Diagnoses associated with dietary supplement use in a national dataset

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ABSTRACT

Objectives: The purpose of this study was to determine if participant diagnosis, as determined by a health care provider, is associated with dietary supplement (DS) use.

Design/setting: Surveys from 1255 study participants aged 34–84, part of the Midlife in the US Study (MIDUS 2 Survey) Biomarker Project, were reviewed. Participant data included pharmaceutical use (prescription and over-the-counter medications (OTC)), clinical symptoms and diagnosis, and laboratory results. Associations were calculated between the above participant characteristics and DS use.

Main outcome measures: Frequency of DS use for physician-reported diagnoses.

Results: Overall prevalence of DS use was 32.4%. Participants taking DS were more often female (p=.048), white (p < 0.001), and older (mean age 57 years, p < 0.001). Participants taking DS reported taking more OTC (p < .001) and prescription medications (p=.024), and had an increased number of chronic conditions (p = .004). Participants reporting physician-diagnosed diabetes were significantly less likely to be taking DS (p = .0066), while participants with eye disease (p = .001), high cholesterol (p=0.041), cancer (p=0.042), and arthritis (p = 0.044) were more likely to be taking DS than those without those conditions. No difference in DS use was found between patients with and without other identified medical conditions. After adjusting for age, race/ethnicity, and gender, only diabetes remained a significant predictor of decreased DS use (OR 0.588, CI 0.388-0.873, p=.01).

Conclusions: Some physician-reported participant diagnoses were associated, positively or negatively, with DS use.

1. Introduction

Integrative health (IH), defined by the National Institutes of Health’s (NIH) National Center for Complementary and Integrative Health (NCCIH), involves the incorporation of “…complementary approaches into mainstream healthcare.”¹ There are a variety of treatment modalities that fall under the umbrella of IH in the United States, including the use of dietary supplements (DS). A DS is a product that is taken by mouth and can contain any of the following ingredients: vitamins, minerals, herbs or botanicals, amino acids, or other substances intended to supplement the diet.²³ Among IH treatments, DS use is consistently one of the most common.⁴ For instance, as per the 2012 National Health and Nutrition Examination Survey (NHANES), up to 52% of the US population reported using DS in the past 30 days.⁵ With respect to economics, the total US expenditure for IH treatments is estimated at $30.2 billion, including $12.8 billion for DS.⁶

The medical literature details many aspects of DS use. For example, national trends of DS use seem to indicate an increase in DS use, with the second highest rate of growth (7.7%) in over a decade documented in 2016.⁵⁻⁶ Of note, even among data that report stable trends of use, there is an annual variability in the popularity of individual DS.⁴⁸ With respect to demographics of DS users, there was an increase in use between 1999–2012 in those 65 and over, but a decrease among those 40–64 years old.⁵ There is some agreement that DS use is more common in some ethnicities (non-Hispanic white) than others⁹ and among women more than men.¹⁰

While the demographics of DS users remain fairly consistent across traditional medical literature, there remains discrepancy about the conditions DS users have and the reasons why they may choose to use DS.¹¹ With respect to diagnoses, adults with multiple chronic conditions (including...
hypertension, CAD, high cholesterol, cancer, diabetes, lung disease, arthritis, and depression) may be more likely to use multivitamins, vitamins, minerals, and non-vitamin or herbal therapies compared to adults without chronic conditions. Other studies have found that those with chronic but not life-threatening conditions were more likely to use DS compared to those with chronic and life-threatening conditions. However, an analysis of the 2007–2010 NHANES reported the most common reasons for using DS were to “improve” or “maintain” overall health and found that organ-specific health reasons were less frequently reported as motivators to use DS. Further research is needed to understand the association of certain conditions with DS use as it pertains to disease prevention and treatment.

With respect to DS documentation, previous studies have prompted study participants choose the type of DS from pre-made lists without the opportunity for the participant to record their particular DS. Furthermore, specific combination products, brand names, or DS dose relevant to actual use may be lacking. There are some concerns that these methodologies for DS documentation may have limited research generalizability, and some experts are recommending a more complete description of DS use to provide standardization among DS studies.

The MIDUS longitudinal study is a national survey intended to investigate the consequences of behavioral and psychosocial factors on health. The Biomarker Project of MIDUS 2 contains data from 1255 participants with clinical and biological assessments added to the medical history questionnaire of a subsample of respondents. The advantages of the MIDUS Biomarker Project include exploration of both self-reported diagnoses and those that originated with the participants’ health care provider. The database includes clinical assessments and laboratory data lending an additional layer of credibility to the information collected. Furthermore, with comprehensive DS use data collected from observation and recording the exact DS by research staff during site visits, there is a level of detail about the specific DS products being used that extends beyond prior studies. Overall, the goal of this study was to utilize the depth of information present in the Midlife in the United States (MIDUS) 2 Biomarker Project database to look for trends in DS use with a focus on participant diagnoses.

2. Methods

2.1. MIDUS 2 project 4 description

The Biomarker Project of MIDUS 2 contains data from 1255 respondents from 2004–2009. These respondents include two distinct subsamples, all of whom completed the Project 1 Survey: (1) longitudinal survey sample (n = 1054) and (2) Milwaukee sample (n = 201). The purpose of the Biomarker Project was to add comprehensive biological assessments on a subsample of MIDUS respondents, thus facilitating analyses that integrate behavioral and psychosocial factors with biology. A complete description of the MIDUS project and methodology is available in prior publications. To augment the self-reported data collected in the MIDUS survey project, participants completed a medical history, self-administered questionnaire, and self-reported sleep assessments (see below).

2.2. Dietary supplement collection and charting

Respondents were instructed to bring all their medications (prescription and OTC) and DS, in the original bottles, to the inpatient study site for review by study personnel. See Table 1, below, for relevant information regarding the three categories documented. Of note, “alternative medicines”, or “Alt Med”, included non-vitamin, non-mineral DS; vitamins and minerals were included under the OTC category in MIDUS.

During the inpatient study visit the research staff recorded medication information including medication name, dosage, frequency and route of administration, and how long the participant has been taking a given medication. In addition, each study participant was asked about their reasons for using a medication on a questionnaire “Why are you taking it?” and responses to this question were recorded verbatim. Standardized protocols as outlined in “Documentation for MIDUS and MIDJA Medication Data” were then applied to code text data describing reasons why participants think they are taking a given medication. Many participants were able to name specific conditions or diseases, but others gave more general responses such as “general health” or “bone health”. Each response was coded into two mutually exclusive sets of categorical codes based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) or a MIDUS code. The MIDUS code utilizes key words and common phrases in participant responses to form a standardized code label for each response. A separate MIDUS Biomarker Project Medical History questionnaire was also used that asked each participant about their extensive medical history including symptoms and conditions. If a participant had a certain symptom or condition, they were asked if it was or was not diagnosed by a physician.

2.3. Statistical analysis

Data were extracted from the MIDUS database to determine the associations between participant characteristics and DS use. Participants taking all DS were identified by the variable B4XAM (number of alternative medications). Participant characteristics considered were doctor diagnosed diseases (heart disease, high blood pressure, anemia, high cholesterol, diabetes, asthma, cancer, arthritis, depression, thyroid disease, glaucoma, and other eye disease), health characteristics (BMI, number of chronic conditions, smoking status), prescription and OTC medication usage, and demographic information (age, gender, white or non-white race).

In an unadjusted analysis, patients were stratified by whether they were taking at least one alternative medication or none. Chi-square tests were used to determine associations between categorical variables and alternative medication use. The Mann-Whitney-Wilcoxon test was used to compare continuous numerical variables and alternative medication use. Despite the high number of unadjusted tests (27 tests), no p-value correction for Type I error rates were applied. When overall significance was found for a variable with more than two categories,
post-hoc analysis was conducted using tests of proportions and correcting the p-value using the Bonferroni method.

The probability of taking an alternative medication with and without one of the doctor diagnosed diseases was reported along with 95% Agresti-Coull confidence intervals.

Adjusted models were fit to determine the association between taking alternative medications and each of the eleven doctor diagnosed conditions while adjusting for age, race (white or non-white), and gender. Estimated odds ratios with 95% confidence intervals and p-values from these models are reported. Significance was assessed with a type 1 error rate of 0.05.

Statistical analysis was performed with R 3.4.3 using the binom package, 1.1-1 by Sundar Dorai-Raj (https://CRAN.R-project.org/package=binom) to calculate confidence intervals.

3. Results

Records from 1255 study participants were extracted. The overall prevalence of participants who take DS was 32.4% (95% Agresti-Coull CI 29.9–35.1), equivalent to an odds of 0.48 (CI 0.426-0.540).

Demographics and diagnostic differences between users and nonusers of DS are listed in Table 2. Participants taking DS tended to be older (p < 0.001), female (p = 0.041), and white (p < 0.001). Participants taking DS reported taking 2.20 supplements on average, and took more OTC (p < 0.001) and prescription medications (p = 0.024) than participants with no DS. DS use was associated with the number of chronic conditions (p = 0.004), but not with body mass index (p = 0.078). Furthermore, an association was found between DS use and tobacco use (p < 0.001); participants taking DS were less often current smokers (6.14%–19.2%, p < 0.001), but there was no difference observed for former smokers (37.1%–30.4%, p = 0.055) or never smokers (56.8%–50.4%, p = 0.100).

With respect to laboratory values (see Table 3), DS users had higher HDL (median 55 to 52, p = 0.017) and lower glucose values (median 96–97, p = 0.018). No difference was found in HbA1c (p=0.212), total cholesterol (p=0.124), triglycerides (p=0.184), LDL (p = 0.403), CRP (p = 0.057), and insulin (p = 0.051).

3.1. Dietary supplement use and diagnosis

With respect to diagnoses, significantly increased DS use was found among participants with eye disease (including glaucoma), cancer, elevated lipids, and arthritis, though these trends were found to be non-significant with the adjusted statistical analysis. Although study participants with physician-diagnosed elevated lipid levels showed borderline increased DS use (unadjusted), there was no difference in mean total cholesterol or triglycerides lab values between groups, though there was higher HDL (median 55 to 52) and lower glucose (median 96–97) amongst DS users.

Table 2
Demographics and health characteristics of DS users and non-users and users of dietary supplements.

<table>
<thead>
<tr>
<th>Measure</th>
<th>No DS</th>
<th>DS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>848</td>
<td>407</td>
<td></td>
</tr>
<tr>
<td><strong>Demographics (count (%))</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race, white</td>
<td>626</td>
<td>352</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Never</td>
<td>427</td>
<td>231</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Current</td>
<td>163</td>
<td>25</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Former</td>
<td>258</td>
<td>151</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Gender, female</td>
<td>465</td>
<td>246</td>
<td>0.041</td>
</tr>
<tr>
<td><strong>Demographics (mean (sd))</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>53.34 (11.74)</td>
<td>56.98 (11.27)</td>
<td>0.004</td>
</tr>
<tr>
<td>BMI</td>
<td>29.98 (6.78)</td>
<td>29.32 (6.28)</td>
<td>0.078</td>
</tr>
<tr>
<td>Chronic conditions</td>
<td>0.92 (1.29)</td>
<td>1.13 (1.39)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Medications (mean (sd))</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DS</td>
<td>2.20 (2.18)</td>
<td>3.22 (2.18)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>OTC</td>
<td>1.68 (1.71)</td>
<td>2.98 (2.94)</td>
<td>0.024</td>
</tr>
</tbody>
</table>

3.2. Laboratory values

<table>
<thead>
<tr>
<th>Measure</th>
<th>No DS</th>
<th>DS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>185.50</td>
<td>188.88</td>
<td>0.124</td>
</tr>
<tr>
<td>CRP</td>
<td>3.18 (5.04)</td>
<td>2.70 (4.16)</td>
<td>0.057</td>
</tr>
<tr>
<td>Glucose</td>
<td>104.06</td>
<td>98.12</td>
<td>0.018</td>
</tr>
<tr>
<td>HDL</td>
<td>54.60 (17.78)</td>
<td>56.97 (18.28)</td>
<td>0.017</td>
</tr>
<tr>
<td>LDL</td>
<td>104.82</td>
<td>127.25</td>
<td>0.184</td>
</tr>
<tr>
<td>HDL</td>
<td>54.60 (17.78)</td>
<td>56.97 (18.28)</td>
<td>0.017</td>
</tr>
<tr>
<td>Glucose</td>
<td>104.06</td>
<td>98.12</td>
<td>0.018</td>
</tr>
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<td>HDL</td>
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</tr>
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</tr>
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<td>54.60 (17.78)</td>
<td>56.97 (18.28)</td>
<td>0.017</td>
</tr>
</tbody>
</table>

4. Discussion

The current analysis both supports and adds to the past literature on DS use. In the MIDUS 2 dataset, higher DS use was seen in study participants who were white, female, of an older mean age, nonsmokers, and who also used OTC and prescription medications. This is not dissimilar from an oft-referenced national study, the 2012 NHANES, which found DS users to be healthy individuals who were older, non-Hispanic white, reported lower alcohol use, and were nonsmokers. Other studies have corroborated the correlation between DS use and the use of OTC and prescription medications.

With respect to diagnoses, significantly increased DS use was found among participants with eye disease (including glaucoma), cancer, elevated lipids, and arthritis, though these trends were found to be non-significant with the adjusted statistical analysis. Although study participants with physician-diagnosed elevated lipid levels showed borderline increased DS use (unadjusted), there was no difference in mean total cholesterol or triglycerides lab values between groups, though there was higher HDL (median 55 to 52) and lower glucose (median 96–97) amongst DS users.

Table 3
Summary statistics and associations of physician-diagnosed conditions between users and non-users of dietary supplements.

<table>
<thead>
<tr>
<th>Measure</th>
<th>No DS</th>
<th>DS</th>
<th>Unadj. p-value</th>
<th>Adj. p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physician diagnosed conditions (count (%))</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart disease</td>
<td>93 (0.5)</td>
<td>52 (0.3)</td>
<td>0.348</td>
<td>0.992</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>305 (1.5)</td>
<td>154 (0.8)</td>
<td>0.519</td>
<td>0.987</td>
</tr>
<tr>
<td>Liver disease</td>
<td>19 (0.1)</td>
<td>9 (0.0)</td>
<td>0.974</td>
<td>0.884</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>97 (0.5)</td>
<td>58 (0.3)</td>
<td>0.156</td>
<td>0.876</td>
</tr>
<tr>
<td>Cancer</td>
<td>104 (0.5)</td>
<td>67 (0.3)</td>
<td>0.042</td>
<td>0.663</td>
</tr>
<tr>
<td>Depression</td>
<td>161 (0.8)</td>
<td>84 (0.4)</td>
<td>0.489</td>
<td>0.469</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>35 (0.2)</td>
<td>13 (0.1)</td>
<td>0.420</td>
<td>0.254</td>
</tr>
<tr>
<td>Arthritis</td>
<td>270 (1.3)</td>
<td>153 (0.8)</td>
<td>0.044</td>
<td>0.241</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>338 (1.7)</td>
<td>187 (0.9)</td>
<td>0.041</td>
<td>0.224</td>
</tr>
<tr>
<td>Diabetes</td>
<td>117 (0.6)</td>
<td>72 (0.4)</td>
<td>0.071</td>
<td>0.179</td>
</tr>
<tr>
<td>Eye disease</td>
<td>179 (0.9)</td>
<td>122 (0.6)</td>
<td>&lt; 0.001</td>
<td>0.089</td>
</tr>
<tr>
<td>Asthma</td>
<td>97 (0.5)</td>
<td>57 (0.3)</td>
<td>0.195</td>
<td>0.053</td>
</tr>
<tr>
<td>Diabetes</td>
<td>121 (0.6)</td>
<td>36 (0.2)</td>
<td>0.007</td>
<td>0.010</td>
</tr>
</tbody>
</table>

(36.2%–30.5%, p = 0.047), compared to study participants without those conditions. No difference in DS use was found between study participants with or without heart disease (p = 0.348), high blood pressure (p = 0.519), anemia (p = 0.071), asthma (p = 0.195), glaucoma (p = 0.420), liver disease (p = 0.974), depression (p = 0.499), or thyroid disease (p = 0.156). After adjusting for age, race, and gender, only diabetes remained a significant predictor of alternative medication use (Fig. 2). Patients with diabetes had a 0.588 times lower odds of taking alternative medications than patients without diabetes of the same age, race, and gender (CI 0.388-0.873, p = 0.01).
diagnosis; normal laboratory values could indicate controlled pathology, or, alternatively, a misdiagnosis. Further analysis of the dataset could help to differentiate the laboratory variables most likely to indicate disease or diagnoses, and most strongly associated with DS use.

The case of physician-diagnosed cancer and borderline, unadjusted, correlation with DS use was less than would have been expected based on the literature. Per the 2012 NHIS, cancer survivors were more likely to report using vitamins and minerals (75% vs. 61%, \( p < .001 \)), as well as non-vitamin/mineral natural products (24% vs. 19%, \( p < .001 \)). The Breast Cancer Quality of Care (BQUAL) Study identified breast cancer patients as the highest users of complementary and alternative medicine among all types of cancer. They found the prevalence of CAM use to be 87% among patients with dietary supplements used in 70% of patients. The current iteration of the MIDUS dataset did not differentiate those participants currently undergoing cancer treatment versus previous cancer diagnosis and treatment. It is not unfathomable, given themes in the medical literature regarding DS safety in oncological cases, that patients undergoing cancer treatment may be dissuaded from DS use by their oncology providers due to potential interactions with conventional treatments.

The only truly significant finding when adjusting for gender, age, and race/ethnicity was a decreased DS use among study participants with physician-diagnosed diabetes. There was, however, no clinically significant difference in mean A1C between DS users and nonusers, potentially indicating that people in this study with diabetes had adequate glycemic control. The lack of an association with DS use, though, is perplexing given that research findings have shown that people with diabetes may use medicinal plants either in association or instead of

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**Fig. 1.** Rates of DS use for participants with and without each of the eleven physician-diagnosed diseases with illustrated 95% confidence intervals and Chi-square \( p \)-values.

**Fig. 2.** Adjusted odds ratios of taking DS between participants with and without each physician-diagnosed disease.
conventional physician-prescribed treatments. The Medical Ex-
Funding sources

interest

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References

5. Conclusions

Participants reporting physician-diagnosed diabetes were sig-
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Declarations of interest

None.

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