Clinical and Patient-Reported Outcomes of Direct-Acting Antivirals for the Treatment of Chronic Hepatitis C Among Patients on Opioid Agonist Treatment: A Real-world Prospective Cohort Study

Bernd Schulte,1,4,9 Christiane S. Schmidt,1,4 Jakob Manthey,1,2 Lisa Strada,1 Stefan Christensen,3,4 Konrad Cimander,5 Herbert Göme,6 Pavel Khaykin,7 Norbert Scherbaum,9 Stefan Walcher,8 Stefan Mauss,6,9 Ingo Schäfer,7 Uwe Verthein,1 Jürgen Rehm,1,11–15 and Jens Reimer1,16

1Centre for Interdisciplinary Addiction Research, Department of Psychiatry, Medical Centre Hamburg-Eppendorf, Hamburg, Germany, 2Institute of Clinical Psychology and Psychotherapy & Center of Clinical Epidemiology and Longitudinal Studies, Technische Universität Dresden, Dresden, Germany, 3Center for Interdisciplinary Medicine Infectious Diseases, Muenster, Germany, 4Department of Gastroenterology and Hepatology, Muenster University Hospital, Muenster, Germany, 5Kompetenzzentrum Suchtmizin, Infektiologie und Cannabis-Therapie, Hannover, Germany, 6MediZentrum Hamburg, Praxis für Suchtmedizin, Hamburg, Germany, 7Praxis MainfrauArzt, Frankfurt am Main, Germany, 8LVR-Hospital Essen, Department of Addictive Behaviour and Addiction Medicine, Medical Faculty, University of Duisburg-Essen, Essen, Germany, 9Schwerpunktpraxis Konzept, Munich, Germany, 10Center for HIV and Hepatogastroenterology, Düsseldorf, Germany, 11Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, Ontario, Canada, 12Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada, 13Faculty of Medicine, Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada, 14Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada, 15Department of International Health Projects, Institute for Leadership and Health Management, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation, and 16Gesundheit Nord, Bremen, Germany

Background. Patient-reported outcomes (PROs) can help to reduce uncertainties about hepatitis C virus (HCV) treatment with direct-acting antivirals (DAAs) among people who inject drugs and increase treatment uptake in this high-risk group. Besides clinical data, this study analyzed for the first time PROs in a real-world sample of patients on opioid agonist treatment (OAT) and HCV treatment with DAAs.

Methods. HCV treatment data including virological response, adherence, safety, and PROs of 328 German patients on OAT were analyzed in a pragmatic prospective cohort study conducted from 2016 to 2018. Clinical effectiveness was defined as sustained virological response (SVR) at week 12 after end of treatment and calculated in per-protocol (PP) and intention-to-treat (ITT) analyses. Changes over time in PROs on health-related quality of life, physical and mental health, functioning, medication tolerability, fatigue, concentration, and memory were analyzed by repeated-measures analyses of variances (ANOVAs).

Results. We found high adherence and treatment completion rates, a low number of mainly mild adverse events, and high SVR rates (PP: 97.5% [n = 285]; ITT: 84.5% [n = 328]). Missing SVR data in the ITT sample were mainly caused by patients lost to follow-up after treatment completion. Most PROs showed statistically significant but modest improvements over time, with more pronounced improvements in highly impaired patients.

Conclusions. This real-world study confirms that DAA treatment among OAT patients is feasible, safe, and effective. PROs show that all patients, but particularly those with higher somatic, mental, and social burden, benefit from DAA treatment.

Keywords. direct-acting antivirals; hepatitis C virus; opioid substitution treatment; patient-reported outcome measures.
Beyond virological response, patient-reported outcomes (PROs) provide important information on overall health, symptoms, burden of disease, and response to treatment and are an important tool to improve patient-centered care, as they are free from third-party interpretation [14]. Thus, more than virological effectiveness alone, improvements in PROs may help to reduce patients’ fears and increase HCV treatment uptake in OAT settings and beyond [10, 15].

Clinical trials and cohort studies [16–18] have shown improved PROs like health-related quality of life, functioning, work productivity, fatigue, depression, and activity among non-PWID populations on DAA treatment. For OAT patients, comparable data are only available from a post hoc analysis of data collected from phase 3 clinical trials [19], and due to their strict inclusion criteria, the findings might be of limited generalizability. Given this, more real-world data are needed to inform patients and providers on PROs among PWID treated with DAA [20, 21]. The aim of the “Interferon-Free Antiviral Treatment of Chronic Hepatitis C Virus Infection Among Opioid Substituted Patients” (INFO) study was to assess the real-world effectiveness, safety, and PROs of DAA treatment among OAT patients in Germany.

**METHODS**

**Study Design and Population**

HCV treatment data of OAT patients were collected in a prospective cohort study under clinical routine conditions. Inclusion criteria comprised minimum age of 18 years, opioid dependence according to ICD-10, OAT for at least 3 months, CHC infection with virus genotypes 1–6, eligibility for DAA treatment according to the respective summary of product (SmPC), and written informed consent (Figure 1). Both HCV treatment–naïve and –experienced patients were eligible. Patients with severely impaired cognitive functioning impeding study participation were excluded. Overall, 328 OAT patients from 19 OAT units (on average 17.3 patients per unit, ranging from 3 to 40) spread across 8 out of 16 German federal states participated. Patient recruitment took place between January 2016 and December 2017, and data collection was finished in October 2018 (last follow-up assessment).

**Clinical and Patient-Reported Outcome Measures**

Clinical effectiveness was defined as a sustained virological response (SVR) at week 12 or week 24 after the end of treatment (SVR12/24). Safety end points were all adverse events (AEs) collected between treatment initiation and week 12 after the end of treatment (tSVR12). An AE was defined as any new untoward medical interventions and concerns with regard to DAA side effects [11–13].

**Figure 1.** Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the INFO study. Abbreviations: CHC, chronic hepatitis C virus infection; DAA, direct-acting antivirals; GT, genotype; ITT, intention to treat (all patients with first dose); MSCL, Mini Symptom Checklist; OST, opioid substitution treatment; OTI-HSS, Opiate Treatment Index Health Symptom Scale; PP, per protocol (only patients with complete data for SVR12 or SVR24); SmPC, summary of product; SVR12/24, sustained virological response at week 12/24 after treatment.
medical occurrence or worsening of a preexisting medical condition of a patient. Clinicians were asked to rate AEs for their intensity (low, medium, high) and for their assumed relationship with the antiviral medication using the categories “no causal relationship,” “unlikely,” “possible,” “probable,” and “certain.” Clinicians provided categorical ratings on medication adherence and tolerability at week 4 (t₄) and at the end of treatment (t₆₀). Moreover, clinicians rated patients’ functioning and illness severity using the Global Assessment of Functioning (GAF) scale [22] and the Clinical Global Impression scales (CGI-S and CGI-I) [23].

Patient-reported outcomes were collected before (t₀), at week 4 (t₄), at the end (t₆₀), and 12 and 24 weeks after the end of DAA treatment (t₄₉₂, t₆₉₂). The 12-item Short Form Health Survey (SF-12) [24] was used to measure health-related quality of life on 2 T-standardized composite scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). We used the German version [25], and we imputed up to 2 missing items per person with the respective mean sample weights, using the method described in Perneger et al. [26]. The Mini Symptom Checklist (MSCL) [27] is the most recent German version of the 18-item Brief Symptom Inventory (BSI-18), contains 3 subscores (depression, anxiety, somatization) and a Global Severity Index (GSI), and is T-standardized on a recent German norm sample. The Opiate Treatment Index Health Symptom Scale (OTI-HSS) is a measure of physical health, comprising a checklist of 50 symptoms that opioid users often experience [28]. At t₄, patients were asked to provide feedback on medication tolerability on the basis of a 4-point Likert scale from “very good” to “poor.” At t₄ and t₆₀, patients gave a 5-item assessment on therapy side effects using 4-point scales (1 = agree, 2 = rather agree, 3 = rather disagree, 4 = disagree) (Table 2). In addition, treatment-experienced patients were asked at baseline to retrospectively assess their previous treatment (Supplementary Table 1). To measure fatigue, concentration, and memory, we self-constructed a 12-item questionnaire (Supplementary Table 2), as preexisting instruments were either heterogeneity of the sample. Around two-thirds of the patients were treatment-naïve, 18.6% had previously been treated with interferon-based protocols (Table 1). Around two-thirds of the patients were treated with (levo-)methadone, and, according to the last 2 urine tests, around a third were actively using illicit drugs (Table 1).

Global functioning scores (GAF) at baseline indicate a high heterogeneity of the sample. Around two-thirds of the patients fell into the medium categories “moderate/mild/slight impairment,” 17.5% were rated as “serious impairment” or worse, and a similar proportion (17.8%) showed “good” or “superior” functioning (Table 1).

Virological Response
Most patients were treated with a sofosbuvir-based protocol, mostly for 12 weeks (Table 1). Seven patients (2.1%) dropped out before week 4, 9 patients (2.7%) were lost before t₄, and 27 patients (8.2%) left the study after EoT. Moreover, there were 21 subjects (6.4%) with partially missing RNA test data who finished the study. A number of 274 patients with SVR₁₂ data plus another 11 patients with missing SVR₁₂ but valid SVR₂₄ data resulted in a sample of 285 patients for the primary outcome measure, SVR₁₂. Seven out of 285 patients had no SVR, which is an SVR₁₂ rate of 97.5% (95% CI 95.0%–99.0%) in the PP sample (n = 285) (Figure 2). For the ITT sample (n = 328),
Table 1. Sociodemographic and Clinical Characteristics of the Patient Sample at Baseline (n = 328)

| % or Mean (SD), Range |
|------------------------|
| Male (n = 328) 77.4 |
| Age (n = 328) 44.5 (8.4), 26–69 |
| Having children (n = 291) 47.4 |
| Living together with children (n = 321) 10.3 |
| Relationship (n = 280) |
| Single 60.7 |
| Relationship, not living together 11.8 |
| Relationship, living together 27.5 |
| Employment (n = 324) |
| Employed (regular full- or part-time) 20.4 |
| Unemployed/disability pension 67.6 |
| Occasional/other 12.0 |
| Living situation (n = 324) |
| Own flat/with partner 65.4 |
| Institutional 19.3 |
| With relatives/friends 8.6 |
| Other/temporary accommodation 5.6 |
| Homeless 0.6 |
| Caucasian ethnicity (n = 322) 98.8 |
| German citizenship (n = 320) 86.6 |
| Migration background (n = 255) 23.2 |
| German language skills (n = 327) |
| Very good/native speaker 85.6 |
| Good 11.0 |
| Poor 3.4 |
| Duration of OAT with their current physician (n = 289), y 4.2 (4.6), 0–23 |
| Overall duration of OAT (n = 311), y 11.3 (7.3), 0–35 |
| Substitution medication (n = 325) |
| D-/L-methadone (liquid or tablets) 67.7 |
| Buprenorphine (with or without naloxone) 20.0 |
| Other (eg, slow-release morphine, diamorphine) 12.4 |
| (Estimated) duration of HCV infection (n = 309), y 13.7 (7.6), 1–38 |
| Liver cirrhosis (n = 328) |
| Cirrhosis, decompensated 2.7 |
| Cirrhosis, compensated 11.0 |
| Cirrhosis, not specified 2.7 |
| No cirrhosis 75.0 |
| Unclear 8.5 |
| Liver fibrosis (n = 328) |
| Metavir score F4/cirrhosis 16.5 |
| Metavir score F1–F3 23.5 |
| No fibrosis 11.6 |
| Unclear 48.5 |
| HCV genotype (n = 327) |
| 1 49.8 |
| 2 2.4 |
| 3 42.5 |
| 4 5.2 |
| HIV status (n = 328) |
| Positive 4.0 |
| Negative 83.8 |
| Unknown 12.2 |
| Previously treated for HCV (n = 328) |
| Never treated 79.9 |
| Interferon-based 18.6 |

Table 1. Continued

| % or Mean (SD), Range |
|------------------------|
| Interferon-free 0.6 |
| Unclear 0.9 |
| Antiviral medication (n = 328) |
| Sofosbuvir & velpatasvir 41.5 |
| Sofosbuvir & ledipasvir 29.3 |
| Glecaprevir & pibrentasvir 12.2 |
| Elbasvir & grazoprevir 10.1 |
| Ombitasvir, paritaprevir, ritonavir, & dasabuvir 4.6 |
| Other 2.4 |
| Treatment duration (planned; n = 326) |
| 8 wk 27.0 |
| 12 wk 70.6 |
| >12 wk 2.4 |
| Treatment duration (weeks between t0 and EoT; n = 311) |
| Up to 10 wk 22.8 |
| >10–14 wk 62.1 |
| >14–18 wk 10.3 |
| >18 wk 4.8 |
| Past 2 urine samples: ≥1 positive sample |
| Cocaine (n = 287) 16.4 |
| Benzodiazepines (n = 285) 30.2 |
| Opiates (n = 287) 34.8 |
| Amphetamines (n = 245) 0.8 |
| Global Assessment of Functioning score (n = 326) |
| ≤30 (unable to function in almost all areas) 1.5 |
| 31–40 (major impairment in several areas) 6.1 |
| 41–50 (serious impairment) 9.8 |
| 51–60 (moderate impairment) 21.8 |
| 61–70 (mild impairment) 21.8 |
| 71–80 (only slight impairment) 21.2 |
| 81–90 (good functioning) 11.7 |
| 91–100 (superior functioning) 6.1 |

Percentages are based on valid numbers, which are indicated in parentheses. Active drug use: ≥1 positive urine samples in the past 12 weeks.

Abbreviations: HCV, hepatitis C virus; OAT, opioid agonist treatment.

Figure 2. Sustained virological response rates (SVR12/24). Abbreviations: ITT, intention to treat (all patients with first dose); PP, per protocol (only patients with complete data for SVR12/24).
the assumption of nonresponse for all 43 missing individuals resulted in an SVR12/24 rate of 84.8% (95% CI, 80.4%–88.5%) (Figure 2). However, 27 of these 43 missing individuals (62.8%) had completed DAA treatment, and 25 of them were HCV-RNA negative at tEoT. In total, among all HCV-RNA-negative patients at EoT (n = 287), 89.9% remained negative until SVR12, 1.4% (n = 4) did not achieve SVR, and 8.7% (n = 25) dropped out.

Safety
Between baseline and tEoT, 151 AEs from 76 patients (23.2% of the total sample) were documented. The most frequently reported AEs were nausea (19×), headaches (14×), fatigue (13×), sleeping problems (9×), anemia (6×), loss of appetite (5×), diarrhea (5×), and heartburn/gastroesophageal reflux disease (5×). Clinicians provided intensity ratings for 139 of these 151 AEs, resulting in 33 AEs (23.7%) with low, 81 AEs (58.3%) with medium, and 25 AEs (18.0%) with high intensity. A causal relationship with the antiviral medication was assessed for 92 of 151 AEs, resulting in 22.8% “no causal relationship,” 25.0% “unlikely,” 31.5% “possible,” 16.3% “probable,” and 4.3% “certain.” The 19 AEs probably or certainly related to DAA medications were anemia (5×), fatigue (4×), nausea (3×), and loss of appetite (2×).

Between tEoT and tSVR12, another 65 AEs from 31 patients were reported. In total, between baseline and tSVR12, this resulted in 216 AEs from 85 persons. Moreover, 6 SAEs were reported between baseline and tSVR12, among them 3 deaths (due to drug overdose, suicide, aneurysm), suicidal thoughts, 1 hospitalization, and 1 pregnancy. No causal relationship between all SAEs and the antiviral treatment was reported.

Table 2. Course of HCV Therapy, Patient- and Clinician-Reported Outcomes—Total Sample

| Table 2 | Course of HCV Therapy, Patient- and Clinician-Reported Outcomes—Total Sample |
| -------- |-------------------------------------------------------------------------------- |
| **Clinician-Reported** | **T0** | **T4** | **EoT** | **SVR12** | **SVR24** |
| Medication adherence (n = 301–288), % | — | Very good: 90.4 | — | Very good: 86.5 | — | — |
| CGI-S (n = 324–256) | 3.06 (1.52) | 2.95 (1.52) | 2.91 (1.50) | 2.82 (1.51) | 2.80 (1.49) |
| CGI-I (n = 280–224) | — | 3.76 (0.64) | 3.65 (0.71) | 3.51 (0.75) | 3.46 (0.78) |
| GAF | 66.34 (17.00) | 68.14 (17.36) | 70.27 (17.39) | 71.14 (16.66) | 71.84 (16.82) |
| Medication tolerability, clinician-reported (n = 318–305), % | — | Very good: 70.1 | — | Very good: 70.5 | — | — |
| SF-12, Physical Component Summary | 43.66 (9.32) | 44.95 (9.14) | 45.12 (9.35) | 45.44 (9.10) | 45.47 (9.05) |
| SF-12, Mental Component Summary (n = 317–241) | 42.35 (11.26) | 45.21 (11.14) | 45.35 (11.18) | 45.73 (11.35) | 45.68 (10.93) |
| MSCL, total score (GSI; n = 327–242) | 56.87 (9.32) | 56.54 (10.27) | 55.96 (11.14) | 55.41 (10.72) | 55.45 (10.87) |
| MSCL, subscale somatization (n = 327–242) | 57.69 (9.63) | 56.56 (9.69) | 56.00 (10.22) | 54.68 (10.11) | 54.94 (10.16) |
| MSCL, subscale depression (n = 327–242) | 58.16 (8.72) | 55.61 (9.62) | 55.41 (9.84) | 55.23 (9.81) | 55.38 (9.92) |
| MSCL, subscale anxiety (n = 327–242) | 57.44 (10.95) | 55.37 (11.32) | 54.89 (11.47) | 54.64 (10.80) | 54.95 (11.33) |
| OTI-HSS (n = 326–237) | 12.17 (7.62) | 11.14 (7.75) | 11.14 (8.32) | 10.14 (8.06) | 10.23 (8.13) |
| Fatigue, concentration, and memory, total scoreb (n = 325–243) | 0.79 (0.71) | 0.72 (0.77) | 0.68 (0.74) | 0.63 (0.68) | 0.66 (0.73) |
| Fatigue, concentration, and memory, subscale fatigueb | 0.93 (0.89) | 0.85 (0.94) | 0.80 (0.96) | 0.70 (0.82) | 0.72 (0.87) |
| Fatigue, concentration, and memory, subscale concentration and memoryb | 0.69 (0.71) | 0.62 (0.75) | 0.60 (0.71) | 0.58 (0.66) | 0.62 (0.70) |

Data are presented as means and standard deviations or %. Categories of clinician-rated medication adherence: “very good” (100% of the medication taken), “good” (at least 90%), “fair” (at least 80%), “poor” (<80%).

Abbreviations: CGI-I, Clinical Global Impression–improvement (ranging from 1 = “very much improved” to 7 = “very much worsened”); CGI-S, Clinical Global Impression–severity (ranging from 1 = “not at all ill” to 7 = “extremely ill”; GAF = Global Assessment of Functioning (0–100; higher scores indicate better functioning); GSI, Global Severity Index; HCV, hepatitis C virus; MCS, Mental Component Summary; MSCL, Mini Symptom Checklist, with GSI (higher scores indicate worse mental health); OTI-HSS, Opiate Treatment Index–health symptoms scale (higher scores indicate worse physical health); PCS, Physical Component Summary; SF-12, Short Form Health Assessment, consisting of PCS and MCS (higher scores indicate better quality of life).

*Altogether, how do/did you feel during HCV treatment? Response options: 1 = agree, 2 = rather agree, 3 = rather disagree, 4 = disagree (n = 310–287).

bHigher scores indicate higher impairments, ranging from 0 = “not at all” to 4 = “very much.”
Adherence and Tolerability (Patient- and Clinician-Reported)

Medication adherence (n = 288) at tEoT was mainly rated as “very good”; that is, patients reported having taken all of the medication (Table 2). Around 90% of both patients and clinicians stated that medication tolerability was either “good” or “very good” (Table 2). The high tolerability ratings are supported by the results of the 5 additional items on therapy side effects and depression, with mean values between 3 (rather disagree) and 4 (disagree) (Table 2). In comparison with previous HCV treatments (94% interferon-based), treatment-experienced patients reported substantially reduced side effects while on the current DAA treatment (Supplementary Table 2).

Physical and Mental Health Outcomes

Health-related quality of life, as measured with the SF-12, was clearly reduced compared with the general population [24, 25], who have mean values (SD) of approximately 50 (10). In our sample, baseline mean PCS (SD) was 43.7 (9.3), and the mean MCS (SD) was 42.4 (11.3). During the course of treatment, MCS showed small but significant improvement (Tables 2 and 3) persisting after treatment, whereas PCS did not change over time. Patients with clearly reduced health-related quality of life at baseline (PCS or MCS < 40) showed a considerable level of improvement, mainly between baseline and t4 (Figure 3).

In the Mini-SCL (MSCL), the Global Severity Index (GSI) indicates, compared with the population mean (SD) of 50 (10), a clearly increased symptom load (t (326) = 17.21; P < .001), consistent over all subscales: somatization, depression, and anxiety (Table 2). In the course of the DAA treatment, all MSCL scores modestly improved, mainly between baseline and t4 (Tables 2 and 3). Patients with higher psychological distress at baseline showed higher improvements over time.

According to OTI-HSS at baseline, patients reported, on average (SD), 12.17 (7.62) physical health symptoms. Similar to other PROs, there were modest improvements over time (Tables 2 and 3); these improvement were more prominent in patients with higher symptom loads at baseline.

The self-constructed 12 items on fatigue, concentration, and memory were divided into 2 subscales: 1 subscale for fatigue and 1 subscale for concentration and memory, as supported by exploratory factor analyses (Supplementary Table 1). Mean values include all patients with no more than 1 missing value per subscale or 2 missing values in total. At baseline, the mean of the total scale “fatigue, concentration, and memory” (SD) was 0.79 (0.71), indicating a mean impairment between 0 (not at all) and 1 (a little) (Table 2); 8.5% of the sample had a minimum value of 0.00, indicating no impairment at all. At the other end of the spectrum, 9.8% had a mean score of 2 or higher, and the maximum value (n = 1) was 3.17. Overall, patients scored higher on the fatigue subscale than on the subscale on concentration and memory (Table 2). Over time, fatigue, concentration, and memory showed higher improvements over time compared with the population mean (SD) of approximately 50 (10).
memory showed modest improvements (Tables 2 and 3), with higher improvements in patients who had more impairments at baseline.

The clinician-reported severity rating CGI-S had, at baseline, a mean score (SD) of 3.06 (1.52) and showed modest improvement over time.

**DISCUSSION**

The aim of this prospective cohort study was to analyze the clinical effectiveness, safety, and PROs of DAA treatment among OAT patients under the conditions of clinical routine treatment in Germany.

The first main study outcome was that DAA treatment among OAT patients is feasible, safe, and results in high SVR rates. Feasibility of DAA treatment in OAT settings is confirmed by the high adherence and treatment completion rates in our sample, also in accordance with previous studies [29, 30]. Compared with clinical data from IFN-ribavirin-based treatment among OAT patients [31] and even compared with previous clinical trials on DAA treatment among OAT patients [32], we found a low prevalence of AEs. Between baseline and EoT, around a quarter of patients reported on average 2 mainly mild AEs like nausea, headache, or fatigue, which are deemed reversible after treatment completion [19]. The high adherence and completion rates and the low number of mainly mild AEs went along with high SVR rates (PP, 97.5%; ITT, 84.5%), comparable to those found in previous studies [5, 8], also from Germany [6]. The lower rate in our ITT sample is a consequence of the conservative assumption treating all missing data on SVR like treatment failures. An alternative, probably more realistic assumption considers that more than half of our dropouts (27 out of 43) completed treatment, and 25 of these 27 patients were RNA-negative at EoT. Given that in the total sample virtually all patients who were RNA-negative at EoT did achieve SVR (98.6%), we have reason to assume SVR in at least 24 of these dropouts. This assumption would result in an SVR_{12/24} rate of 92.1% for the ITT sample.

The second main outcome of this study was that DAA treatment results in improved PROs among OAT patients. In contrast to interferon- and ribavirin-based protocols [31], health-related quality of life does not deteriorate during DAA treatment. Still, compared with the findings of a post hoc analysis of phase 3 clinical trial data on PROs among OAT patients in antiviral treatment [19], the improvements in our study were modest, especially with regard to the PCS of the SF-12. However, as smaller improvements were also found in other real-world populations [33, 34], 1 explanation might be that the exclusion of “difficult-to-treat” patients from registration trials results in better PROs. In our sample, health-related quality of life (PCS and MCS) at baseline was substantially reduced compared with the general population, which is consistent with a recent German large-scale study among OAT patients [35].

Reasons why patients with higher baseline HRQoL impairments reported significant improvements on DAA treatment may be 2-fold. On the one hand, statistical effects need to be considered, such as regression to the mean or ceiling effects among those with very low or very high baseline levels, respectively. On the other hand, CHC is a systemic disease, and a number of metabolic, autoimmune, and neuro-psychiatric extrahepatic manifestations (EHMs) associated with CHC have been described that also affect patients’ health-related quality of life but can be improved or eliminated after successful antiviral treatment [36]. Given this, patients with higher baseline HRQoL impairments might have experienced a stronger increase in HRQoL during and after treatment due to improvements in EHM. In general, the fact that SVR reduces the risk of EHM [37, 38] is another reason why individuals with CHC should be treated, including patients with opioid use disorders.

![Figure 3. Estimated marginal means of the Physical Composite Score (PCS) and Mental Composite Score (MCS) means of the 12-item Short-Form Health Survey (SF-12) for patients with valid data for all measurement points between baseline and tSVR12. Groups are divided according to their baseline PCS/MCS levels (<40 vs ≥40 points).](image-url)
With regard to the other PROs (physical/mental health, fatigue, cognitive impairment), we also found consistent but modest improvements over time, as well as substantial improvements among those with higher impairments. Similar to HRQoL, these findings need to be addressed in further research. The information that especially patients with high self-reported health burden will benefit from PROs on DAA treatment could be relevant for both patients and providers.

Some limitations need to be considered. First of all, as shown in Table 2, no data on the stage of liver disease from more than half of the patients could be obtained, which impeded further analyses on PROs depending on the severity of the liver disease. However, the relevance of the stage of liver disease on HRQoL during DAA treatment might not be as important as presumed. Recent studies show that patients with early and advanced fibrosis have comparable improvements, and other factors like sociodemographic characteristics or psychiatric comorbidities might have a higher impact on HRQoL [35, 39, 40]. Another limitation is that that patient-reported data on fatigue, concentration, and memory need to be carefully interpreted, as they were not assessed with a validated instrument.

CONCLUSIONS

DAA treatment among PWIDs is feasible, safe, and effective. Besides clinical effectiveness, health-related quality of life and other PROs improve during DAA treatment, in particular among those OAT patients with higher somatic, mental, and social burden. These findings may reduce uncertainties about HCV treatment with DAAs in OAT settings in clinical routine treatment, for both patients and providers. Given the high prevalence rates of CHC infections among OAT patients and the excellent therapeutic opportunities in this setting, more investments are needed to improve the linkage to HCV care.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyrighted and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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