**Appendices**

**Appendix A: Example Recommendation Listing with Patient Reported Compliance Ratings**

|  |  |  |
| --- | --- | --- |
| **Recommendation** | **Mean Rated Ease** | **Mean Rated Compliance** |
| **Physical Activity** |  |  |
| Engage in physical activity | 3.76 (1.22) | 4.13 (0.93) |
| Aerobic exercise | 3.49 (1.25) | 3.88 (1.04) |
| Interval training | 3.08 (1.28) | 3.26 (1.21) |
| Use a balance ball or standing desk instead of a usual desk chair | 2.78 (1.34) | 4.67 (0.73) |
| Weight training | 3.23 (1.33) | 3.47 (1.16) |
| **Dietary** |  |  |
| Make changes to your diet | 3.34 (1.06) | 4.54 (0.88) |
| Consume caffeinated coffee only before 2 pm | 4.21 (1.04) | 4.16 (1.23) |
| Consume no carbohydrates for at least 12 hours overnight at least 4 days a week (on average) | 3.32 (1.14) | 3.70 (0.78) |
| Drink 7-14 servings of alcohol per week (for men) or 7 servings (for women) per week | 3.30 (1.30) | 3.16 (1.41) |
| Eat 2-3 servings (half a cup) of berries per week | 4.33 (0.90) | 2.69 (1.42) |
| Eat foods containing Omega 3 fatty acids (like DHA and EPA) | 4.30 (0.99) | 3.56 (1.12) |
| Eat more "lean" protein instead of "fatty" protein | 4.22 (0.78) | 4.23 (0.76) |
| Reduce carbohydrate intake | 3.06 (1.14) | 4.34 (0.80) |
| Specifically reduce 'bad' carbohydrates with a high glycemic index ("empty calories") | 3.17 (1.30) | 3.76 (0.79) |
| **Vitamins/Medications** |  |  |
| Take a Vitamin or Supplement | 4.44 (0.90) | 4.65 (0.76) |
| Cocoa powder or capsules | 3.86 (1.31) | 4.16 (1.23) |
| Folic Acid (Vitamin B9) | 4.46 (0.93) | 3.96 (1.02) |
| Niacin (Vitamin B3) | 4.25 (1.07) | 4.33 (1.17) |
| Omega-3 fatty acids (specifically DHA and EPA) | 3.76 (1.21) | 4.42 (0.94) |
| Take prescribed medications | 4.46 (0.82) | 4.59 (0.81) |
| Vitamin B12 | 4.52 (0.88) | 4.69 (0.68) |
| Vitamin B6 | 4.42 (0.98) | 4.65 (0.75) |
| Vitamin D | 4.42 (0.94) | 4.39 (1.07) |
| **Other** |  |  |
| Avoid computers, electronic devices or texting/email for at least 30 minutes before bed | 3.25 (1.28) | 3.81 (0.73) |
| Join Alzheimer's Universe (www.AlzU.org) | 3.54 (1.26) | 3.38 (1.32) |
| Learn something new (like a new language) | 2.49 (1.20) | 2.81 (1.24) |
| Listen to music | 4.20 (1.02) | 3.99 (1.05) |
| Make a lifestyle change (aside from exercise and diet) | 3.06 (1.20) | 2.93 (1.24) |
| Make more time for yourself to work on your brain-health | 3.09 (1.26) | 3.37 (1.18) |
| Play a musical instrument or learned how to play one | 2.17 (1.16) | 2.32 (1.22) |
| See your primary care doctor | 3.99 (1.06) | 3.92 (1.13) |
| Sleep at least 7-8 hours a night | 3.50 (1.23) | 4.02 (0.95) |
| Socialize with family and friends | 4.28 (0.86) | 4.23 (0.85) |
| Try stress reduction techniques (yoga, acupuncture, meditation, mindfulness training) | 2.93 (1.26) | 3.09 (1.30) |
| Use a health-tracking app | 2.92 (1.35) | 2.89 (1.39) |
| Use the online Alzheimer's Disease - Nutrition Tracking System | 2.36 (0.96) | * 1. 0.85) |

NOTE: Adapted from (1). Patient reported data via 1-5 Likert scale, with 1= Very Difficult and 5= Very Easy. Patients were also asked to report the frequency of their adherence to each individual recommendation and rated this on a 1-5 Likert scale, with 1=Opposed to doing this and 5=All the time.

**Appendix B: Example of Individualized Clinical Approach**

**Case Presentation:** A perimenopausal woman in her late 40s without subjective cognitive complaints may receive on average 20-25 individualized recommendations. Additional clinical history, anthropometrics, blood biomarkers, and cognitive assessments are also considered to personalize care. For example, a past medical history of untreated “borderline” hypertension, insulin resistance, hyperlipidemia, and elevated homocysteine generated specific recommendations that address these comorbidities, such as referral to a preventative cardiologist for management of blood pressure (goal 120s/70s or below) and hyperlipidemia. If homocysteine is elevated, optimizing B-complex (B12/folate/B6) vitamin may be recommended. Limiting high-glycemic foods is recommended for those with insulin resistance. In addition, cocoa flavanols may improve insulin sensitivity as well as blood pressure and memory function. Managing the cardiovascular and metabolic risk factors more optimally can be especially important when results of cognitive testing are found to be in the low-average range in memory, executive function and processing speed. It is common for women in perimenopause to experience hot flashes, night sweats, trouble staying asleep, decreased libido, and general irritability. If these symptoms begin, and labs demonstrate elevated FSH and estradiol levels that have decreased on follow-up, patient education about potential risks/benefits of long-term hormone replacement therapy may be advisable, along with a collaborative discussion with the patient’s treating OB/Gyn physician.

All patients receive exercise counseling based on their level of activity, biomarkers, and anthropometrics. For instance, a patient with abdominal obesity/elevated waist-to-hip ratio and elevated visceral body-fat would be recommended a target amount/type of aerobic-versus-resistance training geared for body-fat reduction. Patients also receive nutritional counseling centered on the Mediterranean-style diet. An APO*ε4* carrier or someone with elevated ApoB cholesterol would be recommended to prioritize intake of fatty fish and extra-virgin olive oil, especially if their diet is already lacking in these areas. APO*ε4* carriers and those with a low red blood cell Omega-3 Index (EPA+DHA) may benefit from Omega-3 fatty acid supplementation.

Recommendations include several other detailed interventions related to sleep and oral hygiene, cognitive and social engagement, stress management, ongoing care with primary care physician, and information on AD prevention clinical trials. An introductory course on AD prevention (10 lessons, 2+ hours of interactive-multimedia content) that has been shown to increase knowledge and willingness to participate in AD prevention clinical trials is also recommended via the online learning portal AlzU.org(2). Any adverse events are recorded during each follow-up, with the treating clinician asking all participants whether they experienced any side effects/harm related to assigned interventions.

**References**

1. Isaacson RS, Hristov H, Saif N, Hackett K, Hendrix S, Melendez J, et al. Individualized clinical management of patients at risk for Alzheimer's dementia. Alzheimer's & dementia : the journal of the Alzheimer's Association. 2019;15(12):1588-602.

2. Isaacson RS, Haynes N, Seifan A, Larsen D, Christiansen S, Berger JC, et al. Alzheimer's Prevention Education: If We Build It, Will They Come? [www.AlzU.org](file:///Users/kiarraakiyoshi/Desktop/www.AlzU.org). J Prev Alzheimers Dis. 2014;1(2):91-8.