Clinical Characteristics of Central European and North American Samples of Pregnant Women Screened for Opioid Agonist Treatment

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Key Words

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Abstract

Background: Little comparable information is available regarding clinical characteristics of opioid-dependent women from different countries. In the present study, women from the USA, Canada and a Central European country, Austria, screened for participation in the Maternal Opioid Treatment Human Experimental Research study, were compared with respect to their demographic and addiction histories. **Methods:** Pregnant women ($n = 1,074$) were screened for study participation using uniformed clinical criteria and instruments. The screening results were compared with regard to exclusion, demographics, drug use, and psychosocial and treatment histories. **Results:** Compared to the screened US and Canadian women, Austrian women were more likely to be younger ($p < 0.001$), white ($p < 0.001$), had significantly lower levels of educational attainment ($p < 0.001$), were less likely to use opioids daily ($p < 0.001$) and more likely to have been prescribed buprenorphine ($p < 0.001$). Compared to both rural and urban US groups, the Austrian group was less likely to have legal issues ($p < 0.001$) and was younger when first prescribed agonist medication ($p < 0.001$). **Conclusion:** The differences between North American and European

groups may offer unique insights concerning treatment and pregnancy outcomes for opioid-dependent pregnant women.

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Introduction

An estimated total of 8 million people worldwide abuse opioids, and women constitute a particularly vulnerable group, especially under circumstances of pregnancy and child care [1]. Internationally, the majority of women in opioid agonist treatment are of childbearing age, yet little comparable information is available regarding clinical characteristics of opioid-dependent pregnant women from different countries [2]. Overall, the benefits of opioid maintenance treatment versus medical withdrawal for the mother outweigh the costs when considering improved prenatal care and the effects on the neonate [3]. However, national differences in treatment modalities, in the regulation of opioids and in prescribing all indicate that the clinical samples may be different and should be tested.

Methadone, a full μ -opioid agonist, is the established maintenance medication for opioid-dependent pregnant women in the USA [4–6], Canada [7] and in most European countries [2], and buprenorphine has recently been

proposed as a valuable addition to the treatment armamentarium due to emerging evidence of a more favorable outcome for the neonate [5, 8–10]. American and European pregnant women can equally benefit from maintenance treatment during pregnancy, yet differences in prescribing exist between the USA, Canada and Austria. In the USA, office-based maintenance treatment has only been established since 2002 with the approval of the buprenorphine-naloxone combination tablet by the US Food and Drug Association; before that, only specialized addiction clinics were allowed to offer treatment, restricting access and availability [11]. In contrast, buprenorphine treatment experience has been gathered in Europe since the mid-1990s, and office-based treatment is common for methadone and buprenorphine. Similar considerations apply to regulations on opioids. The USA have a particularly restrictive drug policy with a major focus on law enforcement concerning drug offences, whereas most European countries have more liberal drug policies.

In the present study, pregnant opioid-dependent women from the USA, Canada and a Central European country, Austria, screened for participation in the Maternal Opioid Treatment Human Experimental Research (MOTHER) study, a randomized, double-blind, double-dummy, flexible-dosing and parallel-group clinical trial involving 8 sites in North America and Europe [12], were compared with respect to their demographic and addiction histories. These issues were selected for comparison between samples because each of them has been reported to influence pregnancy and drug treatment outcome, and to vary geographically [13–16]. The purpose of the present analyses was to gain insight into international differences between samples in an effort to understand the diversity of treatment-relevant variables within this cohort of patients.

Subjects and Methods

As described above, our data were collected as part of the MOTHER study. The participating sites obtained local institutional review board approval, and independent oversight was provided by a data safety monitoring board constituted for this study.

Sites

The 8 participating sites were the following ones: USA – Brown University (Providence, R.I.), Wayne State University (Detroit, Mich.), Johns Hopkins University (Baltimore, Md.), Thomas Jefferson University (Philadelphia, Pa.), Vanderbilt University (Nashville, Tenn.), University of Vermont (Burlington, Vt.); Canada – University of Toronto (Toronto, Ont.); Europe – Medical University of Vienna (Vienna, Austria). The coordinating center for all

sites was the Center for Substance Abuse Research at the University of Maryland (College Park, Md.), and the lead site was the Johns Hopkins University. Each site was sponsored by the US National Institute on Drug Abuse through an independent R01 grant award. The North American sites were considered as 3 groups: rural USA (Burlington, Nashville and Providence), urban USA (Baltimore, Philadelphia and Detroit) and Canadian (Toronto).

Participants

A total of 1,074 opioid-dependent pregnant women were screened for eligibility. In both North America and Europe, participants were interviewed coming either from already established drug treatment programs (e.g. methadone clinics) or various medical clinics, by referral from other physicians (local obstetricians, general practitioners or psychiatrists) and by self-referral, or data were gathered by review of medical charts of women already in treatment. Each site had a different final sample of screened participants: $n = 76$ (Burlington), $n = 45$ (Nashville) and $n = 39$ (Providence) in the rural USA group ($n = 160$); $n = 450$ (Baltimore), $n = 199$ (Philadelphia) and $n = 57$ (Detroit) in the urban USA group ($n = 706$); $n = 37$ (Toronto) in the Canadian group; $n = 171$ (Vienna) in the Austrian group.

Procedures

Instrument of Assessment. Variables assessed at the initial screening were collected using a screening questionnaire developed specifically for the MOTHER trial. The questions were in part dichotomous (yes/no answers) or else multiple choice (a selection of answers was provided, as listed in parentheses below), the rest requested numeric information (i.e. questions on the dosage of the most recent medication). The questions included inquiries about the type of current drug treatment (detox/maintenance, referring to opioid agonist maintenance, i.e. methadone or buprenorphine/none), estimated delivery date, buprenorphine/methadone intake and dose (last 30 days), cocaine use (last 30 days), daily or almost daily opioid use (last 30 days), number of times treated for drug abuse in lifetime, maternal age, estimated gestational age (EGA) in weeks, legal status (not legally involved, parole, probation, impending trial, unknown or other), native language (English, German or Non-English/Non-German), detoxification (yes/no), race/ethnicity (white, black, Hispanic, American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander or other), marital status (never married, married, widowed, divorced, separated or unknown), employment status (employed, unemployed or disabled), pregnancy intention (plan to become pregnant sooner/now/never/don't know/unsure) and history of treatment (how many times prescribed methadone/buprenorphine, age at first prescription of methadone/buprenorphine, last time ingested methadone/buprenorphine, i.e. within the last 48 h/48 h to 1 week/more than 1 week, and highest dose during most recent episode). These questions were posed via interview (face to face or by phone) or by reviewing the medical record.

Eligibility. The eligibility criteria for further screening were age between 18 and 41 years, EGA between 6 and 30 weeks, current opioid dependence and single-fetus pregnancy. Women who reported having had a serious concurrent medical illness, prescription and nonprescription use of benzodiazepines (3 or more times per week) or use of alcohol in the past 30 days were not eligible for study participation. Furthermore, women who reported having pending legal issues, psychiatric reasons, or were non-

Table 1. Screening sample comparison in the MOTHER study of the rural US, urban US and Canadian sites with the European site

	Rural USA (Vermont, Vanderbilt, Brown)	Urban USA (JHU, TJU, Detroit)	Canadian (Toronto)	European (Vienna)	Total	p
Number of women screened	160	706	37	171	1,074	
Met all eligibility criteria ¹	98 (61.3)	324 (45.9)	9 (24.3)	87 (50.9)	518 (48.2)	<0.001
Reasons for exclusion						
Outside age range	2 (1.3)	8 (1.1)	1 (2.7)	3 (1.8)	14 (1.3)	
Low EGA	7 (4.4)	39 (5.5)	0 (0.0)	12 (7.0)	58 (5.4)	
Multiple fetuses	1 (0.6)	7 (1.0)	0 (0.0)	4 (2.3)	12 (1.1)	
Medical condition	14 (8.8)	92 (13.0)	12 (32.4)	10 (5.8)	128 (11.9)	<0.001
No-show	8 (5.0)	8 (1.1)	1 (2.7)	22 (12.9)	39 (3.6)	<0.001
Benzodiazepine use/abuse	14 (8.8)	94 (13.3)	10 (27.0)	27 (15.8)	145 (13.5)	0.025
Detoxification	0 (0.0)	12 (1.7)	2 (5.4)	0 (0.0)	14 (1.3)	0.019
High EGA	16 (10.0)	49 (6.9)	6 (16.2)	22 (12.9)	93 (8.7)	0.019
Legal issue	11 (6.9)	63 (8.9)	3 (8.1)	1 (0.6)	78 (7.3)	<0.001
Psychiatric reason	2 (1.3)	26 (3.7)	2 (5.4)	7 (4.1)	37 (3.4)	
Alcohol abuse/dependence	1 (0.6)	64 (9.1)	4 (10.8)	1 (0.6)	70 (6.5)	<0.001
Language	0 (0.0)	1 (0.1)	0 (0.0)	1 (0.6)	2 (0.2)	
Not dependent	4 (2.5)	4 (0.6)	0 (0.0)	1 (0.6)	9 (0.8)	0.049
Unknown/missing data ²	4 (2.5)	8 (1.1)	3 (8.1)	4 (2.3)	19 (1.8)	

Values in parentheses are percentages. JHU = Johns Hopkins University; TJU = Thomas Jefferson University.

¹ One urban US case was missing data on all eligibility criteria (including reasons for exclusion) and was considered not eligible for the study due to missing data.

² A reason for exclusion was not specified for 18 individuals, and 1 individual was missing all eligibility data.

English- (USA/Canada) or non-German-speaking (Austria) were not eligible to be approached for informed consent.

Statistical Analysis

Comparative analyses were conducted to test significant differences among the 3 groups. Fisher's exact tests were used for categorical data, after determining that all comparisons included at least 1 cell in which the expected value was 5 or less. In cases of a statistically significant Fisher test result, standardized residuals were examined. Analysis of variance (ANOVA) was used to detect differences among continuous variables. In cases of significant F statistics, pairwise comparisons with Bonferroni correction were conducted. Statistically significant p values from the Fisher exact tests are provided, as are the test statistics (F), degrees of freedom and p values for the ANOVA results. For analytic purposes, $p \leq 0.05$ was considered significant. Comparison tests were performed using Stata 10.0 (StataCorp LP, College Station, Tex., USA).

Results

Reasons for Not Being Eligible to Be Approached for Informed Consent

The most common reason for early initial exclusion at the Austrian and urban US sites was cooccurring benzodiazepine use, which was also a frequent reason at the

rural US and Canadian sites (table 1). The most common reason for not being eligible in the Canadian group was the presence of medical conditions. For the rural US group, the most common reason for exclusion was having an EGA above 30 weeks at the time of screening.

Comparative analyses of the 14 potential reasons for exclusion yielded 8 variables with significant differences among the groups. Having a medical condition, 'not showing' for an appointment, benzodiazepine use/abuse, detoxification, having a high EGA, being involved in a legal issue, alcohol use/abuse and nondependence differed significantly across the groups. The investigation of standardized residuals revealed that for 5 variables (medical condition, no-show, high EGA, legal issues and alcohol abuse/dependence), the Austrian site appeared to exclude a comparatively smaller proportion of participants due to medical conditions ($p < 0.001$), legal issues ($p < 0.001$) and alcohol abuse/dependence ($p < 0.001$) in comparison to the other sites. However, the Austrian site appeared to exclude a comparatively higher proportion of participants for not showing up ($p < 0.001$) and having a high EGA ($p = 0.019$) in comparison to the other sites. For the other 3 significant effects, the Canadian site was driv-

Table 2. Comparison of demographic and treatment history characteristics in the MOTHER study of the rural US, urban US and Canadian sites with the European site

	Rural USA (Vermont, Vanderbilt, Brown) (n = 160)	Urban USA (JHU, TJU, Detroit) (n = 706)	Canadian (Toronto) (n = 37)	European (Vienna) (n = 171)	Total (n = 1,074)	Test statistics ¹ p
<i>Demographic characteristics</i>						
Education level, years (n = 982)	11.9 ± 1.6	11.3 ± 1.7	12.4 ± 1.9	9.9 ± 1.8	11.1 ± 1.8	40.0 ± 3, <0.001
Marital status						
Married	25 (15.6)	58 (8.2)	4 (10.8)	24 (14.0)	111 (10.3)	0.001
Not married	121 (75.6)	625 (88.5)	30 (81.1)	141 (82.5)	917 (85.4)	
Unknown	14 (8.8)	23 (3.3)	3 (8.1)	6 (3.5)	46 (4.3)	
Race						
White	144 (90.0)	456 (64.6)	30 (81.1)	169 (98.8)	799 (74.4)	<0.001
Black	1 (0.6)	210 (29.7)	0 (0.0)	0 (0.0)	211 (19.6)	
Other	15 (9.4)	40 (5.7)	7 (18.9)	2 (1.2)	64 (6.0)	
Employment status						
Employed	40 (25.0)	35 (5.0)	8 (21.6)	29 (17.0)	112 (10.4)	<0.001
Not employed	110 (68.8)	640 (90.7)	28 (75.7)	136 (79.5)	914 (85.1)	
Unknown	10 (6.3)	31 (4.4)	1 (2.7)	6 (3.5)	48 (4.5)	
Maternal age, years (n = 1,065)	26.2 ± 5.4	29.4 ± 5.8	27.3 ± 6.0	25.0 ± 5.1	28.1 ± 5.9	35.6 ± 3, <0.001
Legal issues						
Involved	108 (67.5)	486 (68.7)	32 (86.5)	141 (82.5)	767 (71.4)	<0.001
Not involved	33 (20.6)	184 (26.1)	3 (8.1)	25 (14.6)	245 (22.8)	
Unknown	19 (11.9)	36 (5.1)	2 (5.4)	5 (2.9)	62 (5.8)	
Plan to be pregnant						
Sooner/now	20 (12.5)	65 (9.2)	2 (5.4)	43 (25.1)	130 (12.1)	<0.001
Later/never	131 (81.9)	531 (75.2)	28 (75.7)	125 (73.1)	815 (75.9)	
Unknown	9 (5.6)	110 (15.6)	7 (18.9)	3 (1.8)	129 (12.0)	
EGA at screening, weeks (n = 1,061)	17.5 ± 8.6	17.6 ± 8.0	20.9 ± 7.6	18.5 ± 8.3	17.9 ± 8.1	
<i>Cocaine use</i>						
Cocaine use (last 30 days)						
Used in last 30 days	18 (11.3)	401 (56.8)	13 (35.1)	12 (7.0)	444 (41.3)	<0.001
Did not use in last 30 days	138 (86.3)	296 (41.9)	23 (61.2)	154 (90.1)	611 (56.9)	
Unknown	4 (2.5)	10 (1.4)	1 (2.7)	5 (2.9)	19 (1.8)	
<i>Opioid use</i>						
Daily opioid use						
Used daily/almost daily	122 (76.3)	675 (95.6)	36 (97.3)	60 (35.1)	893 (83.1)	<0.001
Did not use daily/almost daily	34 (21.3)	23 (3.3)	0 (0.0)	104 (60.8)	161 (15.0)	
Unknown	4 (2.5)	8 (1.1)	1 (2.7)	7 (4.1)	20 (1.9)	
<i>Tobacco use</i>						
Cigarettes smoked/day (among smokers) (n = 185)	14.0 ± 7.8	13.3 ± 6.4	N/A ²	15.1 ± 8.2	13.9 ± 7.2	

ing the effect for both benzodiazepine use/abuse and detoxification, and the rural US group was driving the effect for not being opioid-dependent.

Demographic, Substance Use and Psychosocial Variables

Compared to the North American groups, Austrian women had less education ($p < 0.001$ for all groups), a

lower maternal age (urban USA: $p < 0.001$), were more often white ($p < 0.001$) and more likely to report planned pregnancies ($p < 0.001$) (table 2). In addition, the investigation of the standardized residuals revealed that legal issues in the Austrian group were contributing to the significant difference among the groups; Austrians had more legal issues than Canadians, but less than the participants from the USA. There also appeared to be differ-

Table 2 (continued)

	Rural USA (Vermont, Vanderbilt, Brown) (n = 160)	Urban USA (JHU, TJU, Detroit) (n = 706)	Canadian (Toronto) (n = 37)	European (Vienna) (n = 171)	Total (n = 1,074)	Test statistics ¹ p
<i>Past and current drug treatment</i>						
Times treated for drug abuse in lifetime (n = 1,021)	3.2 ± 4.2	3.3 ± 3.5	0.7 ± 0.9	2.8 ± 2.6	3.2 ± 3.4	4.6 ± 3, 0.003
Ever prescribed						
Methadone	53 (33.1)	320 (45.3)	28 (75.7)	47 (27.5)	448 (41.7)	<0.001
Buprenorphine	25 (15.6)	16 (2.3)	0 (0.0)	43 (25.2)	84 (7.8)	
Methadone and buprenorphine	31 (19.4)	200 (28.3)	0 (0.0)	47 (27.5)	278 (25.9)	
Neither	39 (24.4)	48 (6.8)	0 (0.0)	26 (15.2)	113 (10.5)	
Unknown	12 (7.5)	122 (17.3)	9 (24.3)	8 (4.7)	151 (14.1)	
Number of times prescribed (among those prescribed)						
Methadone (n = 697)	1.5 ± 1.2	2.2 ± 1.6	N/A	1.5 ± 0.9	2.0 ± 1.5	7.5 ± 2, 0.001
Buprenorphine (n = 362)	1.3 ± 0.6	2.0 ± 1.6	N/A	1.2 ± 0.7	1.7 ± 1.4	
Age first prescribed (among those prescribed)						
Methadone (n = 699)	25.2 ± 4.8	26.3 ± 5.5	22.9 ± 5.8	21.8 ± 3.7	25.5 ± 5.4	9.6 ± 3, <0.001
Buprenorphine (n = 357)	24.6 ± 5.2	25.6 ± 5.8	N/A	21.7 ± 4.7	24.5 ± 5.7	15.0 ± 2, <0.001
Current treatment						
None	60 (37.5)	90 (12.7)	7 (18.9)	16 (9.4)	173 (16.1)	<0.001
Detoxification	3 (1.9)	15 (2.1)	2 (5.4)	0 (0.0)	20 (1.9)	
Maintenance	94 (58.8)	594 (84.1)	27 (73.0)	152 (88.9)	867 (80.7)	
Unknown	3 (1.9)	7 (1.0)	1 (2.7)	3 (1.8)	14 (1.3)	
Type of medication-assisted treatment (last 30 days)						
None	60 (37.5)	127 (18.0)	7 (18.9)	70 (40.9)	264 (24.6)	<0.001
Methadone	80 (50.0)	565 (80.0)	27 (73.0)	54 (31.6)	726 (67.6)	
Buprenorphine	19 (11.9)	7 (1.0)	1 (2.7)	44 (25.7)	71 (6.6)	
Unknown	1 (0.6)	7 (1.0)	2 (5.4)	3 (1.8)	13 (1.2)	
Recency of methadone use (among those prescribed)						
<48 h before	73 (83.9)	445 (84.1)	26 (92.9)	47 (49.5)	591 (80.0)	<0.001
48 h to 1 week before	4 (4.6)	15 (2.8)	1 (3.6)	4 (4.2)	24 (3.2)	
>1 week before	10 (11.5)	61 (11.5)	1 (3.6)	41 (43.2)	113 (15.3)	
Recency of buprenorphine use (among those prescribed)						
<48 h before	18 (32.1)	4 (1.9)		40 (44.4)	62 (17.3)	<0.001
48 h to 1 week before	2 (3.6)	9 (4.2)	N/A	0 (0.0)	11 (3.1)	
>1 week before	35 (62.5)	200 (93.9)		49 (54.4)	284 (79.1)	
Highest dose (most recent episode among those prescribed)						
Methadone (n = 683)	76.3 ± 53.7	71.4 ± 41.9	75.2 ± 41.9	70.2 ± 29.2	72.1 ± 42.1	8.4 ± 2, <0.001
Buprenorphine (n = 206)	15.9 ± 9.7	12.5 ± 7.4	N/A	10.4 ± 5.9	12.4 ± 7.7	

Values denote means ± SD or numbers with percentages in parentheses. JHU = Johns Hopkins University; TJU = Thomas Jefferson University.

¹ An F statistic and degrees of freedom are only reported for the ANOVA. For Fisher's exact tests, only p values are reported.

² There were no smokers in the Canadian group.

ences across the groups with regard to marital status and employment status; however, for marital status and employment status, it appears from the standardized residuals that the results from the rural USA group are driving the effect. There were no significant differences across the groups with regard to gestational age.

With regard to drug use, a comparatively low percentage of Austrian women reported having used cocaine in the past 30 days ($p < 0.001$) and using opioids daily or almost daily ($p < 0.001$). There were no differences across locations with regard to the proportion of women who reported smoking cigarettes.

Past and Current Drug Treatment Experiences

The Austrian group was more likely to report being prescribed buprenorphine only and less likely to report being prescribed methadone only ($p < 0.001$) (table 2). In addition, the Austrian group reported being prescribed methadone fewer times than the urban US group ($p = 0.006$), and the age at first prescription was lower for the Austrian group for both methadone and buprenorphine in comparison to the participants from urban areas of the USA ($p < 0.001$ for both). In addition, the low proportion of European participants who reported having used methadone less than 48 h before, and the high proportion who reported having used it more than a week before strongly contributed to the significance of the Fisher test. Similarly, the high proportion of Austrian participants who reported having used buprenorphine less than 48 h before, and the low proportion who reported having used it more than a week before strongly contributed to the significance of that Fisher test. Finally, with regard to dosage, the participants at the urban US sites reported a greater average highest dose value than the participants at the Austrian site. There were no significant differences across the sites with regard to the highest doses of methadone.

With regard to the differences in the number of times ever treated for drug abuse, the significant effect was driven by the comparatively low average number of times the participants from Canada had been treated. In addition, the standardized residuals showed that the high proportion of participants in the rural USA currently receiving no treatment and the low proportion currently receiving maintenance were driving the effect of current treatment.

Discussion

This study represents the first examination of differences between North American and Austrian women attained in the screening process for a randomized controlled trial of agonist medications conducted in an opioid-dependent pregnant sample. It is striking how different the Austrian and North American samples are when they are compared on demographic and psychosocial characteristics. This is best appreciated in the comparison between the urban US and Austrian groups, with the Austrians being younger, white, married, less educated, more likely to have a planned pregnancy, less involved in legal issues, having fewer medical comorbidities, less likely to have used cocaine in the past 30 days

and less likely to have daily opioid use. This suggests more medically and psychosocially complex patients in the urban USA, and several of these types of variables including polydrug use problems [12] and older age [17] have been shown to be associated with a premature termination of treatment in pregnant drug-dependent patients.

Regarding the study results on legal issues, the percentage of women who were involved in the legal system at the time of screening was high for both the rural (32.5%) and the urban (30.3%) US groups. The Austrian sample had a substantially lower rate of legal involvement (16.4%), a rate comparable to that of the Canadian women (13.5%). While the specific nature of these legal issues was unknown, it could be expected that some portion of them were related to drug issues and another portion to outstanding bench warrants reflecting an unresolved legal status. Similar to many other European countries, Austria has a less repressive drug policy than the USA, including a lower priority given to the prosecution of drug users. The US federal drug control expenditure focuses on law enforcement rather than prevention and treatment [18]. Additionally, the lower legal involvement rates observed in the Austrian sample may, in part, be due to recent developments in the drug treatment systems of several European countries, which focus on alternatives to incarceration for opioid-dependent individuals when addressing drug-related crime.

The comparisons on the drug treatment history variables revealed several interesting observations. First, Austrian women were treated more often with buprenorphine and less often with methadone compared to other groups. This may be due to the fact that buprenorphine has been widely available in Austria since 1999, whereas it had not been approved for use to treat nonpregnant patients in the USA or Canada until 2002 and 2008, respectively. Buprenorphine is still not approved worldwide for use among pregnant women. Second, Austrian women were younger when they were first prescribed either methadone or buprenorphine compared to their rural and urban US counterparts, suggesting that access to treatment in Austria may be more readily available than in the USA. As reflected in our results, access to treatment was a particular problem for the rural US women, a significantly higher percentage of whom had never been prescribed methadone or buprenorphine (24.4%) compared to Austrian women. At the same time, a significantly lower percentage of urban US and Canadian women had never been prescribed either drug compared to Austrian women. This discrepancy may have resulted be-

cause many of the Austrian women who had never received methadone or buprenorphine had been treated with slow-release oral morphine, which for the indication of opioid maintenance treatment is only approved in some European countries, among them Austria [19–22]. The use of slow-release oral morphine was not assessed in the present study.

The Austrian model of treatment coverage builds mainly on office-based treatment as typically seen in France, Switzerland and Austria where 75% of all patients are treated in office-based settings by general practitioners, by a low-threshold treatment approach. In addition, particularly for patients with comorbidities, there are only a small number of specialized clinics which provide both maintenance treatment and additional therapeutic services [23–25]. This system has been shown to produce patient outcomes comparable to those seen in specialized treatment, and it continues to be quite successful [25, 26]. The mainstreaming of treatment helps to overcome barriers to treatment related to geography and stigmatization in the health care system [27, 28].

For the population of pregnant opioid-dependent patients (represented by our screened sample) numerous barriers to treatment persist in the USA, such as a lack of third-party reimbursement, child care and transportation, the last of which may play a greater role for women in rural areas who need to travel a great distance to access treatment [29, 30]. Studies have shown that among drug users in treatment, transportation was the most important barrier to accessing ancillary services [31–33]. Additionally, the stigma associated with maternal substance abuse and the fear of an involvement with child protective services [34] remain complicating issues for pregnant opioid-dependent women worldwide.

Limitations

There are several limitations to this study that bear mentioning. First, the differences in screening modalities may have played a role in the group differences observed. However, the design of the questionnaire with mostly multiple-choice answers probably kept this within tolerable limits. Second, while the amounts of missing data were modest in this screened sample, any missing data provide an opportunity for bias. Third, the survey data were subject to self-report, so that a bias cannot be ruled out and accuracy may not always be a given, especially when reporting on things from the distant past (telescoping effects). Fourth, a more conservative *p* value may also result in a different pattern of results. Fifth, there were considerable differences in screening sample size be-

tween the different sites, which might be explained by differences in the availability of treatment, in the sense that women in already established treatment settings may have been less interested in screening. Sixth, having only 1 European site versus subsamples of 3 rural US groups, 3 urban US groups and 1 Canadian group raises the question of how representative Austria is of Europe as a whole. The 2008 annual report of the European Monitoring Centre for Drugs and Drug Addiction with the title *State of Drug Problems in Europe 2008* describes Austria along with Malta and Italy as the 3 European countries with the highest prevalence estimates for problem opioid use. Certain differences between European countries are evident, so that the Austrian findings are not entirely representative of Europe as a whole. A younger age at first prescription is characteristic of some parts of Europe according to the report which outlines that patients entering maintenance treatment in Austria, Greece, Finland, Ireland and countries that joined the EU after 2004 tend to be younger at their entry into a treatment setting [35]. However, only a selected number of European countries were included in the report, excluding the UK, and it is likely that substantial differences would also be found when, for instance, comparing Eastern to Western European countries. Finally, at the current stage of research, it is unknown to what extent these observed differences are related to maternal and drug treatment outcomes.

Implications

This is the first international analysis of screening data from 2 different continents for opioid-dependent pregnant women. Similar protocols have been applied in the past [6, 36], but they did not include screening women in multiple countries and did not investigate differences in the screening data. The results suggest 3 implications for clinicians and clinical researchers. First, in light of the large number of screened women, this sample likely represents the typical opioid-dependent pregnant woman seeking treatment rather than a selected sample of atypical participants in a clinical trial; thus, conclusions regarding the general population of opioid-dependent pregnant women may be drawn from this sample. Second, there were worrying rates of concurrent benzodiazepine use disorders observed in the entire screening sample across all regions and both continents. This issue is of grave concern not only because of poor psychosocial functioning and treatment response [37–41], but also because of pharmacodynamic interactions with methadone and buprenorphine, leading to significant central nervous system depression [42–44] and death [45–48]. Phy-

sicians need to be more aware of this problem before prescribing benzodiazepines and to have a heightened awareness of psychiatric comorbidities, which often foster concomitant benzodiazepine abuse [49]. Additional significant problems for pregnant opioid-dependent women lie not only in the teratogenic potential of benzodiazepines [50], but also in the possibly prolonged and more severe manifestation of symptoms of the neonatal abstinence syndrome [51]. Third, in the USA, opioid-dependent pregnant women should be screened, assessed, and assisted in legal and financial issues which impair their access to healthcare. Finally, in future research projects with drug-dependent pregnant women, social and geopolitical matters must be considered when developing and implementing treatment protocols.

Conclusion

In summary, our data on demography, psychosocial functioning, drug use and drug treatment suggest that Austrian opioid-dependent women present with multiple

characteristics which suggest an overall milder addiction than North American women, most notably women from the urban USA. Many socioeconomic factors contribute to the greater morbidity of urban American opioid-dependent women and differences documented here may serve to guide policy makers to aim at an amelioration for some of these troubling issues in order to optimize treatment approaches and diminish associated stigma.

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