SUPPLEMENT ARTICLE

Psychoeducation Improves Hepatitis C Virus Treatment During Opioid Substitution Therapy: A Controlled, Prospective Multicenter Trial

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Background. People who inject drugs (PWID) have a high prevalence of hepatitis C virus (HCV) infection. However, PWID are considered "difficult to treat," requiring a specifically adapted treatment setting, including psychosocial support.

Methods. In this prospective, German trial, the impact of psychoeducation (PE) on retention and sustained virologic response (SVR) during HCV therapy among PWID was evaluated. We included 198 patients in opiate substitution therapy, who fulfilled indications for antiviral treatment. All patients received pegylated interferon alfa-2a and ribavirin therapy. Patients in the intervention group (n = 82) received manualized PE sessions.

Results. In patients with HCV genotype 1 or 4 (GT 1/4), PE was associated with increased treatment completion (76% vs 55%, $P = .038$), whereas PE had no such effect among GT 2/3 patients, who showed fewer dropouts and higher SVR rates. Among GT 1/4 patients, a minimum of 5 PE sessions was associated with increased SVR (71% vs 48%, $P = .037$). Multivariate regression analyses confirmed the impact of PE in GT 1/4 and revealed further predictors for retention and SVR, such as preexisting mental distress and adverse events.

Conclusions. In patients with a higher risk of dropout due to GT 1/4 or mental distress, PE was shown to improve retention and SVR. PE is an effective supportive intervention for HCV therapy among PWID.

Clinical Trials Registration. NCT00844272.

Keywords. hepatitis C; antiviral treatment; psychoeducation; injection drug users; retention.

In developed countries, people who inject drugs (PWID) represent the largest subgroup of hepatitis C virus (HCV)–infected patients, with HCV prevalence ranging from 60% to 97% [1]. However, the treatment of PWID is considered difficult. Problems with medication compliance and retention can be exacerbated by neuropsychiatric side effects, which may arise under interferon therapy [2, 3]. Indeed, PWID show a high prevalence of psychiatric comorbidities, predominantly mood and anxiety disorders [4].

Although opioid dependence is no longer an absolute contraindication for HCV therapy, neuropsychiatric concerns may still lead to the exclusion of PWID from interferon treatment [2]. However, a growing number of studies have demonstrated the feasibility of antiviral therapy in this patient population and reported comparable rates of treatment completion and sustained virologic response (SVR) [5–7]. Retention appears to be influenced by psychiatric comorbidity, as preexisting depression was found to reduce treatment completion rates [8]. Given that neuropsychiatric symptoms often arise in HCV treatment and may lead to problems in treatment adherence, it is important to develop and evaluate psychoeducational programs for patients with

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chronic HCV [2]. A growing number of psychosocial interventions including self-help groups, psychoeducation (PE), and case management have been successfully implemented in HCV therapy. However, to date, no controlled trial has systematically investigated these effects. We conducted this prospective, controlled multicenter study to evaluate the impact of PE on retention and SVR. PE is a well-established component in the treatment of chronic mental illnesses, particularly schizophrenia and bipolar disorders [9]. In manualized group sessions, patients are provided with information about the causes and effects of the illness. PE aims to lead to increased understanding and better handling of the disorder, and to reinforce patients' own resources and coping skills. In the treatment of substance abuse, PE has successfully been applied within the German heroin trial [10].

Assuming that an increase in self-responsibility and self-efficacy is of particular importance in this patient population, we hypothesized that patients receiving PE would show higher rates of retention in treatment and SVR. Furthermore, we aimed to clarify the inherent role of PE among other factors influencing retention and SVR, such as genotype, age, and mental stress.

PATIENTS AND METHODS

We included opioid-substituted men and women aged between 18 and 70 years with chronic HCV (genotypes 1–4) infection, verified by polymerase chain reaction (PCR). A minimum stability in opiate substitution treatment (OST) was required, that is, either keeping the last 5 appointments or fulfilling criteria for take-home assignment. Patients had to be drug-naive to the medication provided and not coinfected with human immunodeficiency virus or hepatitis B virus. The usual (contra-) indications for the treatment of chronic HCV, as specified in current treatment guidelines, were adhered to [11, 12]. Psychiatric exclusion criteria comprised of severe comorbid mental disorders, such as untreated major depression or acute psychosis. Concomitant drug use was assessed, but was not an exclusion criterion. All participants gave written informed consent. The study was approved by all ethics committees at participating study sites. Recruitment took place between January 2005 and December 2008 in a total of 24 centers.

An overview of the study design is given in Figure 1. PE was carried out in 7 of 24 study sites, all of which had several years of experience in OST. Assignment to either PE or standard treatment was not randomized, but determined by the respective treatment center. The PE group comprised 82 patients, and 107 patients formed the control group. All participants received pegylated interferon (peg-IFN) alfa-2a and ribavirin, following the guidelines of the German Society for Digestive and Metabolic Diseases [11]. No protease inhibitors or other direct-acting antivirals were used. According to guidelines, patients with genotype 2 or 3 (GT 2/3) were treated for 24 weeks, and those with genotype 1 or 4 (GT 1/4) for 48 weeks.

Psychoeducation

PE group sessions lasted 60 minutes under supervision. The manualized program was especially tailored to PWID in HCV treatment, including the following components:

- Module 1: HCV infection, symptoms, course of illness, interaction with opioid dependence, and risk factors.
- Module 2: HCV treatment, side effects, psychiatric and somatic comorbidities, reinfection and drug use, and risk behavior.
- Module 3: Coping strategies, resources and self-help, effective use of healthcare support, the role of social environment, healthy living, and nutrition.

Each module comprised at least 3 regular sessions, and a variable number of update sessions, to repeat particular topics. In our study, GT 2/3 patients received 12 regular and 5 update sessions, whereas GT 1/4 patients received 12 regular and 10 update sessions. PE started with HCV treatment and was administered weekly, with a break of several weeks between regular and update sessions.

Assessments

Data were prospectively collected at baseline and at defined times during treatment, comprising:

1. Sociodemographic and clinical data (Table 1).
2. Adverse events (AEs): defined as any unintended and unfavorable symptom or disease that appeared during antiviral treatment (such as depressions, insomnia, weight loss), not necessarily related to the antiviral medication.
3. Brief Symptom Inventory: This 53-item self-report questionnaire is a measure of mental stress and psychiatric symptoms on 9 primary dimensions, for example, depression, anxiety, somatization, paranoid ideation. As a measure of symptom severity, the Global Severity Index (GSI) is calculated by summarizing the scores of all completed items. Patients with a normalized T score $\geq$60 (1 standard deviation above the mean) are considered suffering from clinically relevant distress [13].

Primary Outcome Measures

We used 2 different parameters for retention, based on the time of dropout. *Completion of treatment* was defined as completion of the HCV therapy according to the treatment plan, regardless of dropouts in the observation phase. *Completion per protocol* was defined as attendance throughout the entire study, comprising HCV therapy, a subsequent 6-month observation phase, and follow-up assessment. Reasons for dropout were documented (Figure 1). All patients were actively followed for SVR, which was assessed by means of PCR 24 weeks after the end of treatment, regardless of treatment completion.

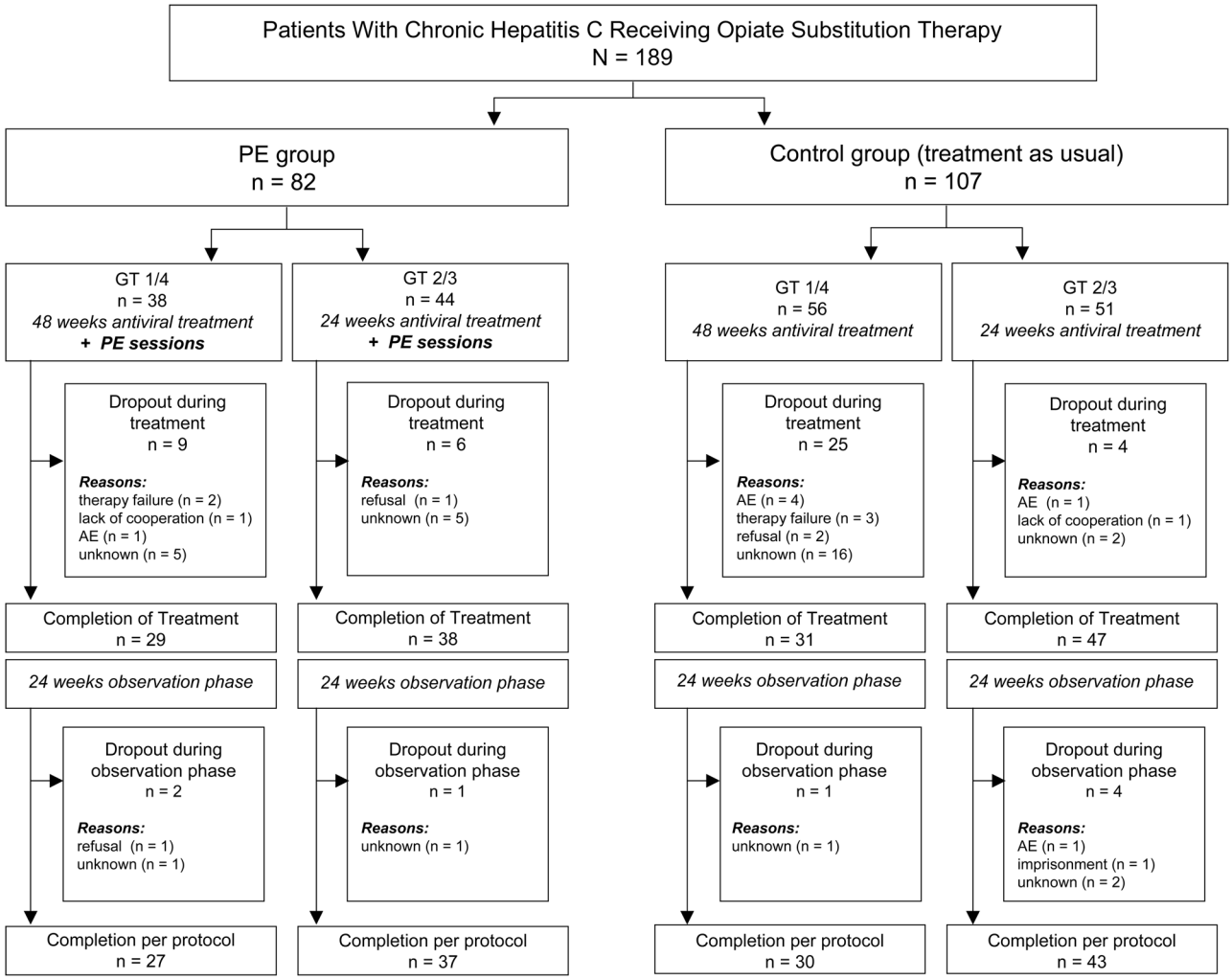

Figure 1. Study design and completion rates. All patients received standard antiviral treatment with pegylated interferon alfa-2a (180 μg/week) and ribavirin (800–1200 mg/day). Abbreviations: AE, adverse event; GT, genotype; PE, psychoeducation.

Statistical Analyses

All analyses were performed using SPSS for Windows, version 16.0. To assess group differences, we used χ^2 tests for categorical data and *t* tests for interval-scaled variables. At first, we determined the differences between PE patients and controls, stratified for genotype (GT 1/4 vs GT 2/3). In a secondary analysis, we compared patients who attended at least 5 PE sessions (PE $\geq$ 5, n = 70) with the remaining sample (PE < 5, n = 119). This 5-session cutoff was based on results from the German heroin trial, where patients with ≥5 PE sessions showed a significantly higher improvement of health status [14] (unpublished data).

To identify other factors influencing retention and SVR, we first conducted bivariate analyses, using χ^2 tests for categorical data or Bravais-Pearson correlations for metric variables, respectively. We subsequently performed unconditional multivariate logistic regression analyses for each primary outcome measure. The significance of predictors was assessed via the Wald χ^2 test, adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated using regression coefficients, and the Hosmer-Lemeshow test was performed to evaluate goodness of fit. The amount of variance explained by the model was estimated using the Nagelkerke R^2 value [15]. For a better interpretation of the results, we determined bivariate correlations (Cramer's V) between all predictors. Generally, all tests of significance were 2-tailed, with a *P* value of ≤.05 being considered statistically significant.

RESULTS

Regarding sociodemographic and clinical characteristics, PE patients and controls differed in age, substitution medication, and treatment center patient/staff ratio (Table 1).

Table 1. Sociodemographic and Clinical Sample Characteristics

Characteristic	Total (N = 189)	PE (n = 82)	Controls (n = 107)	*P* Value
Age, y, mean ± SD	36.4 ± 7.5	34.3 ± 7.0	37.9 ± 7.6	.001
Age ≥40 y	64 (34%)	22 (27%)	42 (39%)	.074
Male	139 (74%)	62 (76%)	77 (72%)	.573
<10 y of education	122 (69%)	58 (71%)	64 (68%)	.704
Employed	85 (46%)	38 (46%)	47 (47%)	.979
HCV genotype				.414
1/4	94 (50%)	38 (46%)	56 (52%)	
2/3	95 (50%)	44 (54%)	51 (48%)	
Years of HCV infection, mean ± SD	8.5 ± 6.1	8.2 ± 6.4	8.7 ± 6.0	.609
Baseline HCV RNA, IU/mL, mean ± SD	1 772 196 ± 3 200 775	1 328 534 ± 2 232 305	2 091 633 ± 3 725 025	.096
GSI, mean ± SD	56.9 ± 12.8	55.4 ± 12.7	58.2 ± 12.8	.167
GSI clinically relevant (≥60)	72 (44%)	30 (40%)	42 (48%)	.288
Substitution dosage[a]				.748
Low	45 (24%)	18 (22%)	27 (25%)	
Medium	114 (60%)	52 (63%)	62 (58%)	
High	30 (16%)	12 (15%)	18 (17%)	
Time in OST				
>6 mo	143 (80%)	64 (78%)	79 (82%)	.478
OST medication				.025
Methadone/diamorphine (n = 2)	150 (80%)	72 (88%)	80 (75%)	
Buprenorphine	37 (20%)	10 (12%)	27 (25%)	
No concomitant drug use[b]	104 (57%)	45 (55%)	59 (60%)	.576
≥1 AE during treatment	123 (67%)	55 (68%)	68 (65%)	.719
Antidepressant medication, before/during treatment	75 (40%)	30 (39%)	45 (42%)	.446
Treatment center characteristics				
No. of OST patients per year	153.03 ± 81.80	150.98 ± 72.68	154.61 ± 88.46	.763
High OST patient to staff ratio (>16)[c]	94 (50%)	32 (39%)	62 (58%)	.010

Abbreviations: AE, adverse event; GSI, Global Severity Index; HCV, hepatitis C virus; OST, opiate substitution treatment; SD, standard deviation.

[a] Dosage categories: methadone: low, <60 mg; medium, 60–100 mg; high, >100 mg. Buprenorphine: low, <6 mg; medium, 6–18 mg; high, >18 mg. Diamorphine: low, <300 mg; medium, 300–700 mg; high, >700 mg.

[b] Negative urinalyses (heroin, cocaine, amphetamines, and benzodiazepines) across all visits; conducted at 9 (GT 2/3) or 13 (GT 1/4) defined times during treatment.

[c] No. of OST patients per year/number of staff members; categories "high" and "low" defined by median-split.

Effects of Genotype

Retention and SVR were lower in GT 1/4 than in GT 2/3: completion of treatment: 64% versus 90%, odds ratio (OR) = .21 (95% confidence interval [CI], .10–.45), $P < .001$; completion per protocol: 61% versus 84%, OR = .29 (95% CI, .15–.58), $P < .001$; SVR: 56% versus 81%, OR = .30 (95% CI, .16–.58), $P < .001$.

Effects of PE

GT 1/4 patients had significantly higher treatment completion when receiving PE (76% vs 55%, OR = 2.60 [95% CI, 1.04–6.49], $P = .038$; Figure 2*A*). The secondary analysis (PE ≥ 5 vs PE < 5) revealed a stronger effect for patients who attended ≥5 PE sessions (completion of treatment: 86% vs 71%, OR = 2.40 [95% CI, 1.10–5.23], $P = .025$; completion per protocol: 84% vs 66%, OR = 2.82 [95% CI, 1.34–5.95], $P = .005$). We found no effect of PE on SVR. However, in GT 1/4 patients, PE ≥ 5 was associated with increased SVR (71% vs 48%, OR = 2.57 [95% CI, 1.05–6.28], $P = .037$; Figure 2*B*). No effects were found for GT 2/3 patients, who showed better treatment outcomes overall.

Other Factors

Age was related to retention and SVR. Mean age of treatment completers was lower than for dropouts (35.8 vs 38.4 years, $P = .042$, $T = 2.045$), and patients <40 years of age had higher SVR (76% vs 55%, OR = 2.62 [95% CI, 1.38–4.97], $P = .003$). Retention, but not SVR, was lower when AEs occurred (completion of treatment: 71% vs 89%, OR = .31 [95% CI, .13–.74], $P = .006$; completion per protocol: 71% vs 82%, OR = .45 [95% CI, .21–.95], $P = .034$). SVR was related to completion of treatment (OR = 23.87 [95% CI, 9.84–57.91], $P < .001$). In bivariate analyses, neither sex, employment, education, partnership,

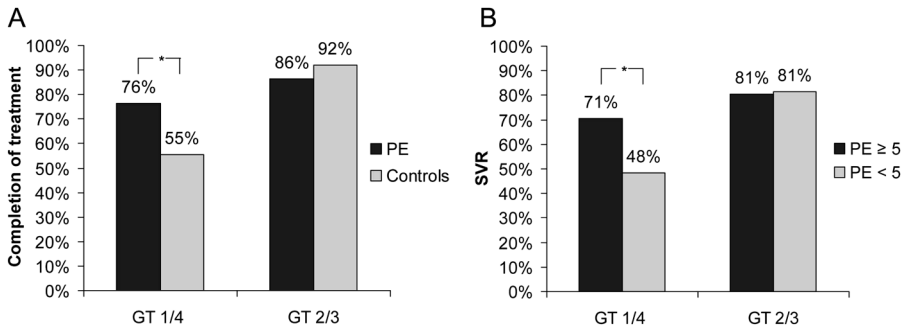

Figure 2. *A*, Completion of treatment depending on genotype (GT) and psychoeducation (PE). GT 1/4 patients receiving PE showed increased completion rates. *Odds ratio (OR) = 2.60 (95% confidence interval [CI], 1.04–6.49), $P = .038$. *B*, Sustained virologic response (SVR) depending on GT and the number of PE sessions. GT 1/4 patients who attended at least 5 PE sessions showed increased SVR rates compared to patients attending fewer or no PE sessions. *OR = 2.57 (95% CI, 1.05–6.28), $P = .037$. Abbreviations: GT, genotype; PE, psychoeducation; SVR, sustained virologic response.

baseline HCV RNA, years of HCV infection, substitution medication, time in substitution treatment, concomitant drug use, antidepressant medication, number of OST patients per year, nor patient/staff ratio were significantly associated with our outcome measures.

Multivariate Analysis (Logistic Regression)

It was hypothesized psychological distress (GSI score ≥60), a more complicated treatment (genotype, AEs), and a short time in OST (<6 months) would negatively influence retention. To determine PE effects on specific patient subgroups, we included interaction patterns for PE with the factors age, GT, AEs, and GSI (baseline score). Age (≥40 vs <40 years), type of OST medication (methadone vs buprenorphine), and OST patient to staff ratio (≤16 vs >16) were included to control for potential center effects.

Results are shown in Tables 2 and 3 and Supplementary Table 1, along with the unadjusted ORs obtained from bivariate analyses.

Significant predictors for completion of treatment were AEs, substitution medication, and the interaction PE × GT, indicating that patients without AEs, patients substituted with methadone, and GT 1/4 patients receiving PE were more likely to complete treatment.

Completion per protocol was significantly predicted by AEs and the interaction PE × GSI. This indicates that patients without AEs were more likely to complete treatment including follow-up, and patients with clinically relevant psychiatric symptoms at baseline showed higher completion rates when receiving PE (80% vs 62%).

SVR was predicted by completion of treatment, AEs, and the interaction PE × AE, indicating that patients who completed treatment were more likely to achieve SVR, along with patients who did not experience AEs. The interaction PE × AE displays the fact that among the small group of 15 patients without AEs and without SVR, 13 individuals were in the control group.

Correlations Between Predictors

Substitution medication was related to substitution dosage ($r = 0.182$, $P = .044$; higher dosages were more frequent in methadone). In small study sites (<80 OST patients per year), OST patient to staff ratios were lower ($r = 0.218$, $P = .003$). Patients with GT 1/4 were more likely to suffer from AEs ($r = 0.172$, $P = .020$). Likewise, patients with a clinically relevant GSI baseline score faced a higher risk of AEs during treatment ($r = 0.255$, $P = .001$). Patients ≥40 years had a higher probability for AEs ($r = 0.172$, $P = .019$), were generally in OST for >6 months ($r = 0.163$, $P = .030$), and were less likely to be substituted with a medium dosage ($r = 0.198$, $P = .025$). AE rates were lower among patients treated in smaller study sites (<80 OST patients per year; $r = 0.183$, $P = .013$), but also in institutions with higher (>16) OST patient to staff ratios ($r = 0.149$, $P = .043$). Furthermore, centers with higher patient to staff ratios had fewer patients with clinically relevant GSI scores ($r = 0.192$, $P = .014$), more patients substituted with buprenorphine ($r = 0.176$, $P = .016$), and more patients substituted with medium or high dosage ($r = 0.177$, $P = .015$). All associations with PE are shown in Table 1.

DISCUSSION

The development and evaluation of appropriate supportive interventions is of particular relevance for improving the feasibility and success of HCV therapy in PWID. To our knowledge, this is the first study that systematically evaluated a standardized PE intervention in the HCV therapy of PWID receiving OST in a prospective, controlled multicenter trial.

In GT 2/3 patients, who showed fewer dropouts overall, PE did not further improve retention. However, a significantly higher rate of completion of treatment emerged in the PE

Table 2. Multivariate Logistic Regression Model for Completion of Treatment

	Unadjusted Analyses			Multivariate Model		
Variable	OR	95% CI	*P* Value	OR	95% CI	*P* Value
PE	1.66	.82–3.36	.156	0.05	.01–33.95	.370
GT 1/4	0.21	.10–.45	<.001	9.76	.26–362.81	.217
Age <40 y	1.91	.96–3.82	.064	0.78	.03–21.21	.885
AE	0.31	.13–.74	.006	0.01	.01–1.23	.061
GSI <60	1.28	.61–2.67	.509	0.07	.01–1.46	.081
Methadone (vs buprenorphine)	1.80	.82–3.97	.142	3.96	1.09–14.39	.037
Time in OST <6 mo	2.61	.86–7.89	.081	1.69	.36–7.81	.504
Large institution (>80 OST patients/y)	0.95	.37–2.39	.905	1.00	.26–3.86	.997
Substitution dosage						.221
Medium vs low	0.66	.30–1.44	.292	0.79	.25–2.53	.689
High vs low	0.75	.26–2.17	.594	0.21	.04–1.27	.089
Staff to patient ratio <0.06	1.11	.57–2.18	.761	1.44	.51–4.12	.493
PE × GT						
GT 1/4	2.56	1.04–6.48	.038	0.04	.01–.58	.018
GT 2/3	0.54	.14–2.05	.359			
PE × age ≥40 y						
<40	1.37	.56–3.38	.490	2.56	.32–20.38	.375
≥40	1.89	.58–6.15	.287			
PE × AE						
≥1 AE	1.65	.74–3.67	.217	11.49	.72–183.09	.084
No AE	1.94	.35–10.86	.447			
PE × GSI						
GSI <60	1.14	.41–3.14	.797	6.82	.75–62.02	.088
GSI ≥60	2.24	.70–7.16	.168			

R^2 (Nagelkerke) = 0.450, goodness-of-fit-test (Hosmer-Lemeshow) $\chi^2(8) = 4.967$, $P = .761$.

Abbreviations: AE, adverse event; CI, confidence interval; GSI, Global Severity Index; GT, genotype; OR, odds ratio; OST, opiate substitution treatment; PE, psychoeducation.

condition in GT 1/4 patients, compared to controls. This effect was more evident when focusing on patients who had attended at least 5 PE sessions (PE ≥ 5). In accordance with previous findings, GT 1/4 patients were more likely to suffer from AEs [16]. The higher dropout rates may therefore be attributed to their higher rate of treatment complications, which could have made additional psychoeducational support more important.

In bivariate analyses, SVR was strongly associated with completion of treatment, followed by genotype and age. This indicates that patients were more likely to achieve SVR if they had GT 2/3, if they were <40 years of age, and if they completed antiviral treatment. All these factors were associated with lower rates of AEs, which therefore emerged as a main predictor for SVR in the multivariate model. We found no overall effect of PE on SVR. However, those GT 1/4 patients who attended at least 5 PE sessions (PE ≥ 5) showed significantly higher SVR rates, which we link back to the positive effect of PE on retention.

The interaction of GSI × PE predicted completion per protocol, indicating that patients with clinically relevant psychiatric symptoms were more likely to complete the study when receiving PE. A comparison of the mean GSI scores between the GSI <60 and the GSI ≥60 group revealed a remarkable difference in preexisting mental stress levels (47.84 ± 8.37 vs 68.55 ± 6.40). This is consistent with the findings of a recent study, reporting decreased retention rates in patients with clinically relevant depression at baseline [8]. Furthermore, our data indicate that GSI ≥60 patients face a higher risk of AEs during antiviral therapy. Both findings confirm the assumption that additional psychosocial support is of particular importance in patients with higher levels of mental distress. Others already recommended the implementation and evaluation of psychoeducational programs, given the high occurrence of neuropsychiatric symptoms in chronic HCV patients in general, and not only among PWID [2]. Future research should further examine the relationships between mental health, psychosocial support, and treatment outcome in larger samples.

Besides focusing on the predictors, it is equally important to look at the factors that did *not* predict our outcomes. It should

Table 3. Multivariate Logistic Regression Model for Sustained Virologic Response

	Unadjusted Analyses			Multivariate Model		
Variable	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Completion of treatment	23.87	9.84–57.91	<.001	35.85	8.76–146.67	<.001
PE	1.18	.63–2.19	.613	0.01	.01–7.77	.183
GT 1/4	0.30	.16–.58	<.001	0.62	.02–17.32	.778
Age <40 y	2.62	1.38–4.98	.003	7.14	.26–197.63	.246
AE	0.59	.30–1.18	.136	0.01	.01–.31	.015
GSI <60 y	1.29	.67–2.49	.443	1.63	.06–46.65	.777
Methadone (vs buprenorphine)	1.25	.59–2.67	.566	1.24	.29–5.24	.774
Time in OST <6 mo	1.41	.61–3.26	.414	0.38	.12–1.24	.110
Large institution (>80 OST patients/y)	0.70	.31–1.60	.396	0.45	.11–1.84	.268
Substitution dosage						.498
Medium vs low	0.51	.25–1.06	.070	0.64	.20–2.10	.462
High vs low	1.00	3.89–2.57	1.000	1.33	.31–5.61	.703
Staff/patient ratio <0.06	1.14	.62–2.11	.673	0.48	.16–1.47	.201
PE × GT						
GT 1/4	1.60	.69–3.71	.275	0.62	.07–5.45	.665
GT 2/3	0.63	.23–1.78	.383			
PE × age ≥40 y						
<40	1.07	.47–2.44	.867	0.74	.01–5.69	.772
≥40	0.99	.35–2.79	.987			
PE × AE						
≥1 AE	0.67	.31–1.41	.292	51.01	3.24–803.38	.005
No AE	6.78	1.38–33.42	.010			
PE × GSI						
GSI <60	1.23	.50–2.99	.650	0.72	.09–5.96	.760
GSI ≥60	0.96	.36–2.54	.934			

R^2 (Nagelkerke) = 0.578, goodness-of-fit-test (Hosmer-Lemeshow) $\chi^2(8) = 6.464$, $P = .595$.

Abbreviations: AE, adverse event; CI, confidence interval; GSI, Global Severity Index; GT, genotype; OR, odds ratio; OST, opiate substitution treatment; PE, psychoeducation.

be emphasized that neither previous time on OST nor concomitant drug use had any influence on retention or SVR. Although we required a minimum stability in OST, defined as attendance at the last 5 appointments, our results indicate that a minimum of several months in substitution treatment before antiviral therapy is not a necessary precondition. Furthermore, concomitant drug use had no negative influence either on retention or SVR. This is consistent with recent findings suggesting that these prerequisites in HCV treatment, as recommended by current guidelines, seem to lack empirical evidence [17, 18]. Choice of substitution medication (methadone vs buprenorphine) served as predictor for completion of treatment. Due to intercorrelations, this finding might also be attributed to substitution dosage, PE, or treatment center.

The most important limitation of this study relates to its naturalistic, nonrandomized design. Only 7 (mostly larger) centers implemented PE, which is reflected in different OST patient to staff ratios (Table 1). To take potential biases into account, we assessed bivariate relationships of patient to staff ratio and size of institution with our outcomes (no significant associations emerged), and we included these factors in the multivariate model. As neither size of institution nor patient to staff ratio predicted any of our outcomes, we do not assume that our results are substantially biased by center effects. A general difficulty in our data analyses were the rather small and unequal sizes of patient subgroups, and the resulting lack of statistical power made it harder to achieve higher levels of significance. Further, the association between PE ≥ 5 and retention could be considered somewhat artificial, because dropouts during the first 5 weeks of treatment were automatically allocated to the PE < 5 group. However, only 7 of the 52 dropouts occurred within the first 5 weeks, of which only 3 patients were in the PE group. In addition, the number of PE sessions attended was not correlated with the number of weeks in treatment; thus, the higher retention rates in PE ≥ 5 are unlikely to result from a methodical artefact.

To summarize, our study provides empirical support for a beneficial effect of PE in the treatment of chronic HCV infection. This is particularly relevant for patients with GT 1/4 and patients with high levels of mental distress, as they have a higher risk of treatment complications and dropout. A very encouraging finding is that, under the condition of attending at least 5 PE sessions, GT 1/4 patients showed significantly higher SVR rates. We therefore consider PE to be a relevant improvement of treatment setting. This study is based on a sample of (former) drug users. However, the differences found in GT and GSI subgroups suggest that PE could be of general importance for other "difficult-to-treat" patients (ie, those with GT 1/4 or high levels of preexisting mental distress). This might also be of relevance for the upcoming protease inhibitors in antiviral HCV treatment [19].

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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