain Qureshi (High School Student, <a href="https://orcid.org/0000-0002-3409-6325">https://orcid.org/0000-0002-3409-6325</a> ), Dolores Becker (Clinical Nutrition Specialist, <a href="https://orcid.org/0000-0001-8668-9491">https://orcid.org/0000-0001-8668-9491</a> ), Umar Farooq (MD, <a href="https://orcid.org/0000-0003-3028-8300">https://orcid.org/0000-0003-3028-8300</a> )
<b>Conflicts of interest (English)</b> List any present or potential conflicts of interest for all authors. (This field may be published.)	The authors declare no potential conflict of interest.
<b>Acknowledgements (English)</b> State funding sources (grants, funding sources, equipment, and supplies). Include name and number of grant if available. (This field may be published.)	
<b>Author contributions</b> (This field may be published.)	Conceptualization: Qureshi Z. Writing - original draft: Qureshi Z. Writing - review & editing: Qureshi Z, Becker D, Farooq U.
<b>Ethics approval (IRB/IACUC) (English)</b> (This field may be published.)	This manuscript does not require IRB/IACUC approval because there are no human and animal participants.

**CORRESPONDING AUTHOR CONTACT INFORMATION**

<b>For the <u>corresponding</u> author (responsible for correspondence, proofreading, and reprints)</b>	<b>Fill in information in each box below</b>
First name, middle initial, last name	Zain, A, Qureshi
Email address – this is where your proofs will be sent	<a href="mailto:zainamerqureshi@gmail.com">zainamerqureshi@gmail.com</a>
Secondary Email address	
Postal address	5002 Pellingham Circle Enola PA 17025
Cell phone number	717-580-8185
Office phone number	
Fax number	

## 1 **Abstract**

2           The Mediterranean Diet has been growing in popularity as preventive medicine has made way  
3 in the healthcare community. Doctors are telling patients to adopt this diet due to its role in lowering  
4 stroke rates and other cardiovascular diseases in both Italy and Greece. These two countries have some  
5 of the lowest stroke numbers in the world, and experts believe this is the result of the diet and lifestyle  
6 of the people of that region. The diet includes foods such as fruits, vegetables, nuts, fish, and olive oil,  
7 along with less cholesterol, saturated fats, and trans fats. These specific foods and combinations of  
8 foods include properties that can prevent high blood pressure. We will explore the capabilities of the  
9 Mediterranean diet in preventing stroke, and the importance of preventive medicine in healthcare.

10  
11 Keywords: Stroke, Nutrition, Preventive Medicine, Mediterranean diet

## 13 **Introduction**

14           A common saying describing the US Healthcare system is that it is not, in fact, considered a  
15 healthcare system, but is a sick care system. This is due to the healthcare system's prioritization of  
16 treating disease after symptoms have presented in a patient as opposed to teaching patients how to  
17 prevent the disease. One of the most prevalent examples of this is stroke. **Some experts say that up to**  
18 **80% of strokes could be prevented through healthy lifestyle choices, which would lead to better control**  
19 **of blood pressure. Eating a healthy diet/better nutrition, engaging in regular exercise, and maintaining a**  
20 **healthy weight all reduce the risk of cardiovascular events (Hankey, 2005).** Usually, preventive

22 medicine is not prioritized in the United States as prevention is not as profitable as treating  
23 symptoms/diseases after they develop (Harrah, 2015). Recently, however, doctors have started to  
24 realize the benefits of preventive medicine to general patient care. This has led to studies and research  
25 that describe what exact measures patients must take to prevent the occurrence of diseases. When it  
26 comes to stroke, some patients in the US assume that if they have a family history they have limited  
27 control over their susceptibility to its occurrence. While family history plays a large part in one's  
28 individual susceptibility to stroke, environmental factors such as weight, nutrition, and exercise also  
29 play a role (Yu et. al, 2019). Practicing a healthy lifestyle does not guarantee the prevention of certain  
30 diseases. However, when looking at the overall occurrence of stroke, it is evident that patients who  
31 improve environmental factors affecting their susceptibility face a significantly decreased risk of stroke  
32 no matter what their genetic risk may be (Peterson et. al, 2015). We will examine the effectiveness of  
33 multiple preventive lifestyle techniques for reduction of stroke risk, **focusing on Mediterranean**  
34 **nutrition and better lifestyle choices.**

35         Stroke is one of the primary preventable burdens on the US healthcare system; it is often  
36 survivable but can lead to numerous disabilities (Bauer et. al, 2014). Preventive medicine can reduce  
37 this burden by treating the precursors to stroke rather than the after-effects. In the year 2000, over half  
38 of all deaths in the US were preventable, and still millions of people die every year from preventable  
39 disease (Mokdad et al., 2004). Proper measures such as screenings, nutritional modifications, increased  
40 exercise, and regular health checks help prevent chronic diseases. Many people are simply unaware of  
41 the steps they need to take in order to stay healthy as they age, and manage diseases they have. Ideally,

42 doctors who practice preventive medicine screen their patient's genetic history and environmental  
43 factors in order to predict their susceptibility to diseases. Then, they recommend personalized  
44 preventive strategies that decrease a patient's risk of disease, such as proper nutrition choices, exercise,  
45 and other preventive measures. Stroke is one of the most effective examples of how prevention can  
46 change one's risk of developing a disease. Every year, more than 795,000 people have a stroke in the  
47 US, and it can cause a loss of cognitive, motor, and sensory function of the brain (Capriotti et. al,  
48 2016).

49

### 50 **Family History's Effect on Stroke**

51 Genetics have a limited but important role in stroke risk. Susceptibility to stroke before age 55  
52 is largely based on family history (Michael et.al, 2006). This is defined as any first-degree relative who  
53 had a stroke before age 55. Identifying this risk should signal to the preventive physician that early  
54 intervention may be key in a patient's health. **While at a young age, family history of stroke is perhaps**  
55 **the most important risk factor, as we age, environmental factors become more powerful predictors.**  
56 **Stroke is usually caused by high blood pressure or other factors when a patient is past the age of fifty-**  
57 **five. A family history remains an important risk factor in patients after the age of fifty-five along with**  
58 **other environmental factors.**

59

### 60 **Introduction to Stroke and Risk Factors**

61           Stroke can be caused due to a blocked artery, or the leaking/bursting of a blood vessel in the  
62 **brain**. A blocked artery, or ischemic stroke, occurs when blood vessels in the brain become weakened  
63 or blocked by fatty deposits, debris, or blood clots. This can be due to a number of factors, but what  
64 usually causes blockages in the brain in elderly patients is high cholesterol (Dietschy et. al, 2001).  
65 Cholesterol is made by the body and consumed through the diet. It is necessary for cell walls,  
66 hormones, vitamin D, and digestion, along with many other bodily functions. However, too much LDL  
67 (low-density lipoprotein) cholesterol, or bad cholesterol, in the blood can be detrimental. It can result in  
68 fatty deposits in blood vessels, which build up and cause narrowing with the potential for blockage.  
69 When this occurs, it causes a stroke. The leaking/bursting of blood vessels in the brain, or a  
70 hemorrhagic stroke, is less common but can be more deadly. This occurs when blood vessels,  
71 specifically in the brain, become blocked to the point where they burst or leak. It is similar to putting  
72 pressure on a balloon to the point where it bursts or leaks air. This is often the result of high blood  
73 pressure (hypertension) which leads to high stress on the walls of the vessel. The blood from a ruptured  
74 vessel then puts pressure on the surrounding cells in the brain. This can significantly damage the cells,  
75 and the affected area of the brain to cease function. There are a multitude of other factors that affect  
76 one's risk for increased LDL cholesterol, high blood pressure, and stroke, such as lack of exercise,  
77 smoking, being overweight, and poor nutrition. These are the major factors that affect one's risk of  
78 stroke past the age of fifty-five. The Mediterranean diet, however, is one of the best interventions to  
79 reduce the risk of stroke, and therefore our best hope to prevent cerebro-vascular events.  
80

## 81 **The Mediterranean Diet**

82           The diet eaten on the Greek island of Crete, most commonly known as the Mediterranean Diet,  
83 is considered by experts to be the most useful in preventing the onset of diseases, such as stroke. It  
84 consists of eating a plant-based diet, including whole grains, vegetables, legumes, fruits, nuts, seeds,  
85 herbs, and spices (Demarin et. al, 2011). In addition, olive oil is the main source of added fat. Olive oil  
86 is a healthy fat as it is monounsaturated and better than the saturated fats and trans fats that are usually  
87 present in American cuisine. These saturated and trans fats contribute heavily to stroke risk. Fish, eggs,  
88 seafood, dairy, and poultry are also included in the Mediterranean diet; however, they are only eaten  
89 occasionally. Red meat is reserved for special events, and eaten very rarely.

90

## 91 **The Mediterranean Diet's Effect on Cholesterol**

92           One of the largest nutritional changes one can make to prevent stroke is to consume less  
93 saturated and trans fats, which reduces LDL cholesterol. The Mediterranean diet has been shown to do  
94 this. Various studies have shown that those who primarily consume a diet similar to the Mediterranean  
95 diet routinely have lower total cholesterol levels than those who do not (Meslier et al., 2020). This  
96 primarily comes from the Mediterranean diet's prioritization of olive oil as the main source of fat, and  
97 the lower consumption rate of unhealthier types of fat. **The olive oil in the Mediterranean diet increases**  
98 **key HDL cholesterol functions, which remove excess cholesterol from arteries, serves as an**  
99 **antioxidant, and keeps blood vessels clear (Hernández et al., 2017). This reduces risk of stroke**  
100 **significantly.** In addition, the Mediterranean diet usually results in decreased consumption of sweets

101 and desserts, which are often high in saturated fat. When less saturated fat is eaten, the body will  
102 produce less LDL cholesterol.

103 As stated previously, cholesterol is a fatty substance that helps build cells in the body. Humans  
104 usually obtain cholesterol through diet. It is critical for survival; however, issues arise when the body  
105 contains an excess of cholesterol. Increased cholesterol creates fatty deposits in the bloodstream, which  
106 can decrease blood flow. If these fatty deposits rupture, they can form a clot, which could cause a  
107 stroke. Studies say that the Mediterranean diet can reduce cholesterol by up to 3x the original amount  
108 (Kastorini et al., 2011), which makes it one of the most effective ways of lowering one's cholesterol.

109

### 110 **The Mediterranean Diet's Effect on High Blood Pressure**

111 High blood pressure is also one of the most prevalent causes of stroke due to increased pressure  
112 on blood vessels in the brain, which can lead to cerebral bleeding and stroke. **A study conducted in**  
113 **Spain suggested that the Mediterranean diet could reverse all changes in blood pressure related to age**  
114 **when compared to a regular diet (Bonaccio, 2012).** This is huge, because age is one of the biggest  
115 contributors to higher blood pressure. If the Mediterranean diet prevents these changes, then one's  
116 blood pressure would not skyrocket as one get older. Therefore, the risk of stroke would remain  
117 controlled despite aging. **Patients who do not follow the Mediterranean diet, however, would still have**  
118 **a higher risk of stroke.** Most of the influence the Mediterranean diet has on blood pressure is based on a  
119 combination of factors, such as healthy eating and increased exercise. The use of olive oil as fat is one  
120 of the most important factors in decreasing blood pressure. Olive oil is high in polyphenols, a



121 micronutrient that occurs naturally in plants, which has a positive effect on blood pressure (Covas et.  
122 al, 2006). Specifically, it enhances the response from the endothelium-derived factors, blunting blood  
123 pressure increase (Linder et. al, 1990). This is what mainly contributes to lower blood pressure through  
124 the mediterranean diet, and significantly decreases one's risk for stroke.

125

## 126 **The Mediterranean Diet's Effect on Obesity and Diabetes**

127 While the Mediterranean diet doesn't specifically limit the number of calories one eats, calories  
128 will usually be less due to the amount of natural and healthy food that is eaten. The average number of  
129 calories one eats a day is approximately 1,527 calories for those that adhere to the Mediterranean diet  
130 (Davis et. al, 2015). In addition, the average number of calories a sedentary person burns in a day is  
131 around 1800 calories. The average number of calories an active person burns in a day is 1900-2200  
132 calories. Thus, whoever follows the Mediterranean diet may be in a caloric deficit, resulting in weight  
133 loss. While different people lose weight at a different pace, being in a caloric deficit has the potential to  
134 decrease obesity. Obesity puts one at a higher risk of stroke due to high total cholesterol levels, and  
135 higher blood pressure (Winter et. al, 2018). Also, with obesity, it is harder for blood to circulate,  
136 contributing to an increased chance of blockage in the brain. In a study, 10 subjects who previously had  
137 coronary artery disease were placed on the Mediterranean diet for 8 weeks along with regular exercise.  
138 They went to weekly informational sessions, and completed food-related questionnaires to analyze  
139 their food intake. The control group, another 10 subjects, were told to go about their daily life with no

140 changes relating to health and nutrition. All 10 subjects in the experimental group had a significant  
141 decrease in weight compared to the control; simply because of diet and exercise. (Noites et. al, 2015).

142 **Obesity also has a very strong correlation with the occurrence of Transient Ischemic Attacks,**  
143 **also known as mini strokes.** These attacks, which can be quite dangerous, are frequently considered  
144 early warning signs of stroke. In fact, up to 15% of people who have a TIA have a stroke within 3  
145 months (Coull et. al, 2004).

146 In addition, obesity can contribute to risk for diabetes due to insulin resistance. This is when  
147 body cells do not respond to regulate a person's insulin production. This also increases the risk of  
148 stroke as diabetes causes the blood vessels to become stiff. This is called arteriosclerosis. It increases  
149 chances of blockage or bleeding of the blood vessels (Abbott, 1987). **The Mediterranean diet reduces**  
150 **the chance of developing diabetes due to healthy eating habits, and less sugary food consumption. A**  
151 **study found that following the Mediterranean diet resulted in lower blood sugar and hba1c levels**  
152 **because of the lack of processed foods within the diet. This improved insulin sensitivity and reduced**  
153 **insulin resistance (Martín-Peláez et. al, 2020).**

154 **Exercise can help combat obesity and diabetes. Social exercise, the act of exercising with a**  
155 **group of people, may be better than solitary exercise, as it contributes to better physical, mental and**  
156 **emotional health (Schuenke et al, 2017) The Mediterranean lifestyle includes social exercise through**  
157 **regular walking and outdoor activities (Sanchez-Villegas, 2016).**

158

159 **Mediterranean Diet's Effect on Patients in Italy**

160 A study was done in Italy that tracked the benefits of the Mediterranean diet on a large scale,  
161 and showcased the benefits of better nutrition on stroke prevention. **The Mediterranean diet was shown**  
162 **to help Italians who suffer from high stroke risk.** While the average Italian usually eats a more  
163 nutritious diet than the average American, the benefits of the Mediterranean diet are much more  
164 effective in preventing diseases such as stroke. The Italian study found that dietary changes reduced  
165 risk of stroke by up to 25% among participants (Iacoviello, 2018).

166

### 167 **Mediterranean Diet's Effect on American Patients**

168 The Mediterranean diet has already been shown to help Americans reduce their risk of stroke, as  
169 well. When it comes to stroke prevention in the US, the Mediterranean diet showed the most promise  
170 out of all secondary interventions in preventing secondary occurrences of stroke. Secondary  
171 interventions are when patients start incorporating preventive measures after they have already had a  
172 stroke in order to lower their risk in the future. These interventions are one of the best ways to gauge  
173 the effectiveness of preventive measures. Five separate studies suggested that the Mediterranean diet  
174 has the most potential in preventing stroke (Dearborn et. al, 2015). **While the Mediterranean diet is not**  
175 **commonly practiced in the US, it has shown to be extremely effective in preventing strokes among all**  
176 **ages and races within the United States among those who adhere to the diet (Dearborn et. al, 2015). A**  
177 **study compared Americans on the Mediterranean diet versus those adhering to a typical American diet,**  
178 **and showed that those adhering to the Mediterranean diet were less likely than their counterparts to**  
179 **suffer from a stroke over two years (American Journal of Cardiology, June 1, 2008)**

180

181 **Benefits of Preventive Medicine**

182           If one has a significant history of stroke, or risk factors for stroke, they can still reduce their  
183 susceptibility to stroke. Stroke is the result of multiple risk factors. Modifying these factors is the best  
184 approach towards preventing stroke. It is easier to prevent oneself from having high LDL cholesterol,  
185 high blood pressure, obesity, and diabetes which all contribute to raising the risk of stroke. The  
186 question, however, is to what extent can we prevent these diseases. Many assume that as they age, their  
187 health will deteriorate and their risk for disease will go up. While this is true, a major reason this is  
188 prevalent is because preventive medicine is not commonly used by the American Healthcare system to  
189 treat those who are susceptible to disease. If preventive measures like the Mediterranean diet were  
190 utilized by the healthcare system, stroke risk would most probably go down. In addition, most patients  
191 would be in better health overall, which would prevent other diseases, including cardiovascular  
192 diseases such as heart attacks. This all has to do with a concept called Healthspan, which explores how  
193 long humans are considered “healthy”. While medication may quickly reduce cholesterol or high blood  
194 pressure, more so than diet changes, they are usually used after one’s health has already gotten worse.  
195 If a patient’s treatment plan utilized preventive measures early on, this would increase their healthspan  
196 as their overall health would be better as they advance through their life. This would make their body  
197 stronger, and if they must face a disease state, such as a heart attack or a stroke, the patient would have  
198 a better chance of surviving the incident. Overall, the Mediterranean diet and other preventive measures

199 do so much more than just prevent stroke. They actually extend healthspan, and a population's ability  
200 to survive dangerous health conditions.

201

## 202 **Recommendations**

203           In order to decrease one's risk of developing a stroke, the Mediterranean diet is the best possible  
204 intervention. When it comes to LDL cholesterol, blood pressure, diabetes, obesity, or exercise, no other  
205 treatment option is able to address each specific risk factor for stroke. As shown throughout the paper,  
206 stroke risk is not inherently based on one's genetic predisposition to the disease, but also on one's  
207 lifestyle choices and health as they age. By preserving one's health span, a patient could be healthier,  
208 could feel healthier, and live longer simply by adhering to a proper nutritional diet and exercise plan.  
209 While medication may be more effective in certain cases and instances, preventive medicine is the most  
210 cost-effective and health-conscious way of avoiding disease. Healthier Americans would mean a lower  
211 strain on the healthcare system, and better diets would mean better overall health for Americans across  
212 the country. Physicians should make these specific recommendations when discussing the  
213 Mediterranean diet with their patients at high risk of stroke. First, they should mention the importance  
214 of low saturated fat and trans fat in their food, which means very little egg yolk, red meat,  
215 sweets/desserts, and full-fat dairy products along with avoidance of processed foods. In addition,  
216 patients should be instructed to focus on eating foods that are plant-based, such as nuts, whole grains,  
217 legumes, vegetables, etc. These provide necessary protein and nutrients to stay healthy. In addition,  
218 olive oil is the main source of added fat in the Mediterranean diet, and doctors must emphasize this as it

219 is the diet's main source of monounsaturated fats and polyphenols, which lower blood pressure. Lower  
220 blood pressure is necessary in preventing stroke and other cardiovascular diseases. Finally, doctors  
221 must emphasize the importance of social exercise. The Mediterranean lifestyle, which includes exercise  
222 as a social event, is important. Patients must understand that in order to reduce their risk of stroke and  
223 adhere to the Mediterranean diet, they must participate in walking groups, yoga classes, weightlifting,  
224 hiking, or any kind of exercise that is done with others. These factors contribute the most to decreasing  
225 a patient's risk of stroke, which can help the US move towards being a country where healthspan  
226 increases, and patients are healthier due to preventive and natural measures versus consumption of high  
227 doses of medication.

228

### 229 **Limitations**

230 While the Mediterranean diet does reduce one's risk of stroke by a substantial amount, some  
231 may argue that it is not the most effective method of preventing stroke. Some Cholesterol drugs, like  
232 statins, can reduce cholesterol as much as 50% or more (Feingold, 2021) at a rapid rate. However,  
233 while the Mediterranean diet may be able to reduce cholesterol by up to 3x the original amount, the  
234 reduction is not as rapid. This effectiveness of treatment is through modification of risk factors of  
235 stroke, which include high LDL cholesterol, high blood pressure, diabetes, and obesity.

236

### 237 **Conclusion**

238           There is no accurate way to determine how much one's environment or genetics contribute to  
239 susceptibility for stroke. A better way to look at the problem is that one cannot change their genetics, so  
240 any aspect of lifestyle changed in a positive way is beneficial for prevention of disease. Since one's  
241 environment is a factor that can be changed, any effort to change it in a positive way is likely to reduce  
242 one's risk of stroke. Personalized medicine is the best way to treat any type of disease. Focusing on  
243 preventing the factors that cause a certain disease will always result in a healthier patient than trying to  
244 treat a disease after its appearance. The core of preventive medicine is individualized attention, which  
245 is why every doctor in the US should be focusing on preventing disease when they first meet with their  
246 patients. Preventive medicine educates patients on lifestyle changes needed in order to preserve health  
247 and reduce risk of diseases. This form of healthcare is best for both patients and doctors, as it reduces  
248 disease and increases overall health, as shown through reduction in stroke and the Mediterranean diet's  
249 effect on prevention.

250  
251  
252  
253  
254  
255  
256  
257

259

260

261

262 **References**

- 263 Widmer, R Jay et al. “The Mediterranean diet, its components, and cardiovascular disease.” The  
264 American journal of medicine vol. 128,3 (2015): 229-38. doi:10.1016/j.amjmed.2014.10.014
- 265 Ojo O, Brooke J. The Use of Enteral Nutrition in the Management of Stroke. *Nutrients*. 2016;  
266 8(12):827. <https://doi.org/10.3390/nu8120827>
- 267 Wirth, R., Smoliner, C., Jäger, M. et al. Guideline clinical nutrition in patients with stroke. *Exp & Trans*  
268 *Stroke Med* 5, 14 (2013). <https://doi.org/10.1186/2040-7378-5-14>
- 269 Corrigan, M.L., Escuro, A.A., Celestin, J. and Kirby, D.F. (2011), Nutrition in the Stroke Patient.  
270 *Nutrition in Clinical Practice*, 26: 242-252. <https://doi.org/10.1177/0884533611405795>
- 271 Foroughi M, Akhavanzanjani M, Maghsoudi Z, Ghiasvand R, Khorvash F, Askari G. Stroke and  
272 nutrition: a review of studies. *Int J Prev Med*. 2013;4(Suppl 2):S165-S179.
- 273 Spence JD. Diet for stroke prevention. *Stroke Vasc Neurol*. 2018;3(2):44-50. Published 2018 Jan 13.  
274 doi:10.1136/svn-2017-000130
- 275 Iacoviello, L. “Diet and Primary Prevention of Stroke: Systematic Review and Dietary  
276 Recommendations by the Ad Hoc Working Group of the Italian Society of Human Nutrition.”  
277 *Nutrition, Metabolism and Cardiovascular Diseases*, Nutrition, Metabolism and Cardiovascular  
278 Diseases, 1 Apr. 2018,  
279 [www.nmcd-journal.com/article/S0939-4753\(18\)30001-2/fulltext#articleInformation](http://www.nmcd-journal.com/article/S0939-4753(18)30001-2/fulltext#articleInformation).



280 Pandian, J. D., Gall, S. L., Kate, M. P., Silva, G. S., Akinyemi, R. O., Ovbiagele, B. I., ... & Thrift, A.  
281 G. (2018). Prevention of stroke: a global perspective. *The Lancet*, 392(10154), 1269-1278.

282 Guzik, Amy, and Cheryl Bushnell. "Stroke epidemiology and risk factor management." *CONTINUUM: Lifelong Learning in Neurology* 23.1 (2017): 15-39.

284 English, Coralie, et al. "The role of diet in secondary stroke prevention." *The Lancet Neurology* (2020).

285 Fisher, Marc, Kennedy Lees, and J. David Spence. "Nutrition and stroke prevention." *Stroke* 37.9  
286 (2006): 2430-2435.

287 Kastorini, Christina-Maria, et al. "The effect of Mediterranean diet on metabolic syndrome and its  
288 components: a meta-analysis of 50 studies and 534,906 individuals." *Journal of the American college of cardiology* 57.11 (2011): 1299-1313.

290 De Pergola, Giovanni, and Annunziata D'Alessandro. "Influence of Mediterranean diet on blood  
291 pressure." *Nutrients* 10.11 (2018): 1700.

292 Altomare, Roberta, et al. "The mediterranean diet: a history of health." *Iranian journal of public health*  
293 42.5 (2013): 449.

294 Abbott, Robert D., et al. "Diabetes and the risk of stroke: the Honolulu Heart Program." *Jama* 257.7  
295 (1987): 949-952.

296 Hankey, G. J. "Preventable stroke and stroke prevention." *Journal of Thrombosis and Haemostasis* 3.8  
297 (2005): 1638-1645.

298 Saulle, R., et al. "A systematic overview of the scientific literature on the association between  
299 Mediterranean Diet and the Stroke prevention." *Clin Ter* 170.5 (2019): e396-e408.

300 Dontas, Anastasios S., et al. "Mediterranean diet and prevention of coronary heart disease in the  
301 elderly." *Clinical interventions in aging* 2.1 (2007): 109.

302 Yang, Ji Hye, et al. "Neogaroooligosaccharides enhance the level and efficiency of LDL receptor and  
303 improve cholesterol homeostasis." *Journal of functional foods* 38 (2017): 529-539.

304 Estruch, Ramón, et al. "Primary prevention of cardiovascular disease with a Mediterranean diet." *New  
305 England Journal of Medicine* 368.14 (2013): 1279-1290.

306 Gotto Jr, Antonio M. "Statins: powerful drugs for lowering cholesterol: advice for patients." *Circulation*  
307 105.13 (2002): 1514-1516.

308 Dearborn, Jennifer L., Victor C. Urrutia, and Walter N. Kernan. "The case for diet: a safe and  
309 efficacious strategy for secondary stroke prevention." *Frontiers in neurology* 6 (2015): 1.

310 Yu, Shumin, et al. "Different types of family history of stroke and stroke risk: results based on 655,552  
311 individuals." *Journal of Stroke and Cerebrovascular Diseases* 28.3 (2019): 587-594.

312 Pandian, Jeyaraj D., et al. "Prevention of stroke: a global perspective." *The Lancet* 392.10154 (2018):  
313 1269-1278.

314 Demarin, Vida, Marijana Lisak, and Sandra Morović. "Mediterranean diet in healthy lifestyle and  
315 prevention of stroke." *Acta clinica Croatica* 50.1 (2011): 67-76.

316 Tektonidis, Thanasis G., et al. "A Mediterranean diet and risk of myocardial infarction, heart failure and  
317 stroke: a population-based cohort study." *Atherosclerosis* 243.1 (2015): 93-98.

318 Tsvigoulis, Georgios, et al. "Adherence to a Mediterranean diet and prediction of incident stroke."  
319 *Stroke* 46.3 (2015): 780-785.

320 Gorelick, Philip B. "Stroke prevention." *Archives of Neurology* 52.4 (1995): 347-355.

321 Hankey, G. J. "Preventable stroke and stroke prevention." *Journal of Thrombosis and Haemostasis* 3.8  
322 (2005): 1638-1645.

323 Mokdad, Ali H., et al. "Actual causes of death in the United States, 2000." *Jama* 291.10 (2004): 1238-  
324 1245.

325 Noites, Andreia, et al. "Effects of the Mediterranean diet and exercise in subjects with coronary artery  
326 disease." *Revista Portuguesa de Cardiologia (English Edition)* 34.11 (2015): 655-664.

327 Coull, Aji, J. K. Lovett, and P. M. Rothwell. "Population based study of early risk of stroke after  
328 transient ischaemic attack or minor stroke: implications for public education and organisation of  
329 services." *Bmj* 328.7435 (2004): 326.

330 Yorks, Dayna M., Christopher A. Frothingham, and Mark D. Schuenke. "Effects of group fitness  
331 classes on stress and quality of life of medical students." *Journal of Osteopathic Medicine*  
332 117.11 (2017): e17-e25.

333 Feingold, Kenneth R. "Cholesterol lowering drugs." *Endotext* [Internet] (2020).

334 Harrah, Scott. "Why Preventive Medicine Is Not Considered Priority in USA." UMHS, UMHS, 1 Apr.  
335 2015, [www.umhs-sk.org/blog/preventive-medicine-considered-priority-usa](http://www.umhs-sk.org/blog/preventive-medicine-considered-priority-usa).

336 Capriotti, Teri, and Teresa Murphy. "Ischemic stroke." *Home healthcare now* 34.5 (2016): 259-266.

337 Paterson, Katherine E., et al. "Mediterranean diet reduces risk of incident stroke in a population with  
338 varying cardiovascular disease risk profiles." *Stroke* 49.10 (2018): 2415-2420.

339 Bauer, Ursula E., et al. "Prevention of chronic disease in the 21st century: elimination of the leading  
340 preventable causes of premature death and disability in the USA." *The Lancet* 384.9937 (2014):  
341 45-52.

342 Michael, Kathleen M., and Marianne Shaughnessy. "Stroke prevention and management in older  
343 adults." *Journal of Cardiovascular Nursing* 21.5 (2006): S21-S26.

344 Dietschy, John M., and Stephen D. Turley. "Cholesterol metabolism in the brain." *Current opinion in*  
345 *lipidology* 12.2 (2001): 105-112.

346 Keys, Ancel. "Mediterranean diet and public health: personal reflections." *The American journal of*  
347 *clinical nutrition* 61.6 (1995): 1321S-1323S.

348 Bonaccio, Marialaura, et al. "The Mediterranean diet: the reasons for a success." *Thrombosis research*  
349 129.3 (2012): 401-404.

350 Covas, María-Isabel, et al. "The effect of polyphenols in olive oil on heart disease risk factors: a  
351 randomized trial." *Annals of internal medicine* 145.5 (2006): 333-341.

352 Davis, Courtney, et al. "Definition of the Mediterranean diet; a literature review." *Nutrients* 7.11  
353 (2015): 9139-9153.

354 Winter, Yaroslav, et al. "Contribution of obesity and abdominal fat mass to risk of stroke and transient  
355 ischemic attacks." *Stroke* 39.12 (2008): 3145-3151.

356 Sánchez-Villegas, Almudena, et al. "The association between the Mediterranean lifestyle and  
357 depression." *Clinical Psychological Science* 4.6 (2016): 1085-1093.

358 Meslier, Victoria, et al. "Mediterranean diet intervention in overweight and obese subjects lowers  
359 plasma cholesterol and causes changes in the gut microbiome and metabolome independently of  
360 energy intake." *Gut* 69.7 (2020): 1258-1268.

361 "Stroke." *Mayo Clinic*, Mayo Foundation for Medical Education and Research, 20 Jan. 2022,  
362 <https://www.mayoclinic.org/diseases-conditions/stroke/symptoms-causes/>

363 Linder, Lilly, et al. "Indirect evidence for release of endothelium-derived relaxing factor in human  
364 forearm circulation in vivo. Blunted response in essential hypertension." *Circulation* 81.6  
365 (1990): 1762-1767.

366 Tuttle, Katherine R., et al. "Comparison of low-fat versus Mediterranean-style dietary intervention after  
367 first myocardial infarction (from The Heart Institute of Spokane Diet Intervention and  
368 Evaluation Trial)." *The American journal of cardiology* 101.11 (2008): 1523-1530.

369 Hernáez, Álvaro, et al. "Mediterranean diet improves high-density lipoprotein function in high-  
370 cardiovascular-risk individuals: a randomized controlled trial." *Circulation* 135.7 (2017): 633-  
371 643.

372 Martín-Peláez, Sandra, Montse Fito, and Olga Castaner. "Mediterranean diet effects on type 2 diabetes  
373 prevention, disease progression, and related mechanisms. A review." *Nutrients* 12.8 (2020):  
374 2236.

375