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Relief of cannabis withdrawal symptoms and cannabis quitting strategies in people with schizophrenia

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Abstract

This study examined the response to cannabis withdrawal symptoms and use of quitting strategies to maintain abstinence in people with schizophrenia. A convenience sample of 120 participants with schizophrenia who had at least weekly cannabis use and a previous quit attempt without formal treatment were administered the 176-item Marijuana Quit Questionnaire to characterize their “most serious” (self-defined) quit attempt. One hundred thirteen participants had withdrawal symptoms, of whom 104 (92.0%) took some action to relieve a symptom, most commonly nicotine use (75%). 90% of withdrawal symptoms evoked an action for relief in a majority of participants experiencing them, most frequently anxiety (95.2% of participants) and cannabis craving (94.4%). 96% of participants used one or more quitting strategies to maintain abstinence during their quit attempt, most commonly getting rid of cannabis (72%) and cannabis paraphernalia (67%). Religious support or prayer was the quitting strategy most often deemed “most helpful” (15%). Use of a self-identified most helpful quitting strategy was associated with significantly higher one-month (80.8% vs. 73.6%) and one-year (54.9% vs. 41.3%) abstinence rates. Actions to relieve cannabis withdrawal symptoms in people with schizophrenia are common. Promotion of effective quitting strategies may aid relapse prevention.

Keywords

Schizophrenia; Cannabis; Drug withdrawal symptoms; Coping behavior; Abstinence

1. Introduction

Cannabis is the most widely used illicit substance, consumed by 125-203 million people worldwide in 2009, an annual prevalence rate of 2.8-4.5% (United Nations Office on Drugs

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and Crime, 2011). In 2010, 17.4 million Americans were current users of cannabis (Substance Abuse and Mental Health Services Administration, 2010). People with schizophrenia have an even higher rate of cannabis use than the general population (Green et al., 2005; Volkow, 2009). The reported range of cannabis use in people with schizophrenia is 17-80% (Fowler et al., 1998; Green et al., 2005; Barnett et al., 2007; Koola et al., 2012); about one-quarter have a lifetime cannabis use disorder (Green et al., 2004; Koskinen et al., 2010).

Cannabis withdrawal in humans is well documented (Budney et al., 2004; Budney, 2006; Budney and Hughes, 2006), based on human laboratory studies (Nowlan and Cohen, 1977; Georgotas and Zeidenberg, 1979; Jones et al., 1981; Haney et al., 1999), longitudinal outpatient self-report studies (Kouri and Pope, 2000; Budney et al., 2001; Budney et al., 2003; Vandrey et al., 2008), inpatient observational studies (Milin et al., 2008), and retrospective self-report studies (Wiesbeck et al., 1996; Hasin et al., 2008; Levin et al., 2010). Withdrawal symptoms impair performance of normal daily activities (Allsop et al., 2012) and may act as negative reinforcement for relapse (Copersino et al., 2006; Levin et al., 2010), suggesting that they have clinical significance.

Cannabis use is detrimental to people with schizophrenia (Bartels et al., 1991; Linszen et al., 1994; Veen et al., 2004; Grech et al., 2005), including association with earlier onset of psychosis (Large et al., 2011), yet very little is known about cannabis withdrawal in this group. In a study of 18 male outpatients with “serious mental illness” and at least weekly cannabis use, 56% reported a history of cannabis withdrawal, although the nature and context of withdrawal were not described (Sigmon et al., 2000). A recent study of 120 participants with schizophrenia (same sample reported in this study) who had made an attempt to stop using cannabis without formal treatment found that 113 (94.2%) experienced withdrawal symptoms during their quit attempt, with 74.2% reporting four symptoms (Boggs et al., 2013).

This study examined the withdrawal relief actions and quitting strategies used by the 120 participants during their “most serious” (self-defined) quit attempt. The goals were to identify ways to better treat cannabis withdrawal and prevent relapse in people with schizophrenia.

2. Methods

2.1 Participants and study design

Over 500 people with psychiatric disorders in the Baltimore, MD metropolitan area were screened from December, 2006 through July, 2011 (Boggs et al., 2013). One hundred and twenty-three met the following eligibility criteria: 18-65 years old, diagnosis of schizophrenia or schizoaffective disorder (DSM-IV-TR criteria), at least one “serious” (self-defined) cannabis quit attempt made without formal treatment while living outside a controlled environment (e.g., hospital or jail), and cannabis use at least weekly over the six months prior to their index quit attempt. Three of these participants were excluded from the sample because they gave inconsistent answers (more than one-year difference) to two separate questions on the duration of abstinence during the index quit attempt, leaving a final sample of 120. Ability to give valid informed consent was evaluated with the Evaluation to Sign Consent instrument (DeRenzo et al., 1998). The Institutional Review Boards of the University of Maryland, Baltimore, the Maryland Department of Health and Mental Hygiene, the Sheppard Pratt Health System, and the National Institute on Drug Abuse Intramural Research Program approved this study. After the nature of the procedures was fully explained, written informed consent was obtained from all participants, who were paid for their participation.

2.2 Procedures and Instruments

Participants were administered the Marijuana Quit Questionnaire (MJQQ), an individually administered 176-item, semi-structured self-report questionnaire (Levin et al., 2010), in paper-and-pencil format over 45-180 minutes. The MJQQ collects information in three domains: demographic data and cannabis use history (chronology, patterns of use, cannabis-associated problems), characteristics of participants' index quit attempt, actions taken to relieve withdrawal symptoms (relief actions), and actions taken to help maintain abstinence (quitting strategies). Forty specific withdrawal symptoms (Table 1) were evaluated. Participants who experienced a withdrawal symptom were asked what relief actions, if any; they took to relieve that particular symptom. In addition, participants were asked whether they used one or more quitting strategies to help maintain abstinence during their index quit attempt (i.e., actions not focused on any particular withdrawal symptom). Participants were also asked to name the one quitting strategy they considered the most helpful. Participants chose from among 22 possible relief actions (Table 2) and from among 16 possible quitting strategies (Table 3) drawn from the literature on spontaneous (i.e., without formal treatment) quitting of alcohol or nicotine use. All participants who did not endorse "quit without help" were counted as using a quitting strategy, even if they did not endorse any specific quitting strategy. This broad definition was used to better capture the prevalence of use of a quitting strategy, even when participants could not name a specific strategy.

2.3 Statistical analyses

Descriptive statistics are reported as N (%), median or mean, and range. Because duration of abstinence was censored for some participants by occurrence of the study interview, the Kaplan-Meier method was used to generate the distributions of time to relapse to cannabis smoking (survival curves); the log rank test was used to determine whether differences in survival time were statistically significant. A Cox regression model was employed to examine the association between using a (self-identified) most helpful quitting strategy (vs. not identifying a most helpful strategy) and relapse, controlling for age, gender, and baseline cannabis use (number of days of use in the month prior to start of quit attempt). All analyses were performed with SAS version 9.1.3 (SAS Institute, Inc; Cary, NC), with two-tailed $\alpha=0.05$.

3. Results

The 120 participants were predominantly male (N=92, 77%) African-Americans (N=75, 62.5%) who never married (N=95, 79%). Mean (range) age at the time of study interview was 41.5 (21-63) years; at the start of the index quit attempt 29.3 (15-59) years. Mean (range) education level was 11.4 (3-18) years. Data on psychiatric characteristics and cannabis and other substance use before and during the quit attempt were previously described (Boggs et al., 2013). The mean (range) interval between start of the index quit attempt and the interview was 9 years (1 day-37years).

113 participants had withdrawal symptoms, of whom 104 (92.0%) took some action to relieve a symptom. The vast majority (90% [36/40]) of cannabis withdrawal symptoms evoked one or more relief actions in a majority of participants experiencing them (Table 1). Among withdrawal symptoms experienced by at least 10% of participants, feeling anxious and craving for cannabis had the highest proportion of participants taking relief actions (95.2% and 94.4%, respectively). Relief actions used by at least half the participants were use of nicotine (N=85, 75%), sleeping (N=68, 60%), engaging in alternative or competing behaviors (N=68, 60%), and eating more (N=64, 57%) (Table 2). Participants used a mean (SD) of 8.5 (5.3) relief actions (median 9.5, mode 10, range 0-19). The number of relief

actions per participant ranged from 0 (9 participants) to 19 (2 participants); the commonest was 10 actions (15 participants).

Almost all (115/120 [95.8%]) participants used one or more quitting strategies (mean [SD] 5.2 [2.8] strategies per participant) to maintain abstinence during their quit attempt (Table 3). The most commonly used quitting strategies were getting rid of cannabis (86, 72%), getting rid of cannabis paraphernalia (80, 67%), stopped associating with people who smoke cannabis (74, 62%), and no longer frequenting places where cannabis was smoked (73, 61%). The quitting strategy most often rated as “most helpful” was religious support or prayer (17, 15%). All except one quitting strategy (acupuncture) was rated at least “moderately helpful” by 80% or more of those who used it (Table 3).

Participants who used a quitting strategy they considered most helpful, compared to those who did not identify a most helpful strategy (even if actually using a strategy), were significantly better in maintaining abstinence after the start of their quit attempt (Fig. 1). They had a significantly longer median duration of abstinence (2.0 years [95% CI 1.0 -6.0] vs. 9.1 months [95% CI 3.0-24.4], respectively, log-rank test $X^2=5.9$, $df=1$, $p=0.02$), with higher one-month (80.8% vs. 73.6%) and one-year (54.9% vs. 41.3%) abstinence rates. After controlling for age, gender and baseline cannabis use, the hazard of relapse for those who used a most helpful quitting strategy was 46% lower than for those who did not identify a most helpful strategy (hazard ratio = 0.54, $z^2 = 5.47$, $p = 0.02$).

There was no significant association between use of any of the 5 quitting strategies most often rated as “most helpful” (stopped associating with people who smoke cannabis, stopped going to places where cannabis was smoked, getting rid of cannabis and cannabis paraphernalia, and religious support or prayer) and likelihood or duration of abstinence (data not shown).

4. Discussion

This is the first study of which we are aware to evaluate the actions taken by people with schizophrenia when they quit cannabis use without formal treatment. Almost all (92.0%) participants took at least one action to relieve cannabis withdrawal symptoms. In a prior study of 104 non-treatment-seeking adults without psychiatric comorbidity, a majority of participants took action to relieve withdrawal symptoms, including 54% who took action to relieve withdrawal anxiety (Copersino et al., 2006). This finding is consistent with the present study, in which 96% of participants with schizophrenia took action to relieve withdrawal anxiety.

96% of our participants used quitting strategies to help maintain abstinence during their quit attempt. This high proportion is consistent with the 88% of people using quitting strategies in a study of 65 adult non-treatment-seeking cannabis users without psychiatric comorbidity (Boyd et al., 2005). Changing one’s environment (getting rid of cannabis, stopping going to places where cannabis was smoked, stopping associating with people who smoke cannabis, getting rid of cannabis paraphernalia) was most often rated as the most helpful quitting strategy in that study, in contrast to the present study, where religious support or prayer was most often rated most helpful. However, religious support or prayer was not listed as a possible quitting strategy in that prior study. Compared to adults without psychiatric comorbidity (Boyd et al., 2005), participants with schizophrenia in the present study used more quitting strategies (5.2 [2.8] vs. 3.2 [2.6]) and a higher proportion used multiple quitting strategies (93% vs. 65% used two or more quitting strategies; 83% vs. 55% used three or more quitting strategies, respectively). These findings suggest that people with

schizophrenia are more likely to use quitting strategies than people without psychiatric comorbidity.

The proportion of participants using quitting strategies (96%) is substantially higher than the 17.5% reported in a meta-analysis of 38 studies of substance users (chiefly alcohol and nicotine) who quit without formal treatment (so-called spontaneous or natural remission) (Sobell et al., 2000). The commonest quitting strategies used by our participants with schizophrenia (avoidance of people, places, and things associated with cannabis, religious support or prayer, and encouragement from family) are similar to the commonly used strategies reported in studies of spontaneous remission from alcohol and nicotine use in people without comorbid psychiatric disorders, e.g., social support, family support, change in residence/avoiding drug areas, finding new relationships, and avoiding old relationships (Sobell et al., 2000; Walters, 2000). Thus, our findings suggest that people with schizophrenia who smoke cannabis take similar relief actions to cope with withdrawal symptoms and help maintain abstinence as do people without psychiatric comorbidity, but take relief actions more often than those quitting cannabis without psychiatric comorbidity or those quitting legal substances.

Some of the actions taken to relieve withdrawal symptoms and maintain abstinence have health implications beyond those related to cannabis use. In particular, increased nicotine and alcohol use during cannabis cessation attempts could contribute to the already high use of these substances by people with schizophrenia (Koola et al., 2012a), with resulting adverse health consequences (Koola et al., 2012b). Increased eating was another potentially unhealthy response to cannabis withdrawal, possibly contributing to the obesity and metabolic abnormalities commonly found in people with schizophrenia (Dickerson et al., 2006). Thus, improved treatment for cannabis withdrawal symptoms might have secondary health benefits in reducing nicotine and alcohol use and overeating in this population and minimizing the possible “reverse gateway” process whereby cannabis use promotes nicotine use (Patton et al., 2005; Humfleet and Hass, 2004).

4.1 Strengths and limitations

This study has several strengths, including the large sample size (N=120) and detailed evaluation of actions taken to relieve 40 individual cannabis withdrawal symptoms, as well as quitting strategies to maintain overall abstinence during a quit attempt.

This study has several limitations. The data were collected by retrospective self-report without external corroboration. However, there is evidence that cannabis users give reliable retrospective self-report about their cannabis use histories (Fendrich and Mackesy-Amiti, 1995; Ensminger et al., 2007) and withdrawal symptoms (Mennes et al., 2009) and that people with severe mental illness can report reliably on their substance use histories (Carey et al., 2001). However, the cognitive impairment associated with schizophrenia may have contributed to missing data about specific relief actions and quitting strategies. Because of the interview procedure, we could not distinguish missing data from failure to take any relief action and so could not resolve some data discrepancies. The MJQQ, unlike the Cannabis Withdrawal Scale (Allsop et al., 2011; Allsop et al., 2012), has not been validated. Finally, participants were a convenience sample of cannabis users from one city in one country, which may limit the external validity of the findings. Despite these limitations, we believe that these data offer a clinically relevant initial look at how people with schizophrenia deal with cannabis withdrawal.

To our knowledge, this is the first study to report what people with schizophrenia do to relieve withdrawal symptoms and maintain abstinence while trying to quit cannabis use without formal treatment. Our participants used quitting strategies similar to those used by

those without psychiatric comorbidity when trying to quit cannabis, alcohol, or nicotine use, and used them at higher rates than those trying to quit legal drugs. Use of such quitting strategies was associated with longer duration of abstinence, although no specific quitting strategy appeared more effective.

The study of “spontaneous” quitting by individuals not in formal treatment may lead to improved psychosocial treatment interventions and novel pharmacologic targets. For example, in this study, withdrawal anxiety, boredom, restlessness, and insomnia were disturbing enough to have relief actions taken by at least 90% of participants experiencing them. This finding suggests that attention to and alleviation of these symptoms would be clinically useful in relapse prevention and improving abstinence.

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Disclosure of interests

Dr. Kelly has received grant support from Bristol-Myers Squibb and Ameritox, Ltd. Dr. McMahon is a statistical consultant for Amgen Inc. All other authors have no interests to declare. Statistical analyses were performed by authors Liu and McMahon. A copy of the protocol can be obtained from the corresponding author at dgorelic@intra.nida.nih.gov. The study was registered with ClinicalTrials.gov on May 19, 2012 (NCT00679016).

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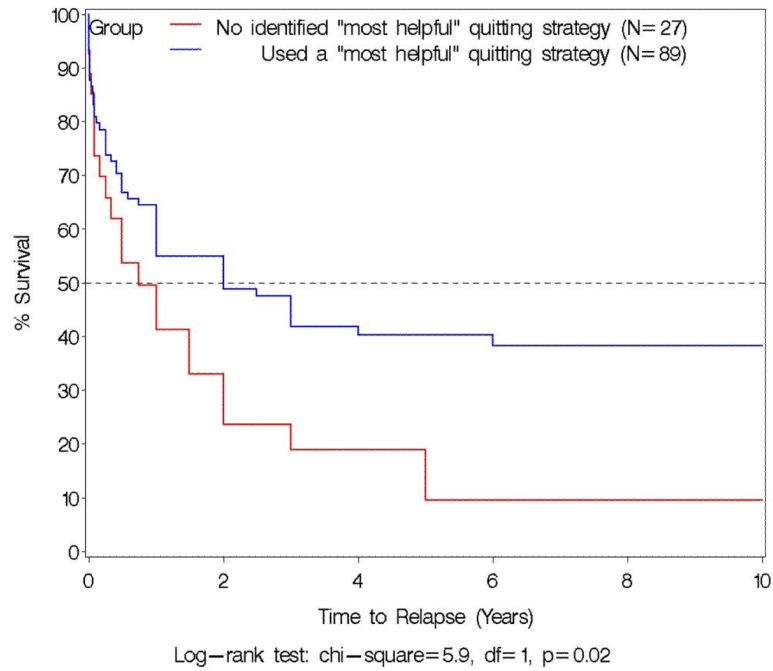


Fig. 1. Association between use of a self-identified “most helpful” quitting strategy (blue line, n = 89) or no use of a “most helpful” strategy (red line, n = 27) and proportion of participants remaining abstinent from cannabis smoking. Time 0 is start of self-defined “most serious” cannabis quit attempt made without formal treatment while not in a controlled environment by 116 regular (at least weekly for 6 months) cannabis smokers with schizophrenia. No relapses occurred after 6 years, so x-axis is truncated at 10 years. The two curves are significantly different by log-rank test: $\chi^2 = 5.9$, $df = 1$, $p = 0.02$. Horizontal dashed line indicates 50% of participants abstinent.

Table 1

Individual Cannabis Withdrawal Symptoms Experienced and Relief Actions Taken by 113 Participants with Schizophrenia.

Withdrawal Symptom	Number who took relief actions/Number who experienced the withdrawal symptom (%)	Number of relief actions used median (range)
Feeling anxious, nervous	60/63 (95.2)	7 (1-17)
Craving for cannabis	67/71 (94.4)	2 (1-17)
Feeling restless	47/51 (92.2)	3 (1-7)
Feeling bored	52/57 (91.2)	3 (1-14)
Upset stomach	10/11 (90.9)	1.5 (1-3)
Nausea	9/10 (90.0)	1 (1-9)
Trouble falling asleep	36/40 (90.0)	3 (1-12)
Waking up during the night	31/35 (88.6)	3 (1-11)
Stomach pain	13/15 (86.7)	1 (1-3)
Feeling sad, depressed	46/54 (85.2)	3 (1-9)
Diarrhea	5/6 (83.3)	1 (1-2)
Sleep less than usual	30/36 (83.3)	3 (1-10)
Feeling irritable, "jumpy"	43/54 (79.6)	2 (1-10)
Headaches	21/27 (77.8)	1 (1-4)
Increase in appetite	27/35 (77.1)	2 (1-7)
Tremor, shakiness	10/13 (76.9)	2 (1-7)
Weight gain	16/21 (76.2)	2 (1-5)
Physical discomfort	6/8 (75.0)	1.5 (1-6)
Physically attacked another person	5/7 (71.4)	3 (1-12)
Sweating	11/16 (68.8)	1 (1-7)
Feeling aggressive	15/22 (68.2)	3 (1-12)
Feeling angry	23/34 (67.7)	3 (1-17)
Vomiting	4/6 (66.7)	1.5 (1-8)
Waking up earlier than usual	18/27 (66.7)	3.5 (1-8)
Chills	8/13 (61.5)	2 (1-7)
Insulted, yelled, or swore at another person	11/18 (61.1)	3 (1-7)
Sleep more than usual	11/19 (57.9)	2 (1-4)
Vivid dreams	19/33 (57.6)	2 (1-8)
Decrease in appetite	16/28 (57.1)	2 (1-7)
Increase in sex drive	8/14 (57.1)	3 (1-9)
Strange dreams	16/29 (55.2)	2.5 (1-8)
Punched or kicked another person	4/8 (50)	2.5 (1-5)
Pulled a knife, gun, or	1/2 (50)	2 (2-2)

Withdrawal Symptom	Number who took relief actions/Number who experienced the withdrawal symptom (%)	Number of relief actions used median (range)
other weapon on another person		
Muscle twitches	5/10 (50.0)	3 (2-7)
Weight loss	4/8 (50.0)	1 (1-2)
Decrease in sex drive	4/10 (40.0)	2.5 (1-3)
Pushed, grabbed, or stabbed another person	2/6 (33.3)	7 (2-12)
Improved memory	4/19 (21.1)	2.5 (1-5)
Threw or broke something	3/10 (30.0)	2 (2-12)
Other sleep problem	1/1 (100)	6 (6-6)

Withdrawal symptoms listed in descending order of frequency of participants taking relief action. "Other sleep problem" listed last because reported by only one participant. Range does not include 0 because of inability to distinguish missing values from a true 0 value.

Table 2

Common Actions Taken to Relieve Cannabis Withdrawal Symptoms by 113 Participants with Schizophrenia Who Experienced Withdrawal Symptoms During Their Index Quit Attempt.

Relief Actions	N (%) Taking the Action
Use of Nicotine	85 (75.2)
Sleep	68 (60.2)
Engage in Alternate or Competing Behaviors	68 (60.2)
Eat More	64 (56.6)
Use of Alcohol	56 (49.6)
Avoid People/Places/Things Associated with Cannabis	56 (49.6)
Actively Ignore	53 (46.9)
Ride out the Discomfort	53 (46.9)
Meditate/Pray	51 (45.1)
Drink more Water	49 (43.4)
Exercise	49 (43.4)
Read Bible	44 (38.9)
Drink more Carbonated Beverages/Soda	43 (38.1)
Have Sex	38 (33.6)
Eat Healthier or Change Diet	34 (30.1)
Think about Negative Effects of Cannabis	32 (28.3)
Use of Vitamins or Herbal Supplements	28 (24.8)
Do Breathing Exercises	27 (23.9)
Use of Cannabis	23 (23.0)
Use of Antidepressants	25 (22.1)
Use of Stimulants	17 (15.0)
Use of Sedatives/Hypnotics	17 (15.0)

Table 3

Quitting Strategies Used to Maintain Abstinence from Smoking Cannabis by 120 Participants with Schizophrenia.

Strategy	Used and helpful N (%)	Didn't use, but might have been effective N (%)	Most helpful N (%)
Rating of helpfulness			
Encouragement from family	55 (45.8)	26 (40)	11 (9.5)
Not at all	4 (7.3)		
Used	51 (92.7)		
Mean (SD)	2.9 (1.2)		
Encouragement from friends	31 (25.8)	43 (48.3)	n/a
Not at all	2 (6.5)		
Used	29 (93.5)		
Mean (SD)	2.4 (1.1)		
Stopped associating with people who smoke cannabis	74 (61.7)	23 (50.0)	13 (11.2)
Not at all	2 (2.7)		
Used	72 (97.3)		
Mean (SD)	3.3 (1.0)		
Stopped going to places where cannabis was smoked	73 (60.8)	27 (57.5)	8 (6.9)
Not at all	3 (4.1)		
Used	70 (95.9)		
Mean (SD)	3.4 (1.0)		
Got rid of cannabis	86 (71.7)	16 (48.5)	11 (9.5)
Not at all	5 (5.8)		
Used	81 (94.2)		
Mean (SD)	3.3 (1.2)		
Got rid of cannabis paraphernalia	80 (66.7)	16 (40.0)	4 (3.5)
Not at all	5 (6.3)		
Used	75 (93.7)		
Mean (SD)	3.3 (1.1)		
Attended a self-help group e.g., AA	44 (36.7)	34 (44.7)	7 (6.0)
Not at all	2 (4.5)		
Used	41 (93.2)		
Mean (SD)	3.3 (1.2)		
Got counseling or psychotherapy	30 (25.0)	57 (64.0)	3 (2.6)
Not at all	1 (3.3)		
Used	29 (96.7)		
Mean (SD)	3.2 (1.1)		
Religious support, prayer	62 (51.7)	25 (43.1)	17 (14.7)

Strategy	Used and helpful N (%)	Didn't use, but might have been effective N (%)	Most helpful N (%)
Rating of helpfulness			
Not at all	2 (3.2)		
Used	60 (96.8)		
Mean (SD)	3.4 (1.1)		
Saw a physician	23 (19.2)	40 (41.2)	2 (1.7)
Not at all	2 (8.7)		
Used	21 (91.3)		
Mean (SD)	2.9 (1.3)		
Took non-prescription medication	5 (4.2)	20 (17.7)	
Used	5 (100)		
Mean (SD)	3.8 (0.4)		
Took prescription medication	19 (15.8)	37 (37.0)	2 (1.7)
Not at all	1 (5.3)		
Used	18 (94.7)		
Mean (SD)	3.2 (1.1)		
Took herbal medicine, vitamins, nutritional supplement	21 (17.5)	33 (34.0)	3 (2.6)
Not at all	4 (19.0)		
Used	16 (76.2)		
Mean (SD)	2.7 (1.5)		
Had acupuncture	11 (9.2)	34 (31.8)	1 (0.9)
Not at all	6 (54.5)		
Used	5 (45.5)		
Mean (SD)	1.6 (1.9)		
Other	13 (11.2)	2 (2.0)	7 (6.0)
Used	12 (92.3)		
Mean (SD)	3.8 (0.6)		
Quit without any quitting strategies at all	73 (60.8)	8 (17.8)	27 (23.3)
Not at all	6 (8.2)		
Used	64 (87.7)		
Mean (SD)	3.2 (1.3)		

"Used" is a combination of a little bit, moderately, quite a bit, extremely, couldn't have quit without it.