Dear Committee Members,

I am pleased to submit my research proposal titled "The Effects of Magnesium Supplementation on Quality of Life in Adults with Epilepsy: A Randomized Controlled Trial" for your review and consideration. This study aims to explore whether daily oral magnesium supplementation at two dosage levels (300 mg/day and 500 mg/day) improves quality of life and clinical outcomes compared to placebo in adults with medically managed epilepsy. This research uses a randomized, placebo-controlled design with repeated measures over six months and will evaluate primary and secondary outcomes including quality of life, seizure frequency, and serum magnesium levels.

Given the prevalence of epilepsy and the limitations of current treatment options, this study is designed to offer insight into the potential role of magnesium supplementation as a low-risk adjunct therapy. The project also aligns with current gaps in literature related to nutritional interventions in neurological disorders and may inform future integrative care strategies for this population.

I welcome the opportunity to discuss any components of the study further and to address any questions from the committee. Thank you for your time and consideration. I look forward to your feedback.

Sincerely,

Laura Thompson, Graduate Student of Applied Science in Nutrition

University of New England

Effects of Magnesium Supplementation on Quality of Life in Adults with Epilepsy:

A Randomized, Placebo-Controlled Trial

Laura Thompson

**APN 755** 

### **Research Question**

Among adults aged 25–65 years with medically managed epilepsy, does daily oral magnesium supplementation at 300 mg or 500 mg for six months improve quality of life compared to placebo?

## Null Hypothesis (H<sub>0</sub>)

There will be no statistically significant difference in quality of life among adults aged 25–65 years with medically managed epilepsy across the three study groups (300 mg magnesium, 500 mg magnesium, and placebo) after six months of supplementation.

## Alternate Hypotheses (H<sub>1</sub>)

- H<sub>1</sub>a: Adults who receive 300 mg/day of magnesium for 6 months will show improved quality of life compared to those who receive a placebo.
- H<sub>1</sub>b: Adults who receive 500 mg/day of magnesium for 6 months will show improved quality of life compared to those who receive a placebo.
- H<sub>1</sub>c: Adults who receive 500 mg/day of magnesium for 6 months will show greater improvement in quality of life compared to those who receive 300 mg/day.

#### **Title**

The Effects of Magnesium Supplementation on Quality of Life in Adults with Epilepsy: A Randomized, Placebo-Controlled Trial

#### **Abstract**

*Background:* Epilepsy is a chronic neurological disorder affecting over 50 million people worldwide. Despite pharmacologic advancements, many individuals continue to experience

reduced quality of life and adverse effects from long-term medication use. Magnesium plays a critical role in neuronal stability and has been suggested to influence seizure threshold and frequency. However, evidence on magnesium supplementation as a supportive therapy in epilepsy remains limited. There is a need for well-designed clinical trials to explore whether magnesium may serve as an effective adjunct to conventional treatment.

*Problem Statement:* Although low serum magnesium has been observed in individuals with epilepsy, there is insufficient evidence evaluating whether supplementation can improve patient-centered outcomes such as seizure control and quality of life. This study aims to address this gap by investigating the effects of daily oral magnesium supplementation on clinical and quality of life outcomes in adults with medically managed epilepsy.

Objectives: This project will evaluate the impact of two doses of oral magnesium supplementation (300 mg/day and 500 mg/day) on quality of life, seizure frequency, and serum magnesium levels over a six-month period, compared to placebo.

#### *Methodology:*

*Impact:* Findings from this study will inform clinical and nutritional approaches to epilepsy management. The results may support the inclusion of magnesium supplementation as a low-cost, adjunctive intervention, potentially benefiting patients, clinicians, and the broader applied nutrition and neurological care communities.

#### Introduction

Epilepsy is a neurological disorder characterized by recurrent, unprovoked seizures caused by abnormal electrical activity in the brain. The condition can result from a range of underlying structural, physiological, or chemical abnormalities. Epilepsy profoundly impacts quality of life, often leading to physical limitations, psychological distress, reduced social engagement, and increased rates of depression and anxiety. For many individuals, medication management alone may not adequately control seizure activity, particularly those with drugresistant epilepsy. Alternative avenues may need to be utilized in conjunction with pharmacological treatments.

Nutrition has emerged as a potential partner to pharmacologic treatment in seizure management. Magnesium, an essential mineral involved in nerve function and neurotransmission, has shown promise in influencing seizure activity and supporting overall neurological health.<sup>3,4</sup> Low magnesium levels have been observed in individuals with epilepsy and are associated with increased seizure frequency and severity.<sup>5,6</sup> Despite this, the relationship between magnesium supplementation and improvements in both seizure control and quality of life remains under-researched.

This study aims to investigate the effects of two different dosages of magnesium supplementation, 300 mg and 500 mg daily, compared to placebo, on quality of life, seizure activity, and serum magnesium levels over a six-month period in adults with medically managed epilepsy.

#### **Background**

Epilepsy is a chronic neurological disorder that affects millions of individuals worldwide. The etiology of epilepsy can be multifactorial, involving chemical imbalances, structural anomalies, and physiological dysfunctions. While antiepileptic drugs (AEDs) are the cornerstone of epilepsy management, approximately one-third of individuals with epilepsy continue to experience seizures despite pharmacologic therapy. This has led to growing interest in alternative approaches, including nutritional strategies, to enhance seizure control and quality of life.

Magnesium plays a critical role in neurological function, including stabilizing neuronal membranes, modulating neurotransmitter release, and reducing neuronal excitability.<sup>4</sup> Its neuroprotective properties suggest that adequate magnesium levels are essential for seizure prevention.<sup>3</sup> Numerous studies have reported that individuals with epilepsy often have lower serum magnesium levels than healthy controls, even when those levels fall within the normal reference range.<sup>5,8</sup> This observation has prompted researchers to explore whether magnesium supplementation can serve as an adjunctive therapy to improve clinical outcomes in epilepsy.

Magnesium supplementation has shown promise in reducing seizure frequency and enhancing neuronal stability, particularly among individuals with drug-resistant epilepsy. However, much of the existing literature focuses solely on serum magnesium levels and their correlation with seizure activity, rather than the impact of magnesium supplementation itself. Additionally, studies investigating supplementation often feature small sample sizes, lack diversity, and do not examine the broader implications of magnesium on quality of life.

Quality of life in epilepsy extends beyond seizure control. Because of what is known about magnesium, supplementation may offer additional benefits, such as improved mood, reduced anxiety, increased independence, and better sleep, which contribute to an overall

improvement in quality of life.<sup>2,10</sup> The Quality of Life in Epilepsy Inventory (QOLIE-31), a validated and widely used tool, measures multiple domains including emotional well-being, social functioning, seizure worry, cognitive effects, and medication side effects. (Appendix A) <sup>10</sup> Few studies have examined how magnesium supplementation might influence these domains comprehensively.

Additionally, research is sparse regarding the optimal dosage and duration of magnesium supplementation for adults with epilepsy. Some evidence supports the safety and potential efficacy of doses ranging from 300 mg to 500 mg daily, but direct comparisons of multiple dosages within a single study are limited.<sup>10</sup> This represents a significant gap in literature.

A randomized, placebo-controlled, blinded clinical trial is needed to examine the effects of two oral magnesium dosages at 300 mg and 500 mg administered daily over six months. Key outcomes should include changes in QOLIE-31 scores, seizure frequency, and serum magnesium levels, with measurements taken at baseline, three months, and six months.

Such a study would address several critical gaps identified in the current literature on epilepsy and magnesium supplementation. A direct comparison of two distinct magnesium dosages would allow for exploration of potential dose-dependent effects on patient outcomes and clarify whether higher doses offer additional advantages or if lower doses are sufficient.

Importantly, the study should go beyond seizure control alone and place greater emphasis on quality of life, using the QOLIE-31<sup>10</sup>, a validated, epilepsy-specific tool that captures the multidimensional impact of the condition. This approach would provide a more comprehensive understanding of how nutritional interventions may influence both clinical and patient-centered outcomes in epilepsy management.<sup>2</sup>,<sup>10</sup>

Incorporating a placebo group enhances the validity of the study and adds confidence to the results by showing whether changes are due to the supplements themselves. Furthermore, by limiting the study population to adults aged 25–65 years who are currently receiving pharmacologic treatment but continue to experience seizures, the research targets a group that stands to benefit most from additional treatments.<sup>9</sup>

By blending known research with new research, the potential findings from this proposed study may help clarify magnesium's therapeutic role as a complementary intervention to existing epileptic medication. Additionally, the results could provide valuable guidance regarding optimal supplementation dosages and contribute to strategies aimed at improving the overall quality of life for individuals living with epilepsy.

## Methodology

#### Research Design

This study will utilize a randomized, double-blind, placebo-controlled clinical trial design, aligning with the objectives of evaluating the effects of oral magnesium supplementation on seizure frequency, serum magnesium levels, and quality of life in adults with medically managed epilepsy. An experimental design is appropriate to establish causality between magnesium supplementation and the observed outcomes, which addresses current gaps in the literature regarding the nutritional management of epilepsy.

### Research Participants

Participants will include adults aged 25 to 65 years with a clinical diagnosis of epilepsy who are currently receiving stable doses of anti-seizure medications. All participants are based on the same criteria and were moved into randomized groups.

• **Inclusion criteria**: Adults aged 25–65, diagnosis of epilepsy confirmed by a neurologist, currently using anti-seizure medications for at least 3 months, and willingness to adhere to supplementation protocols.

**Exclusion criteria**: Individuals with kidney disease, gastrointestinal malabsorption disorders, current use of magnesium supplements or medications known to affect magnesium status, recent changes to epileptic medications, pregnancy or lactation, or those with cognitive impairments that affect consent or survey completion. Participants may be discontinued from the study under the following circumstances:

- Voluntary withdrawal of consent at any time without penalty.
- Noncompliance with study protocols or missed follow-up visits without adequate explanation.
- Occurrence of significant adverse events or safety concerns related to study participation.
- Development of new medical conditions or changes in health status that, in the opinion of the study investigators, preclude continued participation.

Participants will be recruited through multiple strategies, including the distribution of informational flyers in participating neurology clinics and epilepsy treatment centers, as well as direct referrals by healthcare providers managing patients with epilepsy. Recruitment materials

will provide a brief overview of the study objectives, eligibility criteria, and contact information for study personnel.

All individuals expressing interest or referred to the study by providers will undergo a structured prescreening phone interview. This prescreening process will confirm the potential participant meets preliminary eligibility criteria, clarify any exclusion criteria, and answer participant questions and provide an overview of study expectations.

The prescreening interview ensures that all enrolled participants are evaluated according to the same standardized criteria, improving consistency and internal validity. Individuals meeting prescreen eligibility will be invited to an in-person (or secure video) screening visit, during which:

- Detailed eligibility assessments will be conducted, including medical history review and baseline laboratory testing (e.g., serum magnesium levels).
- The study will be explained in full, and any remaining questions will be addressed.
- Participants will complete the informed consent process prior to any study procedures.

Eligible and consented participants will be enrolled and randomly assigned in equal proportions to one of three study groups. Randomization will be conducted using a computer-generated allocation sequence managed by an independent researcher to maintain allocation concealment. All participants will be informed that they may withdraw from the study at any time and that their decision will not impact their medical care or have penalty or consequences.

Sample Size:

A priori power analysis was conducted using G\*Power (Appendix B) to determine the required sample size for this study. Assuming a medium effect size (f = 0.25),  $\alpha = 0.05$ , power = 0.95, and three independent groups, the total sample size needed to detect statistically significant differences using a one-way ANOVA is 252 participants (approximately 84 per group).<sup>12</sup>

To account for a potential 20% attrition rate due to loss of follow-up, withdrawal, or other unforeseen factors, the target enrollment will be increased to 303 participants (approximately 101 per group). This adjusted sample size ensures the study remains feasible yet adequately powered to detect between-group differences in the primary outcomes: quality of life, seizure frequency, and serum magnesium levels across all measurement time points.

#### Intervention

Following the completion of eligibility screening and informed consent, participants will be randomly assigned in equal numbers to one of three study groups:

- **Group 1:** Daily oral placebo capsule
- **Group 2:** Daily oral magnesium supplement (300 mg elemental magnesium)
- **Group 3:** Daily oral magnesium supplement (500 mg elemental magnesium)

All participants will be instructed to take one capsule daily with food, preferably at the same time each day (e.g., with breakfast or lunch) to minimize gastrointestinal discomfort and improve adherence. Supplements and placebos will be visually identical and provided in monthly allotments. Each bottle will be labeled only with participant ID and dosing instructions to maintain blinding.

During the initial study session (Week 0), participants will attend a 45-minute orientation visit that includes:

- A review of their group assignment procedures (without disclosing allocation)
- Detailed verbal and written instructions on how to take the supplement
- Education on potential side effects of magnesium
- Training on how to complete daily adherence logs and seizure diaries
- Instructions on monthly pill count procedures for adherence tracking
- Distribution of the first month's supply of capsules
- Baseline collection of serum magnesium levels and QOLIE-31 assessment

To reduce dietary variability in magnesium intake and minimize confounding, participants will be asked to avoid initiating any new magnesium-containing supplements or multivitamins during the study. They will also be provided with a brief Magnesium Awareness Handout (Appendix C), which outlines common high-magnesium foods (e.g., pumpkin seeds, spinach, almonds, black beans, fortified cereals). Participants will be advised not to intentionally increase or restrict these foods, but to maintain their usual dietary intake. Any major dietary changes should be reported to study personnel.

Monthly check-ins will include review of pill logs, pill counts, and brief dietary recalls to monitor adherence and assess any significant changes in magnesium intake. During these visits, participants will be encouraged to promptly report any adverse effects or changes in medication. Supplement adherence rates will be calculated from monthly pill counts and participant-maintained daily logs, while dropout rates will be tracked across study arms. The incidence of

supplement-related side effects will also be documented based on self-reports collected during follow-up visits and participant logs. All participants and study staff involved in data collection and analysis will remain blinded to group assignments until after final data collection is complete.

#### Ethical Considerations

This study will obtain IRB approval prior to participant recruitment. All participants will complete an informed consent (Appendix D) form outlining study procedures, potential risks, and their right to withdraw at any time without penalty. Data confidentiality will be ensured using coded IDs and secure data storage. Participants will be monitored for adverse events, and any serious safety concerns will be reported to the IRB.

#### Research Setting

This study will be conducted at affiliated outpatient neurology clinics in urban and suburban areas across Nebraska and western Iowa, including sites within the Methodist Health System network. Data collection visits and lab draws will take place at these locations.

#### *Instruments*

- Quality of Life in Epilepsy Inventory (QOLIE-31): A validated, epilepsy-specific instrument assessing emotional well-being, energy/fatigue, cognitive function, medication effects, and social functioning (Appendix A).<sup>13</sup>
- Seizure Activity Logs: Participants will record seizure frequency daily using a structured log, reviewed during each follow-up visit. (Appendix E)

Serum Magnesium Levels: Blood samples will be collected at baseline, 3 months, and 6 months using standard venipuncture. Laboratory analysis will follow Clinical Laboratory Standards Institute (CLSI) procedures for magnesium quantification via colorimetric assay (Appendix F).<sup>14</sup>

#### Data Collection

Descriptive Data Collection: Descriptive statistics will be used to summarize baseline demographic and clinical characteristics of participants. These variables will include:

- Demographics: Age (years), gender (male, female, other), race/ethnicity, and BMI (kg/m²), collected through self-reported questionnaires and measured height/weight at baseline visit
- Clinical history: Duration of epilepsy (years), current anti-epileptic medications, seizure type and frequency, collected through participant interviews and medical record review
- Baseline outcome measures: Serum magnesium levels (mg/dL), seizure frequency (monthly average), and QOLIE-31 total and subscale scores, collected via laboratory testing, seizure diaries, and validated survey administration, respectively

Inferential Data Collection: Data collection at baseline and follow-up data collection at three and six months will be analyzed using inferential statistics, including repeated measures of the QOLIE-31, seizure logs, and serum magnesium levels. Adherence, supplement side effects, and any relevant clinical changes will also be documented at each visit to support subsequent inferential analysis.

Descriptive Data Analysis

Descriptive statistics will be used to summarize baseline demographic and clinical characteristics of study participants. Continuous variables such as age, body mass index (BMI), serum magnesium levels, and QOLIE-31 scores will be reported as means and standard deviations. Categorical variables, including gender, seizure type, and medication use, will be summarized using frequencies and percentages. To assess baseline equivalence among the three study groups (placebo, 300 mg magnesium, and 500 mg magnesium), one-way ANOVA will be applied to continuous variables, while chi-square tests will be used for categorical variables. All data analyses will be conducted using Stata, and statistical significance will be determined using a two-tailed alpha level of 0.05.<sup>15</sup>

#### Inferential Data Analysis

Inferential analyses will be conducted using a series of one-way analyses of variance (ANOVA) to evaluate the effect of group assignment (placebo, 300 mg magnesium, 500 mg magnesium) on each primary outcome variable. The primary outcomes include:

- 1. Quality of life (QOLIE-31 total score)
- 2. Seizure frequency (monthly average)
- 3. Serum magnesium level (mg/dL)

Separate one-way ANOVAs will be conducted for each outcome at each of the three time points (baseline, 3 months, and 6 months) to allow for clear, point-in-time comparisons between groups without assuming a repeated measures structure.<sup>16</sup>

In addition to these point-in-time analyses, one-way ANOVAs will also be performed on mean change scores (baseline to 3 months, baseline to 6 months) for each outcome. This will

allow assessment of whether the magnitude of change over time differs significantly between groups.

If a statistically significant main effect of group is detected in either the time point or change score analyses, Tukey's Honestly Significant Difference (HSD) test will be used for post hoc pairwise comparisons to identify which groups differ significantly. Tukey HSD is selected for its ability to control the Type I error rate across multiple comparisons.<sup>16</sup>

## Significance

Although epilepsy is primarily managed with pharmacological treatment, approximately one-third of individuals continue to experience seizures despite medication. This has led to growing interest in adjunctive, non-pharmacologic strategies to improve seizure control and quality of life. Magnesium, a mineral involved in neuronal excitability and synaptic transmission, has shown potential in this area; however, its role in epilepsy management remains poorly understood. To date, few studies have rigorously assessed the effects of oral magnesium supplementation on seizure frequency or quality of life using randomized, controlled methods.

This study aims to expand and refine the understanding of magnesium's therapeutic potential in epilepsy by evaluating the effects of two distinct supplementation dosages (300 mg and 500 mg) compared to placebo. The randomized, placebo-controlled design allows for the isolation of magnesium's effects while minimizing bias. By assessing seizure frequency alongside patient-centered outcomes, such as quality of life (QOLIE-31 scores), and objective biomarkers like serum magnesium levels, the study offers a comprehensive view of treatment impact. Methodological rigor will be maintained using validated tools, dietary monitoring,

adherence tracking, and intention-to-treat analysis. By integrating clinical, biochemical, and quality-of-life data, this research may offer clearer guidance on the role of magnesium as a low-risk, evidence-based adjunctive therapy for epilepsy. Findings could inform clinical practice, nutritional recommendations, and future large-scale trials.

### **Strengths and Limitations**

This study design offers several notable strengths. The randomized, placebo-controlled approach with blinding of both participants and study personnel minimizes bias and enhances the internal validity of the findings. <sup>16</sup> The inclusion of two magnesium dosages (300 mg and 500 mg) allows for a direct comparison of efficacy and tolerability, providing insight into potential dose-response effects. <sup>3,4</sup> A six-month follow-up period enables the assessment of both short and intermediate-term changes in seizure frequency, serum magnesium levels, and quality of life. Additionally, the use of validated tools such as seizure logs and the QOLIE-31 questionnaire improves the reliability and relevance of measured outcomes. Basic dietary monitoring throughout the study also helps reduce confounding related to external sources of magnesium intake.

However, the study does have several limitations. Recruitment through specialty epilepsy clinics may limit the generalizability of findings to the broader epilepsy population, particularly those not receiving specialty care. Self-reported seizure diaries, while practical for longitudinal tracking, may be subject to recall bias and underreporting. Although dietary intake will be monitored through participant logs and monthly check-ins, it will not be tightly controlled, which could introduce variability in baseline or background magnesium intake. Finally, participant

attrition over the six-month period remains a potential concern, which may impact statistical power despite built-in safeguards through oversampling.

Despite these limitations, this study represents a scientifically rigorous and clinically meaningful investigation into a low-risk, potentially impactful nutritional intervention. Its findings could lay the groundwork for future translational research and inform evidence-based guidance for integrating magnesium supplementation into comprehensive epilepsy care.

#### **Dissemination of Results**

Findings from this study will be disseminated through multiple channels to reach both academic and clinical audiences, as well as individuals with epilepsy and their caregivers.

Results will be submitted for publication in peer-reviewed journals specializing in neurology, epilepsy, and clinical nutrition, such as *Epilepsia*, *Seizure: European Journal of Epilepsy*, or the *Journal of the Academy of Nutrition and Dietetics*. Abstracts will also be submitted for presentation at national and regional conferences, including the American Epilepsy Society (AES) Annual Meeting and the Food & Nutrition Conference & Expo (FNCE).

To extend the impact beyond the academic setting, study summaries will be developed in plain language and shared with participating clinics, patient advocacy groups (e.g., the Epilepsy Foundation), and community health organizations. These efforts aim to improve awareness of magnesium's potential role in epilepsy management and support informed decision-making among patients, caregivers, and clinicians.

The results may also serve as a foundation for future grant applications or collaborative studies involving larger, multi-site trials. Ultimately, this research has the potential to influence

clinical nutrition guidelines, contribute to integrative epilepsy care, and encourage continued investigation into accessible, non-pharmacologic treatment strategies.

#### References:

- Kumar M, Kumar S, Vimsar B. Study of serum magnesium and calcium levels in patients with new onset seizures. J *Med Sci Clin Res*. 2019. Vol. 7, Issue 3, Page: 2455-0450 DOI: https://dx.doi.org/10.18535/jmscr/v7i3.222
- Vaurio, L, Karantzoulis S, Barr WB. The impact of epilepsy on quality of life. In: Chiaravalloti, N., Goverover, Y. 2017. (eds) *Changes in the Brain*. Springer, New York, NY. doi.org/10.1007/978-0-387-98188-8
- 3. Kirkland AE, Sarlo GL, Holton KF. The role of magnesium in neurological disorders. *Nutrients*, vol. 10, no. 6, 2018, p. 730. doi:10.3390/nu10060730. PMID: 29882776; PMCID: PMC6024559.
- Elgar K. Magnesium: A review of clinical use and efficacy. *Nutr Med J.* 2022
   Mar;1(1):79-99. doi: 10.7860/NMJ/2022/69769.19601.
- Abdullahi I, Watila MM, Shahi N, et al. Serum magnesium in adult patients with idiopathic and symptomatic epilepsy in Maiduguri, Northeast Nigeria. *Niger J Clin Pract*.
   2019 Feb;22(2):186-193. doi: 10.4103/njcp.njcp 252 18. PMID: 30729941.
- 6. Krishna, CR, Basha, SJ, Venkateswara Rao, B, Preethi, B. Serum magnesium levels in seizure disorders *J Evol Med Dent Sci.* 2014; Vol. 3, Issue 35, August 14; Page: 9313-9319, DOI: 10.14260/jemds/2014/3202
- Nuñez-Lumbreras MdlA, Rocha L. How far are we from the best preclinical models of drug-resistant epilepsy? *Epilepsy Behav.* 2024;161:110029.
   doi:10.1016/j.yebeh.2024.110029
- 8. Prasad DK, Shaheen U, Satyanarayana U, et al. Association of serum trace elements and minerals with genetic generalized epilepsy and idiopathic intractable epilepsy.

- Neurochem. Res. vol. 39, no. 12, 2014, pp. 2370-2376. doi:10.1007/s11064-014-1439-3. Epub 2014 Sep 26. PMID: 25255736.
- Abdelmalik PA, Politzer N, Carlen PL. Magnesium as an effective adjunct therapy for drug resistant seizures. *Can J Neurol Sci.* 2012;39(3):323-327. doi:10.1017/S0317167100013457
- 10. Siebenbrodt K, Willems LM, von Podewils F, et al. Determinants of quality of life in adults with epilepsy: a multicenter, cross-sectional study from Germany. *Neurol. Res. Pract.* vol. 5, 2023, Article 41. doi:10.1186/s42466-023-00265-5.
- Cook, B. G., Cook, L., & Therrien, W. J. 2018. Group–difference effect sizes: gauging the practical importance of findings from group–experimental research. *LDRP*. 33(2), 56-63. https://doi.org/10.1111/ldrp.12167 (Original work published 2018)
- 12. Kang H. Sample size determination and power analysis using G\*Power software. *J Educ Eval Health Prof.* 2021;18:17:1-12.
- Devinsky O, Vickrey BG, Cramer J, Perrine K, Hermann B, Meador K, Hays RD.
   Development of the quality of life in epilepsy inventory. Epilepsia. 1995
   Nov;36(11):1089-104. doi: 10.1111/j.1528-1157.1995.tb00467.x. PMID: 7588453.
- 14. Clinical and Laboratory Standards Institute. Protocols for Determination of Elements in Biological Fluids and Tissues by Atomic Absorption Spectrometry; Approved Guideline. CLSI Document C14-A3. Wayne, PA: CLSI; 2000.
- Kaliyadan F, Kulkarni V. Types of variables, descriptive statistics, and sample size.
   *Indian Dermatol Online* J. 2019 Jan-Feb;10(1):82-86. doi: 10.4103/idoj.IDOJ\_468\_18.
   PMID: 30775310; PMCID: PMC6362742.

16. Harris JE, Sheean PM, Gleason PM, Bruemmer B, Boushey C. Publishing nutrition research: a review of multivariate techniques-part 2: analysis of variance. *J Acad Nutr Diet*. 2012;112:90.

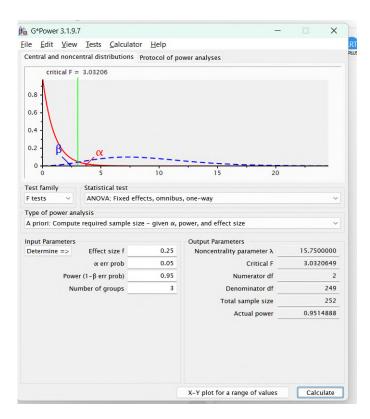
## **Appendices:**

**Appendix A** - QOLIE-31 Questionnaire (attached as a PDF and link below)

Source: RAND Health Care. QOLIE-31 Survey Instrument.

https://www.rand.org/content/dam/rand/www/external/health/surveys\_tools/qolie/qolie31\_survey\_.pdf. Accessed June 30, 2025.

## **Appendix B -** G\*Power Calculations



## Appendix C - Magnesium Awareness Handout

Study Title: Magnesium Supplementation and Epilepsy

Purpose of this Handout:

To help you avoid significant changes in your magnesium intake during the study so we can accurately assess how the supplement affects your health.

## **✓** Please DO:

- Continue eating your usual diet throughout the study.
- Let the research team know if you start or stop any vitamins, supplements, or medications.
- Tell us if you experience any digestive symptoms like diarrhea or stomach cramps.
- Take your assigned capsule once daily with food, at the same time each day.
- Bring your pill bottle and logs to each monthly follow-up

# **X** Please AVOID During the Study:

1. No additional magnesium supplements

Avoid magnesium-containing supplements (including multivitamins or antacids like Milk of Magnesia or magnesium citrate/lactate).

- 2. Don't dramatically change your diet
- 3. Avoid suddenly adding or cutting out large amounts of high-magnesium foods, such as:
  - Pumpkin seeds (1 oz =  $\sim$ 150 mg)

- Almonds (1 oz =  $\sim$ 80 mg)
- Spinach ( $\frac{1}{2}$  cup cooked =  $\sim$ 75 mg)
- Black beans ( $\frac{1}{2}$  cup =  $\sim$ 60 mg)
- Cashews, peanuts, and peanut butter
- Whole grains (brown rice, oats, quinoa)
- Fortified breakfast cereals
- Dark chocolate (1 oz =  $\sim$ 50 mg)
- Avocados
- Bananas
- Edamame

*Note:* You don't need to avoid these foods, just don't increase or decrease them on purpose.

## **Why This Matters:**

This study is testing how magnesium supplements affect quality of life and seizure activity. If you start getting more magnesium from other sources, it may make it harder to understand the effects of the supplement alone.

## **Questions?**

Please contact the study team if you:

- Experience any symptoms
- Need to start a new supplement or medication
- Have questions about foods or how to take your capsule

Appendix D – Informed Consent Form for Participation in a Research Study

Study Title: The Effects of Magnesium Supplementation on Seizure Frequency and Quality of

Life in Adults with Epilepsy

Principal Investigator: Laura Thompson, University of New England

Contact Information: lthompson29@une.edu

**Key Information** 

You are invited to take part in a research study. This form gives you important information

about the study to help you decide whether to participate.

Purpose: To evaluate whether daily magnesium supplementation can improve seizure

control and quality of life in adults with epilepsy.

Procedures: Participants will be randomly assigned to receive either a magnesium

supplement or a placebo for 6 months. Neither you nor the study team will know which

group you are in (this is called a double-blind study).

Duration: Approximately 6 months, with three in-person visits and monthly check-ins.

Voluntary: Participation is entirely voluntary. You may withdraw at any time.

**Purpose of the Study** 

This research is will evaluate the potential benefits of magnesium supplementation in

reducing seizure frequency and improving quality of life in adults with epilepsy.

**Procedures** 

If you choose to participate:

- You will be randomly assigned to one of three groups: 300 mg magnesium, 500 mg magnesium, or placebo.
- You will take one capsule per day for 6 months.
- You will complete quality of life and seizure activity questionnaires at the beginning,
   midpoint, and end of the study.
- You will have blood drawn at baseline, at 3 months, and after 6 months to measure magnesium levels.
- All participants will continue their current medications unless otherwise directed by their healthcare provider.
- All supplements and recording logs will be provided to you.

### **Risks and Discomforts**

- Minor discomfort may occur during blood draws.
- Magnesium may cause gastrointestinal symptoms (e.g., diarrhea, cramping) in some people.<sup>4</sup>
- There is a small risk of allergic reaction or interaction with your current medications.

#### **Benefits**

You may or may not benefit directly from this study. However, your participation may help researchers better understand how magnesium affects epilepsy.

## **Confidentiality**

All data will be coded to protect your identity. Only authorized study staff will have access to your information. Data may be published, but your identity will not be revealed.

Appendix E – Seizure Activity Log	
Participant ID:	
Date Reviewed:	Reviewer ID:

Date	Time of Seizure	Seizure Type	Duration (minutes)	Severity (1-5)	Possible Trigger(s)	Comments/Notes

## **Instructions for Participants:**

- Date: Enter the current date of seizure occurrence.
- Time of Seizure: Record the time the seizure began (approximate is acceptable).
- **Seizure Type:** Describe the type of seizure (e.g., focal aware, focal impaired awareness, generalized tonic-clonic, absence). Use your best knowledge or ask your clinician for help if unsure.
- **Duration:** Estimate how long the seizure lasted in minutes.

• Severity (1-5): Rate severity of the seizure on a scale of 1 to 5, where:						
○ 1 = Very mild (barely noticeable)						
o 3 =	<ul> <li>3 = Moderate (interferes with activity)</li> </ul>					
o 5 =	<ul> <li>5 = Severe (requires assistance or emergency care)</li> </ul>					
• Possible Trigger(s): Note any events or circumstances you think might have triggered						
the seizur	re (e.g., missed medication, stress, lack of sleep).					
• Commen	Comments/Notes: Include any additional observations such as aura, post-seizure					
symptoms, injuries, or medication taken after the seizure.						
To be reviewed by study staff at each follow-up visit.						
Appendix F - Serum Magnesium Level Log <sup>14</sup>						
Participant ID:	Participant ID: Date of Blood Draw:					
	Serum Magnesium					

Timepoint	Date of Sample	Serum Magnesium  Level (mg/dL or  mmol/L)	Laboratory Method	Comments/Notes
Baseline (Pre-			Colorimetric assay per	
study)			CLSI guidelines	

Timepoint	Date of Sample	Serum Magnesium  Level (mg/dL or  mmol/L)	Laboratory Method	Comments/Notes
3 Months			Colorimetric assay per CLSI guidelines	
6 Months			Colorimetric assay per CLSI guidelines	

## **Notes:**

- **Blood Collection:** Blood samples will be obtained by standard venipuncture (blood draw) at scheduled visits.
- Laboratory Analysis: Serum magnesium will be measured using a validated colorimetric assay consistent with CLSI procedures<sup>14</sup> to ensure accuracy and reproducibility.
- Units: Record serum magnesium concentration in mg/dL or mmol/L as provided by the laboratory report.
- Comments/Notes: Record any relevant information such as fasting status, recent magnesium supplementation, or sample quality concerns.