

Natural Product Use for Chronic Pain: A New Survey of Patterns of Use, Beliefs, Concerns, and Disclosure to Providers

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Abstract

Background: “Natural products” (NPs), including dietary supplements, are widely used, yet little is known about NP use for chronic pain and related conditions.

Objective: To develop a new NP survey to better understand reasons for NP use, beliefs, concerns, medication substitution, and provider disclosure.

Methods: Based on similar surveys and input from veteran focus groups and subject matter experts, a new brief NP survey was developed. The survey was piloted among 52 veterans with chronic pain enrolled in Veterans Health Administration (VA) primary care who endorsed NP use at baseline in a pragmatic trial comparing non-drug pain management approaches. Survey data was enriched with sociodemographic and clinical data from a parent trial. Descriptive frequencies and means were calculated.

Results: Of 55 surveys, 52 were completed (response rate, 94.5%). Respondents’ mean age was 57.6 (SD+/-12.5); 42% were women, 21% identified as Black/African American, and 10% Hispanic/Latinx ethnicity. All had chronic pain; 80% experienced disabling pain daily; 67% were prescribed non-opioid pain medication; 15% were prescribed opioids. In the prior 3 months, the mean number of NPs used was 4.6 (SD+/-3.2); 90% reported daily use. Most frequently used NPs were vitamins/minerals (94%), herbals/botanicals (60%); and cannabis (40%); one-third reported substituting NPs for pain medications. The majority endorsed safety concerns about interactions of NPs either with pain medications (55%) or other NPs (52%). Nearly all (98%) believed providers should discuss NP use with their patients, though only 52% had disclosed NP use to their providers.

Conclusions: Among veterans with chronic pain in VA primary care enrolled in a pragmatic trial, a new NP survey revealed prevalent use of multiple NPs concurrently, and in some cases, as substitutes for prescribed medications. Most veterans expressed safety concerns, yet a significant proportion reported not discussing NP use with their providers.

Keywords

dietary supplements, veterans, chronic pain, survey methodology, patient safety

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U.S. Veterans experience high rates of chronic pain with upwards of 60% of veterans reporting 1 or more chronic pain conditions.^{1,2} Moreover, a disproportionate burden of comorbid mental health problems in veterans with chronic pain has been associated with a high prevalence of prescription opioid use and adverse outcomes.³ Thus, recent data and expert consensus have led healthcare systems, including the Veterans Health Administration (VA), to recommend non-pharmacological therapies (e.g., Cognitive Behavioral Therapy, exercise) and complementary and integrative health (CIH) approaches (e.g., yoga, mindfulness), as first line treatments for chronic pain.^{4,5} Natural products (NPs) are the most frequently used form of CIH in the U.S., and are often used alone or in combination with medications among those with chronic pain.^{6,7} Over half of U.S. adults and >70% of U.S. military service members report using NPs.^{8,9}

U.S. retail sales of NPs have increased steadily over the past 2 decades.¹⁰ NPs are non-pharmaceutical substances used to promote health and wellness or for symptom management.¹¹ NPs include dietary supplements (i.e., multivitamins, fish oil), and foods or liquids (i.e., herbal teas and tinctures). NPs may be applied topically (i.e., creams, gels, oils), or inhaled (i.e., aromatherapy). Some low to moderate quality studies indicate that NPs may reduce various pain-related symptoms either through direct effect or as a placebo.^{12,13} Although NPs are generally regarded as safe by patients, side-effects and drug-NP or NP-NP interactions exist.¹⁴⁻¹⁶ NPs are not subject to the same regulatory oversight as drugs regulated by the U.S. Food and Drug Administration, labeling may be misleading,¹⁷ and some NPs contain toxic adulterants.¹⁸ Thus, patient-provider communication is important in ensuring patient safety.

Moreover, patients may not disclose NP use to clinicians,¹⁹ and clinicians and pharmacists do not typically inquire,²⁰ despite reports of NP substitution for medication, adverse side-effects in patients with chronic conditions, and potential medication interactions.²¹ Overall, little is known about the frequency, duration, type, and patterns of NP use, as well as beliefs, attitudes, concerns, and disclosure to health care providers.

Although publicly available national surveys collect information on NPs among U.S. civilians, (i.e., The National Health and Nutrition Examination and the National Health Interview Surveys),²² neither is specific to NP use for chronic pain and co-occurring conditions.²³ Moreover, these population-based surveys are lengthy, and require direct input of product labels or selection of items from long lists of products, which may not be feasible for clinical settings or pragmatic trials.

Given that VA-enrolled veterans with chronic pain are increasing encouraged to taper opioids,²⁴ continued and

expanded use of NPs to self-manage pain and related conditions is likely.²⁵⁻²⁷ However, there are no recent studies that describe the use of NPs for pain management and related symptoms. This study was conducted as a supplement to an ongoing multi-site pragmatic trial, the “wHOPE study,” that compares 2 active non-pharmacological pain management approaches delivered by VA clinicians for veterans enrolled in VA primary care with moderate to severe chronic pain.²⁸ This study aimed to develop and pilot test a brief survey about NP use in veterans with chronic pain that could be used in the ongoing wHOPE trial and potentially, for broader application in other research and clinical care settings.

Methods

Natural Products Survey Development

Between November 2020 and June 2021, our team iteratively developed a new survey to inventory and describe NP use in individuals with chronic pain. First, 2 of the study investigators (KS and TF) with prior training and/or clinical experience in NPs created an initial self-administered paper survey based on their working knowledge of the most frequently used and commercially available NPs for pain. Because chronic pain is typically accompanied by sleep disturbance, stress, depression, PTSD, or anxiety,^{29,30} items assessing NP use for these co-occurring conditions were included.

Next, standing Veteran Engagement Panels (consisting of ≤5 veterans each, not participating in the wHOPE trial) were convened at 2 wHOPE study sites [San Francisco VA Health Care System (SFVAHCS) and VA Connecticut Health Care System] to provide preliminary feedback. All veterans completed this initial survey within 30 minutes, endorsed the importance of asking about NP use for pain, including the use of cannabis, and offered minor formatting and wording suggestions to improve readability and comprehension.

Based on this preliminary feedback, aspects of the survey's appearance, comprehensibility, and content were revised. Next, subject matter experts (SMEs), including 6 researchers and clinicians from across the U.S. with prior experience in NP-related clinical care, survey development, and clinical research were identified. SMEs first individually reviewed the survey and provided written feedback. Next, the study team (KS, TF, and NP) facilitated a group virtual feedback session. SMEs recommended (1) including questions about combination NPs (as opposed to only single vitamins, minerals, or other NPs), (2) narrowing the list of NPs to those primarily used to manage pain, and (3) providing open text response fields for veterans to write in other NPs used. SMEs also provided specific recommendations to

clarify terminology, survey instructions, layout, and administration format.

After making revisions based on SME input and obtaining human subjects approval from the University of California, San Francisco, 13 veterans from the SFVAHCS (not participating in the wHOPE trial) were purposively sampled to participate in 2 separate virtual focus groups composed of roughly 20% female, 20% non-White, and 20% < age 50 to provide representative end-user feedback on the revised draft survey. Prior to the focus groups, veterans were mailed the paper survey, completed it, and provided written feedback about the survey. During the subsequent focus groups veterans recommended that (1) the purpose of the survey be stated upfront, including its relevance to veteran health, (2) “general health” be added as an optional indication for NP use, and (3) clarification be added to ensure respondents disclosed all NPs used, not just those provided by the VA. Veterans were compensated \$50. After further revisions were made based on these suggestions, both a paper NP survey for self-administration and an online version created in REDCap for staff administration by phone were finalized.³¹ Based on focus group and internal testing, the finalized NP survey required 15-20 minutes to complete. The finalized versions and protocol for administration within the wHOPE parent study were approved as an amendment to the existing VA Central Institutional Review Board protocol.

Natural Products Survey

The finalized paper survey was designed for self-administration and self-report. The survey instructed respondents to gather all NPs used in the prior month and refer to them while completing the survey. The survey contained the following 42 items color coded for readability and to facilitate response entry: Natural product(s) used in the last 30 days including multiple vitamins, mixed B vitamins, single vitamins or minerals, single herbal products (e.g., green tea), non-vitamin NPs (e.g., fish oil/omega-3), cannabis (THC- or CBD-predominant, roughly equal, unknown), other NPs used in the past month, and home remedies. Other NPs and home remedies include NPs with multiple ingredients (other than multivitamins and mixed B vitamins), and respondents were instructed to write in name and brand. For each of these items, participants were asked about frequency, duration, and indications for use [pain or mobility and/or co-occurring conditions, including sleep, posttraumatic stress disorder (PTSD) or anxiety, stress, depression, general health, or other reason], and experience, beliefs, concerns, and disclosure regarding NP use ([Supplementary Appendix: Natural Products Survey](#)).

Natural Products Pilot Survey Administration

Study Sample. Between November 2021-May 2022, the finalized NP survey was piloted in a subsample of veterans

participating in the wHOPE trial. Veterans were eligible for wHOPE if they were enrolled in VA primary care, had moderate to severe chronic pain for at least 6 months ascertained by ICD-9/10 diagnostic codes, chart review, and subsequent phone screen, and had no exclusion criteria (i.e., dementia, hospice, relocating). The parent study collected data at baseline on NPs used within 30 days of study enrollment, but no other detail. wHOPE study staff mailed the new NP survey with a feedback form to 55 wHOPE participants at 5 VA study sites across the U.S. who endorsed NP use at baseline. The initial survey was piloted with 50 veterans, including 30% women, 30% non-white, and 30% under age 50, to gather representative feedback to refine the survey for the larger trial. A study coordinator called participants who had not returned the survey by mail within 2 weeks to offer administration by phone. Veterans were compensated \$50 for returning a survey and feedback form.

Data Collection and Analyses. Two study staff each entered the survey data (via manual double data entry) and feedback form into a VA-approved REDCap firewall-protected and encrypted database. Each data field was automated to flag outliers, redundancies, and missing data. When surveys were administered over the phone, data was entered electronically, and quality control occurred via automation in REDCap. The NP survey dataset was enriched with baseline demographic and clinical data from the parent trial (wHOPE). Analysis of the survey responses was descriptive- frequencies for categorical variables and means and standard deviations for continuous variables were calculated. Analyses were conducted using Stata 17.0.³²

Results

Among participants endorsing NP use in wHOPE at baseline, 52/55 veterans completed an NP survey for a response rate of 94.5%. Of surveys completed, 67.3% were returned by mail and 32.7% were conducted by phone (by request). Of the 52 surveyed, mean age was 57.6 (SD \pm 12.5); 42% identified as women, and 63% were White, 21% Black or African American, 15% other races; 10% were of Hispanic/Latinx ethnicity. The majority (81%) completed some college; whereas only 35% reported employment and 52% had annual incomes < \$50,000; 71% reported a military service-connected disability ([Table 1](#)).

Clinically, 88% reported experiencing moderate to severe pain every day with a mean Brief Pain Inventory Severity score of 6.09 (SD \pm 1.16) and Interference score of 6.63 (SD \pm 1.70). At baseline, 67% used non-opioid pain medication only; 15% used opioids plus other pain medication; 17% reported no pain medication. Forty-four percent screened positive for PTSD, 63% for moderate depression, and 35% for symptoms of moderate or severe anxiety ([Table 1](#)).

Table 1. Sociodemographic and Clinical Characteristics of 52 Veterans Completing the Natural Products Survey.

Characteristic	N (%)
Gender	
Male	30 (58%)
Female	22 (42%)
Race	
White/Caucasian	33 (63%)
Black or African/American	11 (21%)
Other, multiple, or unknown	8 (15%)
Hispanic ethnicity	
Not Hispanic or latino	47 (90%)
Hispanic or latino	5 (10%)
Age	
≤49	14 (27%)
≥50	38 (73%)
Education	
High school graduate	10 (19%)
Associates degree or some college	27 (52%)
Bachelor's degree or higher	15 (29%)
Employment	
Working for pay	18 (35%)
Student, not working for pay	2 (4%)
Retired, on disability, or seeking work	32 (62%)
Household income	
<\$50,000	23 (52%)
\$50,000-\$99,999	21 (48%)
Private health insurance*	15 (29%)
Pain severity (brief pain inventory, BPI)	
<5	6 (12)
≥5	44 (88)
Pain interference (brief pain inventory, BPI)	
<5	10 (20)
≥5	40 (80)
Pain medications at baseline	
No pain medications	9 (17%)
Used non-opioid pain medications only	35 (67%)
Used opioid pain medications with or without other pain medications	8 (15%)
PTSD (PC-PTSD-5)	
Negative (0-3)	22 (56%)
Positive (4-5)	17 (44%)
Depression (PHQ-9)	
No, minimal or mild	19 (37%)
Moderate to severe depression	33 (63%)
GAD-7: Generalized anxiety disorder	
No or mild anxiety symptoms	34 (65%)
Moderate or severe anxiety symptoms	18 (35%)

*In addition to VA health care benefit.

The mean number of NPs used (past month) was 4.6 (SD+/- 3.2); 17% used ≥8 or more different NPs; 90% reported daily use; 94% had used NPs for ≥6 months. Veterans reported multiple non-mutually exclusive reasons for NP use (Figure 1). Nearly all (98%) reported use for general health; 63% for pain and/or mobility concerns, 58% for sleep, and 40% for stress. Most (87%) reported use of

NPs for ≥ 2 indications. Categories of NPs used were vitamins and/or minerals, which was reported by nearly all respondents (94%), followed by herbals (non-cannabis) (60%); while 40% reported using cannabis (Figure 2). The most frequently used individual NPs were vitamin D (67%), multivitamins (61%), cannabis products (40%), magnesium (36%), green tea (36%), fish oil/omega-3 (33%) and

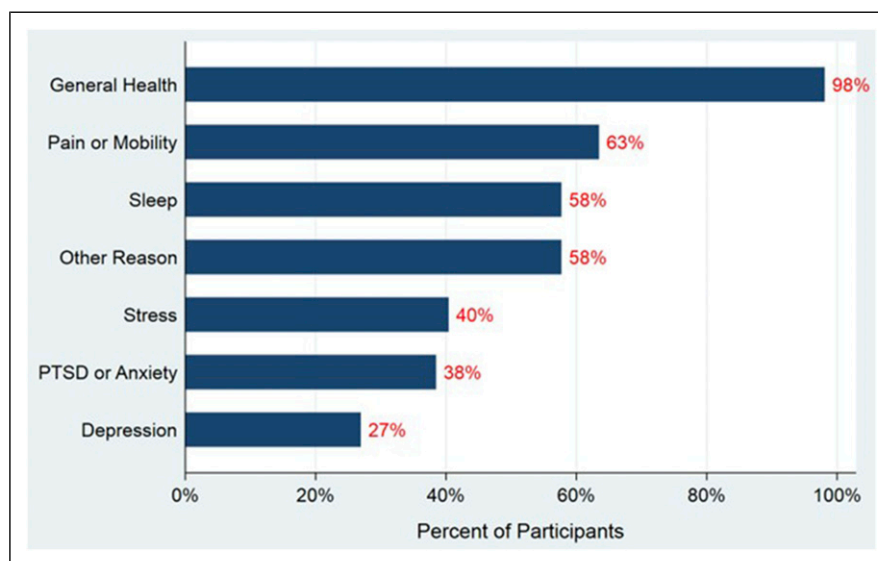


Figure 1. Indications for natural product use in the past 30 days.

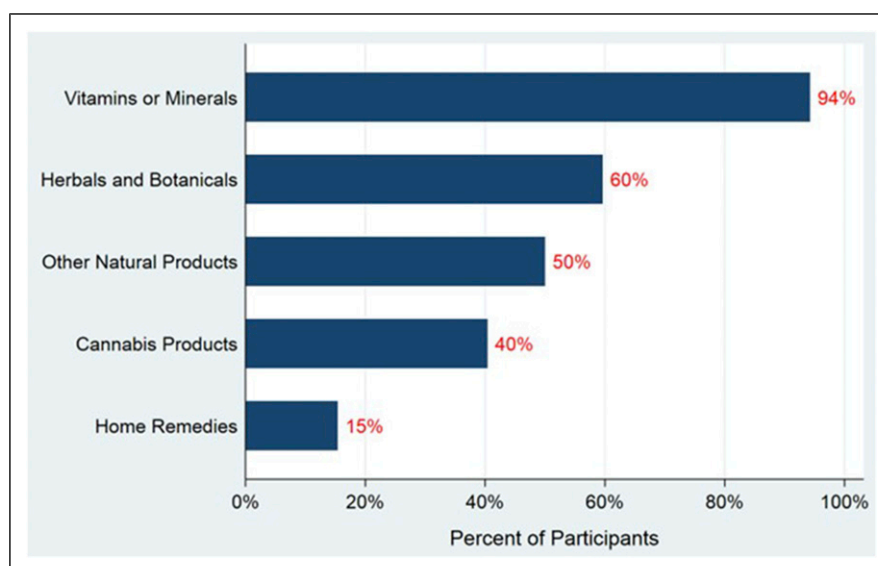


Figure 2. Most frequent categories of natural products used in the past 30 days.

melatonin (33%) (Figure 3). The most frequently reported individual NPs for pain were cannabis products (33%), followed by oral magnesium (13%), multivitamins, turmeric, and capsaicin (12% each), fish oil or omega 3 (10%), and Vitamin D (8%) (Figure 4).

Of the 21 (40%) reporting using cannabis products for all indications, most reported using products that had a mix of cannabidiol (CBD, without the psychoactive component) and tetrahydrocannabinol (THC, the psychoactive component in cannabis). Indications for cannabis among those reporting use were pain or mobility (81%), sleep (62%), PTSD or anxiety (43%), stress (43%), and depression (29%).

Survey respondents described various experiences, attitudes, and practices related to NP use (Table 2). Nearly all (92%) anticipated they would use NPs for pain or related symptoms more often if the VA or other insurance provided them at no cost. Nearly half reported difficulties obtaining natural products; reasons included too expensive (31%), not available through VA (27%), and/or health care provider was not supportive (6%). Notably, nearly a third (29%) reported using NPs in place of pain medications, and of these, the most substituted medications were non-steroidal anti-inflammatories (19%), acetaminophen (17%), medications for neuropathic pain (i.e., gabapentin, 10%) and anti-depressants (8%). Nearly all endorsed the

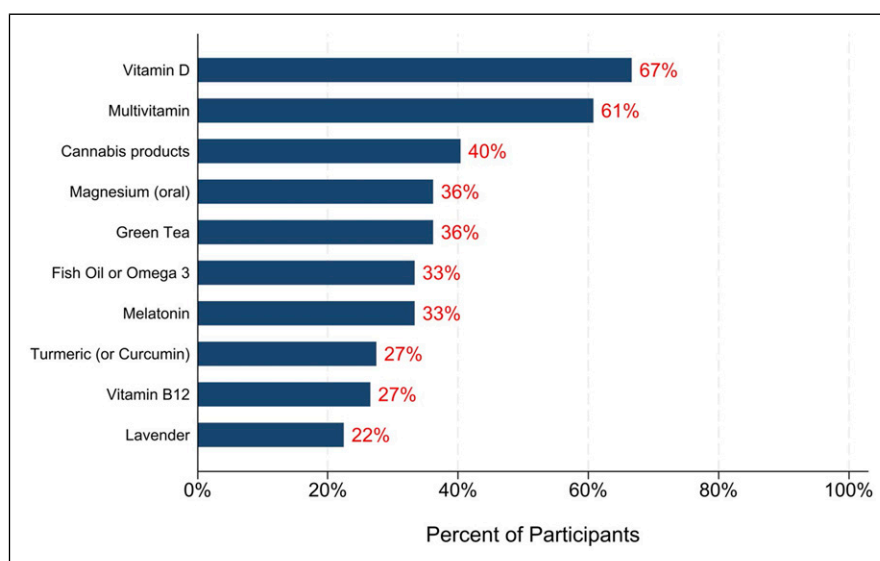


Figure 3. Most frequently reported NPs used for any indication (past 30 days).

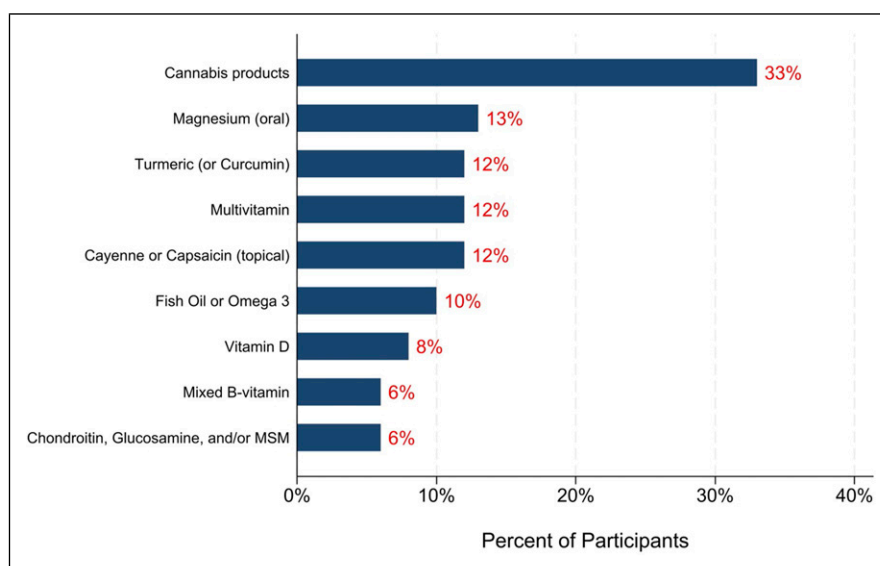


Figure 4. Most frequently reported NPs used for pain in the past 30 days.

importance of provider-patient communication regarding NP use (98%), however, 31% reported that they had unanswered questions about NPs, and only 52% reported discussions with their provider. Among those who did discuss NPs with their providers, veterans observed that providers responded positively or were neutral (85%).

Over one-quarter of respondents believed NPs were safe since they are sold over the counter (27%), or are “natural” (39%), and over half (55%) believed NPs were less harmful than most medications. Nevertheless, roughly half (55% and 52%, respectively) worried about NPs interacting with other prescribed medications or with each other (Table 3).

Fifty-one of 52 respondents provided feedback on the survey itself. The majority “strongly agreed” or “agreed” with the following: (1) the time required to complete the survey was reasonable; (2) the instructions were useful; (3) questions were in a logical order; (4) questions were of interest; (5) were comfortable answering the questions; (6) information needed to complete the survey was easy to find/gather in their homes, and (7) survey accurately captured their NP use.

Discussion

The development of a new natural products survey was motivated by a lack of information about NP use for chronic

Table 2. Veterans' Attitudes and Practices Related to NP Use.

Attitude and Practice	N (%)
How often would you use NPs if VA provided them at no cost or insurance paid?	
Always, very often, or often	45 (92%)
Never or not often	4 (8%)
Do you have unanswered questions about using NPs for pain?	
No	28 (55%)
Yes	16 (31%)
Not sure	7 (14%)
Do you think it is important for your healthcare provider to talk to you about NP use?	
Not important	1 (2%)
Important	20 (20%)
Very important	22 (22%)
Don't know	8 (8%)
Have you had difficulty getting the NPs you want to use for pain or related symptoms?	
No	23 (46%)
Yes	19 (45%)
Don't know	8 (16%)
Have you talked to your (VA) health care provider(s) about your use of NPs for pain or related symptoms?*	
No	22 (44%)
Yes	26 (52%)
Not sure	2 (4%)
Do you have unanswered questions about using NPs for pain?	
No	28 (55%)
Yes	16 (31%)
Not sure	7 (14%)
Have you used natural products in place of 1 or more of your pain medications?	
No	32 (61%)
Yes	15 (29%)

*Among those responding that they did not speak to their VA healthcare providers(s) about NP use, their reasons follow: 55% assumed providers would not support NPs or discussing NPs "wouldn't help"; 23% thought it was "unimportant to bring up"; 9% reported that NPs did not come up in their visit; 23% reported another reason.

pain and related conditions, coupled with the opportunity to capture this information among a diverse group of veterans with chronic pain recruited from VA primary care clinics across the U.S. who were participating in a trial of non-pharmacological pain management approaches and reported NP use at baseline. Moreover, reticence about discussing NP use among patients and clinicians has created a knowledge gap, thus reducing opportunities for informed shared decision-making. The new NP survey not only inventories specific NPs, but also ascertains intensity and indications for use, as well as experiences, beliefs, and practices regarding NPs. Future studies are needed to demonstrate the generalizability and utility of the NP survey in other research and clinical care settings, such as primary care, although, of note, all veterans completing the NP survey were concurrently enrolled in VA primary care and were participating in a

Table 3. Veterans' Beliefs About Natural Products.

Belief	N (%)
I believe natural products are safe because they are sold over the counter	11 (27%)
I believe natural products are safe because they are natural	17 (39%)
I think natural products are less harmful than most medications	24 (55%)
I worry about natural products interacting with medications prescribed to me	24 (55%)
I worry about natural products interacting with each other	23 (52%)
I think natural products are as effective as most medications for pain	15 (36%)
Responded "Don't Know" to 1 or more items	9 (17%)

pragmatic trial in which the study interventions were delivered by VA clinicians using the VA virtual care platform.

In our sample, nearly a third reported substitution of NPs for medications prescribed for pain and co-occurring conditions. One study found that nearly 1 in 5 U.S. adults used NPs instead of their prescribed medications.³³ As our and other studies have shown, patients may substitute NPs for prescribed pain medications because they feel their pain is inadequately treated, they are concerned about medication side-effects, or they believe NPs to be more effective and/or less harmful.³⁴ Of concern, the use of NPs in lieu of pain or other medications could result in non-adherence to prescribed medications, which may lead to harm, especially for patients with underlying serious health conditions (i.e., hypertension, diabetes).^{35,36}

Potential harm from NPs could be prevented by providers inquiring about their patients' use. Nearly all surveyed felt that providers should talk to patients about NP use, and stated they would use NPs for pain or related symptoms if the VA provided them at no cost. Of note, several of the most frequently reported NPs in this study (vitamin D, multivitamins, magnesium) are available on the national VA formulary, such that they may be prescribed at low or no cost. A likely smaller proportion of veterans surveyed reported cannabis use for pain and related conditions, which may represent under-reporting related to the prohibition on cannabis prescribing in the VA as a federal health care system. Some of the expressed barriers and concerns about NPs (e.g., cost, lack of access and information, potential harms, interactions with other NPs and medications) could be mitigated by increased provider involvement, specifically in discussing the risks and benefits of using NPs in the context of underlying health conditions and concomitant medications.^{6,34,37}

Our study revealed, however, that only about half of respondents using NPs had discussed NP use with their providers. Ours and other studies have indicated that since NPs are widely available without prescription and are "natural," they are generally believed to be "safe."³⁸ This may explain

prior observations that individuals are comfortable obtaining most information about NPs from the internet, social media, friends, and family, rather than from their health care providers.^{19,39,40} Also, clinicians and pharmacists generally lack knowledge about NPs, which explains why they may avoid discussions about NPs with their patients.^{41,42} Online databases (e.g., NatMed Pro, Herbs at a Glance, The Nutrition Source, National Institutes of Health Office of Dietary Supplements, and National Center for Complementary and Integrative Health) readily allow clinicians to access non-commercial, independent information about NP efficacy and safety that is updated semi-regularly.⁴³⁻⁴⁷ Broader use of these accessible databases by clinicians would facilitate communication and shared decision-making with patients about NP use, potentially limiting harms and improving the management of chronic pain.⁴⁸

A strength of our study was that our purposive sample of veteran respondents was drawn from primary care clinics at 5 geographically diverse VA facilities across the U.S. and was more inclusive and representative than the general VA population with a higher proportion of women, racial/ethnic minority, and younger veterans. In addition, a higher-than-expected response rate (95%) likely reflects not only follow-up by study staff, but also supports findings from our preliminary focus group testing that veterans found the survey of personal interest, non-threatening, and easy to complete, not surprising as survey development occurred in iterative steps with veteran input and feedback. Also, despite most survey respondents not completing college, unemployed and/or low income, and disabled with multiple comorbid mental health conditions, most participants (67%) completed the paper survey on their own without assistance. Nevertheless, roughly a third requested assistance or expressed a preference for a phone survey. Thus, future iterations must attempt to assure an 8th grade reading level to facilitate broader use and self-administration. This may be challenging however, since reading level is partially determined by multiple syllable words, and the specific names of some NPs have multiple syllables and are lengthy.

A limitation of this pilot study is that preliminary survey findings were limited to a relatively small VA primary care-enrolled veteran population (not a general patient population with chronic pain). In addition, these respondents were enrolled in a pragmatic trial comparing non-pharmacological pain management approaches and endorsed NP use at baseline. Therefore, this sample of veterans likely used more NPs the general population, and perhaps started or increased NP use as a function of trial participation (although the comparator interventions were not focused on NP use). Moreover, this sample may have been biased in favor of NP use, yet respondents still expressed concerns about NPs, challenges in accessing NPs, as well as dissatisfaction about their communication with their providers re: NP use. Following this pilot, the NP survey was revised minimally and was incorporated into the *w*HOPE trial at baseline, 6, and

12 months to determine the effect of the study interventions on NP use for pain management over time; results are forthcoming.

Another limitation is that NP data was collected by self-report only. Respondents were asked to gather all NPs used in the past 30 days and refer to labels while completing the survey. The VA electronic health record (EHR) was not used to validate self-reported NPs because only a minority of veterans have NPs recorded in the EHR and NPs are not systematically updated like other medications because most are not prescribed by VA. The survey was administered during the COVID-19 pandemic and thus home visits were not possible. As video telehealth is more widely used in VA and other healthcare systems, assessments using video/virtual platforms could be leveraged to verify names and brands of NPs. Future studies are needed to further pilot and validate the use of this NP survey in broader veteran and non-veteran populations with chronic pain, and video technology could be used to increase the accuracy/validity of self-report.

In sum, this study on NP use in a small, yet diverse sample of veterans with chronic pain participating in a multi-site pragmatic trial produced an acceptable and feasible survey as well as descriptive information about NPs for pain, an area in which there has been a knowledge gap. Among survey respondents, NP use was intensive and longstanding, and NPs were used for multiple reasons in addition to pain. Respondents also disclosed the substitution of NPs for prescribed medication and lack of disclosure to their providers. While most NPs are generally considered safe, some may be mislabeled, contain adulterants, have side-effects or drug/NP interactions, especially in patients (or veterans) with comorbidities prescribed multiple medications. Although patients strongly endorsed the need to consult their providers about NP use, many clinicians lack knowledge and up-to-date information re: NP use.^{42,48} Fortunately, clinicians can access several online evidence-informed NP databases that may support communication and informed shared decision-making to improve safety and pain-related outcomes in their patients.

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Author Contributions

Termeh Feinberg: Conceptualization, Methodology, Writing-Review & Editing; Liliana Moore: Validation, Investigation, Writing-Review & Editing; Nicole A. Woodruff: Validation, Investigation, Writing-Review & Editing; Natalie Purcell: Conceptualization, Methodology, Investigation, Writing-Review & Editing; Daniel Bertenthal: Validation, Formal Analysis, Writing-Review &

Editing; McCamish: Conceptualization, Project Administration; William R. Becker: Conceptualization, Conceptualization, Methodology, Funding acquisition.

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Supplemental Material

Supplemental material for this article is available online.

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