Health Conditions in Methamphetamine-Dependent Adults
3 Years After Treatment

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Objectives: Medical conditions in methamphetamine (MA) users have not been well characterized. Using both self-report and physical examination data, the aims of this study were to (1) describe the frequency of medical conditions in a sample of MA users 3 years posttreatment; (2) evaluate the association between medical conditions and MA use frequency; and (3) examine the relationship of route of administration with medical outcomes.

Methods: MA-dependent adults (N = 301) who participated in the Methamphetamine Treatment Project were interviewed and examined 3 years after treatment. Medical, demographic, and substance use characteristics were assessed using the Addiction Severity Index and Life Experiences Timeline. Current and lifetime medical conditions, electrocardiogram characteristics, and physical examination abnormalities were assessed.

Results: Among the most frequently reported lifetime conditions were wounds and burns (40.5%, N = 122) and severe dental problems (33%, N = 99), and a significant proportion of the sample evidenced prolonged corrected QT interval (19.6%, N = 43). Although health conditions were not associated with MA use frequency during follow-up, intravenous MA use was significantly associated with missing teeth (odds ratio = 2.4; 95% confidence interval, 1.2–4.7) and hepatitis C antibodies (odds ratio = 13.1; confidence interval, 5.6–30.1).

Conclusion: In this sample of MA users, dental problems and corrected QT prolongation were observed at elevated rates. Although posttreatment MA use frequency was not associated with a majority of medical outcomes, intravenous MA use exacerbated risk for dental pathology and hepatitis C. Longer term follow-up research is needed to elucidate health trajectories of MA users.

Key Words: medical, health, methamphetamine, intravenous, treatment

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Methamphetamine (MA) is a potent and highly addictive stimulant, the effects of which are longer lasting and more harmful to the central nervous system as compared with those of amphetamine.1 According to the most recent National Survey on Drug Use and Health, 10.4 million Americans aged 12 years and older report lifetime use of MA, representing 4.3% of the population.2 Despite significant health risks associated with use, current literature on MA-related medical illness, influenced primarily by case reports and autopsy series, is limited in scope relative to cocaine and other drugs of abuse. Acute and chronic medical conditions affecting multiple organ systems have been documented in MA users, most notably the cardiovascular and central nervous systems.3,4 MA intoxication is responsible for increasing incidences of hospital visits, and the rate at which MA is cited as a factor in emergency department presentations across the nation is rising steadily.5 Although the majority of fatalities related to MA intoxication involve accidents or violence, life-threatening medical consequences related to MA use have been reported, including myocardial infarction, aortic dissection, arrhythmias, pulmonary edema, seizures, and stroke.6–8

Some of the deleterious health-related effects of MA use may be accounted for, at least in part, by its cellular mechanisms of action. As a central and peripheral nervous system stimulant, MA facilitates the release of newly synthesized norepinephrine and dopamine from nerve terminals and, to some extent, blocks their synaptic reuptake.9 The resulting catecholamine surge mediates many of the acute symptoms and physiological changes associated with MA intoxication, including elevated heart rate and blood pressure. Excess circulating norepinephrine may contribute to organ pathology by causing vasoconstriction and ischemia. Likewise, the oxidation of accumulated intra- and extracellular catecholamines may lead to the formation of reactive oxygen species and subsequent cellular toxicity.3,4
Apart from its sympathomimetic effects, other putative mechanisms by which MA use may induce medical illness include direct toxicity to tissues and concurrent effects from other chemical and street drug contaminants. When examining physiologic sequelae of MA use, it is often difficult to differentiate the direct effects of the drug from general health consequences of drug-using lifestyles. Specifically, needle sharing, malnutrition, and concomitant use of other substances, such as tobacco and alcohol, may accelerate and exacerbate the onset and clinical course of MA-associated medical consequences.

In addition to acute physiologic effects including tachycardia, hypertension (HTN), and hyperthermia, MA use may precipitate a range of psychiatric symptoms including depression, insomnia, and anxiety. Severity and chronicity of MA-related psychiatric impairment varies, with reports of persistent psychotic symptoms and cognitive impairment for prolonged periods after drug discontinuation in some individuals. Chronic MA use confers risk of accelerated dental disease and dermato logical problems, including self-inflicted skin lesions in the context of psychotic symptoms. Additionally, MA use has been associated with adverse public health consequences, including the transmission of hepatitis and HIV via needle sharing and risky sexual behaviors.

Although prior investigations have characterized the various medical illnesses observed in stimulant-using populations, relatively few studies have examined the relationship between frequency and duration of drug use and health outcomes. Nevertheless, as would be expected, several studies have demonstrated an association between MA use frequency and medical problems. In a retrospective study of adult MA users who received drug abuse treatment, Greenwell and Brecht reported that prolonged and heavy lifetime MA use conferred an elevated risk of medical problems, particularly in younger individuals. Further characterizing a well-documented link between MA use, high-risk sexual behaviors, and HIV risk, MA use frequency predicted HIV infection rates in a population of men who have sex with men.

Although narrow in scope, the majority of studies examining the relationship between route of administration and health outcomes in stimulant abusers have highlighted poorer health outcomes in intravenous (IV) relative to non-IV users. In a study by Lexau et al., IV cocaine users were more likely to report hepatitis diagnoses and emergency room visits resulting from complications of drug use than those of non-IV users. In comparison with other routes of administration, MA injection was also a stronger predictor of hepatitis C infection in a population of more than 700 treatment-seeking MA users. Likewise, IV drug use history was associated with poorer overall health status in MA-using adults who received treatment for drug abuse, and greater psychiatric symptom severity has been documented in MA injectors relative to noninjectors, including history of chest pain, headaches, or seizures. Additionally, in a study of cocaine users in Australia, the prevalence of physical and psychologic problems did not differ between injection and noninjection users when frequency of use was accounted for. Nevertheless, IV route of administration has been shown to predict severity of dependence, length of use, and drug use frequency in both cocaine and MA users.

In light of mixed findings concerning MA use variables and their association with medical outcomes, the broad aim of the present investigation was to examine the predictive utility of route of administration and MA use frequency in relation to posttreatment health status in a sample of adult MA users. This is the first study to examine both objective and subjective measures of health status in this population. To this end, the aims of this study were to (1) describe the frequency of self-reported medical conditions and physical examination abnormalities in a sample of MA users 3 years posttreatment; (2) evaluate the association between medical conditions and posttreatment MA use frequency; and (3) examine the relationship of route of administration (eg, IV, intranasal, and smoking) with medical outcomes. Based on earlier literature suggesting that drug use frequency and IV route of administration may be associated with poorer medical outcomes, we hypothesized that more frequent posttreatment MA use and IV route of administration would predict greater severity of medical consequences relative to less frequent use and other methods of administration.

METHODS

Subjects

Participants (N = 301) were a subset of 1016 MA-dependent adults who were recruited to participate in the Methamphetamine Treatment Project (MTP), the largest randomized, controlled trial of psychosocial treatments for MA dependence to date described elsewhere. Individuals were excluded from the MTP if they exhibited medical or psychiatric impairment that warranted hospitalization or otherwise compromised their safety as a participant, required medical detoxification from alcohol or other drugs, had been enrolled in another treatment program within the past 30 days, and/or had legal, housing, or transportation problems precluding their safety or ability to participate in treatment.

This study was approved by both the Friends Research Institute and UCLA Institutional Review Boards. After a complete description of the study was provided to the participants, informed consent was obtained. Participants were compensated for their time with up to $200 in gift cards to local stores.

Procedures and Measures

Trained interviewers conducted local face-to-face assessments with study participants approximately 3 years after discharge from treatment. The Addiction Severity Index provided information regarding demographic and substance use characteristics, including preferred route of administration. The Life Experience Timeline interview (LET) was used to quantify MA use in the follow-up period. The LET is a measure adapted from the Natural History Interview in which substance use history is gathered using a month-by-
month timeline approach that links substance use to important life events.

The Health Status Survey provided information about past and current medical conditions within multiple organ systems (skin, cardiac, pulmonary, hepatic, gastrointestinal, genitourinary) as well as infectious diseases, sexually transmitted diseases (STDs), wounds, and injuries. This survey is a 42-item questionnaire derived from a subset of the National Health and Nutrition Examination Survey, an annual survey of health and nutritional trends within the United States conducted by the Center for Disease Control and Prevention. To supplement this information, a subset of questions from a comprehensive Medical History survey that was designed for use in substance using populations were used to assess past-year changes in weight, sleep problems, and sexual problems at 3-year follow-up.

Physical examinations were performed by study physicians at designated health facilities approximately 3 years posttreatment, and results were classified as normal or abnormal within the following categories: (1) general appearance, (2) skin, hair, or nails, (3) head, ears, eyes, nose, and throat, (4) oral cavity (mouth, condition of teeth, or dentures), (5) dentition (presence of missing teeth), (6) pulmonary, (7) cardiovascular (heart rate, rhythm, or murmurs) (8) abdomen, (9) extremities (range of motion, swelling, tenderness, radial and pedal pulses, or presence of varicosity), (10) mental status (mood, affect, memory, attention, concentration), (11) neurologic (cranial nerves, gait, coordination, motor tone and strength, or deep tendon reflexes), (12) movements (tremor, tic, choreoathetosis, or akathisia), and (13) sensory perception (pin prick, light touch, position, vibration).

Blood pressure, height, and weight were measured. Blood pressure was classified as normal or elevated (either systolic blood pressure \( \geq 140 \) and/or diastolic blood pressure \( \geq 90 \)). Body mass index (BMI) was calculated for each subject according to the following formula: weight (lb)/\[\text{height (in)}^2\] \times 703 and were categorized as normal (BMI 18.5–24.9), underweight (BMI <18.5), or overweight (BMI \( \geq 25 \)). Twelve-lead electrocardiograms (Ergs) were obtained according to standard procedures, and results were reviewed and interpreted by a board-certified internist. Based on prior literature, ECG characteristics were selected that may be affected by MA use and included the following: corrected QT interval (QTc) \( >440 \) milliseconds, tachycardia (heart rate \( >100 \) beats/minute), bradycardia (heart rate \( <60 \) beats/minute), and a pooled variable of other ECG abnormalities. QTc intervals were calculated using Bazett’s formula.

Blood samples were collected by venipuncture for clinical laboratory testing. Samples were sent to local Quest Diagnostics laboratories for analysis of standard hematology, blood chemistry, and lipid panels, serum liver assays (including aspartate aminotransaminase [AST], alanine aminotransaminase [ALT], and glutamyl transferase), Rapid Plasma Reagin (RPR), HIV, and hepatitis B and C serostatus. Qualitative immunoassays were conducted to detect hepatitis B virus antibody to the core antigen (anti-HBc) and hepatitis C virus (HCV) antibody (anti-HCV), with positive results indicating a history of recent or past infection with hepatitis B virus or HCV, respectively. Qualitative enzyme immunoassays were also used to screen for the presence of HIV-1 antibodies, with positive results confirmed by Western blot. Agglutination testing was performed for RPR, a screening test for syphilis.

In addition to the infectious disease tests listed earlier, the following variables were selected from the broader laboratory panels to capture measures of general health and potential abnormalities within a range of organ systems: creatinine, AST, ALT, hemoglobin, hematocrit, iron, and albumin. Creatinine, AST, and ALT were classified as normal or elevated; the remaining variables were categorized as normal or low.

Statistical Analysis

For all statistical tests, alpha was set at 0.05. All logistic regression and univariate analyses were run using SAS v.9 software. Primary outcome measures were binary variables of self-reported medical conditions, physical examination findings, and selected laboratory and ECG characteristics. The number of missing teeth was evaluated as both a binary and continuous variable. MA use outcomes included 1 dichotomous “use status” measure and 1 continuous “frequency” measure: (1) use status during the 3-year follow-up period, measured using the Addiction Severity Index (0 = no use; 1 = use on 1 or more days); (2) number of months during which use occurred in the follow-up period, measured by the LET.

The \( t \) tests and \( \chi^2 \) analyses were conducted to compare substance use and demographic characteristics between the original MTP sample (N = 1016) and the subset who completed physical examinations (N = 301). Mixed effects multivariate logistic regression models controlling for sociodemographic factors, lifetime years of MA use, and route of administration were used to determine odds ratios (ORs) of self-reported medical conditions, physical examination findings, and laboratory and ECG abnormalities as a function of MA use frequency in the 3-year follow-up period. Health conditions that were significantly associated with route of administration were subsequently analyzed using the method of recycled predictions to calculate expected probabilities of these outcomes among intranasal users, smokers, and IV users. Predicted values were adjusted for demographic differences between groups using logistic regression for binary outcomes and multiple linear regression for continuous outcomes.

RESULTS

Sample Characteristics

In a follow-up to the MTP, 587 participants consented to participate in psychosocial and medical assessments, an average of 3.1 years after treatment completion (SD = 0.48). Individuals who had participated in the MTP and who were psychologically and medically able to participate in the follow-up were considered eligible. Because of logistical constraints, only a subset of participants who completed health status questionnaires (N = 587) were available to obtain physical examinations (N = 301). Thus, the final sample for
this investigation included 301 individuals who obtained both objective and subjective measures of health. Of these, clinical laboratory test results were obtained for 285 participants, and 245 obtained 12-lead ECGs. Of those who completed health questionnaires, reasons cited for not obtaining physical examinations included moving out of the study area (N = 64); inability to schedule a convenient appointment (N = 63), inability to be located for contact (N = 42), incarceration (N = 36), declining this portion of the assessment (N = 37), not responding to contact attempts (N = 29), and death (N = 3). Documentation was missing for the remainder of participants (N = 12). Results of t tests and χ² analyses indicated that there were no significant differences between the original MTP sample and the subset who obtained physical examinations in age, gender, level of education, employment, marital status, route of administration, or ethnicity except for white subjects, who were represented at a significantly higher rate in the physical examination subset than the MTP sample (70% vs 60%, respectively), χ²(1) = 9.64, P < 0.01. There were significant differences between the pretreatment MTP sample and those who received physical examinations for the number of days of MA use in the past 30 days, t(1315) = −11.44, P < 0.0001, and lifetime MA use, t(1315) = 8.87, P < 0.0001, as would be anticipated given that these measures were administered at pre- and posttreatment, respectively.

Demographic characteristics of the original MTP sample are described elsewhere.28 At 3-year follow-up, the sample consisted of predominantly women (62.1%) and white subjects (70%), with an average age of 37 years (SD = 7.9) and an age range of 21 to 59 years. The preferred route of administration was smoking, followed by injection and intranasal use (Table 1). At follow-up, 22% (N = 66) of the sample reported having been abstinent throughout the follow-up period, and 28% (N = 84) had been using MA heavily (ie, during 26 or more months of follow-up). Participants had used MA an average of 11.1 years (SD = 6.5) at the time of examination. Although 50% (N = 150) of individuals reported using alcohol at follow-up and 31% (N = 93) reported using cannabis, the rates of other drugs of abuse were relatively low (opiates: 12% [N = 36]; sedatives or hypnotics: 8% [N = 24]; cocaine: 3% [N = 9]).

### Frequency of Medical Conditions

#### Self-report

Rates of self-reported medical conditions in this sample of adults 3 years posttreatment for MA dependence are presented in Table 2. Among the most frequently reported lifetime conditions were wounds and burns (40.5%, N = 122), back injuries (34.9%, N = 105), severe dental problems (33%, N = 99), STDs (31%, N = 96), and asthma (28.9%, N = 87). Hepatitis and urinary system (ie, kidney or bladder) illness were reported in 14.6% (N = 44) and 22.6% (N = 68) of the sample, respectively. Of particular interest given the relatively young average age of the sample (ie, 37 years) were a history of stroke in 1.3% (N = 4), myocardial infarction in 2.0% (N = 6), blindness in 1.7% (N = 5), and hearing impairment or deafness in 13.6% (N = 41) of study participants.

<table>
<thead>
<tr>
<th>Characteristic (N = 301)</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, female</td>
<td>187</td>
<td>62.1</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/remarried</td>
<td>70</td>
<td>23</td>
</tr>
<tr>
<td>Divorced/widowed/separated</td>
<td>105</td>
<td>35</td>
</tr>
<tr>
<td>Single</td>
<td>126</td>
<td>42</td>
</tr>
<tr>
<td>Employed</td>
<td>213</td>
<td>71</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>211</td>
<td>70</td>
</tr>
<tr>
<td>Hispanic</td>
<td>39</td>
<td>13</td>
</tr>
<tr>
<td>African American</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Asian</td>
<td>37</td>
<td>12</td>
</tr>
<tr>
<td>Others (American Indian/Alaskan)</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Route of administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>193</td>
<td>64</td>
</tr>
<tr>
<td>Injection</td>
<td>64</td>
<td>21</td>
</tr>
<tr>
<td>Intranasal</td>
<td>44</td>
<td>15</td>
</tr>
<tr>
<td>Mean</td>
<td>37.0</td>
<td>7.9</td>
</tr>
<tr>
<td>Age at follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education, years at follow-up</td>
<td>12.5</td>
<td>1.7</td>
</tr>
<tr>
<td>Days using MA, past 30 at follow-up</td>
<td>4.5</td>
<td>8.6</td>
</tr>
<tr>
<td>Years using MA at follow-up</td>
<td>11.1</td>
<td>6.5</td>
</tr>
</tbody>
</table>

**MA. methamphetamine.**

At the time of interview, weight gain and sleep difficulty during the past year were reported in nearly half of the sample (47.3%, N = 142 and 40.3%, N = 121, respectively). Other commonly cited current health conditions included severe dental problems (21.9%, N = 66), headaches (20.9%, N = 63), asthma (20.9%, N = 63), and arthritis (16.6%, N = 50). Again, given the relatively young average age of the sample, the presence of arthritis in 16.6% (N = 50) and hearing impairment or deafness in 11.3% (N = 34) of the participants were noteworthy findings.

### Physical Examination and Laboratory Studies

The frequencies of physical examination abnormalities and selected clinical laboratory findings are presented in Table 3. Of note, greater than half the sample was overweight (65.7%, N = 150), and more than 40% had abnormalities noted on examination of the oral cavity (41.3%; N = 213). Over half the individuals had missing teeth (64.2%, N = 185), and the average number of missing teeth was 4.6 (SD = 7.1). HTN was observed in 21.5% (N = 195) of participants. Abnormalities on mental status examination (including mood, affect, memory, attention, and concentration) were noted in 16.3% (N = 49) of individuals. Abnormal neurologic findings were present in a significant proportion of the sample; 6.7% (N = 20) evidenced disorders of movement (ie, tremor, tic, akathisia, or choreoathetosis), 11% (N = 33) were noted to have abnormalities on sensory examination, and 13.6% (N = 41) presented with other neurologic problems (ie, cranial nerve findings, abnormal deep tendon reflexes, or problems with gait, coordination, motor strength, or tone).
As reported in Table 3, frequencies of clinical laboratory abnormalities were generally unremarkable. However, elevated rates of hepatitis C antibody and hepatitis B core antibody, indicating prior exposure or current infection with these viruses, were found in 16.3% (N = 45) and 12.9% (N = 24) of participants, respectively. In line with these findings, elevated liver function tests (ie, AST and ALT) were present in approximately 10% of individuals. Rates of HIV infection and RPR, a screening test for syphilis, were very low (1.1%, N = 3), respectively. Compared to previous reports, high rates of elevated creatinine and AST were noted in 27.7% (N = 60) of the sample. These included a combination of abnormal axis deviations (N = 13), heart blocks (N = 10), early or late transitions (N = 9), sinus arrhythmias (N = 8), low voltage (N = 8), old infarcts (N = 6), premature atrial or ventricular complexes (N = 5), nonspecific T-wave changes (N = 4), atrial or ventricular enlargement (N = 3), delayed R-wave progression (N = 3), and early repolarization (N = 1).

### Electrocardiogram

Selected ECG variables are presented in Table 3. Approximately half (49.8%, N = 122) of the participants had at least one ECG abnormality. A prolonged QTc interval was found in a significant proportion of subjects (19.6%, N = 43). Interestingly, an abnormally slow heart rate (ie, bradycardia) was noted in a higher percentage of individuals than rapid heart rate (ie, tachycardia) 9.7% [N = 21] and 3.7% [N = 8]).

### Association of Medical Illnesses with MA Use During Follow-up

In mixed model logistic regression analyses controlling for demographics, lifetime MA use, and route of administration, no significant relationships were found between self-reported lifetime health problems and MA use status during the follow-up period, with the exception of back injury and severe dental problems. Contrary to hypotheses, participants who used MA during the follow-up period were significantly less likely to report a lifetime history of back injury or dental problems than those who did not use MA posttreatment.
(OR = 0.3; 95% confidence interval [CI], 0.2–0.6 and OR = 0.4; 95% CI, 0.2–0.8, respectively). No significant relationships were found between current self-reported health conditions and MA use frequency during the entire 3-year follow-up period or in the 30 days earlier to interview. Likewise, no physical examination, laboratory, or ECG abnormalities were associated with MA use frequency either during follow-up or in the 30 days before examination.

**Association of Route of Administration with Medical Conditions**

In the regression analyses, IV users were significantly more likely to report the following lifetime medical conditions relative to smokers (comparison group): hepatitis (OR = 15.3, 95% CI, 6.4–36.8), dental problems (OR = 2.2, 95% CI, 1.2–4.0), and STDs (OR = 2.1, 95% CI, 1.2–3.9). Intranasal users were significantly more likely than smokers to experience a history of kidney and bladder problems (OR = 2.9, 95% CI, 1.2–7.3). On physical examination, the presence of missing teeth was significantly more likely to be associated with IV use than smoking (OR = 2.4, 95% CI, 1.2–4.7). Other physical examination findings were not significantly related to route of administration. Among clinical laboratory abnormalities, IV users were 13.1 times more likely to have hepatitis C antibodies than smokers (95% CI, 5.6 30.1), but route of administration did not predict the presence of hepatitis B core antibody.

As reported in Table 4, predicted rates of these selected medical conditions were calculated and compared between MA smokers, IV users, and intranasal users. Relative to smokers, analyses indicated that IV users experienced significantly higher lifetime rates of hepatitis, kidney and bladder problems, dental disease, and STDs. IV users also had significantly higher rates of dental illness than those of intranasal users. On physical examination, significantly more IV users evidenced missing teeth than smokers, and the average number of missing teeth within the 2 groups was 6.2 (SD = 2.35) and 3.8 (SD = 2.1), respectively.

**TABLE 4.** Predicted Probabilities of Medical Conditions by Route of Administration

<table>
<thead>
<tr>
<th>Condition</th>
<th>Route of Administration</th>
<th>Injector (n = 78)</th>
<th>Smoker (n = 195)</th>
<th>Intranasal (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime medical conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis (%)†</td>
<td>39.5</td>
<td>5.5</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Kidney/bladder problems (%)‡</td>
<td>29.4</td>
<td>17.7</td>
<td>37.5</td>
<td></td>
</tr>
<tr>
<td>Dental problems (%)‡</td>
<td>47.7</td>
<td>28.9</td>
<td>21.9</td>
<td></td>
</tr>
<tr>
<td>Sexually transmitted diseases (%)‡</td>
<td>43.9</td>
<td>26.8</td>
<td>34.3</td>
<td></td>
</tr>
<tr>
<td>Physical examination conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of missing teeth (%)</td>
<td>76.4</td>
<td>58.8</td>
<td>70.5</td>
<td></td>
</tr>
<tr>
<td>Number of missing teeth*</td>
<td>6.2</td>
<td>3.8</td>
<td>5.9</td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05, significant difference between intravenous and smoking.
†P < 0.05, significant difference between intravenous and intranasal.
‡P < 0.05, significant difference between intranasal and smoking.

**DISCUSSION**

The results of this study of adults 3 years after treatment for MA dependence replicate and extend research suggesting elevated prevalence rates of certain health conditions in stimulant abusers, most commonly related to cardiovascular and neurologic abnormalities, dental disease, and infectious disease risk.11,40 This study is the first to characterize a broad range of current and lifetime medical conditions in previously treated MA users using both subjective and objective measures of health and to examine the relationship of these outcomes to route of administration and MA use frequency. To this end, IV route of administration was found to be associated with a subset of medical outcomes. Contrary to hypotheses, however, frequency of use during the follow-up period did not predict current health conditions as measured by self-report, physical examination, laboratory analyses, and ECG.

**Frequency of Medical Conditions in MA Users**

In line with an emerging body of literature highlighting an association between MA use and poor dentition, a substantial proportion of study participants evidenced significant dental disease, both on physical examination and by self-report. Although a direct causal link between MA use and dental pathology has not been established, elevated rates of caries, missing teeth, and other oral health problems have been observed in MA users.41 Putative cited mechanisms of MA-related enamel erosion include xerostomia (ie, dry mouth) caused by alpha-adrenergic stimulation, compensatory and excessive consumption of soft drinks, poor oral hygiene, and the acidic composition of the drug.15

Findings from this study are also consistent with extant literature describing catecholamine-mediated cardiac toxicity in MA users. The frequency of reported HTN, a known consequence of MA use,42 was more than double that of young adults (age 18–44 years) in the general population (7.3%).43 The considerably higher rate of HTN evident on physical examination relative to self-report may be attributable to factors including underreporting, underdiagnosis, or inconsistent cutoffs used to establish diagnosis. Additionally, the frequency of acute myocardial infarction (AMI) was twice that of cardiovascular disease (including AMI, angina, and coronary heart disease) in younger adults in the United States (1.0%).43 This finding supports multiple citations in the literature to date of amphetamine-related AMI,44,45 including an association between amphetamine and AMI in young users, as suggested by both case reports46 and a recent population-based study.47

Replicating prior literature demonstrating elevated rates of prolonged QTc intervals in MA users,26 QTc >440 milliseconds emerged as the most common ECG abnormality in this sample. Prolonged QTc has also been observed in conjunction with the use of other drugs, including cocaine48 and psychotropics.49 The clinical implications of QTc prolongation in substance users are significant, albeit varied; prolonged QTc may be associated with structural heart disease,50 and individuals with prolonged QTc are susceptible to potentially fatal ventricular arrhythmias. The higher frequency of bradycardia on ECG relative to tachycardia was...
also of interest, as this has not been reported previously in treatment-seeking MA users. Reflex bradycardia has been identified in animal studies after administration of higher doses of MA. In addition, bradycardia may be found as a normal variant in healthy persons or may represent preexisting or acquired conduction deficits.

Finally, in line with well-documented deleterious effects of MA on the nervous system, neurologic symptoms were present in a notable proportion of the sample, as were abnormalities on mental status examination. Although specific conditions were not elucidated and characterization of nervous system impairment was not a primary focus of this study, MA may have deleterious effects on mental status and neurologic functioning in users, including cognitive deficits, psychiatric symptoms, and movement disorders.

**Association of Medical Conditions with Frequency of Use and Route of Administration**

Contrary to hypotheses, posttreatment MA use frequency did not predict current medical conditions, physical examination or laboratory abnormalities, or ECG characteristics. Chronicity of MA use, as measured by lifetime years of use, was included as a covariate in analyses and was not found to be a significant predictor of any health condition. In contrast, limited extant literature has demonstrated a significant association between frequency and chronicity of drug use and medical illness in MA users. Discrepancies in these findings may be attributable in part to differences in design and measured outcomes between studies.

Unexpectedly, MA users who reported a lifetime history of severe dental problems or back injury were significantly less likely to have used MA during the 3-year follow-up period. These findings were not replicated, however, when current medical conditions and physical examination abnormalities were examined, suggesting that these findings were an artifact of recall bias, a limitation of self-report. Findings with extant literature and with objective examination results may not be attributable in part to differences in design and measured outcomes between studies.

Extending prior work investigating the relationship between route of administration and health problems in stimulant users, IV MA use was a significant predictor of several medical conditions. Consistent with prior work, IV MA use was associated with hepatitis C exposure and self-reported history of STDs. These findings are not surprising, given the well-documented link between MA injection, needle sharing, and risky sexual behaviors causing increased transmission rates of hepatitis C, HIV, and other STDs.

Of note, IV route of administration was significantly associated with both subjective and objective evidence of dental disease. The average number of missing teeth in the IV users (6.2) exceeded that found in the general population (1.4 to 4 in 20- to 59-year-olds). Although dental pathology in MA users has been well-documented in prior literature, its relationship with route of administration has not been previously investigated. It is possible that severity and potency of IV MA use exacerbate risk of dental disease relative to other routes of administration through various mechanisms, including xerostomia and poor oral hygiene. Coupled with prior observations of dental disease in users who do not smoke MA, the current findings support the proposal by Shaner et al that corrosion of enamel via acidic contaminants in smoked MA cannot fully explain dental pathology in MA users.

**Limitations**

This study had several potential limitations. First, health conditions were assessed in a relatively young population of MA users at a single time point posttreatment. In light of the possibility that MA exerts cumulative damage over time and that selected medical effects may be delayed, replication with longer follow-up periods is needed to elucidate the health consequences of MA use. Additionally, findings may not be generalizable to MA users not seeking treatment or older users, each of whom may have more severe medical pathology. Second, the ability to determine the effects of treatment on health trajectories was limited, as medical questionnaires were administered 3 years after, but not before treatment. Third, because of limited statistical power, alcohol and other drug use were not controlled for in multivariate analyses, further limiting the ability to ascertain the contribution of these factors to outcomes. Fourth, the study did not use an intent-to-treat design, restricting the ability to examine the full range of illness severity in relation to treatment outcomes. Fifth, because users may alternate routes of administration over time, the effects of IV and other routes of administration might have been underestimated in this study. Finally, because of the significant proportion of subjects lost to follow-up from the original MTP sample, results may not be broadly applicable to treatment-seeking MA users.

**CONCLUSIONS**

Prior research on the long-term health effects of MA use is limited in scope, yet increased knowledge and understanding of the potential medical consequences of MA is important to enhance treatment efforts and services for users. In this relatively young population of previously treated MA users, certain health conditions and laboratory findings consistent with known consequences of stimulant use were observed at elevated rates. For a subset of conditions, disease risk was exacerbated by IV use. Although posttreatment MA use frequency was not associated with a majority of medical outcomes, further research is needed to elucidate physical health trajectories of MA users, effects of treatment on health conditions, etiologies of medical conditions in MA users, and health effects of MA relative to other drugs of abuse.
REFERENCES


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