

## Purpose

To examine magnesium (Mg) status and depression in individuals at risk of suicide via the interplay of dietary Mg intake, serum Mg, dietary and serum Ca:Mg ratios, and the use of medications known to affect the absorption, distribution, metabolism, and/or excretion (ADME) of these electrolytes.

## Materials & Methods

Using baseline data for 103 subjects determined to be at risk of suicide by the Better Resiliency Among Veterans and Non-Veterans with Omega-3's protocol, a randomized control trial (ClinicalTrials.gov Identifier NCT01901887), we analyzed the relationship between serum and dietary Mg markers and five mental health screening tools. Baseline dietary habits were characterized using the USDA Automated Multiple Pass Method (AMPM) 24-h dietary recalls with one in-person interview and followed by a telephone interview within 10 days and the 30-day Diet History Questionnaire (DHQ) Food Frequency Questionnaire (FFQ). The 30-day FFQ, when combined with the set of two AMPM USDA 24-h recalls, mathematically represents the current best estimation tool for determining usual intake of food and nutrients. Due to the variable effects on Mg's ADME by the large number of medications, our primary analyses considered subjects reporting medications with a major effect on Mg, such as proton pump inhibitors (PPI).

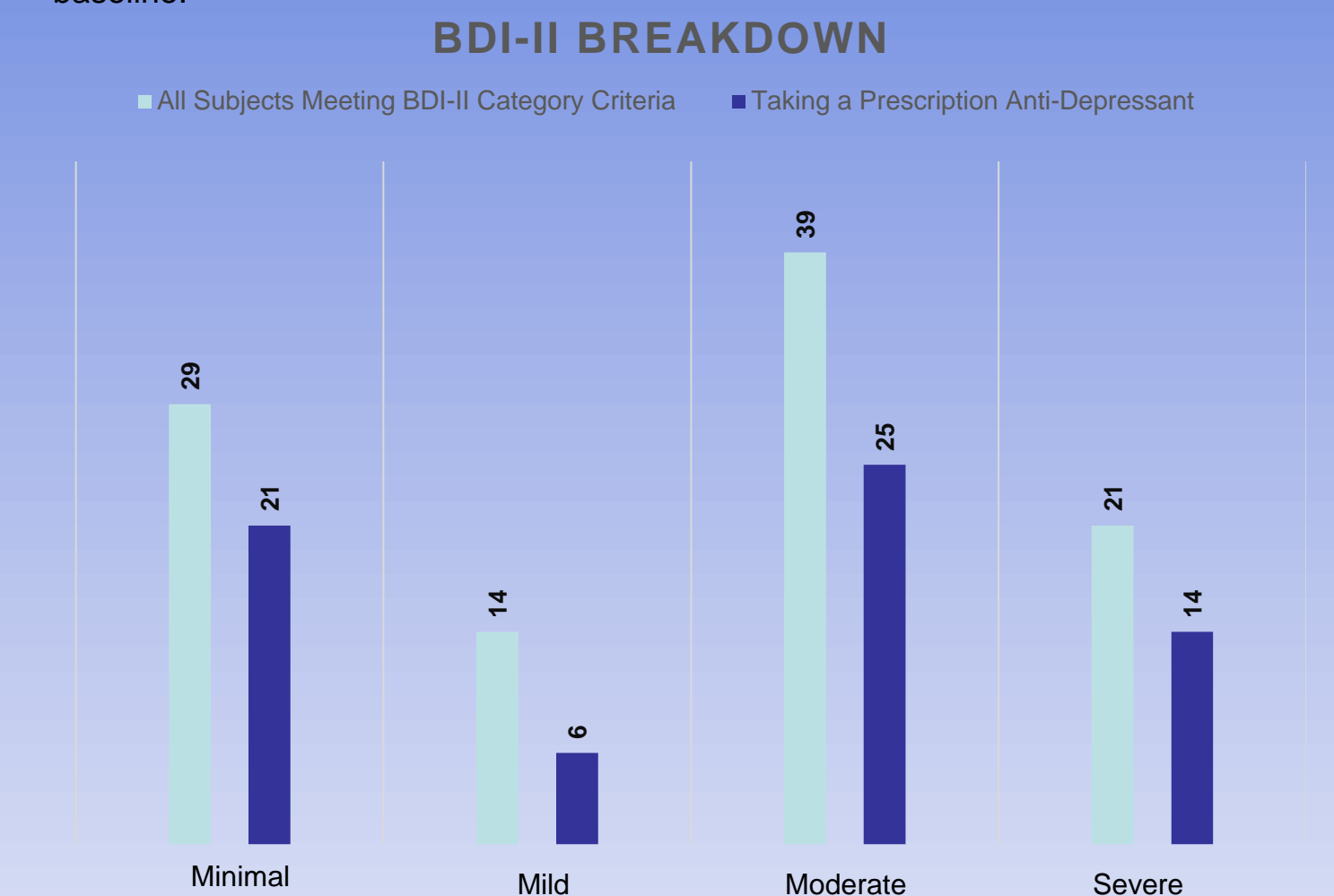
73% of the study population (n=75) met the Beck Depression Inventory (BDI-2) criteria for depression. Of the depressed individuals, 61% reported taking at least one prescription anti-depressant (and as many as 10 or more prescription drugs). Similarly, a subgroup of 18 individuals taking a PPI at baseline met criteria for depression and 11 individuals also reported taking at least one prescription anti-depressant. Mean serum Mg for the entire population was  $2.07 \pm 0.24$  mg/dL, range 0.84 – 2.59 mg/dL (normal 1.7 – 2.2), mean dietary Mg intake was  $298 \pm 131$  mg/day, mean serum Ca:Mg ratio  $4.8 \pm 0.88$ , and mean dietary Ca:Mg ratio  $3.4 \pm 1.6$ . Regarding the correlation between Mg markers and depressive symptoms, outlier points within the data dominated Pearson's *r*, and removing these points showed the remainder of the data to be basically trendless. Spearman's rho and logarithmic analyses also failed to elucidate significant trends or findings.

## Results

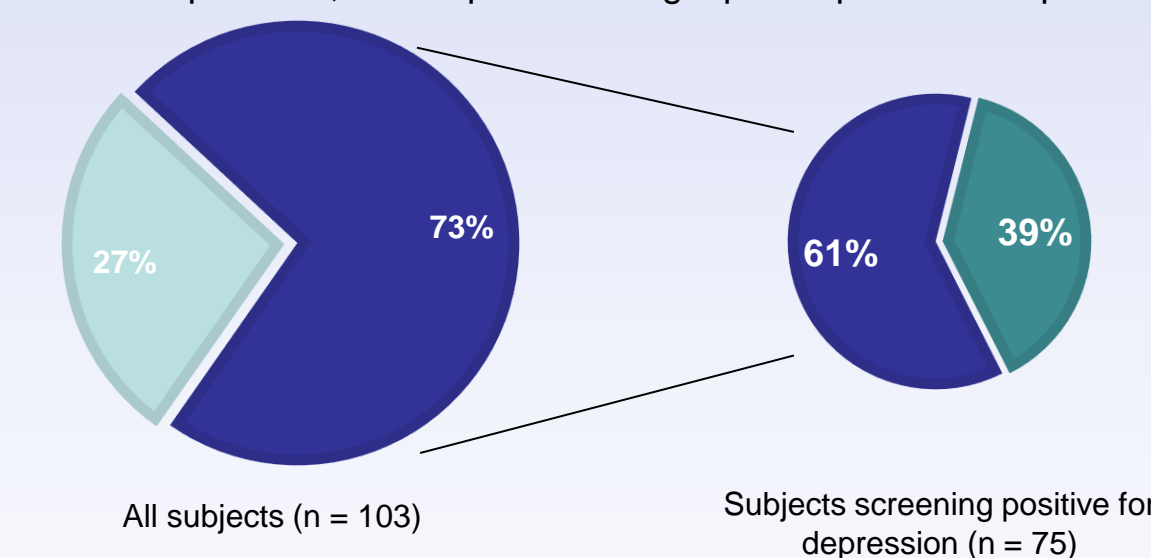
**Table 1. Descriptive Data:** Electrolyte markers of the entire cohort (n = 103) based on categorical BDI-II score.

Electrolyte Marker	BDI-II Depression Category			
	Minimal (n = 29)	Mild (n = 14)	Moderate (n = 39)	Severe (n = 21)
Diet Mg (mg)	324.91 ± 101.7	249.5 ± 80.9	273.94 ± 126.24	341.84 ± 174.6
Diet Ca (mg)	1081.02 ± 487.4	849.05 ± 415.6	936.8 ± 499.72	872.11 ± 375.2
Diet Ca/Mg	3.48 ± 1.6	3.62 ± 1.8	3.63 ± 1.6	2.71 ± 1.2
Serum Mg (mg/dL)	2.01 ± 0.02	2.15 ± 0.22	2.1 ± 0.27	2.06 ± 0.2
Serum Ca (mg/dL)	9.81 ± 0.78	10.06 ± 0.90	9.7 ± 0.72	9.74 ± 0.66
Serum Ca/Mg	4.92 ± 0.54	4.73 ± 0.79	4.77 ± 1.2	4.78 ± 0.61

**Chart 2.** The BDI-II is a 21-item tool used to screen for depression. Each item is rated on a 4-point scale ranging from 0 – 3 based on the severity of each item. Minimum score is 0, and maximum score is 63. Sum total scores are divided into 4 categories: Minimal 0 – 13; Mild 14 – 19; Moderate 20 – 28; Severe 29 – 63. This chart shows the number of subjects from the entire study population meeting criteria for each of the 4 depressive categories (green bar) juxtaposed with the number of individuals in each subgroup who reported taking a pharmaceutical anti-depressant at baseline.



**Chart 1.** Of the majority (73%) of the suicidal study population that screened positive for depression, 61% reported taking a prescription anti-depressant.



## Discussion

No significant relationship between magnesium status and depression was found in a high-suicide-risk cohort, the majority of whom reported depression despite >50% reporting pharmaceutical depression treatment at baseline. Although the relationship between magnesium and depression has been well-studied, there is a relative paucity of data examining the relationship between magnesium status and suicidality. Several subjects were taking multiple medications that can affect Mg status which may have

## References

## **BRAVO Inclusion and Exclusion Criteria**

### **Inclusion Criteria**

- 1) United States (U.S.) military Veterans and non-Veterans ages 18-80 years;
- 2) A suicide attempt in past 6 months, or a suicide attempt during the adult lifetime AND current diagnosis of an episode of depression diagnosed on the Mini International Neuropsychiatric Interview (MINI), or an inpatient admission with suicide risk in the last 6 months, or an inpatient admission with suicide risk during the adult lifetime AND current diagnosis of an episode of depression as diagnosed on the MINI, or positive suicidal behavior or ideation based on a psychiatrist-administered Columbia-Suicide Severity Rating Scale (C-SSRS) and psychiatrist review of participant medical history and physical, or a score of 0 or greater on the Implicit Associations Test – Suicide (IAT-S), or score of  $\geq 9$  on the Beck Hopelessness Scale (BHS) and psychiatrist review of participant medical history and physical;
- 3) Currently under the care of a mental healthcare provider. A release of information from his/her mental healthcare provider is required;
- 4) Capacity to provide written, informed consent;
- 5) Having a stable residence with adequate space to store juice, and ability and willingness to consume 3 fruit juice beverages per day for 6 months.

### **Exclusion Criteria**

- 1) Any unstable medical conditions requiring immediate attention;
- 2) Medical conditions that preclude potential study participation for the duration of the study or any life-threatening medical condition(s) or life expectancy of less than 6 months;
- 3) History of non-febrile seizures;
- 4) Unstable or rapidly progressive neurological disease
- 5) Diabetes mellitus and/or taking hypoglycemic agents
- 6) Regularly taking anticoagulants (including high-dose aspirin, warfarin), taking the medication isotretinoin (Acutane);
- 7) Allergy, hypersensitivity, or intolerance to fish oils or omega-3 fatty acids, any nuts, fruits, fish, rosemary, or milk protein;
- 8) Pregnancy, lactation, or intention to become pregnant within the next 12 months;
- 9) Acute intoxication or withdrawal from alcohol or other substances;
- 10) Body Mass Index (BMI)  $< 18 \text{ kg/m}^2$  or  $> 45 \text{ kg/m}^2$  without medical comorbidities associated with obesity and extreme obesity;
- 11) Evidence of disordered eating or risk of malnutrition based on the Eating Attitude Test-26 (EAT-26);
- 12) History of significant psychiatric instability;
- 13) Any unstable medical conditions requiring immediate attention.