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Physicians' Perceptions and Intent to use McDonald Guidelines for Diagnosing Multiple Sclerosis

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Abstract

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Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system that affects close to 400,000 patients in the United States and roughly 2.3 million people around the world. Because this is a growing global public health concern, researchers and clinicians are calling for a more efficient adoption of these McDonald MS guidelines in clinical practice as outlined in newly diagnosed guidelines. The purpose of this quantitative correlational study was to examine the relationship between the independent variables gender, guidelines knowledge, years in practice and intent to use the McDonald MS guidelines for diagnosing MS among physicians. The diffusion of innovation model was used to help understand and interpret the findings. The study sample consisted of 161 practicing physicians who treat MS patient in the Midwestern United-States recruited using convenience purposeful sampling. Data were collected by electronic survey using Survey Monkey. Binary logistic and multiple logistic regression to test the association between variables yielded no association between variables or the presence of predictor for the outcome. Analysis revealed gender (odds ratio [OR] =1.5; p=.347), knowledge (OR=1.23; p= .600), and years in practice (OR=1.015; p=.404) were not a predictor of intent. These findings contradict research on factors affecting the adoption of new technologies in fields other than treatment of MS. The positive social change impact of understanding factors associated with the adoption of the guidelines by clinicians is a resulting increase in use for effective diagnoses of MS.

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Dedication

I dedicate this page to my wife, children, in-laws, and all those diagnosed with

MS.

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I would like to acknowledge and thank the University staff for their incredible

support.

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Chapter 1: Introduction to the Study

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system that affects close to 400,000 patients in the United States and roughly 2.3 million people around the world (Tullman, 2013), which has led to a growing global public health concern. (World Health Organization, 2016). Guidelines exist to help patients with diagnosing and treatment of MS. However, researchers and clinicians are calling for a more efficient adoption of these guidelines in clinical practice (Harris, 2009). The McDonald guidelines may improve disease diagnosis, predict disease progression, and improve clinical outcome (Harris, 2009). The topic of the study is physicians' perceptions and intent to use MS McDonald guidelines for diagnosing MS. Appropriate use of guidelines by frontline clinicians could result in earlier detection of MS, reducing associated morbidity and mortality associated with the disease. Study findings may impact secondary and tertiary MS prevention efforts in the community. This chapter includes a discussion of the background, research questions (RQs), purpose of the study, and theoretical framework for the study.

Background

Physicians' perceptions on the use of MS guidelines are hampered due to the lack of understanding for the etiology of MS, lack of specificity, and cost (Harris, 2009). However, it is necessary for clinicians to have appropriate understanding of the etiology, as well as a guideline that they can correctly use. This can make a difference in public health because as the prevalence of MS is increasing, quality of care for these patients is becoming a growing concern. The National MS society has reported the prevalence of

MS to be 2.3 million individuals worldwide and 400,000 in the United States (Tullman, 2013). In the United States prevalence estimates are 90 per 100,000, and 10,000 new cases are diagnosed each year or 200 new cases per week (Pohlman et, al., 2010). MS can affect individuals between the ages of 20 and 50.

The current diagnostic tools for MS include MRI of the brain and spinal cord, lumbar puncture to evaluate cerebrospinal fluid (Villoslada, 2010). But there is a need for clinicians to correctly use guidelines, which could provide intervention to prevent advanced MS disease. Guidelines that currently exist focus on myelin loss, spinal cord disease, gray matter, and subcortical demyelination (Villoslada, 2010). The discovery of innovated guidelines will depend on significant advances in proteomics and microarray gene and antigen analysis (Gandhi et, al.,2013). Although guidelines currently exist for MS, there is a need for clinicians to correctly use McDonald guidelines for diagnosing MS to improve community care and clinical outcomes (Martin et, al., 2006). But there is little research about clinicians' level of knowledge and perceptions of the use of guidelines for diagnosing MS. Findings from this study will contribute to closing this gap in the literature. The purpose of this quantitative correlational study is to examine the association between physician factors and characteristics that may be associated with their intent to use guidelines for early diagnosis and prevention of advanced forms of MS.

Problem Statement

Physicians find it clinically valuable to have a measuring tool such as guidelines to definitively diagnose, identify reoccurrence, and treat MS (Mehr, 2015). However, there is a lack of consistent guidelines to diagnose and treat MS (Harris, 2009). Not

correctly using measurable tools for accurate, early diagnosis results in poor clinical outcomes for the community suffering from MS (Mehr, 2015). The correct use of guidelines by front line clinicians is needed so that patients can be diagnosed and treated more effectively to prevent reoccurrences of MS related complications (Harris, 2009). But there is not enough research on what clinicians know about guidelines when diagnosing MS along with their attitudes and beliefs particularly when looking at physician gender, McDonald MS guideline knowledge, and years in practice. With this study, findings may encourage use of MS guidelines to diagnose and treat patients, which may lead to earlier detection and improved patient outcomes.

Purpose

The purpose of this quantitative correlational study was to examine the relationship between the independent variables gender, McDonald MS guideline knowledge, and years in practice, and the dependent variable of intent to use guidelines. The variables were analyzed with correlation, bivariate, and multivariate logistic regression. This study may impact MS prevention efforts by indicating factors that affect use of guidelines to diagnose and treat MS patients.

Research Questions and Hypotheses

The research questions (RQs) and accompanying null and alternative hypotheses for this study are:

RQ1: What is the association between gender and the intent to use the guidelines?

Null Hypothesis: There is no association between gender and intent to use the guidelines.

Alternative Hypothesis: There is an association between gender and intent to use the guidelines.

RQ2: What is the association between guidelines knowledge and intent to use the guidelines.

Null hypothesis: There is no association between guidelines knowledge and intent to use the guidelines.

Alternative Hypothesis: There is an association between guidelines knowledge and intent to use the guidelines.

RQ3: What is the association between years in practice and intent to use the MS guidelines?

Null Hypothesis: There is no association between years in practice and intent to use the guidelines.

Alternative Hypothesis: There is an association between years in practice and intent to use the guidelines.

RQ4: To what extent do gender, guideline knowledge, and years in practice predict intent to use the guidelines?

Null hypothesis: Gender, guidelines knowledge, and years in practice do not predict intent to use guidelines.

Alternative Hypothesis: Gender, guidelines knowledge, and years in practice predict intent to use guidelines.

Theoretical and Conceptual Framework for the Study

I used the Diffusion of Innovation Model to help me understand and interpret my findings (Rogers, 1995). This model was appropriate because it looks at the how, why, and at what rate technology can spread. Adoption means that a person does something differently than what they had previously done, and the key to adoption is that the person must perceive the idea, behavior, or product as new or innovative (Rogers, 1995). The steps in diffusion consist of knowledge, persuasion, decision, implementation, and confirmation. Though the diffusion of innovation model is important when evaluating technology acceptance and sustainability (Aizstrauta, 2014), in the context of this study, it takes this type of new adoption for clinicians to realize the importance of guidelines for MS since there is an underutilization of guidelines with MS patients. The clinical use of guidelines in early detection and risk assessment will recognize an important health care need of detecting and monitoring MS at its earliest stage. The Diffusion of Innovation Model helped me in my understanding of the data from the study.

Nature of the Study

This study was a quantitative cross-sectional correlation study in which I examined the association between gender, McDonald MS guideline knowledge, and years in practice and clinicians' intent to the use the guidelines. This methodology was appropriate for the study because it allowed me to quantify the association between the variables. Independent variables in the study were gender, McDonald MS guideline knowledge, years in practice, and the dependent variables was intent to use the guidelines. I developed an electronic survey using Survey Monkey to collect data from

161 practicing physicians from the Midwest who are in private practice or practicing at major medical centers.

Definitions

The following section includes a list of key constructs and their definitions.

Multiple sclerosis (MS): Demyelinating and chronic disease of the central nervous system in which the insulating covers of nerve cells in the brain and spinal cord are damaged. This construct will measure how well biomarkers detect MS (Loma, 2011).

Gender: Biological designation of male or female (Miguez, 2014).

Guideline's knowledge: Knowledge is the level of understanding and knowledge about the McDonald MS guidelines (Guo, 2014).

Assumptions

The first assumption was that physicians' knowledge about McDonald MS guidelines may be varied. The second assumption was that guideline clinical use may be varied, and clinicians responded truthfully to the questions on the survey. The advantages are these more robust guidelines are clinically useful for clinicians to make a proper diagnosis and treatment plan for the patients (Housley et, al., 2015).

Scope and Delimitations

The scope of the study focused on the selected physician characteristics gender, McDonald guideline knowledge, and years and practice and the dependent variable intent to use. I explored intent to use the McDonald guidelines only, not their actual use. The populations included in the study include physicians who diagnose and treat MS patients across the Midwest, and the exclusion includes population outside of the Midwest.

Limitations

The limitations of this cross-sectional correlational methodology are that it is not used to analyze behavior or establish cause and effect. The limitations to external validity consisted of population and ecological validity. Another limitation is recall bias as this is a main drawback to surveys.

Significance

Although McDonald MS guidelines may exist for MS there is a need for clinicians to correctly use of guidelines for diagnosing MS to improve community care (Martin et, al., 2006). But there is little research about clinicians' level of knowledge and perceptions of the use of guidelines for diagnosing MS. The public health concern for MS in the community is the growing prevalence, disability, and cost of MS; with better use of guidelines this burden could be reduced. Addressing clinicians' perceptions can improve their quality of care, cost, and access within the healthcare system. The appropriate use of McDonald MS guidelines by frontline clinicians could result in earlier detection and more effective treatment of MS thus reducing associated morbidity and mortality.

Summary

The prevalence of MS is growing including the diagnosis of MS. The purpose of this quantitative correlational study was to examine the association between physician characteristics that may be associated with their intent to use the McDonald guidelines for early diagnosis and prevention of advanced forms of MS. It is important to examine the association between physician factors and clinical factors like gender, McDonald MS guideline knowledge, and years in practice with the intent to use the guidelines to better

understand their implementation or lack of implementation in practice. Increased and consistent use of the McDonald MS guidelines could result in earlier detection and more effective treatment of MS thus reducing associated morbidity and mortality associated with the disease. Roger's Diffusion of Innovation Model was used to help me understand and interpret my findings (Rogers, 1995). Data for this study were collected through an electronic survey that was emailed to practicing clinicians from across the Midwest and at major academic institutions. Chapter 2 includes a detailed literature review on MS and the methodology.

Chapter 2: Literature Review

The implementation of guidelines by front line clinicians is needed so that patients can be diagnosed and treated more effectively to improve patient outcomes and establish more valid diagnostic tests and immunotherapies (Harris, 2009). For instance, the McDonald MS guidelines can be used to definitively diagnose, identify reoccurrence, and treat MS (Mehr, 2015). However, there is a need for a more efficient adoption of these guidelines (Harris, 2009). It has been challenging to establish an effective guideline because of the clinical and pathophysiological complexities of the disease (Katsavos et, al., 2013). This understanding of which mechanism is most relevant is challenging in deciding which is the appropriate therapeutically immunotherapy choice.

At present, the clinical application of neutralizing antibodies interferon beta as a guideline is what clinicians are using to treat MS even though it lacks specificity and sensitivity, and with current validation studies that are currently occurring, cerebral spinal fluid (CSF) analysis of fetuin-A and other markers, such as ostepontin could be routinely used and a more effective option (Harris, 2014). The current study discussed possible guidelines that are relevant and include HLA-DRB1, polymorphisms, oligoclonal bands, vitamin D, TOB-1, ApopE. S100B and conventional and nonconventional imaging techniques to name a few (Katsavos et, al., 2013). But without an effective guideline it is difficult to personalize the treatment with an effective immunotherapy. The clinical management of patients with MS can improve with a reliable biomarker and improve clinical outcome (Harris, 2014), which can be done using the McDonald guidelines. This

chapter includes the literature search strategy and a comprehensive review of the relevant literature on MS and the McDonald guidelines.

Literature Search Strategy

The databases used included the library resources at the Washington University School of Medicine in St. Louis, St. Louis University School of Medicine, Lindenwood University in St. Louis, and search engines included EBSCO host, google scholar. The key search terms included were *MS and guidelines, current research and development with MS guidelines, current challenges or limitations of MS guidelines, and clinical factors associated with clinician's intent to use the guidelines.* The years searched included 2015-2020 for data and peer reviewed articles.

Theoretical Framework

I used the Diffusion of Innovation Model to help me understand and interpret my findings (Rogers, 1995). This diffusion of innovation model is used to evaluate technology acceptance and sustainability (Aizstrauta, 2014), determining the how and why technology spreads. This model is appropriate for my study because it takes this type of new adoption for clinicians to realize the importance of guidelines for MS.

Literature Review

Epidemiology of MS

MS is an acquired inflammatory and neurodegenerative immuno-mediated disorder of the central nervous system, and its distinguishing features consist of inflammation, demyelination, and primary and secondary axonal degeneration (Pugliatti et, al., 2006). The clinical presentation of MS consists of visual and sensory disturbances,

limb weakness, gait problems, and bladder and bowel symptoms that often accompany irreversible functional disability over time (Puglatti et, al., 2006).

MS affects 400,000 people in the United States and 2.5 million people worldwide (Puglatti et, al., 2006). The prevalence estimates are 90 per 100,000 population and MS symptom age can start anywhere from 20-50 to 80 years old, but mean age is 32 (Williamson, 2009). The lowest prevalence has been in the Texas area, intermediate in the Missouri area, and highest in the Ohio area (Williamson, 2009). The United States MS prevalence is highest among women, aged 40 to 59 years old and non-Hispanics, and approximately 85% of affected people have a relapsing-remitting course, and an unsteady course of exacerbations and remissions (Williamson, 2009). The latitude increase gradient in MS incidence over the last 25 years tied to regions closer to the equator, and an increase in the female to male ratio among MS cases (Alonso, 2008). Europe is considered a higher region for MS with 30,000 per 100,000 and higher prevalence and incidence tended to be higher in the Northern regions of the United Kingdom and in the Nordic countries, suggesting the importance of the role of latitude (Kingwell et, al., 2013). In Europe, the MS incidence is 4.3 cases per 100,000 and the total prevalence in Europe the past three decades is 83 per 100,000 and higher rates in northern country and a female to male ratio around 2.0 (Pugliatti et, al., 2006).

Some of the proposed causes of MS include genetics, smoking, and reproductive factors (Alonso, 2008; Poorolajal et, al., 2017) The literature has also demonstrated that the incidence of MS in influenced by numerous factors, including patient gender, age, duration of illness, ethnicity, season, latitude, serum vitamin D levels, smoking, stress,

infectious diseases, pregnancy, and assisted reproduction (Kalincik, 2015). Additional factors that influence MS incidence include population genetics, the interplay between genes and a geographically determined physical environment, socioeconomic structure including the availability of medical facilities (Tullman, 2013). Additional research shows that besides the established MS associated risk factors insufficient sun exposure, dietary intake, Epstein-Barr virus infection, and obesity during adolescence all play an important role and can lead to more cases of MS (Olsson et, al., 2017). In addition, personality has been considered a difference in overall health and well-being, and those individuals with a type D or distressed personality with MS tend to have poorer outcomes (Strober, 2016). However, early-stage MS patients who had adequate levels of vitamin D had a 57% lower rate of new brain lesions, a 57% lower relapse rate, and a 25% lower yearly increase in lesion volume than those with lower levels of vitamin D (Harvard School of Public Health, 2016).

Public Health Impact of MS

There is significant evidence that MS as a neurological disorder poses a great threat to public health. MS disease characteristics significantly affect dimensions of quality of life (Rezapour et, al., 2017). Major depression prevalence in those diagnosed with MS in the 18 to 45-year-old range was high at 25.7% (Patten et, al., 2003). Not only can depression be a public health concern for these MS patients, but there may be a greater risk of harm to the MS patients due to substance abuse including alcohol and illicit drug use in people with MS because of the possible magnification of motor and cognitive impairments (Bombardier et, al., 2004).

MS Prevention History and Current State of the Science

As stated, MS can be caused by strong environmental factors that include vitamin D status, infection with Epstein Barr virus, and cigarette smoking (Ascherio, 2008). More importantly genetic factors play a significant factor as well as the strongest risk factor for MS is family history (Ascherio, 2008). The keys to MS prevention with these genetic risk factors are the systemic screening of the whole genome. A large international consortium has been established to identify the genetic determinants of MS as the HLA-DRB1 locus has been linked along with additional loci to an MS risk (Asherio, 2008). Other prevention methods for environmental causes of MS include moving to area of lower latitudes because of the importance of the correlation of vitamin deficiency at higher latitudes and MS incidence. (Asherio, 2008). Vitamin D effectively reduces the risk of MS; thus, it is important to provide supplementation in adolescents and young adults. Because of the correlation of smoking to MS, if smoking was eliminated, up to 6% of the MS cases could be prevented (Asherio, 2008). Further, to prevent MS from further progressing in diagnosed individuals, there are many recommended therapies (McNamara et, al., 2017). However, MS is progressive disease with no cure, therefore MS may worsen in some patients despite everything the patient and physician do (Murray, 2006).

MS Diagnostic History and Current State

MS diagnostic history in the 1980's relied on the evidence of at least two relapses typical of MS and evidence of white matter in more than one site in the central nervous system (Murray, 2006). New research has shown new criteria known as McDonald criteria which incorporates clinical and laboratory data, while looking at MRI imaging to

demonstrate multiple areas of involvement and involvement over time (Murray, 2006).

These McDonald criteria also include the Barkhof-Tintore MRI criteria, which include

three of the four elements and at least one gadolinium enhancing lesion or 9 T2

hyperdense lesions, at least one infratentorial lesion, at least one juxtacortical lesion, and

at least 3 periventricular lesions, and a spinal cord lesion can substitute any of the above

brain lesions (Inglese, 2006) The current diagnostic criteria for MS are based on lesions

within the central nervous system that demonstrate dissemination in space and time

(Rovira, et, al., 2015). The high sensitivity of the MRI in the depiction of plaques in the

brain and spinal cord has made this technique valuable for diagnosing MS (Rovira et, al.,

2015). In addition, an MS diagnosis is dependent on a detailed medical history, careful

neurological examination, and additional paraclinical investigations such as MRI imaging

scans, CSF, evoked potentials, and blood tests (Inglese, 2006). The implementation of

MRI imaging reveals multifocal white cerebral white matter lesions in more than 95% of

patients and in 75-85% of these are focal spinal lesions (Inglese, 2006). However, no

single test including a tissue biopsy can provide a definite diagnosis of MS. The past few

years have seen improvement in the development of laboratory and imaging approaches

to the diagnosis of MS, but the use of diagnostic guidelines is important as well.

Lack of Correct and Consistent Use of McDonald Guidelines

One of the biggest challenges for clinicians is that the disease prognosis and

individual therapeutic outcomes can be difficult to predict with MS (Harris, 2014),

making it important to have a reliable guideline to detect MS and treat MS patients

(Harris, 2009).

Some of the clinical parameters that physicians use depends on MS relapse rates, MRI outcomes, and various changes in disability scores (Harris, 2009). Thus, there is an unmet need for more sensitive and specific MS guidelines to better effectively diagnose and treat MS. With more consistent and accurate guidelines, the clinicians will have an accurate measurable tool that is better able to better assess and predict medical therapy outcomes (Harris, 2009).

Despite the need for consistent guidelines, research on the etiology of MS is still ongoing because it is difficult to confirm the exact etiology or cause of MS along with understanding of the mechanism that is driving the disease (Harris, 2009). But MCAM (melanoma cell adhesion molecules) are a potential diagnostic guideline for MS, as the data show that the expression of the molecule on T cells correlates with MS disease activity (Muccilli, et, al., 2017). The strength in this approach is that researchers are looking for additional correlations across various disease states including a correlation to melanoma in trying to identify a new diagnostic guideline. The weakness in this approach is whether the peripheral expression of melanoma cell adhesion molecules can also predict MS relapses.

Additionally, "NMO-IgG antibodies became the first clinically useful diagnostic guideline that looked at a subgroup of patients with classic MS" (Comabella, 2014). All molecular guidelines used at present in MS clinical practice are the proteins, and those that measure humoral immune response are easier to integrate into clinical practice (Comabella, 2014). Further, CSF is one of the most informative body fluids in which to measure guidelines of disease because the pathological processes of the patients with MS.

However, the CSF is obtained by an invasive procedure that restricts repeated collection and can make it challenging in clinical practice.

Thus, the use of diagnostic guidelines detected in other body fluids such as IgG oligoclonal bands in tears may warrant further investigation for better application in clinical practice (Comabella, 2014). The ideal test to appropriately measure a guideline should have solid analytical and clinical precision and should be clinically useful to improve patient outcomes.

Infectious agents have also been suggested to have a role in terms of environmental factors in MS. This includes the gastrointestinal commensal bacteria having been implicated in the pathogenesis of autoimmune diseases like MS. Identifying a unique gastrointestinal and oral bacteria derived lipedipeptide, Lipid 654, which is produced by commensal bacteria and functions as a human and mouse like Toll-like receptor 2 ligand, may help in the diagnosis of MS (Farrohki, et, al., 2013). Lipid 654 is expressed at significantly lower levels in the serum of patients with MS compared to healthy individuals (Farrohki, et, al., 2013). But there is still no clear pathogenesis of MS as several theories exist out there regarding the exact cause and mechanism of the disease (Farrohki et, al., 2013).

Peer-reviewed evidence also validates clinicians' use of McDonald MS guidelines because of its effectiveness for diagnosing MS, across other therapeutic areas that have the same type of mechanism as MS. Clinicians should implement this measure tool because there is an immediate need to improve patient outcome and personalized medicine. The correlation is important because these protein and antibody factors helps

clinicians with an intent to use a specific guideline and thus guide their therapeutic treatment.

Other important peer- reviewed articles show that a biomarker blood test can determine the type of MS someone has with an accuracy of 85 to 90 %, and thus improve patient outcome by allowing clinicians to adapt to treatments faster (Farrohki et, al., 2013). A potential guideline that involves tryptophan in which researchers look at the importance of that being known to be involved in brain inflammation. A reliable guideline will guide personalized treatment for each patient, which will improve patient outcomes. However, further research is still needed on this diagnostic guideline, as there are other diseases associated with inflammation and neurodegeneration besides MS and that includes Alzheimer's, Parkinson's, and Lou Gehrig's disease (Farrohki, et, al., 2013).

Separating MS from other neurodegeneration and inflammatory conditions with this guideline and trying to separate from Alzheimer's or Parkinson's disease can be challenging considering the various disease states that have inflammatory conditions, so there is a need for a precise guideline.

Studies show that using high throughput body profiling by MALDI-TOF mass spectrometry, small proteins and peptides have been detected as promising candidate guidelines for disease diagnosis and disease progression of MS (Teunissen et, al., 2011). The strength of this study is the potential for promising clinical biomarkers for clinicians to adapt to, and the weakness with this is still investigating MALDI-TOF mass spectrometry and how this plays a significant role in MS guidelines. The rationale for this study is that it provides physicians another opportunity to use guidelines considering

potential new candidates for MS disease diagnosis like mass spectrometry that have not existed before. The correlation with this study is clinical factors that are produced from electric and magnetic fields and a clinician's intent to use a guideline (Teunissen, et, al., 2011).

These research studies support this because it discusses the importance of the development of these process specific therapies which will be impossible without the use of guidelines that reflect the targeted process and how this target process can aid in the more rapid screening of therapeutic agents as well (Bielekova, 2004). This is crucial because having this process-specific guideline is a reason why it cannot serve as a surrogate for a clinical outcome because of the complexity of MS (Bielekova, 2004). The strength of this study is that with more of a targeted approach it will help the therapeutic approach and aid in a more rapid screening process and in the development of therapeutic agents. The weakness in this approach is that there is a high degree of complexity of understanding MS because of the complexity of the disease and the difficulty of finding a single guideline (Bielekova, 2004).

The rationale for this approach is a clinician's intent to use a McDonald MS guideline by understanding this as a measurable tool that has a great ability to be targeted specifically for MS patients since challenges do exist that are being presented by being such a complex disease. The correlations are important that are presented in this study because the importance of identifying clinical factors through an effective screening process is important in MS along with the development of immunotherapy agents. The controversy with this study is the complexity of MS and how the complexity of the

disease will be difficult to identify a single guideline to improve clinical outcome (Bielekova, 2004).

The findings from the following studies demonstrate an important point because this study shows significant changed expression of selected extracellular miRNA in plasma of MS patients. This is important because these observations may help suggest that miRNA subsets may be potential guidelines for MS activity (Kacperska, et, al., 2015). The strengths of this study are that even though an ideal guideline of MS has still not been found, the strength is that a group of endogenous, single-stranded noncoding RNA molecules shows promise (Kacperska, et, al., 2015). With a better understanding of microRNA profiles in each disease may aid in a quicker and accurate diagnosis while also having universal prognostic factors. The weaknesses of this study are that the use of miRNA expression differs depending on a stage of MS whether it is relapse vs remission.

The rationale for this approach is significant because these miRNA molecules could aid in a quicker and accurate diagnosis (Kacperska et, al., 2015). This is important because a quicker and accurate diagnosis will improve patient outcome for MS patients. The correlation in this study is important because looking at clinical factors such as microRNA profiles of patients provides physicians with an intent to use guidelines and effective immunotherapy treatments. The controversy with this study is that more research needs to be done in this area especially in turn how useful in clinical practice these new guidelines could really be effective.

The study supports the significance of this because it discusses the neuroinflammatory imaging guidelines this could provide accurate and more complete

picture of MS, which in turn will help with therapeutic strategies. The strengths of this study are that it provides another perspective at looking at identifying guidelines and provides a complete picture of MS, especially our understanding of acute lesion pathophysiology and its noninvasive follow-up. This is relevant because this approach will provide in vivo sensitive and specific look at MS components to improve the diagnostic performance, the pathophysiology, and our ability to follow the course of this disease when looking at the future of therapeutic development and monitoring (Tourdias, 2013). The weakness of this study is the complex cascade of events that could take place with acute inflammatory lesions like cell recruitment and edema formation. There can be an issue with this because there are other guidelines of consequences of acute inflammation like matrix digestion by metalloproteinase, acute demyelination, and axonal injury (Tourdias, 2013).

The rationale for this study is that it provides another angle at looking at potential guidelines for MS, especially from an imaging perspective. These MRI and positron emission tomography markers of neuroinflammation will be a valid approach to assess the neurodegeneration component of MS, particularly the axonal loss and incomplete remyelination (Tourdias, 2013). The correlation is important in this study because clinical factors of inflammation provide clinicians with an intent to use a guideline and effective immunotherapy. "The controversy around this study is that there are other markers of inflammation that need to be considered here, so the research is still ongoing in identifying a single inflammatory guideline including looking at neuroimaging (Tourdias, 2013).

Further research validates that these proteins semaphorin 7A and ala-B-dipeptidase can play an important role as CSF biomarkers (Canto, et, al., 2014). The strengths of this study are that it provides some validation of specific proteins as biomarkers while using different techniques in individual CSF samples. The weakness is that in this study there were other proposed proteins as candidates for guidelines were not validated in the individual CSF samples.

The rationale for this study is to look at how different proteins play a role in guidelines, and which ones are more specific than others in determining an appropriate guideline candidate for MS (Canto, et, al., 2014). The correlation is relevant because of the clinical factors of particular proteins that patients may exhibit and a clinician's intent to use a guideline and effective immunotherapy. The controversy with this study is trying to identify which proteins are more valid than others as the study has identified appropriate candidates and not valid candidates for potential guidelines.

Additional studies are crucial because additional studies discuss the glial potassium channel KIR4.1 as potential guideline. According to the research antibodies against KIR4.1 were observed in 46.9% of patients with MS, but were essentially absent in people with other neurological diseases and healthy donors (Wunsch et, al., 2014). The strengths of this study are significant because the impact of immune responses against antigens of gastric parietal cells on the KIR4.1 reactive antibody in patients with MS is clinically significant (Wunsch et, al., 2014). The weakness of this study is that in the data only 2 of 19 serum IgG positive MS patients also had detectable levels of KIR4.1

antibody in the CSF so there still needs to further clarity on the research (Wunsch et, al., 2014).

The rationale for this study is that KIR4.1 antibody could play an important role in identifying new guidelines for clinicians. The correlation in this study is clinical factors associated with KIR4.1 antibody are an important because this provides validation for clinician's intent to use a guideline when patients have these KIR4.1 antibody. The controversy with this study is the clarity that needs to be confirmed regarding KIR4.1 antibody as research is still ongoing regarding showing resulting pathological effects in the CNS and gut (Wunsch et, al., 2014).

Additional study is important because it looks at the activation of the kynurenine pathway of tryptophan metabolism results from chronic inflammation like MS. Also, the kynurenine pathway of the tryptophan metabolism is highly inducible in inflammatory environments, and that changes in KP may be associated with MS (Kim, et, al., 2017). The strength of this study is that researchers are constantly considering biochemical pathways that are causing MS like the KP pathway. Also, the conclusions of the study show a strong association with KP parameters and MS subtype. The weakness associated with this study is this study only looked at tryptophan and unfortunately was not capable of looking at downstream KP metabolites (Kim et, al., 2017).

The rationale for this study is that additional biochemical pathways exist in looking at identification of MS guidelines and further validates this as a viable option as a guideline. The correlation with this study is important because this shows clinical factors that patients may have because of disruptions in these biochemical pathways and a

clinician's intent to use guidelines. The controversy with this study is that it did not look at other downstream KP metabolites (Kim et, al., 2017).

Furthermore, additional articles show that 40% of MS cases studied it shows detectable alpha-GA1C reactivity, which is potentially indicative of a particular type of MS in terms of disease course and severity (Menge et, al., 2005). The strength of this study is that mechanisms have been postulated with galactocerebroside and how this can be implemented in the near future. The weakness of this study is that pathophysiological explanation for the delayed response is not known. The rationale for this study is exploring additional novel findings which demonstrate guideline capability for MS diagnosis, staging, and prognosis (Menge et, al., 2005). The correlation that is important in this study is clinical factors such as patients having these enzyme disruptions with galactocerebroside and a clinician's intent to use guidelines and immunotherapy. The controversy with this study is the need for clarity around the pathophysiological explanation with MS.

The importance of this study demonstrates that immunophenotyping of CSF cells in MS is becoming more important to correlate cellular subsets with different disease activity and remission (Alvermann et, al., 2014). The strength of this study is that characterization of CSF cells allows researchers to understand MS pathogenesis and to provide appropriate guidelines, individual prognosis, and treatment decisions (Alvermann et, al., 2014). The weakness of this study is that other leukocyte populations including natural kills cells, monocytes, and dendritic cells show variation as well (Alvermann et, al., 2014). The rationale for this study is considering additional perspective on intent to

use guidelines. The correlation with this study is how these CSF clinical factors can play a role in clinician's intent to use guidelines and immunotherapy. The controversy with this study is that several other leukocyte populations need to be further examined.

The next study shows that lipid dysregulation plays a role in MS progression of disability. The strength of this study is the identification of novel cholesterol subsets and plasma triglycerides in MS patients including the use of the treatment of simvastatin (Alvermann et, al., 2014). The weakness of this study is that these results were independent of age and sex. The rationale for this study is to demonstrate the importance that lipid dysregulation plays with people with MS as it pertains to progression and disability. The correlation is important because clinical factors like lipid dysregulation plays a role in clinician's intent to identify a guideline. The controversy with this study is that these results are independent of age and sex, and also could discriminate disease state with high specificity and sensitivity (McKechnie, 2017).

Additional studies are important to address because this states that a useful guideline in MS would allow for early identification of MS patient subsets and guide their personalized treatment plan. The study discusses that the only robust guidelines utilized in current practice are the MRI and CSF oligoclonal bands, but both which provide limited prognostic information (Butterworth et, al., 2015). The strengths of this study are that the study succeeded in showing a gene SLC9A9 associated with treatment response. "The study discusses altered gene expression could lead to altered glycosylation, an important mechanism regulation inflammation, implicating gene variation in regulation of proinflammatory lymphocyte activation and thereby disease

activity" (Butterworth et, al., 2015). The weaknesses in this study are that some plasma levels in MS have not demonstrated sufficient specificity and sensitivity to be a viable guideline.

The rationale for this study is that it shows that robust guidelines solutions do exist but do not provide enough information to create the most efficient prognostic measurable tool (Butterworth et, al., 2015). This study discussed other options including gene expression which can play an important role in the inflammatory process and MS. The correlation in this study is that patients that exhibit gene expression led to clinician's intent to use guidelines for future immunotherapies. The controversy within this study is the challenge to develop a guideline with efficient prognostic solutions since robust guideline exist, but not enough to produce prognostic information that clinicians are expecting.

After an extensive search of the literature, I did not find other studies that used gender, years in practice or knowledge about a targeted content to predict intent. However, there are other recent studies that examine gender as a predictor for an outcome. Wlodarczyk (2020) examined gender and predictors of post-MI HRQoL (health-related quality of life) and found a difference between female and male survivors of a myocardial infarction (Wlodarczyk, 2020) Additional studies focused on gender included patient gender differences in the prediction of medical expenditures (Bertakis, 2010) and gender differences in determinants and consequences of health and illness (Vlassof, 2007).

Review of the Proposed Methodology

The research design for the proposed study was a quantitative correlation study to examine the relationship between the independent variables including gender, McDonald MS guideline knowledge, and years in practice, and the dependent variable intent to use the guidelines.

Lynd (2014) used correlation and regression analysis first study looked at quantitative analysis of MS patients' preferences for drug treatment as the objective was to elicit patients' preferences for different attributes of MS drug therapy (Lynd et, al., 2014). The second study looked at a comparative quantitative study of axonal injury in active, inactive, and remyelinated lesions with MS. The objective of this study discussed the importance of magnetic resonance studies of MS lesions indicate that axonal injury is a major correlate of permanent clinical deficit (Kornek et, al., 2000). The third study is a quantitative study of water diffusion in MS lesions and normal appearing white matter using Echo-Planar imaging. "The objective of this study shows that diffusion-weighted imaging is able to identify MS lesions with severe tissue disruption" (Flippi et, al., 2000). These additional citations and references demonstrated the quantitative methodology is sound and has been used by other researchers. Specific to my proposed analysis method of binary logistic regression several studies have been found in the literature. Boamah analyzed predicting social trust with give demographic variables from a national sample of individuals who participated in the General Social Survey (GSS). (Boamah, 2015). Schober (2021) analyzed the association between the induction technique and the risk of hypoxemia while controlling the potential confounders (Schober, 2021). Bucor (2017)

examined binary logistic regression instrument for assessing museum indoor air impact on exhibits (Bucor, 2017).

Summary and Conclusions

The major themes in the study include the role of epidemiology of guidelines in MS, the public health impact of MS, MS prevention history and current state, the MS diagnostic history and current state, and finally the lack of correct and consistent use of guidelines along with additional studies with my proposed methodology. I addressed the importance of how prevalent MS is and the need for clinicians to use an effective guideline to not only help MS patients but also the field of public health. The development and use by clinicians' of effective McDonald MS guidelines, the public health field can be positively impacted because effective guideline use this will lead toward more personalized and targeted care for these patients in order to improve patient outcome. The study highlighted a call from the profession to use the MS guidelines in clinical practice. There is a clinical need for not only MS, but also across other therapeutic inflammatory areas that have the same type of mechanism. Furthermore, with this study it provides clinicians another opportunity to use guidelines considering potential new candidates for MS disease diagnosis like mass spectrometry that have not existed before. Another major theme in this study is that it provides another perspective at looking at potential guidelines for MS, especially from an imaging perspective. These MRI and position-emission tomography markers of neuroinflammation will be an excellent approach to assess the neurodegeneration component of MS, particularly the axonal loss and incomplete remyelination (Tourdias, 2013). These are important studies

because clinical factors of inflammation provide clinicians with an intent to use guidelines and effective immunotherapy. Finally, the importance of having a sustainable measurable MS guideline is critical in the field of medicine and public health as patient outcome will improve along with improvement on the economic burden of patients in society. An effective MS guideline tool provides a solution for clinicians to effectively diagnose, monitor, and treat MS patients with more accuracy and precision to improve patient outcome. In Chapter 3, I discuss the research design and rationale, methodology, threats to validity all of which was an important aspect in this research.

Chapter 3: Research Method

The purpose of this quantitative study was to explore the relationship between selected physician characteristics including gender, McDonald MS guideline knowledge, and years in practice and intent to use the new guidelines for diagnosing MS. I collected data with a survey administered by email to practicing physicians from across the Midwest. The study addressed what physician characteristics might be associated with intent to use McDonald MS guidelines for the diagnosis, monitoring, prevention, and treatment of MS. The major sections of this chapter include a description of the research design and rationale, methodology, threats to validity, and summary.

Research Design and Rationale

This was a quantitative study with bivariate and regression analysis. The independent variables included gender, McDonald MS guidelines knowledge, and years in practice, and the dependent variable was intent to use the guidelines for the diagnosis and prevention of MS. A quantitative research design was appropriate given the nature of the RQs. The time and resource constraints consisted of waiting for the return of the survey data from the physicians with their busy schedules seeing patients. A detailed and specific follow up reminder email was provided to the physicians to encourage them to take and return the survey. In addition, I emailed reminders every week throughout the duration of the data collection phase of the research project.

Research Questions and Hypotheses

The RQs and accompanying null and alternative hypothesis for this study are:

RQ1: What is the association between gender and the intent to use the guidelines? Null Hypothesis: There is no association between gender and intent to use the guidelines.

Alternative Hypothesis: There is an association between gender and intent to use the guidelines.

RQ2: Research question: What is the association between guidelines knowledge and intent to use the guidelines?

Null hypothesis: There is no association between guidelines knowledge and intent to use the guidelines.

Alternative Hypothesis: There is an association between guidelines knowledge and intent to use the guidelines.

RQ3: Research question: What is the association between years in practice and intent to use the MS guidelines?

Null Hypothesis: There is no association between years in practice and intent to use the guidelines.

RQ4: To what extent do gender, guideline knowledge, and years in practice predict intent to use the guidelines?

Null hypothesis: Gender, guidelines knowledge, and years in practice do not predict intent to use guidelines.

Alternative Hypothesis: Gender, guidelines knowledge, and years in practice do predict intent to use guidelines.

Methodology

Population

The target population was practicing physicians (neurologists and primary care physicians) in the Midwest who diagnose and treat MS patients. The study population was practicing MD and D.O physicians who were either in private or hospital-based practice.

Sampling and Sampling Procedures

The study population consisted of MD and D.O. physicians across several states (Missouri, Illinois, Kansas, Oklahoma, Iowa, Arkansas, Nebraska) in the Midwest who treat MS patients. Convenience sampling was used because of constraints of time and other resources. I chose to purposefully sample physicians residing in states near where I live in Missouri. The study participants were identified with an online search of all neurologists and primary care physicians in network who treat MS patients within the Midwest. Potential participants were invited via email to participate in the study. Those who agreed were asked to take a survey using Survey Monkey. Physicians who do not treat these types of MS patients or who currently use the guidelines were excluded from the study.

Procedures for Recruitment, Participation, and Data Collection

Recruitment Procedures

The steps for recruitment included emailing invitations to the physicians to participate in the study. I determined eligibility, ensuring that that the participants treat MS patients, through online searches of potential participants' specialty and exact patient

population. This included both the neurologists and primary care physicians holding an

M.D. or D.O degree and license to practice medicine in their state. I screened potential

candidates using a short screening questionnaire when they accessed Survey Monkey. I

then provided access to a previously developed self-administered survey on Survey

Monkey. The participants provided informed consent acknowledgement on the first page

before they took the survey to ensure that privacy and informed consent was respected.

For collecting data, I implemented response validation in which I made sure respondents

submitted their answers in the right format. Follow up procedures included my contact

information and email had any of these physicians wanted to contact me for a follow up

interview, live visit, or phone call.

Minimum Sample Size Calculation

I calculated the minimum sample size needed for this study using the G Power

calculator for sample size computation for binary logistic regression (Faul, et

al.,2009). This calculation was based on one dichotomous independent variable, gender

(male/female) and the dichotomous outcome, intend to use or do not intend to use the

McDonald guidelines for diagnosing MS. Because of the lack of published research on

the use of the McDonald guidelines, and based on my personal experiences working with

physicians who treat MS, I hypothesized that male physicians were more likely to state

intent to use the guidelines than women physicians. However, the final gender

distribution of the sample consisted of 47% male physicians and 53 % female

physicians.   Thus, assumptions were made that 50% of male physicians and 30% of

female physicians would state their intent to use the McDonald guidelines. It was

determined that a minimum sample size of 312 respondents would be needed for the

analysis for an odds ratio (OR) of 2.3, and 95% power (see Figure 1). I attempted to

recruit at least 500 respondents to increase the power of the study. However, despite

several attempts to recruit more potential participants, I was not able to achieve the 500

goal. The final sample size for this study was 161 physicians.

Figure 1

G Power Output for Sample Size Calculation for Binary Logistic Regression,
Dichotomous Independent, and Dependent Variable

Options:	Large sample z-Test, Demidenko (2007) with var corr	
Analysis:	A priori: Compute required sample size	
Input:	Tail(s)	= Two
	Odds ratio	= 2.3333333
	Pr(Y=1|X=1) H0	= 0.3
	α err prob	= 0.05
	Power (1-β err prob)	= 0.95
	R² other X	= 0
	X distribution	= Binomial
	X parm π	= 0.47
Output:	Critical z	= 1.9599640
	Total sample size	= 312
	Actual power	= 0.9500790

Procedures for Informed Consent

The informed consent process involved giving adequate information concerning

the study, providing sufficient opportunities for the participants to consider all options,

responding to the subject's questions ensuring that the subject had comprehended this

information while obtaining the participants voluntary agreement. For informed consent,

a drafted word document with a voluntary agreement for physicians to participate in this

research using the Walden Informed Consent template was provided. This informed

consent was provided in written format, sent by email to each participant who indicated a

willingness to participate. The physicians understood the research and the risks involved

within a written consent. If reading the informed consent document and they have

questions, they would respond to questions by email within 48 hours of receipt. There

will be immediate follow up to the physician if there are any missing data. The survey

was non-anonymous and confidential was guaranteed with informed consent. This was

designed to capture any reported changes or final questions that the physicians may have,

and physicians were able to contact me directly via email or phone. No physicians

contacted me regarding follow up. Also, the study was approved by the Walden (IRB #

01-21-20-0311462).

Data Collection

Data was collected in writing via an electronic survey accessed by participants

online using the Survey Monkey software. Data was collected from March 2020-August

2020. The survey had five parts including: the screening tool for eligibility, the informed

consent form, the demographic data form, the main survey questions, and closing

paragraph and form (see Appendix A). The sampling frame included all the physicians

with an MD or DO degree and license to practice medicine in their state in community

practice which included neurologists and primary care physicians who treat MS patients

in the Midwest.

Consensus Validity for the Survey

To increase the internal validity of the survey that I developed, I consulted with a

panel of three practicing physician/experts on MS who reviewed the content of the survey

for accuracy and construct validity to achieve consensus validity. The names and contact

information of the panelist were provided to my committee chair for review and approval.

Results of the review were made available to my committee members. The panelists

provided encouraging feedback that the survey being used was accurate with the study.

Pilot Study

I conducted a small pilot study prior to implementing the main study. I selected

three physicians similar to the physicians in my main study in order to test my sampling

strategy, the ease and logic of taking the survey-on Survey Monkey, and completeness

and clarity of my survey data collection instrument. I first received approval from the

IRB before conducting the pilot study. As a result of the pilot study and encouraging

feedback from the three physicians I proceeded to the next steps. I did not do any analysis

of data with the pilot study. Overall, I received positive comments from the three

physicians regarding the sample strategy feedback, ease and logic of taking survey, and

completeness and clarity of my survey data collection instrument.

Data Analysis

Since my outcome of interest is physicians' perceptions and intent to use

McDonald MS guidelines for diagnosing MS, I used binary logistic regression for the

bivariate analysis.

The software used for the analysis was SPSS version 27. My data preparation and

cleaning plan included checking and dealing with missing data, linearity, outliers,

multicollinearity, and homoscedasticity. The primary RQs for this study were: RQ1:

What is the association between gender and the intent to use the guidelines? RQ2: What

is the association between McDonald MS guideline knowledge and intent to use the guidelines? RQ3: What is the association between years in practice and intent to use the MS guidelines? RQ4: To what extent do gender, guidelines knowledge, and years in practice predict intent to use the guidelines?

The analysis plan included a descriptive analytical component consisting of the use of percentages distributions and measures of central tendency to describe the population and the responses to attitude, knowledge, beliefs, and behaviors of the diagnostic tool (See Table below) The analysis plan included an inferential statistical plan with the bivariate analysis and multiple logistic regression for the multivariate analysis and predictor modeling. (See Table 1 below) The results were interpreted with confidence intervals as confidence intervals are important when analyzing the results of statistical analysis to help interpret the P-values obtained.

Data Analysis Matrix

Table 1 shows a summary of the overall data analysis plan for the study. Please see Appendix B for the Mock Tables used in the data analysis. The three specific predictor variables are gender, McDonald MS knowledge of Guidelines, and years in practice.

Table 1

Data Analysis Plan for Study

Study Objective or Research Questions	Concept	Data Source	Level of Measurement	Analysis Procedures	Logistic Regression
RQ I. What is the association between gender and the intent to use the guidelines	Association between gender and intent to use	Survey instrument	Binary	Binary logistic regression	Binary Logistic Regression
RQ II. What is the association between guideline knowledge and intent to use the guidelines	Association between guideline knowledge and intent to use. Measured by a short quiz question and dichotomous score by Pass/Fail	Survey instrument	Binary	Binary logistic regression	Binary Logistic Regression
RQ III. What is the association between years in practice and intent to use the guidelines	Association between years in practice and intent to use	Survey instrument	Binary	Binary logistic regression	Binary Logistic regression
RQ IV. To what extent do gender, guideline knowledge, and years in practice predict intent to use the guidelines	Association between gender, guidelines knowledge, and years in practice and intent to use	Survey instrument	Multivariate	Binary logistic regression	Multiple Logistic regression

Threats to Validity

The threats are relevant to my proposed study because of my quantitative study design in which a survey was used to collect data. In the design of my study, the threats to external validity consist of population and ecological validity, while the internal threats consist of statistical regression and selection. The reasons these are external threats is population validity is this type of external validity that can create assumptions regarding extrapolation of the entire population as a whole. The internal threats of statistical regression because the scores of individuals may be extremely high or low, and selection can be an internal threat based on the comparability before the study.

Ethical Procedures

Ensuring that participants can refuse to participate without repercussions is an ethical guarantee that was included in this study. Although this study was confidential, it was not fully anonymous since the participants could be traced through their IP address. The treatment of the data was kept confidential and only used solely for the purpose of the study. Protection of the data collected and implementing storage practices to ensure privacy were applied. Strict care was taken to avoid breaches of confidentiality in which information is provided to others. I submitted an application to the IRB for permission to collect data for the pilot and main study and was granted permission (IRB: 01-21-20-0311462). I stored the data in my office in a locked cabinet in a file folder for the duration of the study and will keep the data for a minimum of five years.

Summary

The methodology used was a quantitative correlational study. Data was collected by electronic survey using the survey monkey software. Data was be kept confidential and used solely for the purpose of the study. Protection of the data collected and implementing storage practices was applied and enforced for the participants not to discuss the survey outside of the research context. In Chapter 4, I present my research findings.

Chapter 4: Results

The purpose of this quantitative correlational study was to examine the relationship between the independent variables gender, McDonald MS guidelines knowledge, and years in practice, and the dependent variable of intent to use guidelines among practicing physicians in Missouri, Kansas, Oklahoma, Iowa, Illinois, and Nebraska. I examined the association among gender, knowledge, and years in practice and intent to use the guidelines. The RQs and accompanying null and alternative hypothesis for this study are:

RQ1: What is the association between gender and the intent to use the guidelines? Null Hypothesis: There is no association between gender and intent to use the guidelines.

Alternative Hypothesis: There is an association between gender and intent to use the guidelines.

RQ2: Research question: What is the association between guidelines knowledge and intent to use the guidelines?

Null hypothesis: There is no association between guidelines knowledge and intent to use the guidelines.

Alternative Hypothesis: There is an association between guidelines knowledge and intent to use the guidelines.

RQ3: Research question: What is the association between years in practice and intent to use the MS guidelines?

Null Hypothesis: There is no association between years in practice and intent to use the guidelines.

Alternative Hypothesis: There is an association between years in practice and intent to use the guidelines.

RQ4: To what extent do gender, guideline knowledge, and years in practice predict intent to use the guidelines?

Null hypothesis: Gender, guideline knowledge, and years in practice do not predict intent to use the guidelines

Alternative Hypothesis: Gender, guidelines knowledge, and years in practice do predict intent to use the guidelines.

Chapter 4 includes a description of a pilot study conducted, data collection, reporting of findings from descriptive statistics and inferential analysis of the data, and a summary.

Pilot Study

I recruited three physicians similar to the physicians in my main study in order to test my sampling strategy, the ease and logic of taking the survey on Survey Monkey, and completeness and clarity of my survey data collection instrument. Data from the pilot study participants was not included in the main study. There were no results from the pilot study as the purpose was get the administrative protocol established. I first received approval from the IRB before conducting the pilot study. There were no changes needed to my data collection protocol, the survey content, or the participant recruitment strategies. Permission was then obtained from my committee and the IRB to proceed to the data collection for the main study. I did not do any analysis of the data during the pilot study.

Data Collection

Data were collected in writing via an electronic survey accessed confidentially by participants online using Survey Monkey. The survey had five parts: the screening tool for eligibility, the informed consent form, the demographic data form, the main survey questions, and closing paragraph and form. The sampling frame included all the neurologists and primary care physicians who treat MS with an M.D. or D.O. degree and license to practice medicine in Missouri, Kansas, Oklahoma, Iowa, Illinois, and Nebraska. Data were collected from April 2020 to July 2020. A total of 161 participants completed the survey, though the original goal was to recruit 500 participants. Despite several attempts to increase the response rate with multiple email reminders no additional participants were recruited. Participants provided demographic information that included gender, race, McDonald MS guidelines knowledge and years in practice. Data were analyzed using version SPSS 27.

Descriptive Statistics

The study sample included 75 males (46.60%) and 86 females (53.40%). Most were not Hispanic or Latino (n=141, 87.00%). The average years in practice was 11.18 (M = 11.18; SD= 10.51). There were 21 Hispanic or Latino (13.00%) and 141 not Hispanic or Latino (87.00%). One participant was American Indian or Alaska native (0.60%), 12 were Asian (7.40%), 13 were Black or African American (8.00%), 4 were Native Hawaiian or another Pacific Islander (2.50%), and 132 were White race (81.50%). The average years in practice was 11.18 (M=11.18; SD = 10.51). Fifteen participants

were very likely to use guidelines (9.30%), whereas 68 were very unlikely to use

guidelines (42.00%).

Table 2

Descriptive Characteristics of Study Sample

Variable	N	%
Gender		
Male	75	46.60
Female	86	53.40
Ethnicity		
Hispanic or Latino	20	13.00
Not Hispanic or Latino	141	87.00
Race		
American Indian or Alaska Native	1	0.60
Asian	11	7.40
Black or African American	13	8.00
Native Hawaiin or Pacific Islander	4	2.50
White	132	81.50
Total	161	

Table 3

Geographic Distribution of Survey Respondents

Geographic distribution	Yes (Number)%	No (Number)%	Total (Number)%
Private practice	0(0) %	161(100) %	161(100) %
Hospital	161(100) %	0(100) %	161(100) %
Totals	161(100) %	161(100) %	161(100) %

Table 4

Participants Who Stated Intent to Use Guidelines

Intent to use guidelines	Yes (Number)%	No (Number)%	Total (Number)%
Yes	42(26.6) %	119(42) %	161(100) %
No	119(42) %	42(26.6) %	161(100) %
Totals	161(100) %	161(100) %	161(100) %

Data Coding

Data were coded as gender 0 = female, and 1 = male, guideline knowledge given

for 0=fail and 1 = pass, years in practice was discreet, and intent to use 0 = no intent, and

1 = intent to use.

Bivariate Logistic Regression Analysis

A logistic regression analysis was conducted to assess the association between the

predictor variable, gender, and the outcome, the likelihood of stated, intent to use the

McDonald guidelines. (see Table 5). The null hypothesis tested for the adjusted OR is the

probability of being in the target group is equal to the probability of not being in the

target group (*OR=1).* The adjusted OR (.674) is less than 1.0, indicated a negative

association between gender and stated intent to use the McDonald guidelines. The P

value of the Adjusted OR is .322 and substantially greater than Alpha threshold of (.05)

and therefore not statistically significant. The Confidence Interval for the Adjusted OR

(lower: = 308; upper: =1.473) crosses 1.0 and is not statistically significant. Therefore,

the null hypothesis is not rejected. Gender is not associated with intent to use the

McDonald guidelines.

Table 5

Bivariate Analysis: Gender

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	95% C.I. for EXP(B) Upper
Step 1[a]	Gender (1)	-.395	.399	.979	1	.322	.674	.308	1.473
	Constant	-.298	.275	1.176	1	.278	.742		

A logistic regression analysis was conducted to assess the association between the predictor variable, knowledge, and the outcome, the likelihood of stated, intent to use the McDonald guidelines. (see table 6) The null hypothesis tested for the adjusted OR is the probability of being in the target group is equal to the probability of not being the target group ($OR = 1$). The adjusted OR (1.065) is greater than 1.0, indicated a positive association between gender and stated intent to use the McDonald guidelines. The p value of the adjusted OR is .873 and substantially greater than Alpha threshold of (.05) and therefore not statistically significant. The Confidence Interval for the adjusted OR (lower=:.493; upper=:2.300) crosses 1.0 and is not statistically significant. Therefore, the null hypothesis is not rejected. Knowledge is not associated with intent to use the McDonald guidelines.

Table 6

Binary Logistic Regression: Knowledge and Years in Practice

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	95% C.I.for EXP(B) Upper

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B) Lower	95% C.I. for EXP(B) Upper
Step 1ᵃ	Knowledge(1)	.063	.393	.025	1	.873	1.065	.493	2.300
	Constant	-.486	.259	3.502	1	.061	.615		

A logistic regression analysis was conducted to assess the association between the predictor variable, years in practice, and the outcome, the likelihood of stated, intent to use the McDonald guidelines. (see Table 7) The null hypothesis tested for the OR is the probability of being in the target group is equal to the probability of not being in the target group (*OR*=1). The OR (1.016) is greater than 1.0, indicated a positive association between years in practice and stated intent to use the McDonald guidelines. The p value of the OR is .379 and substantially greater than Alpha threshold of (.05) and therefore not statistically significant. The Confidence Interval for the OR (lower: =.981; upper: =1.051) crosses 1.0 and is not statistically significant. Therefore, the null hypothesis is not rejected. Years in practice is not associated with intent to use the McDonald guidelines.

Table 7

Binary Logistic Regression: Years in Practice

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B) Lower	95% C.I. for EXP(B) Upper
Step 1ᵃ	Years in Practice	.015	.018	.775	1	.379	1.016	.981	1.051
	Constant	-.627	.275	5.188	1	.023	.534		

Multivariate Analysis

A multivariate regression analysis was conducted to assess the relationship and predictive value of the independent variables, gender, McDonald MS guideline knowledge, and years in practice and the dependent variable, the intent to use guidelines.

The sample included in the analysis was 106 instead of 161 due to the recoding of the

dependent variable to make it dichotomous to conduct the multivariate binary logistic

regression. The logistic regression equation is log(p/1-p) = 0.384*gender +

0.214*guideline knowledge + 0.015*years in practice.

The first step was to conduct a test multicollinearity test with the following

results. Results indicated no collinearity with a variance inflation factor of 1.0 for gender,

and 1.1 for knowledge and 1.1 years in practice.

The next step in the analysis was to conduct and examine a null regression model

where no independent variables were included in the analysis. The classification

accuracy for Block 0 (62%; p=.013) indicated a modest level of classification accuracy.

The interpretation of the results is that p = .013, therefore it is significant, and = .612 is

the odds ratio and that it is not significant. (see Table 8) The interpretation of the

confidence interval is that it is not statistically significant.

Table 8

Multivariate Analysis for Intent to Use Guidelines

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 0	Constant	-.491	.198	6.135	1	.013	.612

Multiple Logistic Regression Model

The final step was to test the regression model that included all independent

variables and the dependent variable. The omnibus test of coefficients model included the

independent variables as well as the dependent variables and tests the predictive capacity

of the model. There was no statistically significant difference between the Log-likelihood

of the baseline model and new model, with a chi-square of 2.044, df=3, and sig.=.563.

The predictive value of the regression model is not very high. The Nagelkerke R square

value (.026) indicates the amount of variation accounted for in the dependent variable,

indicating a small variation. The Hosmer and Lemeshow test for goodness of fit for

logistical regression models. predictive value of the regression model is not very high.

The result here (Chi-square = 5.529 Sig = .700) is non-significant. The null hypothesis is

rejected. The contingency (Table 9) indicates substantial differences between expected

versus observed values for most of the deciles, indicating the weakness of the model.

Table 9

Contingency Table for Hosmer and Lemeshow Test

		Intent_to_use_guidelines = No		Intent_to_use_guidelines = Yes		Total
		Observed	Expected	Observed	Expected	
Step 1	1	5	5.836	4	3.164	9
	2	7	9.028	7	4.972	14
	3	6	5.743	3	3.257	9
	4	7	9.513	8	5.487	15
	5	7	6.882	4	4.118	11
	6	3	3.099	2	1.901	5
	7	10	8.009	3	4.991	13
	8	9	6.711	2	4.289	11
	9	9	7.015	3	4.985	12
	10	5	6.164	7	5.836	12

The classification accuracy for Block 1 is indicated by 61.3% as the overall

percentage correct that was predicted regarding intent to use the guidelines. The

regression model classification accuracy was not an improvement over the null model, in

fact it was lower. (Null Model = 62%; Regression Model = 61.3%).

The variable in equation is provided in table 9. The Wald statistic show that the model is not significant as it does not add anything to the model. The Exp (B) are values for the regression equation predicting the dependent variable from the independent variable. The Exp (B), the odds ratio was not statistically significant.

Table 10

Variables in the Equation

	B	SE	Wald	df	Sig.	Exp(B)	95% Cl Lower	95% CI Upper
Step 1[a] Gender (1)	.384	.408	.886	1	.347	1.468	.660	3.266
Knowledgeable (1)	.214	.408	.275	1	.600	1.239	.557	2.758
Years in Practice	.015	.018	.697	1	.404	1.015	.980	1.051
Constant	-.947	.392	5.825	1	.016	.388		

Summary

It was hypothesized that gender, knowledge of the new treatment guidelines, and years in medical practice (independent variables) would predict intent to use the McDonald MS guidelines (dependent variable) among physicians who treat multiple sclerosis. A correlational analysis was conducted to assess the linear relationship between all the variables of interest. There were positive but non-significant relationships between the variables. A test for collinearity revealed the near absence for collinearity for each independent variable (Gender 1.0 and 1.1 for knowledge 1.0 for years in practice). Bivariate regression analysis for each independent variable and the dependent variable indicated no statistically significant predictive power for each independent variable and the outcome. The regression omnibus model had a poor predictive capacity for the

outcome according to the analysis. (p = .563) Chapter 5 includes the interpretation of the

findings, limitations of the study, and recommendations for further study.

Chapter 5: Discussion, Conclusions, and Recommendations

The purpose of this quantitative correlational study was to examine the relationship between gender, McDonald MS guideline knowledge, and years in practice, and intent to use the guidelines. The guidelines improve both the quality of care and patient outcomes when correctly used by physicians and a adherence to the McDonald clinical guidelines helps clinicians make appropriate clinical diagnosis and treatment plans for MS patients. A test for collinearity revealed the near absence of collinearity for each independent variable, with variance inflation factors of 1.0 for gender, 1.1 for knowledge and 1.1 for years in practice. Bivariate regression analysis for each independent variable and the dependent variable indicated no statistically significant predictive correlation between each independent variable and the outcome. Lastly, the regression omnibus model had a poor predictive capacity for the outcome. (Exp (B)=.612; $p = .563$)

Interpretation of the Results

Test for Collinearity

The test for collinearity revealed the near absence of collinearity for each independent variable with variance inflation factors of 1.0 for gender, and 1.1 for knowledge and 1.1 for years in practice. Little or no collinearity allows the model a better change to detect of each independent variable on the outcome if there is one. Yet, in this study even with no collinearity my model was not a good model. This finding of non-significant relationships between other variables did not support my hypothesis based on previous research.

Bivariate Analysis

Bivariate regression analysis for each independent variable and the dependent variable indicated no statistically significant predictive power for each independent variable and the outcome. My findings contradict the studies that have shown gender to be a strong predictor or the outcome. For example, Carrol (2017) found that females have a greater intent to use medical apps to improve their health compared to their male counterparts, and females with higher education were more likely to use medical apps to improve their healthcare outcomes. (Carrol, et, al.,) Deshpande (2009) also analyzed gender and intent to eat a healthy diet among students, showing that males students reported a lower intention to consume a healthy diet than did females (Deshpande, et, al., 2009). Thus, gender and intent does exist, which contradicts my study findings.

Multivariate Analysis

The multivariate analysis for all independent variables combined and the dependent variable indicated no statistically significant predictive power for the model. My findings contradict previous studies using multivariate analysis that showed gender to be a significant predictor. For example, Khatun (2017) showed that intention to use mHealth services was high for both genders (Khatun et, al., 2017). Ng-Sueng (2016) also analyzed gender as a predictor of the intent to choose a medical specialty like obstetrics/gynecology and dermatology over general practice, suggesting that females had an intent to choose obstetrics/gynecology, pediatrics, pediatric surgery, dermatology, and oncology (Ng-Sueng et, al., 2016).

Survey Results

Fifteen participants were very likely to use guidelines (9.30%), 26 were somewhat likely to use guidelines (17.30%). 51 were neutral (31.50%) and 68 were very unlikely to use guidelines (42.00%). Therefore, most were unlikely to use the guidelines, which is supported in the peer-reviewed literature by Ghezzi (2018), who suggested that the guidelines are not set rules, but rather only serve as a clinical guide for decision making (Ghezzi, et, al., 2018). This means that some physicians do not see the importance and will not follow suggestions.

Additional significant information regarding the survey is knowledge of the guidelines. The majority were familiar with the guidelines, yet most said they were unlikely to use them. Previous research has also shown that clinicians follow the guidelines, and they agree that outcomes are improved, but they are not using them because even though guidelines are clear and relevant, often they can still derail quality improvement efforts. (Nelson, 2016). Further research has indicated that there was a lack of agreement with the recommendations with a lack of evidence and environmental factors (Luggenberg et, al., 2009). In my study the results showed that guideline knowledge did not predict outcome.

Limitations of the Study

A key limitation is the small sample size ($N = 161$), which limits the power of the analysis to detect an effect if there is one. This lessened the likelihood to find a significant result and decreased the external validity, and the ability to generalize the findings to other similar populations. Another limitation is the sampling method, which

was convenience, non-random sampling and affected the external validity of the findings because the population did not have an equal chance of being selected.

Recommendations

Recommendations for further studies include studies with a larger sample size to include more clinicians' from around the country. This will increase the power of the study to detect an effect if one exists. Additional recommendations for developing a survey and questionnaire in the future include adding more questions to the survey to capture a larger amount of data. This additional information would include institutional policies that clinicians' have abide by along with added survey questions to test clinicians' awareness of educational tools they have access to in order to educate them around their intent to use the guidelines.

Implications

The goal of this study was to examine physician characteristics that might be associated with intent to use the McDonald MS guidelines. Knowing which factors are associated with intent to use could help develop interventions to encourage their use. Widespread and consistent intent to use guidelines could change how clinicians' approach MS and provide them with the tools and knowledge to make more informed diagnostic and treatment decisions to improve outcomes. MS significantly affects quality of life (Rezapour et, al., 2017), which is important consideration in policy-making decisions and health care outcomes in the public health field.

Conclusion

MS is a growing global public health concern. (World Health Organization, 2016). As MS becomes more prevalent, it is more important to continue to follow the McDonald MS guidelines to ensure adequate diagnosis and further treatment for MS patients. Although this study did not confirm if there are physician characteristics factors that might predict intent to use the guidelines, it is worth replicating the study with a larger sample size to increase the power of the study. Increasing the physician's perceptions and intent to use guidelines for diagnosing MS may allow for continued quality of care and improved outcomes to continue to promote evidence-based medicine.

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Appendix A: Survey Questions

A. **PART 2: Demographic Information:**
  1. **How old were you on your last birthday? (Please fill in a number)**

  _____

  2. **What is your Gender? (Instructions-Choose the best answer)**
  A. Male
  B. Female
  C. Other_____
  D. Prefer not to answer

  3. **What is your ethnicity? (Instructions-Choose the best answer)**
  A. Hispanic or Latino
  B. Not Hispanic or Latino

  4. **What is your race? (Instructions-Choose the best answer)**
  A. American Indian or Alaska Native
  B. Asian
  C. Black or African American
  D. Native Hawaiian or other Pacific Islander
  E. White

  5. **How many years have you been in practice? (Please fill in a number)**

  _____

  6. **What is your intent to use the guidelines for biomarkers in the diagnoses of MS? (Instructions: Choose the best answer)**
     A. Very Likely
     B. Somewhat likely
     C. Neutral
     D. Very unlikely

C. **Part 3: Knowledge on Guidelines**:

7. **The McDonald diagnostic criteria were established in 1997?**
   (Instructions-Choose the best answer)

A. True

B. False

8. **The McDonald diagnostic criteria were revised to clarify the**
   meanings of attack, dissemination and positive MRI? (Instructions-
   Choose the best answer)

A. True

B. False

9. **There have been recent advances in the McDonald Diagnostic**
   Criteria? (Instructions-Choose the best answer)

A. True

B. False

10. **According to Clinical Guidelines it is important to diagnose MS on**
    the basis of MRI findings alone? (Instructions-Choose the best
    answer)

A. True

B. False

11. **According to Guidelines clinicians should counsel people with newly**
    diagnosed MS about specific treatment options? (Instructions-
    Choose the best answer)

A. True

B. False

12. **Specific criteria for diagnosing PPMS have not changed?**
    (Instructions-Choose the best answer)

A. True

B. False

13. **According to the Guidelines there are recommendations to use the**
    presence of oligoclonal bands in CSF to make the diagnoses of MS?
    (Instructions-Choose the best answer)

A. True

B. False

14. What is your intent to use the guidelines for biomarkers in the diagnoses of MS? (Instructions: Choose the best answer)
    E. Very Likely
    F. Somewhat likely
    G. Neutral
    H. Very unlikely

15. According to the Guidelines both symptomatic and asymptomatic MRI lesions can be considered in determining DIT (dissemination in time) and DIS?(dissemination in space) (Instructions: Choose the best answer)
    A. True
    B. False

16. According to the Guidelines rapidly evolving severe RRMS is only sensory symptoms only? (Instructions-Choose the best answer)
    A. True
    B. False

Appendix B: Mock Tables

Table B1

Distribution of Gender of Study Participants (N = x)

Gender	Yes (Number)%	No (Number)%	Total (Number)%
Male	( ) %	( ) %	( ) %
Female	( ) %	( ) %	( ) %
Totals	( ) %	( ) %	( ) 100%

Table B1

Geographic Distribution of Participants (N = x)

Geographic distribution	Yes (Number)%	No (Number)%	Total (Number)%
Private practice	( ) %	( ) %	( ) %
Hospital	()%	( ) %	( ) %
Totals	( ) %	( ) %	( ) 100%

Table B2

Number and Percent of Participants Who Stated Intent to Use Guidelines (N = x)

Intent to use guidelines	Yes (Number)%	No (Number)%	Total (Number)%
Yes	( ) %	( ) %	( ) %
No	( ) %	( ) %	( ) %
Totals	( ) %	( ) %	( ) 100%

Table B3

Bivariate Statistical Analysis

Independent Variable	Dependent Variable	Chi Square Value	DF	Sig
Gender	Intent to Use Guidelines			
Guidelines Knowledge	Intent to Use Guidelines			
Years in Practice	Intent to Use Guidelines			

Table B4

Output for Multiple Logistic Regression Analysis

Outcome: Intent to Use Guidelines	Regression Coefficient	Chi Square	P Value	Odds Ratio	Confidence Interval (95% CL)
Intercept					