

## SPECIAL ARTICLE

# Marijuana as Antiemetic Medicine: A Survey of Oncologists' Experiences and Attitudes

By Richard E. Doblin and Mark A.R. Kleiman

A random-sample, anonymous survey of the members of the American Society of Clinical Oncology (ASCO) was conducted in spring 1990 measuring the attitudes and experiences of American oncologists concerning the antiemetic use of marijuana in cancer chemotherapy patients. The survey was mailed to about one third (N = 2,430) of all United States-based ASCO members and yielded a response rate of 43% (1,035). More than 44% of the respondents report recommending the (illegal) use of marijuana for the control of emesis to at least one cancer chemotherapy patient. Almost one half (48%) would prescribe marijuana to some of their patients if it were legal. As a group, respondents considered smoked marijuana to be somewhat more effective than the legally available oral synthetic dron-

abinol ([THC] Marinol; Unimed, Somerville, NJ) and roughly as safe. Of the respondents who expressed an opinion, a majority (54%) thought marijuana should be available by prescription. These results bear on the question of whether marijuana has a "currently accepted medical use," at issue in an ongoing administrative and legal dispute concerning whether marijuana in smoked form should be available by prescription along with synthetic THC in oral form. This survey demonstrates that oncologists' experience with the medical use of marijuana is more extensive, and their opinions of it are more favorable, than the regulatory authorities appear to have believed.

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**M**ARIJUANA (smoked) has been reported to be effective in treating emesis associated with cancer chemotherapy,<sup>1,4</sup> but its use is currently prohibited by law.<sup>5</sup> The main psychoactive ingredient in marijuana, tetrahydrocannabinol (THC; dronabinol), was approved in 1985 by the Food and Drug Administration (FDA) for use in the treatment of emesis. As marketed under the trade name Marinol (Unimed, Somerville, NJ) and synthetically formulated in sesame oil in gelatin capsules to be taken orally, almost 100,000 doses were prescribed in 1989.<sup>6</sup>

Litigation concerning the rescheduling of marijuana to permit its medical use has been making its way through the courts since 1972.<sup>7</sup> The central issue in the longstanding administrative and legal dispute, argued before the United States Court of Appeals (DC Circuit) on March 4, 1991,<sup>8</sup> is whether or not marijuana has a "currently accepted medical use in treatment in the United States." This is the standard for rescheduling required by the Uniform Controlled Substances Act of 1970,<sup>5</sup> which

created the current system of drug scheduling. The Act does not further specify the standard.

In September 1988, after 2 years of Drug Enforcement Administration (DEA) administrative hearings, DEA Administrative Law Judge Francis Young issued a recommendation in favor of rescheduling marijuana. He ruled that the appropriate standard for current acceptance is identical to the one established for a successful defense in medical malpractice cases, which requires only that the medical practice at issue be accepted by a "respectable minority" of physicians.<sup>9</sup> Ironically, the 1955 medical malpractice case that established this standard involved a lawsuit against an oncologist for the unsuccessful use of chemotherapy, which was then new and did not have the approval of the American Medical Association. The court stated that as long as there was no infallible cure and the doctor "did not engage in quackery by representing that he had one," the support of a respectable minority of peers would be sufficient to avoid malpractice liability. The court remarked "We [the court] are not physicians and we have no light on the subject except such as is shed by the testimony of physicians. . . ."<sup>10</sup>

On December 29, 1989, the Administrator of DEA rejected Judge Young's recommendation and refused to reschedule marijuana on the grounds that medical use of marijuana was not

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*Address reprint requests to Dr Mark A.R. Kleiman, Program in Criminal Justice, Kennedy School of Government, 79 JFK St, Cambridge, MA 02138.*

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currently accepted. The Administrator used an eight-part standard for determining current acceptance similar to the "safety and efficacy" standard used by the FDA to approve the marketing of new drugs by pharmaceutical companies.<sup>11</sup> The DEA first articulated this standard in another rescheduling case in 1987, after the United States Court of Appeals (1st Circuit 1987) rejected its contention that FDA new drug approval itself was the appropriate standard.<sup>12</sup> On April 26, 1991, the United States Court of Appeals (DC Circuit)<sup>13</sup> ruled that DEA's standard was impossible to meet, and was therefore invalid. The court remanded to the DEA its ruling rejecting Judge Young's recommendation in favor of the rescheduling of marijuana.

The extent of oncologists' acceptance of medical use of marijuana remains a disputed issue. Dr Ivan Silverberg, an oncologist and witness in the DEA hearings, testified, "There has evolved an unwritten but accepted standard of treatment within the oncologic community which readily accepts marijuana's use."<sup>14</sup> On the other hand, the DEA characterized the medical use of marijuana as a "cruel and dangerous hoax."<sup>15</sup> In a newspaper interview, DEA Associate Chief Counsel Steven Stone suggested that only a fringe group of oncologists accepted marijuana as an antiemetic. Stone remarked, "The Judge seems to hang his hat on what he calls a 'respectable minority of physicians.' What percent are you talking about? One half of one percent? One quarter of one percent?"<sup>16</sup> This report of oncologists' experiences with and attitudes about marijuana as an antiemetic is based on a survey of these specialists conducted in the spring of 1990.

#### SUBJECTS AND METHODS

A random sample of the United States-based members of the American Society of Clinical Oncology (ASCO) was surveyed. The membership of ASCO, the only formal association of clinical oncologists in the United States, comprises about 80% of the approximately 5,000 board-certified oncologists and almost 60% of the approximately 11,700 oncologists in the United States, including academic and research-oriented oncologists as well as clinicians in private practice. The survey was conducted independently of ASCO sponsorship.

The survey, responses to which were anonymous, was sent to about 35% (N = 2,430) of the total United States-based ASCO 1989 membership (N ≈ 6,830). The 1,035 surveys returned resulted in a response rate of 43%, representing 15% of United States-based ASCO members and 9% of all oncologists in the United States. Of the respondents, 57

(6%) returned the survey unanswered, indicating that they did not treat patients. Other respondents did not answer every question. The data analysis is based on the total number of respondents answering each particular question.

The survey initially elicited personal information about the oncologist's year of graduation from medical school and size of practice. Oncologists were then asked to estimate the proportion of their cancer chemotherapy patients for whom the currently available antiemetics provided adequate relief or caused significant problems with side effects.

Respondents were asked how frequently they prescribed Marinol, whether any of their patients had used marijuana as an antiemetic, whether they had directly observed or discussed marijuana's medical use with patients, and whether they had ever recommended that a patient try marijuana.

Oncologists were also asked to estimate the proportion of their patients who reported effective emetic control or negative side effects from using marijuana or Marinol, to directly compare the safety and efficacy of marijuana and Marinol, and to estimate what proportion of their patients experienced net benefits from their use of marijuana.

Oncologists were further asked to respond to the statements "Marijuana can be effective in the control of emesis," "Marijuana can be used safely in the control of emesis," "Marijuana should be given an accepted place in the antiemetic armamentarium," and "I find the use of Marinol in the control of emesis to be a legitimate, currently acceptable medical practice" by indicating strong agreement, agreement, strong disagreement, disagreement, or no opinion. Oncologists were also asked, if marijuana were legal, whether they would prescribe it to "many," "few," or "none" of their patients or if they "needed more information."

#### RESULTS

Ten percent of the respondents graduated from medical school in the 1980s, almost one half (48%) of the respondents graduated from medical school in the 1970s; almost one third (31%) in the 1960s; 9% in the 1950s; and 2% in the 1940s. In 1989, almost one half (49%) of the respondents had an annual patient population of more than 225; almost one quarter (24%) treated between 150 and 225 patients; 18% treated between 75 and 150 patients; and 9% treated 75 or fewer patients.

Two hundred nine (21%) of oncologists reported that the available medicines provided inadequate relief to half or more of their patients (Fig 1). More than half (520, 54%) of the respondents reported that the available antiemetics caused significant problems with side effects in more than a "few" of their patients (Fig 1).

Slightly more than 70% (686) of respondents reported that at least one of their patients had used marijuana as an antiemetic and that they had

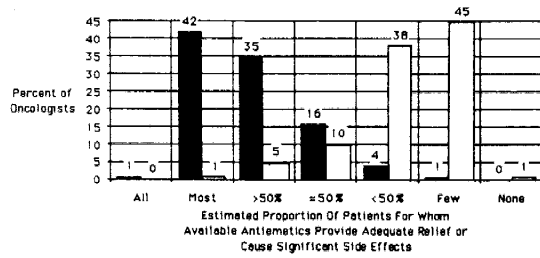


Fig 1. Reported efficacy (■) and side effects (□) of available antiemetics. Percentages do not equal 100% due to rounding.

directly observed or discussed marijuana's medical use with that patient(s). Marinol had been prescribed by 557 respondents (57%).

A surprising proportion of respondents (432, 44%) said they had recommended marijuana to at least one patient. Only six respondents noted that they did so as part of a legally authorized research protocol. Not surprisingly, respondents who treated more than 150 patients per year were more likely to have recommended marijuana than respondents treating fewer than 150 patients (46% v 34%,  $P < .05$ ). Respondents who graduated from medical school in the 1950s, the 1960s, or the 1970s had statistically similar rates of recommending marijuana (1950s, 46%; 1960s, 44%; 1970s, 44%). However, those who graduated during the 1980s had a significantly lower rate (30%,  $P < .05$ ).

*Efficacy of Marijuana and Marinol*

Three hundred eighty-five respondents (64%) stated that marijuana was effective in 50% or more of their patients, and 266 (56%) reported the same of Marinol (Fig 2). The difference is statistically significant ( $P = .008$ ).

Of the 277 respondents (28%) who felt they had sufficient information to compare marijuana directly with Marinol in terms of efficacy, 44% believed marijuana to be more effective, 13% believed Marinol to be more effective, and 43%

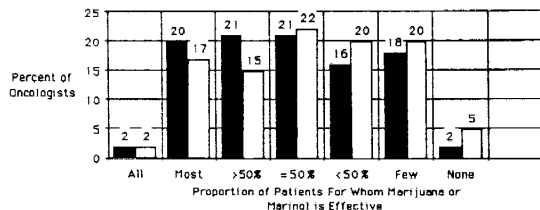


Fig 2. Marijuana (■) and Marinol (□): efficacy ratings. Percentages do not equal 100% due to rounding.

thought they were about equally effective. Of those who reported a preference ( $N = 157$ ), 121 (77%) thought marijuana was more effective than Marinol. The difference between 77% and 50% (the null hypothesis) is statistically significant below the .0001 level.

Six hundred eight respondents (63%) agreed with the statement affirming the efficacy of marijuana in the treatment of emesis (9% "strongly agreed" and 54% "agreed"), and 77 respondents (8%) disagreed (2% "strongly disagreed" and 6% "disagreed"). Two hundred eighty-three (29%) had no opinion. Of the respondents with opinions ( $N = 685$ ), 89% believed marijuana to be effective in the control of emesis. Of respondents to a question concerning net benefits ( $N = 644$ ), 409 (64%) reported that 50% or more of their patients experienced net benefits from marijuana. Only 15 (2%) reported that none of their patients experienced net benefits from marijuana.

*Safety of Marijuana and Marinol*

Two hundred twenty-four respondents (235, 47%) stated that the use of Marinol caused negative side effects in 50% or more of their patients, and 235 (40%) reported the same about marijuana (Fig 3). The difference is statistically significant ( $P = .018$ ).

Of the 288 respondents (29%) who felt they had sufficient information to compare marijuana with Marinol in terms of side effects, 20% believed marijuana to cause fewer problems with side effects, 23% believed Marinol to cause fewer problems, and 57% thought they were equal. Slightly more than half, 52% (65), of those who reported a preference (124) reported Marinol to cause fewer problems with side effects. The difference between 52% and 50% is not statistically significant ( $P = .596$ ).

Four hundred seventy-eight respondents (49%)

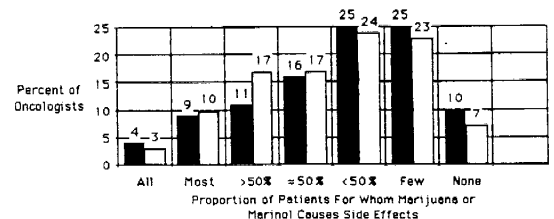


Fig 3. Marijuana (■) and Marinol (□): side effects ratings. Percentages do not equal 100% due to rounding.

agreed with the statement affirming that marijuana could be safely used in the treatment of emesis (6% "strongly agreed" and 43% "agreed"), and 131 (14%) disagreed (4% "strongly disagreed" and 10% "disagreed"). Three hundred sixty-one (37%) had no opinion. Of the respondents with opinions ( $N = 609$ ), almost four fifths (79%) believed that marijuana could be safely used to control emesis.

Almost half (423, 44%) of the respondents reported that they believe marijuana to be both safe and efficacious. Of respondents with opinions on both safety and efficacy ( $N = 577$ ), 73% believe marijuana to be both safe and efficacious. There were no significant differences in positive opinions of marijuana's safety and efficacy between respondents who treated 150 patients or fewer annually and those who treated more than 150 patients annually, or among respondents who graduated in different decades.

Three hundred twenty respondents (33% of all respondents) stated that marijuana should be accepted (5% "strongly agreed" and 28% "agreed") and 279 (29%) felt that it should not (7% "strongly disagreed" and 22% "disagreed"); 364 (38%) expressed no opinion. Of the 599 respondents with opinions, 53% favored making marijuana available by prescription. The surplus of positive over negative opinions is within the bounds of sampling error ( $P = .092$ ). There were no significant differences in rate of acceptance by size of patient population. However, respondents who graduated in the 1950s were significantly less likely to accept the medical use of marijuana (22%) than respondents who graduated in the 1960s (35%), the 1970s (34%), or the 1980s (39%) ( $P < .05$ ).

When asked whether Marinol should be accepted, 705 respondents (73%) agreed (20% "strongly agreed" and 53% "agreed") and 83 (9%) disagreed (2% "strongly disagreed" and 7% "disagreed"); 177 (18%) had no opinion. Of the 788 respondents with opinions, 89% accept the medical use of synthetic THC.

Almost half of the respondents (440, 48%) would prescribe marijuana to at least a few patients (4% to "many," 44% to "few") if it were legal; 200 (22%) would not prescribe it; and 274 (30%) said they would need more information. The 48% who would prescribe marijuana if it were legal is only slightly less than the 54% who have

prescribed Marinol, which is legally available. Of those oncologists who had previously recommended marijuana to at least one patient ( $N = 432$ ), 279 (65%) would prescribe marijuana to at least a few patients if it were legally available. Of those oncologists who had not recommended marijuana to at least one patient ( $N = 550$ ), 161 (29%) report that they would prescribe marijuana to at least a few patients if it were legally available.

## DISCUSSION

Although substantial, the response rate of 43% makes it difficult to determine precisely the views of the entire ASCO membership. The views of the sample who returned the survey may differ significantly from the views of those who did not. Since ASCO itself does not compile membership statistics for age, year of graduation from medical school, or patient population size, respondents cannot be compared with the full membership in these respects. However, no obvious anomalies in their characteristics were observed. Furthermore, the distribution of postmarks by state on the returned surveys—the main information available with which to evaluate response bias—very closely matched the geographic distribution of the survey forms mailed. Although there is nothing specific to suggest the presence of response bias, it cannot be ruled out. Therefore, all reported statistics should be considered indications of the general range of support for various propositions, rather than precise determinations.

The central empirical question the survey was designed to answer was whether a significant minority of the members of the ASCO supported the rescheduling of marijuana to permit its use in the treatment of nausea associated with cancer chemotherapy. The response rate is sufficiently large to resolve that question conclusively.

Of all oncologists with opinions responding to our survey, 54% supported rescheduling. Possible response bias makes it impossible to determine precisely whether a majority of the population with opinions actually holds that view. Ascertaining whether a significant minority of the population supports rescheduling is much simpler. A sensitivity analysis varying the degree of acceptance of the medical use of marijuana by nonrespondents to the survey suggests that support for rescheduling marijuana is indeed present in at

least a significant minority of our population. In the hypothetical event that all nonrespondents and all respondents without opinions were actually opposed to rescheduling, 13% of oncologists would remain in favor of rescheduling. If all nonrespondents and respondents without opinions were actually for rescheduling, 85% would support prescription availability of marijuana.

The survey data suggest that adding marijuana to the existing armamentarium of antiemetic agents would result in substantial benefits to patients. Oncologists believe smoked marijuana to be roughly as safe as legally available, oral synthetic THC (Marinol) and somewhat more effective. Of the oncologists responding to our survey, 44%—73% of those with opinions—consider marijuana both safe and efficacious.

Oncologists may prefer to prescribe smoked marijuana over oral THC for several reasons. The bioavailability of THC absorbed through the lungs has been shown to be more reliable than that of THC absorbed through the gastrointestinal tract,<sup>17-18</sup> smoking offers patients the opportunity to self-titrate dosages to realize therapeutic levels with a minimum of side effects, and there are active agents in the crude marijuana that are absent from the pure synthetic THC.

Although the survey did not ask whether marijuana or Marinol might be safer or more effective when used with specific patient groups, in space set aside for comments, 42 oncologists mentioned either that older patients had more problems with side effects from both Marinol and marijuana or that patients who had side effects tended to be inexperienced with marijuana. The increased prevalence

of side effects in older patients may be a cohort effect and not an age effect. Marijuana and Marinol may be most useful in younger or marijuana-experienced patients.

More than four in 10 respondents (44%) report that they have recommended the (illegal) use of marijuana to control emesis to at least one cancer chemotherapy patient. The fact that so many physicians have advised patients to commit an illegal act to obtain marijuana suggests a substantial discrepancy between clinical and regulatory opinions. Almost half (48%) would prescribe it to some of their patients if it were legal.

The survey reported here of the opinions and experiences of clinicians is not a controlled clinical study of the use of marijuana as an antiemetic. Nevertheless, this survey demonstrates that oncologists' experience with the medical use of marijuana is more extensive, and their opinions of it are more favorable, than the regulatory authorities appear to have believed. It appears that current regulations create the somewhat anomalous situation that a substantial fraction of all practicing oncologists at least occasionally commit an act—ie, counseling a patient to acquire and use a controlled substance—that constitutes a crime and that at least in principle could lead to the revocation of their license.

#### ACKNOWLEDGMENT

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