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## Impact of Non-Pharmacological Treatment Methods and Lifestyle Modification on Multiple Sclerosis Symptoms and Progression

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**Impact of Non-Pharmacological Treatment Methods and Lifestyle Modification on  
Multiple Sclerosis Symptoms and Progression**

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NURS 695: Alternative Plan Paper

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### **Abstract**

Multiple sclerosis is a chronic, neurological, autoimmune condition that is characterized by unpredictable demyelination of the central nervous system. Multiple sclerosis remains one of the most debilitating neurological diseases for young adults, affecting an average of 2.5 per 100,000 people worldwide.

The objective of this research was to further assess the efficacy of non-pharmacological treatment methods for symptom management and disease progression for multiple sclerosis. A systemic literature review was conducted using 4 research databases: American Search Premier, Medline, Cochrane, and CINAHL. Studies were included if they addressed nonpharmacological treatment approaches to multiple sclerosis. A total of 21 research articles were used to assess inclusion or exclusion criteria.

What the research concluded was that there was not definitive evidence to prove that any non-pharmacological treatment method would guarantee a decrease in disability or increase in overall quality of life for patients with multiple sclerosis. However this body of research did show that non-pharmacological interventions could provide some benefit and none of these non-pharmacological treatment methods were harmful, thus validating the safety and potential benefit to be implemented in practice. Much more research needs to be conducted to look specifically at different nonpharmacological treatment approaches for the management of multiple sclerosis as varying symptoms make it difficult to pinpoint the exact benefit that each nonpharmacological approach may have.

*Keywords:* multiple sclerosis, non-pharmacological, treatment, lifestyle modification, disease progression, smoking, diet, exercise

## **Impact of Non-Pharmacological Treatment Methods and Lifestyle Modification on Multiple Sclerosis Symptoms and Progression**

Multiple sclerosis is a chronic autoimmune, condition that is characterized by inflammation and demyelination of the central nervous system (Amatya et al., 2013). Multiple sclerosis occurs more commonly in women. Multiple sclerosis is an autoimmune disorder that has an unclear etiology, and can be associated with long-term effects, complications and, decreased quality of life. Multiple sclerosis has the capacity to cause severe disability in those affected by the disease. There are different forms of multiple sclerosis, each with varying degrees of disability. Different forms of multiple sclerosis include relapsing remitting, primary progressive, and secondary progressive. Relapsing remitting forms of multiple sclerosis consist of periods of inflammation and exacerbation followed by periods of returning to baseline, or remission. Primary and secondary progressive forms of multiple sclerosis occur when a person slowly progress in their disease process without the ability to return to their baseline functioning (Amatya et al., 2013). Secondary progression typically occurs in adults after they have had relapsing-remitting multiple sclerosis. At this stage, the patient will continue to have relapses but will not experience remission. Primary progressive forms of multiple sclerosis occur initially when the diagnosis is not consistent with relapsing-remitting. In this form of multiple sclerosis, the initial disease course consists of relapse and absence of remission. Once a person has a diagnosis of multiple sclerosis, they typically have a prolonged life period of at least 40 more years. Because of this, it is likely for a person to have a prolonged disease process and progression of disability, making it imperative that patients with multiple sclerosis obtain treatment to prevent severe disability and improve quality of life (Amatya et al., 2013).

In recent decades, there has been a dramatic increase in the amount of effort that has been placed on assessing different types of treatment modalities for multiple sclerosis. Treatment for multiple sclerosis can come in a variety of forms. Pharmacological treatment methods have been extensively studied and are ever changing. However, non-pharmacological treatment approaches to the management of multiple sclerosis is an area of medicine that is much less researched. There is a variety of non-pharmacological treatment options that had been researched for symptom management for multiple sclerosis. The objective of this literature review is to examine the evidence pertaining to the efficacy of non-pharmacological treatment methods for symptom management and impact on the disease progression of multiple sclerosis.

### **Background**

The exact cause of multiple sclerosis remains unknown however environmental and immunological factors may play a part. Over the past decades, there has been a rapid increase in the incidence and prevalence of multiple sclerosis throughout the world. Some think that this may be due to the change in dietary and lifestyle habits, although there is no definitive cause of the increasing number of patients with multiple sclerosis (Matveeva et al., 2018). Environmental factors that have been attributed to the development of multiple sclerosis include inadequate vitamin D levels, tobacco use, obesity, genetic predisposition, infection with the Epstein Barr virus, and geographic location (Matveeva et al., 2018). Worldwide, multiple sclerosis affects over 2.5 million people. Multiple sclerosis is the most present in the northern hemisphere. There is currently no cure for multiple sclerosis. However, measures can be implemented to help with symptom management.

Clinical manifestations for patients with multiple sclerosis can be variable and dependent on the person. Some of these manifestations can include vision loss, weakness, ataxia, spasticity,

tremors, sensory loss, cognitive impairment, and bowel and bladder dysfunction (Amatya et al., 2013). Pharmacological methods have proven to help with symptom relief and disease progression. However, non-pharmacological treatment methods can also help with symptom management and prevention of relapses. With the increasing numbers of multiple sclerosis cases worldwide, there has also been an increasing interest and amount of research conducted on treatment options. As a result, there has been an increasing amount of evidence on non-pharmacological treatment for prevention of multiple sclerosis progression. Much of the research on non-pharmacological treatment is also focused on quality of life. Some of the non-pharmacological treatments that have been heavily researched include diet, exercise, and smoking cessation. When measuring the outcomes of non-pharmacological treatment, data is often collected from subjective report. Symptoms measured subjectively include spasticity, fatigue, pain relief, and overall quality of life.

Much of the focus on autoimmune conditions and their treatment relies on pharmacological management. The significance of non-pharmacological management in the treatment of multiple sclerosis is also gaining relevance with increasing research. Many factors go into treatment for multiple sclerosis, some of which are difficult to obtain due to cost and availability. The benefit of non-pharmacological treatment is the ease of accessibility and affordability for patients. With the increasing rates of patients being diagnosed with multiple sclerosis, there is an increased importance that is being placed on treatment options. In the primary care setting, management will be collaborative and based on patient preferences, providing education, and sharing clinical evidence.

Recognizing the importance of managing symptoms and delaying disease progression can be pivotal for the health outcomes of the patients diagnosed with multiple sclerosis. When

assessing outcomes for non-pharmacological treatment for patients with multiple sclerosis, it is important to ask the questions about if treatment is effective in minimizing impairment, effective in minimizing the burden of care, an improving quality of life (Amatya et al., 2013).

### **Clinical Question**

Based on the clinical significance of this area of interest, a Population-Intervention-Outcome (PIO) question was formatted to help guide a systemic literature review (Melnik & Fineout-Overholt, 2015). *Among adults living with multiple sclerosis (P), how do non-pharmacological treatment methods and/or lifestyle modification (I) impact disease progression and symptom management (O)?* The working hypothesis is that non-pharmacological treatment methods for multiple sclerosis will aid in symptom management and alter disease progression for patients who carry an established diagnosis.

### **Clinical Significance for Advanced Practice**

A multi-disciplinary approach is needed to manage care for patients with the diagnosis of multiple sclerosis. The modalities that are involved in treatment can be rather complex. To this point, multiple sclerosis remains one of the most challenging neurological diseases to understand and treat (Matveeva et al., 2018). There has been an increase in the amount of knowledge that is known about mechanisms that may trigger and drive multiple sclerosis allowing for individualized therapy in the advanced practice setting (Matveeva et al., 2018). Providers must place increased accountability on patients with multiple sclerosis for managing their care and engaging in positive health promoting behaviors. In the advanced practice setting, motivational interviewing, educating, and encouraging healthy behavior through non-pharmacological

approach can lead to better health outcomes and improved quality of life for patients with multiple sclerosis.

### **Methods**

A comprehensive literature review was conducted between 10/1/2019 and 11/15/2019. Databases that were selected for reviewed included Academic Search Premier (ASP), Cumulative Index of Nursing and Allied Health Literature (CINAHL), Medline, and Cochrane Database of Systematic Reviews. These databases were selected in order to provide a comprehensive review of the available literature. Articles were limited to full text, peer-reviewed, and abstract available. All articles were published after the year of 2006. For reference, refer to Appendix A. Keywords that were used for research included “multiple sclerosis,” “non-pharmacological,” “treatment,” “smoking,” “exercise,” “diet,” “lifestyle,” “lifestyle modification,” and “disease progression.” For specific keyword combinations and yielded results for every database assessed, reference Appendix B. For every keyword combination, results were reviewed if there were 10 or less results. A total of 21 studies were identify as potentially pertinent to the clinical question based on review of title and abstract; these studies were further reviewed for inclusion and exclusion criteria.

### **Inclusion and Exclusion**

Articles that were related to non- pharmacological methods for disease management were included. Studies were eliminated if they focused only on pharmacological management. An extensive amount of research was conducted on lifestyle modifications including smoking, diet, and exercise. Studies that focused on psychological interventions were excluded, as these were more pertinent to quality of life rather than disease alteration. Another study that was often brought up was done over a five-day course at a residential treatment center (Hadgkiss et al.,



2013). These studies were excluded as they were short-term and did not give indications of disease modification, but rather focused on quality of life. Articles that addressed non-pharmacological methods for treatment of symptoms, such as chronic pain, fatigue, or spasticity, were included. All studies that only addressed quality of life as an indicator of non-pharmacological intervention were excluded. Of the 21 studies that were examined through review of the abstracts, 13 met inclusion criteria. See Appendix C for detailed information related to the rationale for each study that was included or excluded. See Appendix D for the data abstracted from the studies included in the systemic review. Each study was fully reviewed for findings pertinent to the clinical question.

### **Literature Review**

There have been a multitude of studies that have been completed on non-pharmacological treatments for multiple sclerosis. Emerging themes among the research include lifestyle modification of diet, exercise, and smoking cessation. Along with that, there are individualized studies that focus on more specific non-pharmacological treatments such as the use of transcutaneous electrical nerve stimulation and hyperbaric oxygen therapy. This literature review will identify the findings in each of these sub-categories of interest.

### **Non-Pharmacological Treatments**

Muscle spasticity is among one of the many debilitating side effects of the progression of multiple sclerosis. Spasticity causes things such as stiffness, spasms, or tightness in any of the extremities. On average 60 to 80% of patients with multiple sclerosis will experience spasticity at some point during their disease process (Amatya et al., 2013). Spasticity can be one of the leading causes of disability and instability for patients with multiple sclerosis. Long term complications of spasticity can include muscle contractures, pain, pressure injuries, and inability

to adequately perform activities of daily living. This associated symptom of multiple sclerosis is extremely challenging to manage. In one study, spasticity management was investigated through the evaluation of nine randomized control trials (Amatya et al., 2013). This study investigated physiotherapy, electromagnetic therapy, and transcutaneous electrical nerve stimulation as non-pharmacological treatment methods for spasticity in patients with multiple sclerosis. When training muscle spasticity, the goal for management is to create goals and rehabilitation in order for patients to maintain a functional quality of life (Amatya et al., 2013). Due to the risks, costs, access issues, and unpredictable results associated with surgical procedures to treat spasticity, nonpharmacological interventions are often the mainstay of treatment and management. The biggest barrier regarding current evidence in research related to spasticity for patients with multiple sclerosis is the lack of known benefits (Amatya et al., 2013). This study examined rehabilitation programs in the inpatient, outpatient, and in home settings. The study concluded that there was an extreme amount diversity in the outcomes.

### ***Transcutaneous Electrical Nerve Stimulation***

Amatya et al. (2013) also assessed transcutaneous electrical nerve stimulation intervention. There was no statistically significant difference between patients who received therapy versus patients who did not receive therapy and their overall report of reduction in muscle spasm (Amatya et al., 2013). Researchers concluded, there was not enough evidence to support the routine use of transcutaneous electrical nerve stimulation for the treatment of spasticity (Amatya et al., 2013). However, the quality of this evidence is limited due to the inadequate amount of studies in research that has been conducted. This study did highlight gaps in the literature that are present when attempting to draw conclusions from this research on non-pharmacological treatment for spasticity (Amatya et al., 2013).

### ***Hyperbaric Oxygen Therapy***

When conducting research on non-pharmacological treatment approaches to multiple sclerosis, one area was also mentioned that was not quite as common. This was hyperbaric oxygen therapy for the decrease in disease progression. This study was a meta-analysis that looked at hyperbaric oxygen therapy and the benefits it may have in slowing the disease process. A total of 9 trials were looked at in this article with a total of 504 participants (Bennett et al., 2011). Two of the trials did show a positive result in the decreasing of multiple sclerosis development when using hyperbaric oxygen therapy. The remaining 7 trials reported no evidence of treatment effect (Bennett et al., 2011). Due to the lack of evidence there is not enough consistent support for the benefit of hyperbaric oxygen therapy for the treatment of multiple sclerosis. The cost is extremely high as well and may not be justified due to the lack of evidence. However given there was positive benefit seen, more research is needed to validate the routine use of hyperbaric oxygen therapy for multiple sclerosis (Bennett et al., 2011).

### **Lifestyle Modification**

#### ***Tobacco Cessation***

Smoking tobacco and smoking cessation is a lifestyle factor that has been studied with multiple sclerosis. One meta-analysis of 11 studies assessed the relationship of tobacco use to worsening disability in multiple sclerosis patients (Heydarpour et al., 2018). Disability due to smoking was measured using an expanded disability status scale (EDSS) or the multiple sclerosis severity scale (MSSS). According to some of the research included in the meta-analysis, there was significant disability in patients with multiple sclerosis who smoked tobacco and some studies revealed no significant disability (Heydarpour et al., 2018). One of the studies that was

assessed in this meta-analysis looked at the pathophysiology of the respiratory system and patients with multiple sclerosis. This study found that patients with multiple sclerosis inevitably have a weakened immune systems and pulmonary function. Because of this, their lungs are also weekend. The study found that patients with multiple sclerosis that smoke had a significant reduction of CD4+ cells compared to other smokers who do not have multiple sclerosis. This leads to decrease clearance of smoke particles and an increase in inflammatory response due to smoking in patients with multiple sclerosis (Heydarpour et al., 2018).

This meta-analysis concluded was that smoking does increase disability for patients with multiple sclerosis. However, it also concluded that it did not increase the risk of worsening the severity of multiple sclerosis (Heydarpour et al., 2018). What this means is that for patients with severe disability due to multiple sclerosis, smoking has a strong likelihood of making that disability worse. However, for patients with multiple sclerosis and no significant disability, smoking may not make the multiple sclerosis symptoms develop or worsen (Heydarpour et al., 2018). Since this article was published, further studies have been conducted that assess smoking cessation and multiple sclerosis. However, many of these studies focus collectively on lifestyle change rather than isolating smoking cessation thereby revealing a gap in the research literature (Heydarpour et al., 2018). Along with that, there lacks a standardized way to assess disability due to smoking which has led to a variety of study methods related to smoking and multiple sclerosis.

### ***Diet***

Dietary modifications are another lifestyle consideration for multiple sclerosis symptoms that is very prevalent in research. In one study, the researcher implemented a five day residential workshop that promoted a low-fat, plant based, seafood, high vitamin D, omega-3

supplementation diet (Marck et al., 2018). The participants in the study had to have had experienced one relapse in the prior year. A questionnaire was used to assess dietary habits. After this workshop, the participants were assessed at the one year and three year mark. There were a total of 76 participants at the one year mark in 78 participants at the three year mark (Marck et al., 2018). The majority of these patients, 73%, had a diagnosis of relapsing-remitting multiple sclerosis. What the study found was that there were improvements in health outcomes one year after the intervention and there was substantial and sustained improved health outcomes three years after the workshop. The goal of this study was to assess if lifestyle changes were maintainable for patients with multiple sclerosis. The study concluded that, over time, patients with multiple sclerosis were able to sustain healthy lifestyle choices that led to a decrease in their overall disability. One of the biggest limitations of this study was the small sample size as well as all of the data being self-reported (Marck et al., 2018).

One study looked at overall brain atrophy that was due to poor diet for patients with multiple sclerosis (Jakimovski et al., 2019). This study compared patients with multiple sclerosis to healthy controls. The participants in the study had to implement lifestyle-based behavior and their brain was imaged through MRI over a five-year period. What the study found was that patients with multiple sclerosis who had an unhealthy diet had a higher accrual of brain lesions over a five year period (Jakimovski et al., 2019). The study looked at the Mediterranean diet and the effects that it may have on multiple sclerosis. This diet includes fruits, vegetables, whole grains, and reduced sugar and red meat (Jakimovski et al., 2019). Given that poor diet was correlated with higher lesion accrual, and there were weaker associations with diet alcohol and tobacco, it could imply that there is an independent process that diet contributes to brain atrophy

for patients with multiple sclerosis. What this study concluded was that healthy lifestyle caused a decrease in brain atrophy and lesion accrual (Jakimovski et al., 2019).

Dietary factors and obesity have been known to play a significant role for patients with multiple sclerosis. In one study, the westernized diet was investigated as it may play a significant role in the development and worsening of multiple sclerosis. The westernized diet is high in salt, fatty acids, flavonoids, and saturated fats. A diet high in salt has been correlated to enhance disease exacerbation and new lesion development. Salt also can affect T cells which alter the macrophage response (Matveeva et al., 2018). This causes a suppression of the anti-inflammatory properties that a macrophage possesses. The role that fats play in the development and progression of multiple sclerosis is linked to their effect on inflammation and increasing relapse risk (Matveeva et al., 2018). Flavonoids play a role in multiple sclerosis development in that they suppress monocytes and limit the uptake of myelin by macrophages. However, there is mixed evidence because certain flavonoids, such as scutellarin, may aid in central nervous system repair (Matveeva et al., 2018). What this study concluded was that more research should be done on the specific mechanisms that different types of food in the westernized diet may contribute to the development and progression of multiple sclerosis (Matveeva et al., 2018).

### ***Exercise***

When assessing approaches to lifestyle modification, exercise is a topic that is often studied. There is extensive research examining the relationship between exercise and its effect on overall functioning for patients with multiple sclerosis. One study looked at formal exercise in a variety of exercise techniques and their ability to maintain and improve functional capacity for patients with multiple sclerosis (White & Dressendorfer, 2004). One of the major things that was assessed was muscle strength as well as mobility. Disability for patients with multiple sclerosis

was often related to a reduced mobility, poor balance, abnormal gait, and muscle weakness. Exercise and strength training can play a significant role in decreasing disability for patients with multiple sclerosis. Much of the research that is conducted on exercise related to multiple sclerosis has to do with decreasing disability and improving quality of life. Another significant thing to think about for patients with multiple sclerosis is their long-term use of corticosteroids. Corticosteroids have been shown to decrease bone density in patients with and without multiple sclerosis. Given that patients with multiple sclerosis are already at an increased risk of premature osteoporosis, bone health is very important. Strength training and resistance training can help to preserve bone density for patients with multiple sclerosis with the hope of decreasing the likelihood of osteopenia, osteoporosis, or skeletal related disability. When looking at an exercise program for patients with multiple sclerosis it should be carefully considered with physical limitation taken into consideration. Physical therapy is another option that may be used when formulating an exercise plan for patients with multiple sclerosis. When looking at this study, the biggest limitation is lack of randomized control trials comparing patients who exercise versus patients who do not. There is also an increase need for further research to be conducted on the role that specific exercise routines play in the hindering of multiple sclerosis development (White & Dressendorfer, 2004).

Another study specifically focusing on activity was conducted. The studies assessed walking intensity and walking activity as a mechanism for preventing progression of multiple sclerosis. This study used this step watch activity monitor to assess the number of steps that were taken by patients who have had multiple sclerosis. The study looked at step count, walking intensity, and walking duration (Neven et al., 2016). What this study found was that patients with multiple sclerosis were not meeting the recommended duration or intensity of walking every day.

In order to achieve benefits from walking the intensity and duration needs to be high enough (Neven et al., 2016). Another thing to consider for patients with multiple sclerosis is their potential inability to sustain walking for long periods of time. What the study concluded was that patients with multiple sclerosis may be active but are not active enough to have significant benefit from walking. The problem with this is that some patients are unable to walk for a sustained period due to fatigue, making them outliers in the study (Neven et al., 2016). The biggest drawback in the study is that it is difficult to often assess stamina for patients with multiple sclerosis due to other contributing factors such as fatigue.

Other studies assessed fatigue related to multiple sclerosis and interventions that could be completed to aid in the relief of fatigue. As mentioned with exercise, fatigue can be a significant barrier for treatment. Fatigue is very common for patients with multiple sclerosis so assessing daily fatigue is important when formulating an exercise plan. Treating fatigue can lead to overall positive health benefits for patients with multiple sclerosis. In one study, aerobic exercise, strength, cooling methods, and yoga was shown to have a positive effect on fatigue in patients with multiple sclerosis (Pozzilli et al., 2006). Both depression and fatigue can negatively affect cognitive development for patients with multiple sclerosis. In turn, this can have a significant effect on quality of life. Another study thoroughly discussed pharmacological interventions to manage fatigue for patients with multiple sclerosis. This study also looked at nonpharmacological interventions such as physical exercise for the treatment of fatigue. As mentioned previously, this may be controversial because exercise may help with fatigue but a patient with multiple sclerosis may not be able to exercise due to fatigue. What the study found was that there was a significant lack in protocols and evidence related to the treatment of fatigue for patients with multiple sclerosis (Brenner & Piehl, 2016).



Another study looked at positive role that lifestyle played for overall well-being for patients with multiple sclerosis. This study used a variety of screening tools that assessed mental functioning, sleep, fatigue, stress, and disability management (Strober et al., 2018). This study looked at overall wellness and using a holistic approach to increase overall quality of life for patients with multiple sclerosis (Strober et al., 2018). What the study found was that lifestyle habits including diet, exercise, social participation, and intellectual activities were positively correlated with overall well-being for patients of multiple sclerosis (Strober et al., 2018). Because of this, there was a decrease in overall disease burden. The biggest drawback to this study was that data was collected by subjective questionnaire rather than objective assessment. Along with that, it was a small sample size consisting of only 248 participants (Strober et al., 2018).

### **Discussion**

Multiple sclerosis is one of the most debilitating autoimmune disorders. There has been an extensive amount of new research that has been conducted on different types of treatment options. As a result of this research there is a variety of findings based on varied methods and interventions studied. When conducting research on non-pharmacological treatment, topics that were consistently discussed included smoking, exercise, dietary, and overall healthy lifestyle. There were also outliers in the research that assessed different nonpharmacological treatment such as hyperbaric oxygen therapy and transcutaneous electrical nerve stimulation. When looking at multiple sclerosis, there is such an array of symptoms that a patient may experience. Because of this, there is an array of non-pharmacological approaches that may also be completed to help with those symptoms.

In terms of non-pharmacological treatment, some research findings were more convincing than others. Healthy lifestyle in the form of smoking cessation, exercise, and dietary restrictions did prove to be beneficial for patients with multiple sclerosis. Much of the studies that were completed on lifestyle modification concluded that, when smoking cessation, healthy diet, and exercise take place, a patient with multiple sclerosis was able to have some form of symptom relief. Although much of the research is limited, or focused on one specific area, there did prove to be benefit. Hyperbaric oxygen therapy is a newer area of research and has been beneficial to some patients though not found to be statistically significant. The common characteristics of these patients was that they had a definite diagnosis of multiple sclerosis, had not had periods of exacerbations in the past three to twelve months, had received no recent immunotherapy, and had no other contraindications to receiving hyperbaric oxygen therapy. (Heard & Bennett, 2011). Transcutaneous electrical nerve stimulation is more aimed at symptom management rather than disease progression or modification. Although it may help with the short-term symptom management, it has not been proven to provide any long-term beneficial effects.

There is still an extensive amount of research that needs to be done when assessing nonpharmacological treatment approaches for patients with multiple sclerosis. When looking at lifestyle factors, the most commonly researched areas including tobacco use, diet, and exercise, though there remains a significant amount of discrepancy in the research. However, when looking at this body of research, the one commonality was that non-pharmacological treatment interventions and recommended lifestyle modifications never caused worsening of symptoms or disease progression. Considering this, it does reveal that nonpharmacological treatment methods are safe, easy, cost effective, and have the potential for providing some benefit.

## **Implications for Practice**

In the field of research for non-pharmacological treatment and lifestyle modification approaches to multiple sclerosis, there is still much research that needs to be completed. When considering recommendations, the first would be to increase research on different types of exercise and the benefits that it may have for decreasing disability for patients with multiple sclerosis as it has been proven to be beneficial. Currently, there is an array of evidence that provides evidence that exercise can be beneficial though not enough evidence to fully support one type of exercise over another. When considering walking and fatigue management, more research should be conducted on types of exercise that may be beneficial for patients who are immobile due to their high level of disability. If a patient with multiple sclerosis has significant disability, it is important to investigate what types of exercise may be completed by those patients that may be beneficial for preventing further disability and improving quality of life.

The biggest problem in research for non-pharmacological treatment approaches to multiple sclerosis is the variety of symptoms in disability that each patient may face. There should be more research conducted on dietary contributions and factors that may play a part in the development and progression of multiple sclerosis. Much of the research that is currently available focuses on how to improve symptoms rather than how to prevent multiple sclerosis from occurring due to healthy diet, or if that is even possible.

Research for smoking tobacco during multiple sclerosis is abundant. Research does support that smoking cessation may decrease the severity of disability for patients with multiple sclerosis. However, it does not conclude that smoking sensation at the beginning of a multiple sclerosis diagnosis will alter the disease progression. More research should be conducted on the

overall effect that smoking tobacco has on the development and progression of multiple sclerosis, rather than just effect it has on the overall disability.

When looking at nonpharmacological treatment approaches to multiple sclerosis, the biggest benefit is that these interventions have not been found to be harmful for patients with multiple sclerosis. Exercise, lifestyle changes, and smoking cessation are beneficial in all patients whether they have multiple sclerosis or not. It is important to educate patients that these interventions may or may not aid in symptom management or disease progression of multiple sclerosis, but they are beneficial for improving overall health.

### **Conclusion**

Multiple sclerosis is an autoimmune, demyelinating, central nervous system disease. It can affect people throughout their lifetime and be detrimental to their quality of life. The field of research for multiple sclerosis is ever changing with new medications constantly available. However, at this point there is no cure for multiple sclerosis. Because of that, nonpharmacological treatment approaches can be used in combination with pharmacological treatment approaches to aid in overall quality of life and lack of disease progression.

There is an overall lack of evidence available supporting the use of non-pharmacological treatments and lifestyle modifications for multiple sclerosis. There is a gap in the literature in education that may be provided to patients that is concrete and evidence based. Due to the lack of harmful side effects, patients with multiple sclerosis should be provided with non-pharmacological options to manage their symptoms and lessen disability while also explaining that they may or may not be beneficial when looking strictly at their multiple sclerosis, as well as educating on the possible benefits that they may experience.

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- White, L. J., & Dressendorfer, R. H. (2004). Exercise and multiple sclerosis. *Sports Medicine*, 34(15), 1077–1100. <https://doi-org.ezproxy.mnsu.edu/10.2165/00007256-200434150-00005>

## Appendix A

### *Database Search Description*

<b>Database</b>	<b>Restrictions Added to Search</b>	<b>Dates included in database</b>	<b>General Subjects covered by database</b>
Academic Search Premier (ASP)	Full Text, Academic Journals, Peer Reviewed	2006-2019	Provides citations and abstracts to articles, as well as full text of articles
CINAHL	Full Text, Academic Journals, Abstract Available	2006-2019	Provides full text access to e-books about nursing and 29 core nursing journals. Also provides citations and abstracts to articles, books, dissertations, proceedings, and other materials about all aspects of nursing and allied health
Medline	Full text, Peer Reviewed	2006-2019	Provides citations and abstracts to articles covering
Cochrane Database of systematic Reviews	Full Text	2006-2019	Evidence-based data that contains full text articles, as well as protocols focusing on the effects of healthcare.



## Appendix B

### *Data Abstraction Process*

<b>Key Words</b>	<b>Hits in ASP</b>	<b>Hits in CINAHL</b>	<b>Hits in Medline</b>	<b>Hits in Cochrane</b>
“Multiple Sclerosis” and “Non-pharmacological”	8*	4*	4*	2*
“Multiple Sclerosis” and “Treatment”	5,550	1,075	71	16
“Multiple Sclerosis” and “Smoking”	130	28	613	0
“Multiple Sclerosis” and “Exercise”	921	569	1585	5*
“Multiple Sclerosis” and “Diet”	185	68	821	1*
“Multiple Sclerosis” and “Treatment” and “Non-pharmacological”	8*	4*	55	0
“Multiple Sclerosis” and “Lifestyle”	214	111	345	0
“Multiple Sclerosis” and “Lifestyle Modification”	22	8*	36	0
“Multiple Sclerosis”, “Disease Progression” and “Non-pharmacological”	1*	0	13	0

\*-Indicates articles reviewed for match with systematic review inclusion criteria

### Appendix 3

#### *Characteristics of Literature Included and Excluded*

<b>Reference</b>	<b>Included or Excluded</b>	<b>Rationale</b>
Amatya, B., Young, J., Khan, F., & Amatya, B. (2018). Non-pharmacological interventions for chronic pain in multiple sclerosis. <i>Cochrane Database of Systematic Reviews</i> , (12).	Included	Non-pharmacological methods for chronic pain management for patients with MS
Amatya, B., Khan, F., La Mantia, L., Demetrios, M., Wade, D. T., & Amatya, B. (2013). Nonpharmacological interventions for spasticity in multiple sclerosis. <i>Cochrane Database of Systematic Reviews</i> , (2).	Included	Assess the effectiveness of non-pharmacological interventions for the treatment of spasticity in adults with MS
Bennett, M. H., Heard, R., & Bennett, M. H. (2011). Hyperbaric oxygen therapy for multiple sclerosis. <i>Cochrane Database of Systematic Reviews</i> , (8).	Included	Hyperbaric oxygen therapy for slowing the disease process of MS
Brenner, P., & Piehl, F. (2016). Fatigue and depression in multiple sclerosis: Pharmacological and non-pharmacological interventions. <i>Acta Neurologica Scandinavica Supplementum</i> . 134, 47-54.	Included	Non-pharmacological approaches to symptom management and fatigue in patients with MS
Messinis, L., Kosmidis, M. H., Lyros, E., & Papatheanasopoulos, P. (2010). Assessment and rehabilitation of cognitive impairment in multiple sclerosis. <i>International Review of Psychiatry</i> , 22(1), 22–34.	Excluded	Focuses on neurological assessment and cognitive rehabilitation as well as pharmacological treatment approaches
Neate, S. L., Taylor, K. L., Jelinek, G. A., De Livera, A. M., Simpson, J. S., Bevens, W., & Weiland, T. J.		Focuses on partners of people living with MS and their relationships.

<p>(2019). On the path together: Experiences of partners of people with multiple sclerosis of the impact of lifestyle modification on their relationship. <i>Health &amp; Social Care in the Community</i>, 27(6), 1515–1524.</p>	<p>Excluded</p>	
<p>Hadgkiss EJ, Jelinek GA, Weiland TJ, Rumbold G, Mackinlay CA, Gutbrod S, &amp; Gawler I. (2013). Health-related quality of life outcomes at 1 and 5 years after a residential retreat promoting lifestyle modification for people with multiple sclerosis. <i>Neurological Sciences</i>, 34(2), 187–195.</p>	<p>Excluded</p>	<p>Quality of life after 5-day stay at residential retreat where non-pharmacological treatment methods were implemented</p>
<p>Heydarpour, P., Manouchehrinia, A., Beiki, O., Mousavi, S. E., Abdolalizadeh, A., Lakeh, M. Moradi, &amp; Sahraian, M. A. (2018). Smoking and worsening disability in multiple sclerosis: A meta-analysis. <i>Acta Neurologica Scandinavica</i>, 138(1), 62–69.</p>	<p>Included</p>	<p>Meta-analysis on smoking and worsening disability for patients with diagnosed multiple sclerosis</p>
<p>Jakimovski, D., Weinstock-Guttman, B., Gandhi, S., Guan, Y., Hagemeyer, J., Ramasamy, D. P., Fuchs, T., Browne, R., Bergsland, N., Dwywe, M., Ramanathan, M., Zivadinov, R. (2019). Dietary and lifestyle factors in multiple sclerosis progression: Results from a 5-year longitudinal MRI study. <i>Journal of Neurology</i>, 266(4), 866–875.</p>	<p>Included</p>	<p>Lifestyle risks studied over 5 year longitudinal study assessing lifestyle on MS disease progression</p>
<p>Jelinek, G. A., De Livera, A. M., Marck, C. H., Brown, C. R., Neate, S. L., Taylor, K. L., &amp; Weiland, T. J. (2016). Associations of lifestyle, medication, and socio-demographic factors with disability in people</p>	<p>Included</p>	<p>Focuses on healthy lifestyle and the association with disability with an international MS sample. Did not specify interventions that were made, but rather lifestyle modifications as a whole.</p>

with multiple sclerosis: An international cross-sectional study. <i>PLoS ONE</i> , 11(8), 1–12.		
Marck, C. H., De Livera, A. M., Brown, C. R., Neate, S. L., Taylor, K. L., Weiland, T. J., Hadgkiss, E., Jelinek, G. A. (2018). Health outcomes and adherence to a healthy lifestyle after a multimodal intervention in people with multiple sclerosis: Three year follow-up. <i>PLoS ONE</i> , 13(5), 1–13.	Included	Assess health outcomes 3 years after lifestyle modification interventions
Matveeva, O., Bogie, J. F. J., Hendriks, J. J. A., Linker, R. A., Haghikia, A., & Kleinewietfeld, M. (2018). Western lifestyle and immunopathology of multiple sclerosis. <i>Annals of the New York Academy of Sciences</i> , 1417(1), 71–86.	Included	Assess the impact of the western diet on the progression and development of MS
Moss, B., Rensel, M., Hersh, C., Moss, B. P., Rensel, M. R., & Hersh, C. M. (2017). Wellness and the Role of Comorbidities in Multiple Sclerosis. <i>Neurotherapeutics</i> , 14(4), 999–1017.	Excluded	Assess the role of already existing comorbidities on the progression of MS
Neven, A., Vanderstraeten, A., Janssens, D., Wets, G., & Feys, P. (2016). Understanding walking activity in multiple sclerosis: step count, walking intensity and uninterrupted walking activity duration related to degree of disability. <i>Neurological Sciences</i> , 37(9), 1483–1490.	Included	Investigate the step count for patients with MS to assess the amount of time and intensity that patients with MS are exercising
Nortvedt, M., Riise, T., & Mæland, J. (2005). Multiple sclerosis and lifestyle factors: the Hordaland	Excluded	Assess quality of life for patients with MS who have high BMI, smoke, or consume alcohol.

Health Study. <i>Neurological Sciences</i> , 26(5), 334–339.		
Pozzilli, C., Sbardella, E., de Giglio, L., & Tomassini, V. (2006). Treatment of multiple sclerosis-related fatigue: Pharmacological and non-pharmacological approaches. <i>Neurological Sciences</i> , 27, s297–s299.	Included	Non-pharmacological treatment for fatigue management compared to pharmacological management
Ploughman, M., Austin, M., Stefanelli, M., Godwin, M., Ploughman, M., Austin, M., & Godwin, M. (2010). Applying cognitive debriefing to pre-test patient-reported outcomes in older people with multiple sclerosis. <i>Quality of Life Research</i> , 19(4), 483–487.	Excluded	Qualitative cognitive debriefing study done via patient questionnaire looking at quality of life
Reider, N., Salter, A. R., Cutter, G. R., Tyry, T., & Marrie, R. A. (2017). Potentially Modifiable Factors Associated with Physical Activity in Individuals with Multiple Sclerosis. <i>Research in Nursing &amp; Health</i> , 40(2), 143–152.	Excluded	Lifestyle modifications to increase ability to complete physical activity
Strober, L. B., Becker, A., & Randolph, J. J. (2018). Role of positive lifestyle activities on mood, cognition, well-being, and disease characteristics in multiple sclerosis. <i>Applied Neuropsychology: Adult</i> , 25(4), 304–311.	Included	The use of adjunct lifestyle modifications for severity and frequency of MS relapses
Thomas, P. W., Thomas, S., Hillier, C., Galvin, K., Baker, R., & Thomas, P. W. (n.d.). Psychological interventions for multiple sclerosis. <i>Cochrane Database of Systematic Reviews</i> , (1).	Excluded	Assess the effectiveness of psychological interventions for patients with MS.

White, L. J., & Dressendorfer, R. H. (2004). Exercise and multiple sclerosis. <i>Sports Medicine</i> , 34(15), 1077–1100.	Included	Focuses on physiology alteration with exercise implementation in patients with MS
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## Appendix 4

### *Literature Review Table of All Studies Included*

<b>Citation</b>	<b>Study Purpose</b>	<b>Pop (N), Sample Size</b>	<b>Design/Level of Evidence</b>	<b>Variables</b>	<b>Findings</b>	<b>Conclusion</b>
Amatya, B., Young, J., Khan, F., & Amatya, B. (2018).	Investigate the effectiveness of non-pharmacological therapies for chronic pain for patients with MS (PwMS)	10 Studies	Level I Literature review of all published RCTs and CCTs	Non-pharmacological therapies for chronic pain such as transcutaneous electrical nerve stimulation (TENS), heat or cold therapy, supportive braces, exercise, biofeedback, and relaxation	No statistically significant association for non-medication treatment for chronic pain management for PwMS	Many studies contained low number of participants. More research needs to be conducted with more participants to determine effectiveness
Amatya, B., Khan, F., La Mantia, L., Demetrios, M., Wade, D. T., & Amatya, B. (2013).	Investigate effectiveness of non-pharmacological therapies for spasticity for PwMS including TENS and exercise	9 Studies	Level I RCTs using GRADE tool as meta-analysis was not possible due to heterogeneity of	Non-pharmacological therapies for spasticity	No statistical significance for non-pharmacological treatment for spasticity for PwMS	Wide variety of non-pharmacological methods are used for spasticity, but more thorough trials need to be done to build evidence

			included studies			for spasticity
Bennett, M. H., Heard, R., & Bennett, M. H. (2011).	Investigate efficacy and safety of Hyperbaric oxygen therapy for treatment of MS	10 studies, 504 participants	Level I RCTs meta-analysis	Hyperbaric oxygen therapy versus sham therapies for MS	No statistical significance to verify a benefit for hyperbaric oxygen therapy for treatment of MS	Hyperbaric oxygen therapy cannot be justified for routine treatment for MS
Brenner P, Piehl F. (2016).	Compare pharmacological versus non-pharmacological therapy for fatigue and depression in PwMS	NA	Level IV Cohort Study	Pharmacological versus non-pharmacological treatment for fatigue and depression for PwMS	Pharmacological treatment for fatigue is modest, non-pharmacological benefit demonstrates some efficacy although not statistically significant. Very few studies are conducted on depression.	Further research is needed to refine treatment protocols.
Heydarpour, P., Manouchehrinia, A., Beiki, O., Mousavi, S. E., Abdolalizadeh, A., Lakeh, M. Moradi, & Sahraian,	Investigate environmental factors, focusing on smoking, to alter the physiology of MS	11 articles	Level I Meta-analysis	Smoking cessation and decreased expanded disability status scale (EDSS) and multiple sclerosis severity scale (MSSS)	Smoking increased EDSS however it had no effect on MSSS or T2 lesion volume	Insignificant findings were contributed to a small number of studies, different study techniques, and variations



M. A. (2018).						in disability reports.
Jakimovski, D., Weinstock-Guttman, B., Gandhi, S., Guan, Y., Hagemeyer, J., Ramasamy, D. P., Fuchs, T., Browne, R., Bergsland, N., Dwywe, M., Ramanathan, M., Zivadinov, R. (2019).	Assess lifestyle risk factors linked to cardiovascular disease and MS outcomes	175 PwMS 42 controls	Level II Single RCT	Followed patients for 5 years, obtained baseline and follow-up MRIs and assessed changes based on diet and lifestyle changes	Lifestyle contributes to increased and enhanced brain atrophy in PwMS	Lifestyle modifications may prove to be beneficial for PwMS and reducing the effect and potential for brain atrophy
Marck, C. H., De Livera, A. M., Brown, C. R., Neate, S. L., Taylor, K. L., Weiland, T. J., Hadgkiss, E., Jelinek, G. A. (2018).	Assess adopting and adhering to lifestyle modification intervention's long-term	95 PwMS	Level IV Cohort Study	Follow PwMS for 1 year and 3 year follow-ups from a 5 day workshop on lifestyle modifications to assess PwMS physical and mental health	Decrease in disability from baseline to 1-year and 3-year follow-up. Fewer patients had relapses when continuing healthy lifestyle interventions	Lifestyle modification that is sustainable is beneficial to PwMS. It may also decrease the need for pharmacological therapy
Matveeva, O., Bogie, J. F. J., Hendriks, J. J. A.,	Study environmental factors and dietary habits and	NA	Level V Meta-Synthesis	Assess how the westernized diet and disturbance	The advancement of molecular mechanisms that drive	A westernized lifestyle contributes to the risk

Linker, R. A., Haghikia, A., & Kleinewietfeld, M. (2018).	the correlation between MS development			s in the sleep circadian rhythm to understand the etiology of MS	MS can lead to specialized dietary treatment approaches	assessment for PwMS. However, more research is needed to increase the understanding on why that occurs
Neven, A., Vanderstraeten, A., Janssens, D., Wets, G., & Feys, P. (2016).	Assess step count, intensity, and duration of walking in correlation to degree of disability of PwMS	64 PwMS	Level II RCT	Assess PwMS step count, duration and distance over a 2,3,6,10,12, 14 minute period	Step count in PwMS was lower than the recommendations, which negatively influenced disability scores	PwMS should be encouraged to step at a moderate intensity for longer periods of time to decrease their degree of disability.
Pozzilli, C., Sbardella, E., de Giglio, L., & Tomassini, V. (2006).	Assess pharmacological and non-pharmacological treatment approaches to fatigue caused by MS	NA	Level V Meta-Synthesis	Assess different pharmacological approaches to treatment in combination to non-pharmacological treatment approaches	Treatment for fatigue related to MS should be approached from a multifactorial perspective incorporating pharmacological and non-pharmacological treatment approaches	In patients with mild fatigue due to MS, yoga, aerobic exercises, cooling therapy, and energy conservation are best paired with pharmacological treatments for

						decreased fatigue.
Strober, L. B., Becker, A., & Randolph, J. J. (2018).	Assess if daily activities can be used as an adjunct therapy to reduce severity of MS symptoms	248 PwMS	Level II RCT	Assess if healthy nutrition, exercise, and social engagement impacts function for PwMS	Engaging in positive lifestyle activities have positive effects on MS and disease management	A holistic approach to treating MS is best as it considers varying aspects of patient functioning and helps to achieve the overall goal of optimal health for those living with MS using exercise and temperature control
White, L. J., & Dressendorfer, R. H. (2004).	Investigate formal exercise and lifestyle as early treatment approaches to treatment for PwMS	NA	Level I RCTs	Implementing exercise programs that are designed to increase fitness, muscle strength, and mobility	Early implementation of exercise for PwMS to reduce increased function decline	Contrary to the previous belief that exercise would magnify MS related symptoms, it is now shown to be beneficial for PwMS to be active to promote better overall health and delayed

						disease progression .
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