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Vitamin B_{12} Intake Correlated to Physical and Mental Improvements in Multiple Sclerosis Specific Quality of Life

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Abstract Current literature fails to provide individuals with multiple sclerosis (MS) specific dietary recommendations to advance quality of life (QOL). Due to the important structural and functional roles of vitamin B_{12} in the nervous system, the purpose of this research was to determine possible correlations between dietary intake of vitamin B_{12} and self-reported quality of life (QOL) among individuals with MS. The National MS Society and MS Foundation were used to recruit volunteers age 18 and older with a clinical diagnosis of MS. After the initial response (n = 89), 46 participants completed an online demographic survey/questionnaire and the MS Quality of Life-54 (MSQOL-54). Additionally, participants (n=23), completed a 3-day food record utilizing *MyPyramid Tracker*. Increased consumption of vitamin B_{12} (M=4.63 ± 3.44 µg) was positively correlated to the MSQOL-54 Subscales, *Emotional Well-Being*, *Health Perceptions*, *Health Distress*, and *Overall QOL*, as well as, to the QOL Composite Summary score for Mental Health. Individuals who consumed 5.0 µg or more of vitamin B_{12} exhibited significantly higher QOL scores for eight of the twelve Subscales, including *Pain* and *Overall QOL* (p<0.01). Additionally, both of the QOL Composite Summary scores (Physical and Mental) were significantly higher (p<0.01) than individuals who consumed less than 5.0 µg of vitamin B_{12}. Dietary intake studies like this one can assist in producing dietary guidelines for individuals with MS, which are currently absent from the *Nutrition Care Manual*. Since MS currently has no known cure, efforts of healthcare professionals should focus on influencing QOL through specific micronutrient intake recommendations, especially vitamin B_{12}. Increased vitamin B_{12} requirements may be needed for individuals with MS to achieve greater QOL.

Keywords *Multiple Sclerosis; Quality of Life; Vitamin B_{12}*

1. Introduction

The Academy of Nutrition and Dietetics has produced a medical nutrition therapy diet guide, the *Nutrition Care Manual*, to aid healthcare professionals in recommending appropriate dietary guidelines to individuals with a wide variety of illnesses and disease states (approximately 50 listings, including three neurological disorders). Dietary guideline recommendations specific to multiple sclerosis (MS) are currently not addressed or specified in this widely used and well respected resource. The purpose of this research was to determine possible correlations between dietary intake, specifically vitamin B_{12} and self-reported quality of life (QOL) among individuals with MS.

The National Multiple Sclerosis Society (NMSS) (2012) stated that about 400,000 individuals in the United States and over 2.5 million people worldwide have been diagnosed with MS, a chronic, immune-mediated inflammatory and neurodegenerative disease of the central nervous system (CNS), with an etiology that is not yet fully understood. In MS, the immune system attacks the myelin sheath of nerve cell fibers in the brain and spinal cord [1]. As a result of the autoimmune attack, the myelin sheath becomes damaged, resulting in inflammation and lesions that disrupt messages to and from the CNS [2; 3]. Individuals with MS have demonstrated poorer QOL in the areas of physical symptoms, mobility, emotional life and social interaction compared with persons having other chronic diseases. Many researchers have attributed poorer QOL to the unpredictable course of the disease and the variable symptoms: fatigue, pains, bowel and bladder dysfunction and impairment of mobility and visual acuity [4]. Many other symptoms associated with MS can greatly affect an individual's QOL. Symptoms can be described further as multidimensional experiences along four dimensions, intensity (strength or severity), timing (frequency and duration), level of distress (degree of discomfort), and quality (how the symptom feels) [5].

Various studies have pointed out the possibility of a potential relationship between MS and vitamin B_{12}. The serum B_{12} levels of MS patients are lower than those seen in healthy individuals [6; 7], and multiple researchers have recommended further exploration of this connection. Previous findings have suggested there may be an association between the time of onset for the first neurological symptoms, and a person's vitamin B_{12} status [8]. Vitamin B_{12} and Folate serum levels are typically taken initially during introductory MS diagnosis to rule out nutritional micronutrient deficiencies [9]. This is due to the fact that vitamin B_{12} deficiency and MS share similar manifestations in their physiology [10]. Increased dietary vitamin B_{12} intake may be beneficial in combination with current immunotherapies in patients with MS and has shown promising results when implemented [11]. Results from one study show that malabsorption of vitamin B_{12} may exist in almost 12% of the MS population [12]. Commonality of low vitamin B_{12} levels in association with patients diagnosed with MS poses the question of MS patients' physiological needs for vitamin B_{12}. A 2011 meta-analysis examining the relationship of vitamin B_{12} and other micronutrients in patients diagnosed with MS shows a direct relationship between low vitamin B_{12} levels and patients diagnosed with MS [13].

2. Materials and Methods

2.1. Participants

A sample (n = 49) of individuals living in the United States with a declared medical diagnosis of MS, all of which were at least 18 years old, participated in this study. Out of the 83 individuals who showed interest in the study, 49 of them (59%) completed the Multiple Sclerosis Online Survey, and of those participants, 23 of them (47%) went on to additionally complete a self-administered 3-day food record. The majority (92%) of the participants were Caucasian (n = 45), and all of the participants who completed both parts of this study were female. Of the 49 total participants, 36 of

them (74%) had relapsing-remitting MS, four (8%) had progressing-relapsing MS, five (10%) had secondary progressive MS, three (6%) had primary progressive MS and one participant had benign MS (2%). Of the 23 participants who completed both parts of this study, 87% of them had relapsing-remitting MS.

2.2. Recruitment

After approval from a large, Midwestern university's Institutional Review Board (IRB), the recruitment process began and was conducted according to IRB specifications. Permission was requested and granted by the NMSS to publicize information regarding this study on their website page "Surveys and other Research Studies." Permission was also granted by the NMSS to personally email each state or regional chapter's representative. Every chapter was asked to announce this study on their website, provide information about the study in their monthly newsletters, and included in their chapter's listserv e-mailings. The Multiple Sclerosis Foundation (MSF) was similarly contacted requesting permission to assist in the recruitment process and support groups across the United States were contacted inviting members to participate in this study. Lastly, the researcher's university listserv was employed to gather participants who might meet the criteria (medical diagnosis of MS and over the age of 18 years).

2.3. Instruments and Data Collection

Each participant was first instructed to complete the Multiple Sclerosis Online Survey using the hyperlink provided to them in an email. Upon review of the informed consent, participants indicated their willingness to participate by checking the appropriate box, allowing them to begin the two-part online survey. The first 13 questions contained the Personal Background Questionnaire, which, with permission, was modified from the Personal and Family Questionnaire [14]. This tool gathered demographic information regarding household income, ethnic background, marital status, time since diagnosis, type of MS, current period of relapse or remission, employment status, and current medication regiment. Lastly, the participants were asked to type in their individual MyPyramid Tracker User ID provided by the researcher in the email. This aided the principal investigator in identifying and linking the participants' online surveys to their specific self-administered 3-day food record. The individual participants were not identifiable beyond their assigned User ID and were not required at any time to include other personal identifiers.

The second part of the online survey, the MSQOL-54 (Multiple Sclerosis Quality of Life-54), began immediately after the Personal and Family Questionnaire. The MSQOL-54 is a multidimensional health-related quality of life measure that combines both generic and MS-specific items into a single instrument [15]. This 54-item instrument generated 12 Subscales (*Physical Health, Role Limitations due to Physical problems, Role Limitations due to Emotional issue problems, Pain, Emotional Well-Being, Energy, Health Perceptions, Social Function, Cognitive Function, Health Distress, Sexual Function*, and *Overall QOL*) along with two additional questions, one regarding *Change in health* and the other pertaining to *Satisfaction with sexual function*. These two additional questions are referred to by the researcher as the two Independent Categories. Two composite summary scores were calculated as products of the various Subscales, the *Physical Health Composite Summary* score and the *Mental Health Composite Summary* score. Past researchers have concluded that in spite of the lengthy time of administration, the MSQOL-54 is still favorable and reliable for detecting the QOL in any period of MS, including remission [16]. The results also indicated that MS-specific measures of QOL might be used for detecting the effectiveness of treatment during the relapse period in patients with MS. Due to the nature of MS, QOL may vary greatly over the course of a week or a month depending on the occurrence and/or the severity of an exacerbation or relapse. The MSQOL-54's ability to show effectiveness during any period of the disease has been noted as an important characteristic of this instrument [4].

Following the completion of the Multiple Sclerosis Online Survey, a hyperlink directed the participants to MyPyramid Tracker. This free, online-based dietary self-assessment tool was part of ChooseMyPlate.gov, and translated the principles of the 2005 Dietary Guidelines for Americans (DGA) and other nutrition standards developed by the USDA and Department of Health and Human Services [17]. This tool was used by the participants to perform a self-administered 3-day food record, including everything eaten or drank over the course of three consecutive days, preferably including at least one weekend day, and complete with quantities and specific preparation methods for each item. This type of dietary assessment is preferred since it does not rely heavily on subject's memory and is not as invasive or time-consuming compared to other methods [18-22].

Educational materials attached to the email, provided information on common serving sizes and detailed step-by-step instructions on how to complete a self-administered 3-day food record using MyPyramid Tracker. The educational materials used by participants in this study were adapted from the public domain tool, MyPyramid Tracker Tutorial. Detailed instructions and educational materials can reduce human error and has been shown to be effective in populations with a severe illness [18; 23].

Once the participants accessed MyPyramid Tracker, they were asked five additional demographic questions pertaining to age, gender, entry date, height, and weight. Participants then proceeded to record all foods and beverages consumed over the course of their first day by searching the USDA food database, which is linked to MyPyramid Tracker. Many of the food choices included specified preparation or cooking methods, and required the participants to select serving sizes and number of servings they consumed for each item. The educational materials provided by the researcher included serving size information by comparing different serving volumes to common objects (a baseball = 1 cup), further enhancing the participant's chance of recording an accurate food record [18; 23]. This process was repeated for all foods and drinks consumed by each participant over the course of three days.

2.4. Analysis of the Data

Participants' results from the MSQOL-54 questions were scored using the MSQOL-54 scoring form [15]. Each available answer per question corresponded to a pre-set numerical value. Every question, besides the two questions that inquired about *Change in health* and *Satisfaction with sexual function*, was part of one of the 12 diverse Subscales. Scores for each question relevant to a specific Subscale were added together and then divided by the total number of questions that corresponded to that Subscale. Subscale scores were based on a 0-100 scale, zero being the worst QOL. To determine the Composite Summary scores multiple Subscales were added together based on the nature of their content (mental or physical) and the sum was divided by the number of Subscales included in the Composite Summary. Eight of the Subscales (*Physical Function, Health Perceptions, Energy, Role Limitations – Physical, Pain, Sexual Function, Social Function* and *Health Distress*) were used to calculate the Physical Health Composite Summary score and five of the Subscales (*Health Distress, Overall QOL, Emotional Well-Being, Role Limitation – Emotional* and *Cognitive Function*) were used to calculate the Mental Health Composite Summary score. *Health Distress* was the only Subscale designed to be calculated in both Composite Summary scores [15].

Participants' MyPyramid Tracker accounts were accessed weekly to collect data from individuals who had recorded three days of food entry. The daily consumption over the course of the 3-day food record was used to calculate the mean consumption per individual participant. MyPyramid Tracker provided information regarding 30 different dietary components, including vitamin B_{12}. The

participants' mean vitamin B_{12} consumption over the course of the three days was used for statistical analysis.

2.5. Statistical Analysis

Once all the data were entered and calculated from the MSQOL-54, including results from the Personal Background Questionnaire, data were analyzed using SPSS v.19 for statistical analysis. MyPyramid Tracker's results were collected in a similar fashion using an Excel spreadsheet to record data over time. When the data collection period ended, only the means of the 3-day food records were entered into SPSS v.19 and used in data analysis. Correlation analysis was utilized to determine if a relationship existed between vitamin B_{12} intake and any of the 12 Subscales, two Independent Categories or two Composite Summary scores. Additionally, multiple independent *t*-tests were used to determine if QOL differences existed based on specific vitamin B_{12} intake levels.

3. Results

Possible relationships between vitamin B_{12} intake and Subscale, Independent Categories and Composite Summary scores of the MSQOL-54 were examined. The mean scores for Subscales, Independent Categories and Composite Summary scores of the MSQOL-54 are detailed in (Table 1). The mean vitamin B_{12} intake was 4.63 ± 3.44 µg, with consumption levels ranging from 1.00 µg to 13.60 µg.

Table 1: *Overall Results of the MSQOL-54*

MSQOL-54 Subscales	Scores[1]
Physical Health	75.65 ± 32.94
Role Limitation (Physical)	35.87 ± 32.71
Role Limitation (Emotional)	79.71 ± 39.87
Pain	72.32 ± 25.26
Emotional Well-Being	77.74 ± 14.71
Energy	42.0 ± 25.97
Health Perceptions	54.78 ± 27.36
Social Function	68.12 ± 32.63
Cognitive Function	60.43 ± 28.48
Health Distress	66.74 ± 30.36
Sexual Function	65.59 ± 29.01
Overall QOL	72.75 ± 20.66
MSQOL-54 Independent Categories	
Change in Health	50.0 ± 26.11
Satisfaction with Sexual Function	57.61 ± 35.7
MSQOL-54 Composite Summary	
Physical	60.29 ± 24.84
Mental	73.4 ± 19.04

[1]Data are presented as mean ± SD, *n*= 23

There was a positive, moderately strong, and statistically significant relationship between vitamin B_{12} intake and the Subscale *Emotional Well-Being* (*r* (21) =0.52, *P* =0.010). Additionally, three other Subscales displayed a positive, moderate, and statically significant relationship to vitamin B_{12} intake, *Health Perceptions* (*r* (21) =0.44, *P* =0.034), *Health Distress* (*r* (21) =0.45, *P* =0.030) and *Overall QOL* (*r* (21) =0.47, *P* =0.024). Similar significance was found for the *Mental Health Composite Summary* Score. There was a positive, moderately strong, and statistically significant relationship between vitamin B_{12} intake and the *Mental Health Composite Summary Score* (*r* (21) =0.47, *P* =0.025).

Due to the statistically significant correlation between vitamin B_{12} intake and some measures of the MSQOL-54, vitamin B_{12} intake and QOL scores were further assessed through multiple independent *t*-tests. The Recommended Dietary Allowance (RDA) (2.4 µg) was used to assess if consumption at levels recommended influenced QOL. The mean scores for the participants who consumed less than the RDA were not significantly different compared to the mean scores for the participants who consumed at or above the RDA for vitamin B_{12} (Table 2).

Table 2: *MSQOL-54 Scores Based on Vitamin B_{12} Intake compared to the Recommended Dietary Allowance (RDA)*[1]

MSQOL-54 Subscales	Vitamin B_{12} Intake	
	≥2.4µg[2]	<2.4µg[3]
Physical Health	76.18 ± 33.71	74.17 ± 33.68
Role Limitation (Physical)	36.76 ± 32.01	33.33 ± 37.64
Role Limitation (Emotional)	84.31 ± 35.59	66.67 ± 51.64
Pain	76.57 ± 19.7	60.28 ± 36.48
Emotional Well-Being	81.18 ± 11.02	68.0 ± 20.24
Energy	44.35 ± 26.49	35.33 ± 25.6
Health Perceptions	57.65 ± 28.51	68.33 ± 24.22
Social Function	73.04 ± 30.83	54.17 ± 36.42
Cognitive Function	57.65 ± 31.48	68.33 ± 27.79
Health Distress	72.65 ± 33.62	50.0 ± 26.18
Sexual Function	69.61 ± 26.52	54.17 ± 27.39
Overall	76.66 ± 21.95	61.68 ± 11.7
MSQOL-54 Independent Categories		
Change in Health	50.0 ± 26.52	50.0 ± 27.39
Satisfaction with Sexual Function	61.77 ± 32.01	45.83 ± 45.87
MSQOL-54 Composite Summary		
Physical	63.3 ± 23.81	51.75 ± 27.94
Mental	76.69 ± 18.81	64.07 ± 17.94

[1]Sample consisted of all non-pregnant females between 24-64 y.
[2]Data are presented as mean ± SD, *n*= 17.
[3]Data are presented as mean ± SD, *n*= 6.

Another independent *t*-test was implemented to determine if individuals who consumed at least 5.0 µg had QOL scores different from individuals who consumed less than 5.0 µg. Participants who consumed 5.0 µg or more of vitamin B_{12} had MSQOL Subscale scores for *Physical Health* (*M*=92.50 ± 9.35) and *Health Perceptions* (*M*=76.67 ± 16.02) greater than participants who consumed less than 5.0 µg (*M*= 69.70 ± 36.33) and (*M*=47.06 ± 26.58). The difference between means for *Physical Health* and *Health Perceptions* were statistically significant at the *P*<0.05 level (*t* (20.28) = 2.37, *P*= 0.028) and (*t* (15.01) = 3.22, *P*= 0.019) respectively.

Additionally, participants who consumed 5.0 µg or more of vitamin B_{12} had QOL Subscale scores for *Role Limitation-Emotional* (*M*=100.00 ± 0.00), *Health Distress* (*M*=85.00 ± 13.04), and *Emotional Well-Being* (*M*=88.67 ± 6.89) greater than participants who consumed less than 5.0 µg (*M*= 72.55 ± 44.47), (*M*=60.29 ± 32.33) and (*M*=73.88 ± 14.91). The difference between means for *Role Limitation-Emotional*, *Health Distress,* and *Emotional Well-Being* were statistically significant at the *P*<0.05 level (*t* (16) = 2.55, *P*= 0.022), (*t* (20.33) = 2.61, *P*= 0.017) and (*t* (18.98) = 3.23, *P*= 0.031).

The last Subscale score that showed a significant difference between groups was the Subscale *Pain.* Participants who consumed 5.0 µg or more of vitamin B_{12} had a mean score for *Pain* (*M*=88.89 ± 7.65) that was greater than participants who consumed less than 5.0 µg (*M*= 66.47 ±

26.83). The difference between means for *Pain* was statistically significant at the *P*<0.01 level (*t* (20.71) = 3.11, *P*= 0.005).

The Independent Category *Social Function* exhibited a significant difference between means scores. Participants who consumed 5.0 µg or more of vitamin B_{12} had a *Social Function* mean score (*M*=86.11 ± 15.52) that was greater than participants who consumed less than 5.0 µg (*M*= 61.77 ± 34.99). The difference between means for *Social Function* was statistically significant at the *P*<0.05 level (*t* (19.46) = 2.30, *P*= 0.033).

Participants who consumed 5.0 µg or more of vitamin B_{12} had MSQOL mean scores for *Physical Health Composite Summary* (*M*=76.09 ± 8.38) and *Mental Health Composite Summary* (*M*=86.79 ± 7.66), greater than participants who consumed less than 5.0 µg (*M*= 54.71 ± 26.45) and (*M*= 68.67 ± 19.72). The difference between means for *Physical Health Composite Summary* and *Mental Health Composite Summary* was statistically significant at the *P*<0.01 level (*t* (20.97) = 2.94, *P*= 0.008) and (*t* (20.58) = 3.17, *P*= 0.005).

Also, participants who consumed 5.0 µg or more of vitamin B_{12} had a mean score for *Overall QOL* (*M*=88.05 ± 4.64), greater than participants who consumed less than 5.0 µg (*M*= 67.36 ± 21.48). The difference between means for *Overall QOL* was statistically significant at the *P*=0.001 level (*t* (19.43) = 3.73, *P*= 0.001).

4. Discussion

In this present study, Subscales that were found to have three of the lowest mean scores were *Role limitation- Physical, Energy, and Health Perceptions* (Table 1). These three Subscales may be decreased due to their relationship with depression and fatigue, two of the most common and disabling symptoms, as well as, important predictors of QOL [24; 25]. Increased vitamin B_{12} intake led to statistically significant improvement in, *Health Perceptions,* and others QOL measures that can be assimilated with either depression or fatigue, *Emotional Well-Being*, *Health Distress, Overall QOL* and the summative *Mental Health Composite Summary Score*. These QOL indicators allude to the fact that individuals may have felt less depressed compared to individuals consuming less vitamin B_{12} based on their reported QOL.

While QOL benefits were observed with increased vitamin B_{12} intake, further analysis regarding specific intake levels may help to identify an appropriate dietary recommendation for individuals with MS, which is missing from the literature. Much of the current dietary advice is centered on a general healthy diet with micronutrient recommendations consistent with Dietary Reference Intakes, which for vitamin B_{12} equates to 2.4 mcg per day. Participants who consumed 5.0 mcg or more, as seen in this study, showed improvements directly related to many common symptoms of MS, including a great overlap with the two most prevalent symptoms, depression and fatigue.

Vitamin B_{12} intake has recently been shown to be correlated with reduction in pain levels in a number of medical conditions, including neuropathy [26]. While neuropathy is not caused by MS, manifestations of MS in the CNS are similar to the damage to the peripheral nervous system seen in neuropathy. Other studies have found that decreased plasma vitamin B_{12} can impair physical performance, but correctable through dietary consumption [27]. Vitamin B_{12} is also known to potentially have a role in the maintenance of neurophysiological health, cognitive health, and function [28-31]. Existing literature is clear; vitamin B_{12} can positively affect mental health and physical functioning, which is concurrent with the results presented here, and further supports the importance of vitamin B_{12} for normal physiological functioning and QOL [32-35]. Current dietary recommendations for individuals with MS may be too simplistic or general for this complex

disease. Findings here, while just preliminary, suggest that QOL may be improved significantly with intake levels of 5.0 mcg of vitamin B_{12}, double the current RDA for this population.

Suspected reasons as to why individuals with MS may need to consume greater dietary vitamin B_{12} may be due to the nature of MS and the possible connection to pernicious anemia (PA) noted by earlier researchers [36; 37]. It has been observed in multiple studies that the occurrence of PA is significantly increased in MS samples [37; 38]. The manifestation of mild macrocytosis has also been shown to be statistically significant among individuals with MS with low levels of vitamin B_{12} [38]. Irregularity in vitamin B_{12} metabolism, may explain the enlargement of red blood cells without the clinical diagnosis of PA [10; 36].

Treatment options for MS have been previously described in great detail [39] and thus will not be discussed in depth here. Reductions in serum vitamin B_{12} levels in individuals with MS treated with Copaxone and Interferon-h have been noted and attributed partially to the drug's role in enhancing the need for vitamin B_{12} for myelin repair [11]. Another common drug therapy prescribed to individuals with MS that may influence vitamin B_{12} status are corticosteroids and are often used for individuals experiencing an acute relapse [40]. This approach has been observed, in high doses, to lead to a decrease in both cerebral spinal fluid (CSF) and serum levels of vitamin B_{12} [41]. Often used in conjunction with corticosteroid treatment are medications such as histamine receptor-2 (H2R) antagonist, proton pump inhibitor (PPI) or antacid to combat the prevalent dyspeptic pain associated with corticosteroids [40]. Despite which drug therapy is used to treat this side effect, the goal is to raise the gastric pH either directly or indirectly. When administered over long periods of time, a vitamin B_{12} deficiency may develop due to the increased gastric pH contents as a result of the decreased acid production. This has been observed in previous literature, particularly in older individuals and those experiencing atrophic gastritis [42-44].

Future research in the area of dietary intake and MS is necessary. Current treatments cannot cure the disease or reverse its progression, so alternative treatments are needed. Most importantly, patients need treatments that can preserve abilities as long as possible, optimize function, and promote QOL at all stages of the disease. With the potential role that vitamin B_{12} has shown in QOL amongst the physical and mental dimensions and possible drug-nutrient interactions, an increase in dietary vitamin B_{12} intake above current the recommendation is justified.

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