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Original Article

# Suboptimal adherence to brain health recommendations in patients pursuing anti-amyloid antibody therapy for Alzheimer's disease: Report from the Brain Health Vital Signs project

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ABSTRACT

*Background:* Consensus is consolidating around a set of lifestyle and medical factors that can promote brain health and reduce the risk of dementia for older adults and further decline for those with early Alzheimer's disease (AD) and related disorders. Little is known about the degree to which recommended brain-healthy behaviors have been adopted by patients with early AD pursuing anti-amyloid antibody therapy (AAT), a proactive group interested in doing what is under their control to help preserve cognitive and functional status. Here, initial results of a clinically relevant quality improvement study are reported.

*Objective:* To determine the extent to which patients pursuing AAT for AD adhere to consensus-based brain health recommendations.

*Participants:* One hundred fifty patients with mild cognitive impairment (MCI) or mild dementia due to AD seeking AAT were studied and compared to a group of 117 patients with MCI or mild dementia who were not pursuing AAT.

*Measurements:* Using a clinical survey tool developed for the project, patients were assessed on 15 modifiable risk factors for cognitive decline and dementia, including 11 via e-survey (diet, physical activity, cognitive activity, sleep, social engagement, smoking status, alcohol consumption, hearing, vision, mood/stress, and purpose in life) and 4 via electronic medical record (EMR) (blood pressure, BMI, LDL cholesterol level, and HbA1c). For each factor, the percentage of each of the two patient groups that was not optimally adhering to brain health-related guidelines was calculated. For each individual, the total number of factors not optimally being followed was determined.

*Results:* Less than 3% of patients with early AD pursuing AAT were following or had anthropometric measures/lab values in line with all 15 brain health recommendations. The five factors with the lowest adherence rates involved physical activity, mood/stress, HbA1c, blood pressure, and BMI, with 44–63% of the AAT group suboptimally following consensus-based guidelines. For 11 of 15 factors, >25% of the group were not adhering to guidelines. No robust differences in degree or pattern of adherence to guidelines were observed between patients pursuing and not pursuing AAT. There were no data in the EMR for HbA1c in >42% of patients and for LDL in >23% of patients in either group.

*Conclusions:* Suboptimal adherence to brain health recommendations may be common among patients with early AD, whether they are pursuing AAT or not. These results suggest that healthcare systems may need to develop more effective strategies and individualized interventions for addressing modifiable risk factors for cognitive decline and dementia, and more efficacious procedures for ensuring that relevant, actionable data associated with brain health are updated in the EMR.

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## 1. Background

The financial, emotional, and social costs of Alzheimer's disease and related dementias (ADRDs) are staggering at both the population and individual levels [1–3]. Over the last decade, the concept of brain health and its relationship to dementia risk and cognitive decline has gained increasing attention. Evidence that adopting brain-healthy behaviors and addressing potentially modifiable lifestyle factors can lower the risk of cognitive decline and dementia, and reduce further decline in early ADRDs, has led health organizations to develop and promulgate guidelines, and influenced the lay media, public health entities and public consciousness more generally [4–6].

There is growing consensus about factors that can promote brain health and reduce the risk of cognitive decline and dementia. Table 1 summarizes modifiable risk factors recognized by a variety of major health organizations and published reports, and highlights areas of convergence. Despite growing awareness about these modifiable risk factors, there are substantial barriers to the adoption of consensus brain health guidelines, including limited motivation, time, social support, and financial resources [7–9]. Moreover, the optimal ways to assess patients' brain health and then implement consensus-based recommendations in clinical care settings remain to be determined [10].

Within this context, to help address this "implementation gap," we developed the Brain Health Vital Signs (BHVS) project, a quality improvement initiative at our academic medical center. Further details about design and goals of BHVS will be detailed in a future publication. Briefly, the project aims to assess the brain health of patients in clinical settings and then pilot clinically embedded educational and other interventions to target modifiable risk factors for cognitive decline. In this first phase, we are focused only on brain health assessment. We have been collecting cross-sectional, brain health information ("brain health vital signs") of patients in two settings: 1) a highly specialized clinic for patients with early Alzheimer's disease (AD) pursuing anti-amyloid antibody therapy (AAT) and 2) our general cognitive neurology subspecialty clinic. To assess modifiable risk factors for individual patients, we developed an instrument, the "BHVS Score," composed of 15 factors chosen from dementia prevention and care guidelines (Table 1), which reflects level of adherence to consensus-based recommendations.

Understanding the pattern and degree of adherence to brain health recommendations in different sub-populations of patients is essential for tailoring education and other clinical interventions at the group level. If, for example, we look at the current landscape of treatment for early AD, evidence suggests that maximizing healthy behaviors and addressing systemic vascular and metabolic disease are critical for protecting brain health and potentially slowing cognitive and functional decline [11,12]. Many clinical guidelines (e.g., from the American Heart Association [13], European Interdisciplinary Council on Aging [14], American College of Cardiology [15], Canadian Consensus Conference [16]), and published reviews (e.g., JAMA Clinical Reviews on Dementia [17,18]) emphasize that the importance of addressing modifiable risk factors applies to not only adults at risk but also to patients with MCI and mild dementia. Little is known about the extent to which brain-healthy behaviors have been adopted by AD patients pursuing AATs, a growing population receiving clinical care. This report focuses on the modifiable brain health risk factors, as measured by BHVS scores, of patients with MCI or mild dementia due to AD who were evaluated for the novel AAT lecanemab over its first ~18 months of availability at our center. This project was designed to be descriptive and cross-sectional, rather than experimental, consistent with recent reports that have sought to characterize patients receiving this new class of medication [19,20]. To be evaluated for AATs, patients had to be referred to our center's AAT treatment program, the Mass General Brigham (MGB) Alzheimer Therapeutic Program (ATP), which has sites at Brigham and Women's Hospital (BWH) and Massachusetts General Hospital. If patients pursuing AATs were found to have limited adherence to brain health guidelines, it would leave open the question about whether they were, none-the-less, following recommendations more closely than patients not seeking AATs. To address this issue, we evaluated a comparison group of patients with similar diagnoses and demographic profiles from the BWH general cognitive neurology subspecialty clinic who were not seeking AAT.

Pursuit of lecanemab therapy requires a striking commitment, including infusions every two weeks, multiple imaging studies, potential out-of-pocket expenses, and the acceptance of the risk of amyloid-related imaging abnormalities (ARIA) and other side effects. Because patients pursuing lecanemab exhibit proactive behavior to do what is under their control to impact disease trajectory, we reasoned that they would demonstrate relatively high adherence to brain health recommendations and more closely follow consensus guidelines than matched counterparts not seeking AAT. Failure to observe this outcome would further highlight the challenges facing healthcare systems interested in addressing modifiable risk factors for cognitive decline and dementia and suggest the need to allocate more resources to develop and implement lifestyle interventions in addition to expensive pharmacologic

**Table 1**
Modifiable risk factors.

| | AHA Essential 8 | Lancet 2024 | Alzheimer's Association | World Health Organization | Institute of Medicine | National Academy of Science | MGH Brain Health Center |
|---|---|---|---|---|---|---|---|
| Physical Activity | X | X | X | X | X | X | X |
| Healthy Weight | X | X | X | X | | | X |
| Health Blood Pressure | X | X | X | X | X | X | X |
| Healthy Blood Glucose Levels | X | X | X | X | X | | X |
| Health Blood Lipid Levels | X | X | ~ | X | | | X |
| Healthy Diet | X | | X | X | | | X |
| Not Smoking | X | X | X | X | X | | X |
| Healthy Sleep | X | | X | | X | | X |
| Social Engagement | | X | X | X | X | | X |
| Formal Education | | X | X | | X | | |
| Cognitively Stimulating Activities | | | X | X | X | X | |
| Limit Alcohol Use | | X | ~ | X | | | X |
| Manage Depressive Stress | | X | ~ | X | | | X |
| Manage Hearing Loss | | X | ~ | X | | | |
| Manage Visual Loss | | X | X | | | | |
| Decrease TBI | | X | X | | | | |
| Decrease Air Pollution | | X | ~ | | | | |
| Decrease Use of Meds with Anticholinergic Properties | | | | | X | | |
| Find Meaning in Life | | | | | | | X |

**Note.** The Xs represent the modifiable risk factors identified by specific health organizations or published reports.

ones.

## 2. Methods

### 2.1. ATP patient group

One group enrolled in BHVS were patients being evaluated at the BWH site of the MGB ATP for consideration of treatment with lecanemab during the first 18 months of its availability at our center. To be evaluated in ATP, patients with early AD had to express an interest to their specialty or primary care provider(s) to be referred. The medical records of referred patients were reviewed by ATP clinical staff. If patients fulfilled preliminary ATP eligibility requirements on a standardized checklist, an intake appointment was scheduled.

Most (~95%) of patients in our group met all lecanemab eligibility criteria established by the MGB ATP, which largely followed published appropriate use criteria [21]. These included: a clinical diagnosis of MCI or mild dementia due to AD (based on performance of instrumental and basic ADLs), a Mini-Mental State Examination (MMSE) of ≥22 or Montreal Cognitive Assessment (MoCA) of ≥15, absence of a clinical diagnosis of Lewy body disease-spectrum or frontal-temporal lobar degeneration-spectrum syndromes, and a positive CSF or amyloid-PET AD biomarker. We also included patients who met diagnostic, biomarker, and cognitive/level of functioning criteria but were later deemed ineligible for other reasons, most commonly exclusionary findings on a baseline MRI scan.

### 2.2. Cognitive neurology patient group

We enrolled a second group of patients in the BHVS project who were receiving care in a general cognitive neurology subspecialty clinic, during the period of the first 18 months of lecanemab availability at our center. They had diagnoses of MCI or mild dementia due to AD or other, non-AD conditions, such as vascular cognitive impairment. The patients from this Cognitive Neurology group were *not* pursuing lecanemab and did not need AD biomarker tests or scores in a certain range on recent cognitive and daily functioning tests.

### 2.3. Brain health vital signs (BHVS) assessment: survey plus EMR data

For each BHVS patient, personal information about 15 key lifestyle and behavioral risk factors that contribute to overall brain health was obtained. For 11 of these, information was collected through an e-survey, and included diet, physical activity, cognitive activity, sleep, social engagement, smoking status, alcohol consumption, hearing, vision, mood/stress, and purpose in life. (**Supplemental Figure 1** contains a copy of the e-survey.) For the four additional factors, blood pressure, body mass index (BMI), LDL cholesterol level, and hemoglobin A1 (HbA1c), data were extracted from each patient's EMR using Clinical Data Pull (CDP) within MGB's REDCap Clinical Data Interoperability Services (CDIS) module [22].

The most recent available data were used. Blood pressure and BMI values at or around the time of a patient's ATP or Cognitive Neurology visit were utilized. LDL cholesterol and HbA1c levels used were the most recent values in the prior 18 months to when the survey was sent. If no results were found within 18 months, they were recorded as missing. Patients who lacked data from four or more of the 15 factors were excluded. In addition to collecting information on key lifestyle and risk factors, the survey gathered demographic data such as age, sex, race, years of education and level of financial comfort. Patients were also asked about existing medical diagnoses and a family history of Alzheimer's disease or related dementias.

### 2.4. Survey distribution and completion

Between December 2023 and May 2025, the BHVS e-survey was distributed as a REDCap link through MGB's EMR messaging system (Patient Gateway). A message accompanying the link explained the purpose of the survey and requested that patients complete it prior to their upcoming visit. For most patients who did not complete the survey by the day of their appointment, a project coordinator tried to meet them in-person following their check-in to facilitate survey completion using a laptop. A unique record ID was generated for each patient. Except as noted below, a week prior to their appointment, all patients being evaluated in one of the ATP clinics were sent surveys. A total of 234 ATP patients were sent surveys;122 were delivered before an initial visit, 60 before a follow-up visit, and 52 were not associated with a specific visit. The latter group were patients seen in the first 11 weeks of the ATP, prior to the start of the BHVS project. These patients were not approached at follow-up visits if they did not complete the questionnaire online.

Of the 234 ATP patients sent surveys, 162 (69.2%) completed them. Twelve were excluded because they did not meet cognitive or functional eligibility requirements for lecanemab (i.e., had a level of severity beyond mild dementia). Thus, we report on results of 150 ATP patients. One hundred forty-two met all eligibility criteria, and eight patients met all cognitive and daily functioning criteria but were later determined to be ineligible for treatment. **Supplemental Figure 2** presents a modified Consolidated Standards of Reporting Trials (CONSORT) flow chart for the ATP patient group.

During each week throughout this initial BHVS project enrollment period, four patients from the Cognitive Neurology clinic who had upcoming visits scheduled were randomly selected using Google's random number generator (Google LLC, Mountain View, CA). The survey was transmitted two weeks prior to an established care visit. A total of 285 cognitive neurology patients were sent surveys, of which 260 appeared eligible for the current study because their records indicated a diagnosis of MCI or mild dementia. Of these 260 patients, 141 (54%) completed the survey. Twenty-four of the 141 were then excluded after more detailed chart review; 14 were too impaired, with dementia beyond the mild stage, seven were cognitively normal or had subjective cognitive impairment, and three had an inadequate data set. Thus, we report on the survey results of 117 Cognitive Neurology patients. **Supplemental Figure 3** represents a modified CONSORT chart summarizing this information.

The MGB institutional review board (IRB) reviewed the BHVS project and determined that informed consent and ongoing regulatory oversight were not required, as it was developed as a patient quality improvement program.

### 2.5. BHVS score calculation

A BHVS score for each patient was then generated, ranging from 0 to 30 points, using both e-survey and EMR-extracted data. Each of the 15 lifestyle and behavioral risk factors was assessed for how well the individual adhered to published, recommended guidelines for that factor using a "3-point" scoring system (0–2 points) toward the total score. A score of 2 was given for optimal adherence, 1 for partial adherence, and 0 if recommended guidelines were not followed at all for that factor. The total number of factors not being optimally followed by a patient was also recorded (0–15). Table 2 summarizes the BHVS scoring system and provides references for the cut-off values used.

The BHVS survey differs from several other dementia risk-assessment tools in terms of its purpose and factor weightings. The survey and scoring system were created as a practical tool to help patients and their providers identify personal risk factors they could work to modify, rather than as risk prediction/calculation tools to employ serially and in conjunction with other clinical data. Regarding factor weightings, other tools differentially weight each factor's contribution to a composite score by employing a variety of strategies, often for the purpose of risk stratification for treatment algorithms. Approaches have included using logistic regression coefficients from a single long-term cohort study (e.g.

**Table 2**
BHVS scoring system.

| FACTOR | 2 POINTS | 1 POINT | 0 POINTS |
|---|---|---|---|
| **Diet**[1] [28,29] | I follow a healthy diet most of the time | I occasionally follow a healthy diet | I rarely follow a healthy diet |
| **Physical Activity**[2] [27] | ≥25 min moderately demanding exercise most days per week | ≥25 min moderately demanding exercise a few days per week | ≥25 min moderately demanding exercise rarely or not at all |
| **Cognitive Activity**[3] | I often engage in activities that stimulate my mind | I occasionally engage in activities that stimulate my mind | I rarely engage in activities that stimulate my mind |
| **Sleep** [30] | >7 h/night | 5–7 h/night | Usually <5 h/night; almost never >7 h |
| **Social Engagement** | Strong support system; many relationships | Few close relationships | I often feel isolated or lonely |
| **Smoking Status** [31] | I don't smoke cigarettes | I occasionally smoke cigarettes | I often smoke cigarettes |
| **Alcohol Consumption** [32] | Female: <4 drinks/week<br>Male: <8 drinks/ week | Female: 4–7 drinks/ week<br>Male: 8–14 drinks/week | Female: ≥8 drinks/week<br>Male: ≥15 drinks/week |
| **Hearing** [7] | I have never had hearing problems, OR I wear hearing aids most of the time and don't have difficulty hearing | I have hearing problems OR<br>I only wear hearing aids some of the time | I have hearing problems and have not received treatment OR<br>I do not wear my hearing aids |
| **Vision/corrected vision** | Vision problems rarely interfere with day-to-day activities | Vision problems interfere with day-to-day activities ≤weekly | Vision problems interfere with day-to-day activities almost daily |
| **Mood/Stress** | I almost never feel sad and/or overwhelmed | I occasionally feel sad and/or overwhelmed | I often feel sad and/or overwhelmed |
| **Sense of Purpose** | I agree with the statement "I have a sense of purpose in life" | I somewhat disagree with "I have a sense of purpose in life" | I disagree with the statement "I have a sense of purpose in life" |
| **HbA1c** [33] | < 5.7% | 5.7% - 6.4% | > 6.4% |
| **LDL level** [34,35] | < 100 | 100–159 | >159 |
| **Blood Pressure** [36] | SBP <130 | SBP 130–140 | SBP >140 |
| **BMI** [37] | 18.5 –24.99 kg/m$^2$ | 25 – 29.99 kg/m$^2$ | ≥30 kg/m$^2$ or <18 kg/m$^2$ |

CAIDE [23]), estimating relative risk based on a literature review of the relationship between each risk factor and the incidence of dementia (e.g., LIBRA [24]), or employing a modified Delphi process in partnership with practitioners and patients (e.g., Brain Care Score [25]). In line with the purpose of BHVS and to prioritize health surveillance, simplicity and patient communication, each of the BHVS factors was weighted equally, which followed the approach of the Essential 8 by the American Heart Association [26].

In keeping with this approach, the wording of alternative responses to BHVS survey questions was developed to be pragmatic and patient centered. For many factors (e.g., social engagement, healthy diet, hearing difficulties), choices were framed using terms such as "often," occasionally," or "rarely/never," a method similar to the one adopted by the Brain Care Score survey for questions about stress, social relationships, and meaning in life [25]. A more quantitative approach was taken for factors such as sleep, physical activity, HbA1c, LDL cholesterol, BMI, and blood pressure. Notably, we chose a 3-point scoring system for each factor, given the BHVS project's overall goal of motivating patients with suboptimal scores to adopt healthier behaviors and improve their lab values. Three-point (or more) graded systems allow for recognition of gradual progress and foster a growth mindset by acknowledging effort and complexity; they avoid binary feedback ("adhering/non-adhering") that can be simplistic or discouraging. For example, for cognitive activity, patients received 2 points if they "often engage in activities that stimulate [their] mind", 1 point if they "occasionally" engage, and 0 points if they "rarely" engage. We also tried to simplify survey choices. For instance, we did not ask patients to calculate the total number of hours per week in which they participated in moderately demanding physical activity (for which we provided a definition), where the recommended duration is 150 min per week [27]. Rather, patients were asked whether they participated in ≥25 min of moderately demanding exercise most days per week (2 points), a few days per week (1 point), or rarely or not at all.

### 2.6. BHVS reports

After the BHVS score was calculated, two reports were generated: a patient report and a provider report. See **Supplementary Figure 4** for an example of a patient report. More detailed information about these reports and other aspects of the overall BHVS project will be addressed in a future publication.

### 2.7. Outcome measures and analysis

Descriptive statistics were used to summarize the main features of the dataset. For each factor, the percentage of the patient group (ATP, Cognitive Neurology) that was not optimally following brain health-related guidelines (i.e., had scores of 0 and 1) was calculated. For each patient, the number of factors not being optimally followed was determined. For each of the four factors extracted from the EMR, the percentage of each group's missing data was calculated.

In addition, each patient's overall adherence rate was calculated as a patient's total BHVS score (0–30) divided by the maximum possible score from their available data, as sometimes one or more factors were missing. If data for any factor were missing, 2 points for each missing factor were subtracted from 30, reducing the denominator value for that patient. Thus, each patient's overall adherence rate was expressed as a percentage of the maximum possible score for their available data. For example, if a patient's data were only available for 14 factors (resulting in a maximum score of 28) and their total BHVS score was 19, their adherence rate would be 19/28 = .68.

Outcome measures were first analyzed separately for the ATP and Cognitive Neurology. Potential differences between several subgroups of the ATP group (e.g., patients with MCI vs with mild dementia, first 25 vs. last 25 patients) were examined using Student *t*-test. Comparisons between the two patient groups were assessed using two-way analysis of variance (ANOVA), with patient group and diagnostic category as the independent variables. When appropriate (e.g., comparisons of categorical data such a sex), non-parametric statistics (e.g., chi-square) were employed. Regression analyses were then used to determine the independent variables that contributed to outcome measures (i.e., number of factors being suboptimally followed and percent adherence), controlling for the other independent variables. Sensitivity analyses were completed to examine whether results comparing the ATP and Cognitive Neurology patient groups would remain consistent when restricting the Cognitive Neurology group to only those diagnosed with underlying AD. Significance level was set at $\alpha = .05$.

## 3. Results

### 3.1. Patients and demographics

Table 3 summarizes patient characteristics of the ATP (n = 150) and Cognitive Neurology (n = 117) groups. For the ATP group, the mean age

**Table 3**
Patient characteristics.

| | ATP (n = 150) M(SD) or % | Cognitive Neurology (n = 117) M(SD) or % | P-value |
|---|---|---|---|
| Age | 74.6 (6.7) | 75.0 (9.1) | >.7 |
| Female | 57.3% | 52.9% | >.17 |
| Years of Education | 16.1 (2.7) | 16.0 (2.7) | >.8 |
| Diagnosis | | | >.5 |
| Mild Cognitive Impairment | 74% | 71% | |
| Mild Dementia | 26% | 29% | |
| MMSE [1] | 25.2 (3.2) | 25.2 (4.8) | >.99 |
| Race/Ethnicity | | | >.4 |
| White | 92% | 93.1% | |
| Black | 1.3% | 1.7% | |
| Asian | 2.7% | 0% | |
| Hispanic | 2% | 3.4% | |
| No data | 2% | 1.7% | |
| Level of Financial Well-being [2] | | | <.005 |
| Just getting along | 5.8% | 18.4% | |
| Reasonably comfortable | 43.8% | 44.7% | |
| Very comfortable | 50.4% | 36.9% | |

[1] For the Cognitive Neurology group, 110 patients had cognitive test scores. MoCA scores were converted to MMSE in 69 patients.
[2] Data are only available for 137 ATP patients and 103 Cognitive Neurology patients.

was 74.6 years old, mean education was 16.1 years, mean MMSE score was 25.9; ~57% were female, 92% were white, 94% reported being reasonably comfortable or very comfortable financially, 74% were diagnosed with MCI and 26% with mild dementia. Unsurprisingly, the mean MMSE score for the MCI subgroup (M = 25.9; SD = 2.9) was greater than for the subgroup with mild dementia (M = 23.0; SD = 2.9, p < .001).

There were no differences between the ATP and the Cognitive Neurology groups for age, years of education, percentage of each group who were female, percentage diagnosed with MCI vs. mild dementia, and racial/ethnic group, both nearly all white. The financial comfort level differed between groups (p < .005). The ATP group had a higher proportion of patients who identified as being "very financially comfortable" and the Cognitive Neurology group had a higher proportion who felt that they were "just getting by" financially. Cognitive test scores were available for 110 patients in the Cognitive Neurology group. MoCA scores (n = 69) were converted to MMSE scores following published recommendations [38]. Using these available data, the overall MMSE scores (or MoCA converted to MMSE) did not differ between ATP and Cognitive Neurology patient groups, nor were there differences between patient groups in MMSE scores among the MCI only or mild dementia only patients.

### 3.2. ATP patient group

#### 3.2.1. Percent of ATP patient group not optimally following brain health recommendations

Fig. 1**a** illustrates the percentage of the ATP Group *not* optimally following brain health recommendations for each of the 15 factors, which ranged from 63% for physical activity to 1% for smoking. For 11 of the 15 factors, more than 25% of patients, for 7 of the 15 factors, more than 35% of patients, and for 4 of the 15 factors, more than 50% of patients were not optimally adhering to brain health recommendations. Less than 3% of the 150-patient ATP group were following, or had anthropometric measures/lab values in line with, all 15 of the brain health recommendations we queried (see **Supplemental Figure 5**). On average, ATP patients were not following optimal brain health guidelines for 4.9 (SD=2.2) of the 15 factors. Fifty-five percent were not adhering to brain health recommendations for 5 or more of the 15 factors, with 24% not adhering to recommendations for 7 or more factors (**Supplemental Figure 5**).

#### 3.2.2. Adherence rates between subgroups of ATP patients

Patients with MCI exhibited a slightly lower average number of factors not being optimally followed (M = 4.7; SD = 2.2) than patients with mild dementia (M = 5.3; SD = 2.3) but differences were not statistically significant (p = .15). Patients with MCI exhibited slightly higher mean adherence rates than patients with mild dementia (M = .79; SD = .10) vs. M = .76; SD = .12), but differences were not statistically significant (p = .15). No difference in the average number of factors not being optimally followed was found between the first 25 ATP patients ("early adopters" of lecanemab therapy) vs. last 25 patients (M = 4.1; SD

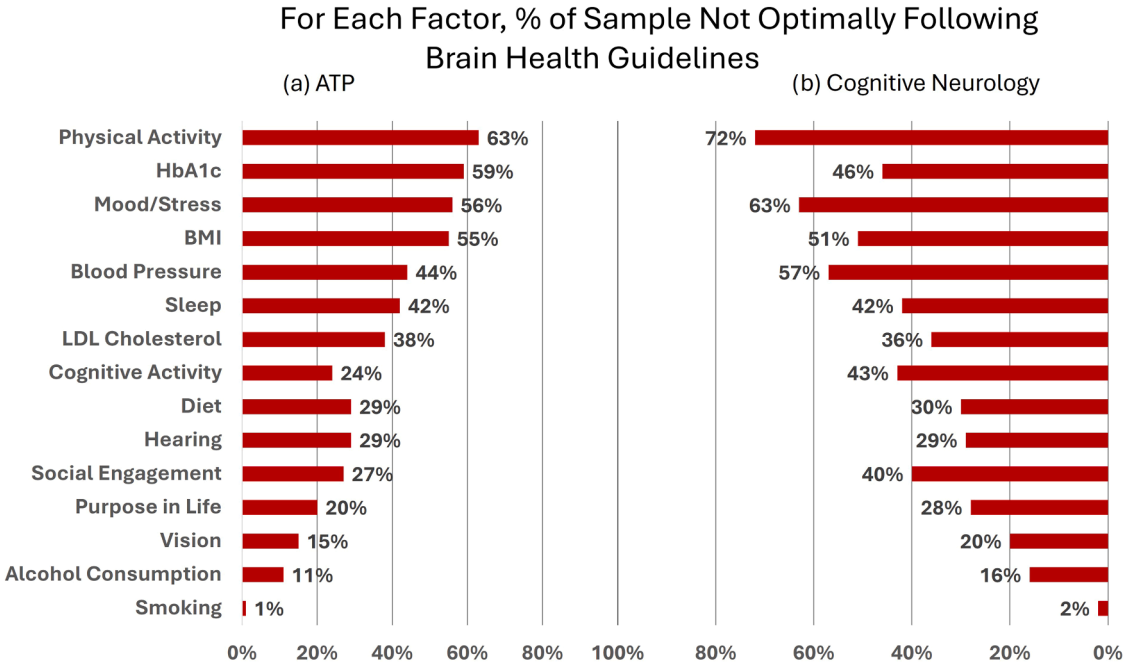


**Fig. 1.** Illustration of the percentage of the a) ATP patient group and b) Cognitive Neurology patient group not optimally following brain health recommendations for each of the 15 factors.

= 2.1 vs. M = 4.7; SD = 2.3, p = .33) or the first 50 vs last 50 patients (M = 4.5; SD = 2.1 vs. M = 4.9; SD = 2.2, p = .36). The average number of factors not being optimally followed did not differ (p = .41) between patients who met all lecanemab therapy eligibility criteria established by the MGB ATP program (n = 142) and patients who met all diagnostic, cognitive, and functional requirements for lecanemab therapy but were later deemed ineligible for treatment for other reasons (n = 8).

### 3.3. Percent of cognitive neurology patient group not optimally following brain health recommendations

Fig. 1**b** highlights the percent of the Cognitive Neurology group *not* optimally following brain health recommendations for each of the 15 factors, which ranged from 72% for physical activity to 2% for smoking. For 12 of the 15 factors, more than 25% of the group for 9 of the 15 factors, more than 35% of patients, and for 4 of the 15 factors, more than 50% of the group were not optimally adhering to brain health guidelines. Like the ATP group, less than 3% of the Cognitive Neurology group were adhering to all brain health recommendations queried. On average, patients in this group did not follow optimal brain health guidelines for 5.4 (SD = 2.3) of the 15 factors. Two-thirds of the group were not adhering to brain health recommendations for 5 or more of the 15 factors, with almost one third (31.6%) not adhering for 7 or more factors (see **Supplemental Figure 5**).

### 3.4. Missing HbA1C and LDL cholesterol data from the EMR records of patients

For the ATP patient group, no data were found in the EMR within the cutoff period used to define missing data (18 months prior to their initial visit) in 42% of patients for HbA1c in and 23% of patients for LDL. For the Cognitive Neurology patient group, no data were found within 18 months of their BHVS enrollment visit in 46% of patients for HbA1c and 25% of patients for LDL. (See **Supplemental Table 1**). There were no differences between groups in the percentage of missing data for HbA1c (p = .60) or LDL (p = .78).

### 3.5. Comparisons between the ATP and cognitive neurology groups

For both patient groups, the same risk factors were among the five factors with the lowest adherence rates (physical activity, mood/stress, HbA1c, blood pressure, BMI), although the exact order differed between groups (Fig. 1). Four of the five factors with the highest adherence rates were the same across patient groups (smoking, alcohol consumption, vision, purpose in life), as were four of the five factors in the middle between the lowest and highest adherence rates (sleep, cognitive activity, LDL cholesterol, diet). Differences between the ATP and Cognitive Neurology patient groups in level of adherence for each factor was examined using the chi-square statistic (i.e., each patient was assigned 0 = suboptimal; 1 = optimal). A Bonferroni correction was applied for 15 comparisons, requiring a value of < .003 for significance. None of the pairwise tests were statistically significant. (Of note, only comparisons for social engagement and blood pressure were significant (p = .013 and p = .021 respectively) before a Bonferroni correction was applied.)

Two-way analysis of variance (ANOVA), with patient group (ATP, Cognitive Neurology) and diagnostic category (MCI, mild dementia) as the independent variables and number of factors being suboptimally followed as the dependent variable revealed no main effect of patient group (p = .30) or diagnostic group (p = .46) and no interaction between patient group and diagnostic group (p = .21). A similar pattern of results emerged when examining percent adherence: no main effect of patient group (p = .10) or diagnostic group (p = .11), and no interaction between the two variables (p = .53).

Regression analysis was conducted to determine variables contributing to the outcome measures (i.e., number of factors suboptimally being followed and percent adherence). The dependent variables included patient group, diagnostic group, age, sex, years of education, MMSE score (or MoCA converted to MMSE), level of financial comfort and missing data for HbA1c alone (n = 64), LDL alone (n = 11), both HbA1c and LDL (n = 53), neither HbA1c or LDL (n = 139). Missing data for level of financial comfort (n = 28) was treated as a fourth category for this factor (i.e., just getting by, reasonably comfortable, very comfortable, and information not available). Missing data for years of education (n = 23) and MMSE (n = 7) were imputed using the multiple-imputation predictive mean matching estimate provided by SPSS.

Table 4 summarizes the models developed, which yielded very similar results for both outcome measures. Importantly, patient group, diagnostic group, age, sex, and MMSE score did *not* contribute to the model. Patients with more years of education had fewer factors suboptimally being followed (p = .005) and higher percent adherence (p = .001). Compared to patients who reported that they were "just getting along financially," patients who were reasonably comfortable, very comfortable, or who did not answer the question had fewer factors suboptimally being followed (p = .029, .059, and .006, respectively) and higher adherence rates (p = .014, .068, and .005, respectively). Patients who were missing values for HbA1c but not LDL had fewer factors being followed suboptimally (p = .002) and higher percentage adherence (p = .012) than patients for whom HbA1c data were available. These findings are consistent with the observation that a high percentage of the patients with HbA1c data were not optimally following guidelines (Fig. 1), which likely had an adverse effect on the group average.

### 3.6. Sensitivity analysis for the subgroup of cognitive neurology patients diagnosed with underlying AD

Although the ATP and Cognitive Neurology groups had similar percentage of patients with MCI and mild dementia, the Cognitive

**Table 4**
Linear regression analyses predicting number of suboptimal factors and percent adherence (*N* = 267).

| | Number of Suboptimal Factors | | | Percent Adherence | | |
|---|---|---|---|---|---|---|
| | β (SE) | [95% CI] | p | β (SE) | [95% CI] | p |
| Clinic Group [ref = Cognitive Neurology clinic] | | | | | | |
| ATP clinic | -.428 (.26) | [−.948 – .092] | .106 | .026 (.01) | [−.0004 – .052] | .054 |
| Diagnosis [ref = MCI] | | | | | | |
| Mild dementia | .274 (.33) | [−.377 – .926] | .408 | -.021 (.02) | [−.054 – .011] | .199 |
| MMSE Scores | -.043 (.04) | [−.119 – .032] | .255 | .002 (.002) | [−.002 – .006] | .34 |
| Age | -.018 (.02) | [−.052 – .016] | .289 | .0002 (.002) | [−.0003 – .001] | .731 |
| Education | -.159 (.06) | [−.27 – −.049] | **.005** | .009 (.003) | [.004 – .015] | **.001** |
| Female | .238 (.26) | [−.279 – .756] | .365 | -.002 (.01) | [−.028 – .024] | .901 |
| Financial comfort [ref = just getting along] | | | | | | |
| Reasonably comfortable | −1.02 (.46) | [−1.93 – −.106] | **.029** | .058 (.02) | [.011 – .104] | **.014** |
| Very comfortable | -.905 (.48) | [−1.84 – .033] | .059 | .044 (.02) | [−.003 – .091] | .068 |
| Did not disclose | −1.63 (.59) | [−2.79 – −.474] | **.006** | .084 (.03) | [.025 – .143] | **.005** |
| Missing Groups [ref = not missing HbA1c or LDL] | | | | | | |
| Missing HbA1c not LDL | 1.01 (.32) | [−1.63 – −.384] | **.002** | .04 (.02) | [.009 – .072] | **.012** |
| Missing LDL not HbA1c | -.747 (.67) | [−2.06 – .563] | .263 | .019 (.03) | [−.047 – .085] | .572 |
| Missing both | -.666 (.35) | [−1.35 – .021] | .057 | -.006 (.02) | [−.041 – .028] | .717 |
| Intercept | 11.52 (1.76) | [8.06 – 14.978] | **.000** | .484 (.09) | [.31 – .657] | **.000** |

***Note.*** Model statistics for the number of suboptimal factors: $F(12, 251.8) = 3.99$, $p<.001$. Model statistics for percent adherence: $F(12, 251.8) = 3.97$, $p<.001$.

Neurology group included patients with non-AD disorders. Within the Cognitive Neurology patient group (n = 117), 62 patients (53%) were diagnosed with MCI or mild dementia due to probable AD and 55 (47%) had MCI/mild dementia due to non-AD conditions (e.g., vascular cognitive impairment, Lewy Body disease, multifactorial). There were no differences between Cognitive Neurology patients diagnosed with AD and those without AD in terms of number of factors suboptimally being followed (p = .61) or percent adherence (p = .68). Comparing the 62 Cognitive Neurology patients diagnosed with AD to the 150 ATP patients all with AD, there were no differences in the number of factors suboptimally being followed (p = .24) or percent adherence (p = .12).

## 4. Discussion

The major goal of this study was to examine the degree to which patients with early AD pursuing anti-amyloid therapy (AAT) are following consensus-based recommendations regarding brain-healthy behaviors and have optimal anthropometric and laboratory values related to vascular and cognitive health. This study utilized data collected for the ongoing Brain Health Vital Signs (BHVS) quality improvement project at our center, aimed at assessing brain health risk factors, providing feedback, and, in the future, offering interventions for patients with or at risk for cognitive disorders.

The most salient finding is that a sizeable portion of individuals with early AD pursuing AAT are not adhering to many brain health recommendations that may reduce their risk of further cognitive decline. For the five factors associated with the lowest adherences rates (physical activity, HbA1c, mood/stress, BMI, and blood pressure), the percentage of the ATP group *not* optimally following recommended guidelines ranged from 63% to 44%. For the next six factors (sleep, LDL cholesterol, cognitive activity, diet, hearing, and social engagement), 42% to 27% of the group were not fully following recommendations for brain health. On average, patients in the ATP group were not adhering to optimal brain health guidelines for approximately five of the 15 factors queried and almost a quarter of this group was not adherent for 7 factors.

We had reasoned that early adopters of AAT for AD might pursue "every avenue" to optimize their brain health and reduce their risk of further decline [39,40]. As such, we wondered whether they would follow overall brain health recommendations more closely than peers, which motivated our comparing them to a similar sample of patients not pursuing AAT in our center. This outcome, however, was not observed. ANOVA, regression analyses, and comparison of adherence to each of the 15 factors using the chi square statistic, demonstrated no robust differences in the degree or pattern of adherence to guidelines between the two groups. Both groups demonstrated the lowest adherence rates for the same five risk factors, and there were no statistically significant differences in the number of factors being optimally followed or the percent adherence.

Although there may have been undetected and meaningful group differences, and our descriptive study was not designed to make causal inferences, the results' main message seems clear: a substantial number of cognitively impaired older patients who are receiving specialty care are not following consensus-based brain health guidelines. The reasons why both groups in this study had low adherence to brain health recommendations are likely myriad. These may include patient (and care partner) lack of knowledge regarding the strong connection between lowering brain health risk factors and slower decline in early ADRDs, the difficulties adopting healthier behaviors due to typical barriers preventing positive behavior change (e.g., poor motivation, time constraints, financial limitations [41,42],) and the sub-optimal management of medical conditions and other modifiable risk factors by the patients' broader care team [43–45].

We do not believe that the study's main findings that our patients with early AD have sub-optimal adherence to brain health guidelines is due to cognitive impairment that reduces their ability to carry out recommendations. If this were the case, one might expect lower adherence rates in patients with mild dementia than in those with MCI, which we did not observe. We suspect that behaviors reported by our patient groups reflect long-standing habits that individuals developed prior to the onset of MCI or mild dementia.

An unexpected finding was the large percentage of patients for whom there were no data in the EMR for HbA1c (>42% for both groups) and LDL (>23% for both groups) for at least 18 months prior to survey completion. One hypothesis about this finding is that the routine evaluation of patients organized by many dementia specialists may not include checking if patients have current HbA1c and LDL lab results and/or ordering them if missing. We would advocate that dementia specialists assess whether up-to-date HbA1c and LDL values are available in the EMR, and if not, order the appropriate test(s). If abnormal values are discovered, the specialist could either pursue further evaluation and treatment or communicate with a patient's other providers to manage the underlying condition.

### 4.1. Limitations and concerns

#### 4.1.1. Population-based evidence vs. prospective brain health interventions

Brain health recommendations most often reflect robust, population-based information about risk factors [7,25,46,47]. There is much less certainty about the effect of brain-healthy behaviors on disease occurrence or slowing of decline on an individual level. Importantly, despite this uncertainty, many clinicians and health organizations strongly recommend adopting brain-healthy behaviors in patients at risk for cognitive decline as well as those already exhibiting cognitive impairment and dementia. There is evidence suggesting the benefit of intensive blood pressure control [48], as well as multimodal interventions for cognitively normal patients at increased risk of cognitive decline and dementia. For example, the FINGER and US POINTER studies demonstrated statistically significant effects on changes in behavior, cognition, and measures of metabolic and vascular health [49–51].

There has been less research on the impact of adopting brain-healthy behaviors in patients who already have a diagnosis of MCI or mild dementia. As noted in the Introduction, numerous published clinical guidelines [13–16] and reviews [17,18] advocate that modifiable risk factors be addressed in patients with MCI and mild dementia. There is evidence that optimizing healthy behaviors and managing metabolic and vascular disease in such patients may slow cognitive and functional decline [11,12]. Several small exercise or multimodal intervention studies have demonstrated maintenance or improvement of cognitive function, cardiorespiratory fitness, and/or physical health in patients with MCI [52–57]. Of note, in a recent study of 51 patients with MCI or mild dementia due to AD, those who were randomized to 20 weeks of an intensive lifestyle modification intervention exhibited improvement in cognitive and functional status, whereas the usual-care control group demonstrated declines [55].

#### 4.1.2. Challenges regarding accurate measurement and specific cutoff scores used

One limitation of our study is uncertainty about the accuracy of the survey-collected data. Eleven of 15 factors relied on patient self-report rather than more objective measures. Patients may miscalculate the frequency of their participation in, for example, cognitive, social or physical activity or the average number of hours in which they sleep. Self-report is also vulnerable to recall and social desirability biases, an issue that is not unique to our survey but applies to other similar ones (e.g., Brain Care Score, LIBRA2) [25,58,59]. These kinds of biases seem likely to yield an overestimate by patients of their degree of adherence to brain-healthy behaviors.

Concerns can also be raised about the more objective data from the EMR, as, for example, blood pressure measurements may not have been taken in accordance with standardized procedures [60]. Moreover, we used a single reading of a patient's systolic blood pressure (SBP), which may have yielded misleading results. To help address this concern, we

randomly selected 20 ATP patients and found two previous BP readings in the patient's EMR that had been taken closest to the single value we used. We then averaged the SBP over the three readings and used that value for comparison. We found no difference in the group's mean SBP between the single reading (M = 134; SD = 18) and average reading (M = 135; SD = 8, p = .63). Also, the calculated mean overall adherence rates across all factors for these 20 patients did not differ when using the single versus averaged SBP value. At the individual patient level, concerning BHVS scores should be viewed as a "starting point," signaling potential red flags that may require additional attention from patients and/or their providers. Importantly, limited adherence to brain health recommendations should not automatically be interpreted as reflecting a lack of effort. For example, although in many cases suboptimal vision in patients can be improved by updating the prescription for their glasses or undergoing cataract surgery, in other cases, such as severe macular degeneration, options for addressing vision loss may be very limited.

We recognize that for some brain health risk factors, the specific cutoff values we used to assign points for level of adherence are subject to debate. A similar criticism can be made of the scoring systems of other brain health indices, used as both clinical and research tools (e.g., Brain Care Score, LIBRA2) [25,58]. For example, our scoring rules for alcohol consumption approximated published guidelines from the CDC [32]; the lowest (least) adherence score (0 points) was given for women having ≥8 drinks/week and men having ≥15 drinks/week. However, there has been growing evidence that any amount of alcohol consumption can be injurious to the brain [61]. As another example, we set the optimal level of LDL cholesterol at <100 mg/dL based on National Cholesterol Education Program guidelines in the U.S., but are aware that for patients with other cardiovascular risk factors or a history of coronary artery disease, sometimes considered "high risk" or "very high risk," the goal should be lower (e.g., <70 mg/dL [34,35]. In terms of blood pressure, we followed suggestions by the International Society of Hypertension and designated SBP<130 as being normal [36]. However, blood pressure guidelines are evolving as a reflection of the growing evidence for the additional benefit of a SBP goal of <120 mmHg, particularly in high-risk populations. Thus, an even larger percentage of our groups would have been classified as not adhering to guidelines if we had used more stringent thresholds for optimal values.

#### *4.1.3. Challenges to generalizing study results across populations*

The sociodemographic characteristics of the patient group being evaluated for AATs in our program are not representative of the overall U.S. or global populations. This challenges the generalizability of our findings about adherence to brain health recommendations among patients with early AD. Our sample was nearly all white, highly educated, and financially comfortable. Nonetheless, this sociodemographic profile overlaps with that of patients in the ALZ-NET registry in the U.S., which is tracking patients being considered for or receiving AATs [62]. This restricted sociodemographic profile, shared by the ALZ-NET cohort and ours, raises broader and critical questions about social and structural barriers that are interfering with early diagnosis of patients and access to new AD therapeutics for all [19,63].

We suspect that patient groups more representative of the US population socioeconomically would have lower adherence rates than found in our study. Research suggests that, generally, higher income and education are associated with greater adoption of healthy behaviors [46,64]. Consistent with this finding, we observed that patients who reported "just getting by" financially and those with fewer years of education were less successful at following brain health guidelines presumably because of facing greater barriers to an optimal, brain-healthy lifestyle. Brain health assessment efforts like BHVS need to include patients from a wide, representative range of socioeconomic statuses, geographic origins, and race and ethnicities to fully account for how sociodemographic factors might impact adherence to brain health recommendations, and, ultimately, patient motivation and clinician success with improving targeted behaviors.

Our aim was to describe adherence to recommendations regarding some risk factors for cognitive decline within a sub-population of MCI and mild dementia patients. Cross-sectional, descriptive studies like ours cannot address many important, clinically relevant questions. Longitudinal studies are necessary to determine whether limited adherence to brain health guidelines precedes cognitive decline and whether pursuing AATs changes behavior and lifestyle choices. More research is needed to ascertain the BHVS program's effectiveness in facilitating discussions between patients and their clinicians, increasing awareness about brain health and the patient-specific modifiable dementia risk factors that need attention. Well-designed, controlled studies are required to determine the most efficacious and cost-effective ways to facilitate changes in behavior and to evaluate whether patients seeking AATs who are more adherent to consensus-based recommendations exhibit slower cognitive and functional decline.

## 5. Conclusion

In summary, for many patients with early ADRDs, a significant gap persists between available knowledge about the benefits of following consensus-based, brain health recommendations and the real-world adoption and maintenance of brain-healthy behaviors and optimal anthropometric and lab values. The Brain Health Vital Signs (BHVS) project is a protocol embedded within clinical care for assessing brain health risk factors. It is aimed at narrowing this "implementation gap" for patients within health systems. The reasons for this gap are complex, and solutions must meaningfully address the numerous social, structural and psychological barriers that hinder the achievement of optimal brain health for all [65–67]. Our study highlights that even among AD patients who by seeking novel AATs demonstrate a strong commitment to doing what is in their power to help preserve cognitive and functional status, we find that suboptimal adherence to brain health recommendations is extremely common. Evidence and expert consensus suggest that a combination of pharmacological and non-pharmacological (behavioral) interventions may be the most promising approach to successfully treat early AD patients [68–70].

Healthcare systems are funding expensive disease-modifying pharmacological therapies. Our findings, especially if confirmed by additional research, suggest that it may be time for them to increase their investment in developing more effective, system-wide strategies and tangible, individualized interventions for addressing modifiable risk factors for cognitive decline and dementia for all patients under their care. In addition, more efficacious procedures are needed to ensure that relevant, actionable data associated with brain health are collected and updated in the EMR.

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## Consent statement

The MGB institutional review board (IRB) reviewed the BHVS project and determined that informed consent and ongoing regulatory oversight were not required, as it was developed as a patient quality improvement program.

## Data statement

De-identified data are available upon request.

## Declarative AI use statement

The authors used no generative AI or AI-assisted technologies in the manuscript preparation process.

## CRediT authorship contribution statement

**Kirk R Daffner:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Conceptualization. **Kayla Riera:** Writing – original draft, Project administration, Formal analysis, Data curation. **George R Ghorayeb:** Formal analysis, Data curation. **Brittany M McFeeley:** Writing – review & editing, Project administration, Formal analysis. **Emma Weizenbaum:** Writing – review & editing. **Kim Willment:** Writing – review & editing. **Seth A Gale:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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## Supplementary materials

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