Acute hepatitis C virus infection among men who have sex with men

Epidemiology, diagnosis, treatment, and outcomes

Newsum, A.M.

Publication date
2020

Document Version
Other version

License
Other

Chapter 4

High treatment uptake in HIV/HCV-coinfected patients after unrestricted access to direct-acting antivirals in the Netherlands

Anne Boerekamps*, Astrid M. Newsum*, Colette Smit, Joop E. Arends, Clemens Richter, Peter Reiss, Bart J.A. Rijnders, Kees Brinkman^, Marc van der Valk^, on behalf of the NVHB-SHM hepatitis working group and the Netherlands ATHENA HIV observational cohort

*/^ Both authors contributed equally to this manuscript

Published in *Clinical Infectious Diseases*, 2018 Apr 17;66(9):1352-1359

Abstract

Background: The Netherlands has provided unrestricted access to direct-acting antivirals (DAAs) since November 2015. We analyzed the nationwide hepatitis C virus (HCV) treatment uptake among patiens coinfected with human immunodeficiency virus (HIV) and HCV.

Methods: Data were obtained from the ATHENA HIV observational cohort in which >98% of HIV-infected patients ever registered since 1998 are included. Patients were included if they ever had 1 positive HCV RNA result, did not have spontaneous clearance, and were known to still be in care. Treatment uptake and outcome were assessed. When patients were treated more than once, data were included from only the most recent treatment episode. Data were updated until February 2017. In addition, each treatment center was queried in April 2017 for a data update on DAA treatment and achieved sustained virological response.

Results: Of 23,574 HIV-infected patients ever linked to care, 1471 HCV coinfected patients (69% men who have sex with men [MSM], 15% people who [formerly] inject drugs, and 15% with another HIV transmission route) fulfilled the inclusion criteria. Of these, 87% (1284 of 1471) had ever initiated HCV treatment between 2000 and 2017, 76% (1124 of 1471) had their HCV infection cured; DAA treatment results were pending in 6% (92 of 1471). Among MSM, 83% (844 of 1022) had their HCV infection cured, and DAA treatment results were pending in 6% (66 of 1022). Overall, 187 patients had never initiated treatment, DAAs had failed in 14, and a pegylated interferon-alfa–based regimen had failed in 54.

Conclusions: Fifteen months after unrestricted DAA availability the majority of HIV/HCV-coinfected patients in the Netherlands have their HCV infection cured (76%) or awaiting DAA treatment results (6%). This rapid treatment scale-up may contribute to future HCV elimination among these patients.

Introduction

Treatment with combinations of direct-acting antivirals (DAAs) is short, safe and highly effective in curing chronic hepatitis C virus (HCV) infection [1]. However, its high cost has led to restricted reimbursement in many countries. In the Netherlands, the first all-oral DAA regimens became available for chronic HCV infection in June 2014, but initially only for patients with severe liver fibrosis, defined as liver fibrosis stage F3 or higher (METAVIR scoring system). These fibrosis restrictions also applied to patients with human immunodeficiency (HIV) infection.

On 1 November 2015, the Dutch government, among other countries in the world, expanded the reimbursement criteria and made DAA treatment possible for all patients with chronic HCV, regardless of their fibrosis stage. Scaling up HCV treatment is one of the interventions that, combined with increased harm reduction strategies and scaling up of testing, may lead to a lower incidence and prevalence of HCV infection and eventually to its elimination [2, 3].

Here we describe the national HCV treatment uptake in HIV/HCV-coinfected patients in the Netherlands, using data from the AIDS Therapy Evaluation in the Netherlands (ATHENA) HIV observational cohort. This cohort captures data on >98% of patients with HIV and in care in the Netherlands and is therefore highly representative of the overall Dutch HIV/HCV epidemic.

Methods

ATHENA cohort

HIV care in the Netherlands is provided by 26 designated treatment centers. As an integral part of HIV care, the HIV Monitoring Foundation (Stichting HIV Monitoring) is responsible for prospectively collecting demographic data and relevant HIV and treatment data, as well as data on comorbid conditions, including viral hepatitis coinfection, from HIV-infected persons living in the Netherlands and receiving care in one of these treatment centers. In addition, residual plasma from HIV viral load assays is stored in each center. This data collection is known as the ATHENA cohort [4]. The ATHENA cohort was initiated in 1998 and captures data from >98% of all patients with diagnosed HIV infection who are in care in the Netherlands. Data collection is still ongoing, and the database of the ATHENA cohort is locked and updated twice a year. This article includes the data from the February 2017 database lock, 15 months after unrestricted access to DAAs in the Netherlands. Furthermore, on 15 April 2017, each center was queried about HCV-infected patients whose treatment status was uncertain and/or whose sustained virological response (SVR) status had been pending in February 2017, in order to render data as up to date as possible.

Ethics statement

At its inception, the ATHENA cohort was approved by the institutional review boards of all participating centers. Individuals can opt out after being informed by their treating physician of the purpose of data and sample collection. Data are pseudonymized and made available to investigators in a coded form. Coded data may be used for scientific purposes without further consent. For the purpose of our analysis, only existing data have been used and therefore no additional review or consent has been necessary.

Included patients

A patient was considered linked to care if he or she had visited one of the 26 HIV clinics at least once and had not opted out of inclusion in the ATHENA cohort. Patients were included in the present analysis if they had ≥1 positive HCV RNA test result and if their HCV had not spontaneously cleared (HIV/HCV-coinfected patients defined as "linked to care"). Spontaneous clearance was defined as a negative HCV RNA test results after a positive result without initiation of HCV treatment. To label the HIV/HCV-coinfected patients who were "retained in care" on 1 February 2017, patients were excluded if they had died, had moved abroad or were lost to follow-up. Lost to follow-up was defined as the absence of a clinical visit after 1 January 2016.

Variables of interest

Included patients were assessed for age, sex, country of origin, HIV transmission route, last known CD4 cell count and HIV-1 RNA measurement, the usage of combination antiretroviral therapy (cART), the presence of severe liver fibrosis, the usage of any HCV treatment, and the outcome of their last HCV treatment. HIV transmission route was used as a proxy for HCV transmission route. Severe liver fibrosis was defined as liver fibrosis stage F3 or higher (METAVIR scoring system), based on most recent available liver biopsy or transient elastography result (≥9.5 kPa). SVR was defined as a negative HCV RNA test result ≥24 weeks after the end of HCV treatment with a pegylated interferon-alfa–based regimen or as a negative HCV RNA test result ≥12 weeks after the end of HCV treatment with DAAs (SVR12).

HCV treatment cascade

Treatment uptake and outcome were assessed using a treatment cascade. In this cascade, every patient was depicted only once based on his or her most recent treatment. For example, if a patient was first treated unsuccessfully with a pegylated interferon-alfa–based regimen and subsequently with DAAs resulting in SVR12, only the last treatment was accounted for in this cascade. First, the proportion of patients who had received treatment was calculated. Second, the proportion of patients who had completed any treatment was calculated. Last, the proportion of patients who reached SVR was calculated. For every step in the cascade, the "gap" was also described (respectively the untreated patients, patients with ongoing treatment or awaiting SVR12 results and unsuccessfully treated patients).

Statistics

We used Chi square tests to compare categorical variables. Differences were considered statistically significant at P <0.05.

Results

HIV/HCV-coinfected patients

Of 23,574 HIV patients ever registered as having been linked to care on 1 February 2017, 2503 had ≥1 positive HCV RNA test result. After exclusion of patients whose HCV had spontaneously cleared (n=514), 1989 HIV/HCV-coinfected patients who had ever been linked to care remained. Of these 1989 patients, 321 had died (of whom 42 had a confirmed liver-related death), 83 had moved abroad, and 114 were lost to follow-up (median duration of being lost to care, 5 years; interquartile range, 2–11 years), resulting in 1471 coinfected patients who were still retained in care in February 2017 (Figure 1) and were included in the current analysis. Of these HIV/HCV-coinfected patients retained in care, 90% were male (1325 of 1471) and 67% were born in the Netherlands (983 of 1471; Table 1). The most commonly reported HIV transmission route was men who have sex with men (MSM) (69%; 1022 of 1471), followed by a history of injecting drug use (15%; 224 of 1471). For the remaining 15% (225 of 1471), HIV transmission had occurred through another route or had an unknown route. HCV genotype 1 was the most prevalent (61%; 896 of 1471), followed by HCV genotypes 4 and 3 (18% and 9%, respectively). Seventeen percent of patients (244 of 1471) had liver fibrosis of stage F3 or higher.

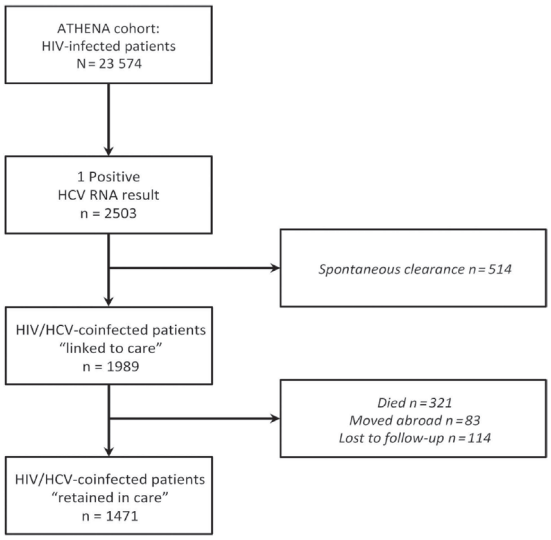

Figure 1. Flowchart of included patients
ATHENA, AIDS Therapy Evaluation in the Netherlands; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

Table 1. Baseline characteristics of included patients in February 2017

	Patients, No.[a]					
Characteristic	**Retained in care (n=1471)**	**Untreated (n=187)**	**Ever treated (n=1284)**	**SVR achieved (n=1124)**	**Ongoing treatment/ awaiting SVR (n=92)**	**Treatment failure (n=68)**
Age, median (IQR), y[b]	50 (44–56)	51 (43–57)	50 (44–56)	50 (44–56)	49 (42–55)	49 (46–55)
Sex						
Male	1325	150	1175	1027	86	62
Female	146	37	109	97	6	6
Region of origin						
The Netherlands	983	102	881	775	61	45
Western Europe	161	22	139	126	9	4
Sub-Saharan Africa	35	5	30	28	0	2
Caribbean/Latin America	99	20	79	69	5	5
Other	193	38	155	126	17	12
HIV transmission route						
MSM	1022	72	950	844	66	40
PWID	224	65	159	127	18	14
Heterosexual contact	127	35	92	81	2	9
Other/unknown	98	15	83	72	6	5
Ever used cART	1454	179	1275	1118	91	66
cART regimen at HCV treatment initiation						
2 NRTIs + INI	NA	NA	422	NA	NA	NA
2 NRTIs + NNRTI	NA	NA	412	NA	NA	NA
2 NRTIs + r/PI	NA	NA	202	NA	NA	NA
Other	NA	NA	128	NA	NA	NA
None	NA	NA	120	NA	NA	NA
HCV genotype						
1	896	95	801	704	53	44
1a	676	59	617	548	40	29
1b	94	21	73	65	6	2
Subtype not specified	126	15	111	91	7	13
2	69	10	59	53	5	1
3	131	27	104	92	6	6
4	258	28	230	196	19	15
Other/unknown	117	27	90	79	9	2
Liver fibrosis score F3 or higher[c]	244	25	219	192	13	14
Treatment						
Currently used DAA-regimen	NA	NA	702	598	90	14
Older regimen[d]	NA	NA	582	526	2	54

cART, combination antiretroviral therapy; DAA, direct-acting antiviral; HCV, hepatitis C virus; HIV, human immunodeficiency virus; INI, integrase inhibitor; IQR, interquartile range; MSM, men who have sex with men; NA, not applicable; NNRTI, non-nucleoside reverse-transcriptase inhibitor; NRTIs, nucleoside reverse-transcriptase inhibitors; PWID, persons who (formerly) injected drugs; r/PI, ritonavir-boosted protease inhibitor; SVR, sustained virological response.

[a] Data represent No. of patients unless otherwise specified.

[b] Age as of 1 February 2017.

[c] METAVIR scoring system.

[d] Interferon-alfa, or pegylated interferon-alfa with or without ribavirin and with or without boceprevir or telaprevir.

Treatment uptake and outcome

Of the included 1471 HIV/HCV-coinfected patients, 1284 had ever initiated HCV treatment between 2000 and 2017 (Figure 2). Of these, 582 had been treated with an old HCV regimen (interferon-alfa, or pegylated interferon-alfa with or without ribavirin and with or without boceprevir or telaprevir), and 702 had received or were still receiving a currently used DAA regimen (Figure 3). Of those treated with DAAs, 259 (37%) were previously treated with pegylated interferon-alfa–based antiviral regimens.

A total of 187 patients had never started any form of HCV treatment, and 68 were in need of retreatment because prior HCV treatment had failed. Of these 68 patients, DAAs had failed in 14 and a (pegylated) interferon-alfa–based regimen had failed in 54.

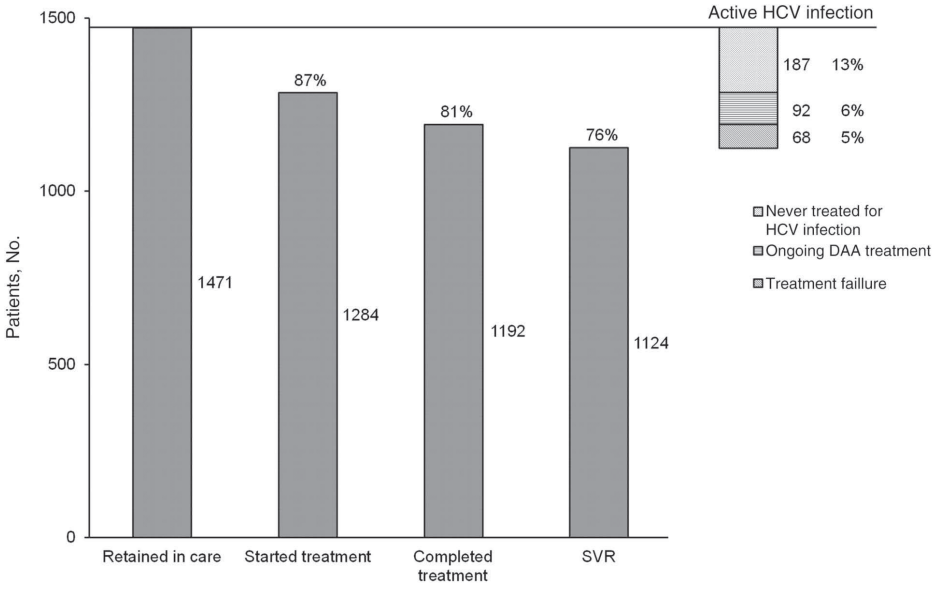

Figure 2. Treatment cascade of the Dutch population coinfected with human immunodeficiency virus and hepatitis C virus (HCV) until 1 February 2017
DAA, direct-acting antiviral; HCV, hepatitis C virus; SVR, sustained virological response.

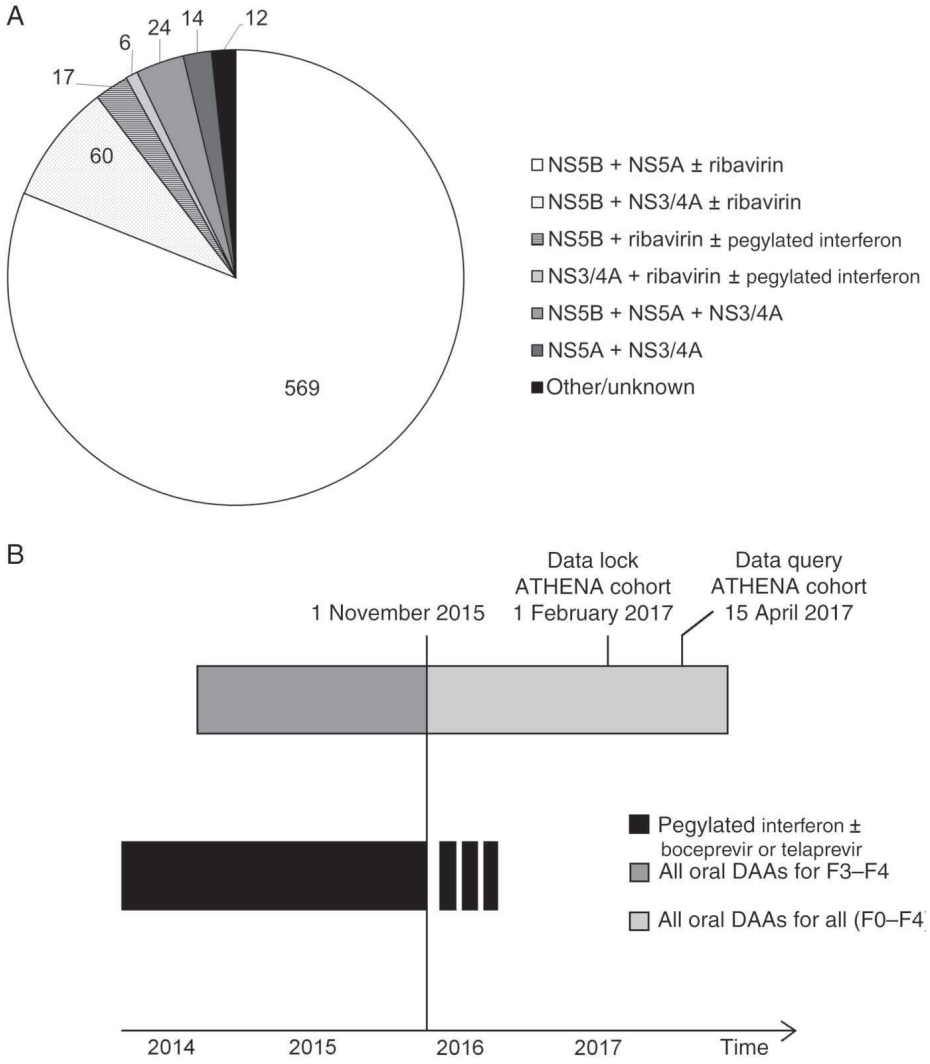

Figure 3. A, Direct-acting antiviral (DAA) regimens used in the Dutch population coinfected with human immunodeficiency virus and hepatitis C virus. Numbers in graph represent numbers of patients. B, Schematic overview of availability of DAAs with regard to liver fibrosis stage over time.
ATHENA, AIDS Therapy Evaluation in the Netherlands.

Based on their last received treatment, 1124 of the 1192 patients (94%) who were known to have completed their HCV treatment reached SVR (Figure 2). When analysis was restricted to patients known to have completed DAA treatment, 98% reached SVR12 (598 of 612). At the time of analysis, 76% (1124 of 1471) of the HIV/HCV-coinfected patients retained in care had reached SVR, and DAA treatment was still ongoing or treatment results were pending in 6% (92 of 1471). Overall, only 255 patients remain to be treated.

Of the 1284 patients who ever started treatment, 743 started their last treatment in 2014, 2015 or 2016. Shortly after unrestricted access to DAAs, 176, 226 and 86 patients started treatment in the fourth quarter of 2015 and the first and second quarters of 2016, respectively; in all other quarters, the number of patients who started treatment was <50 (Figure 4).

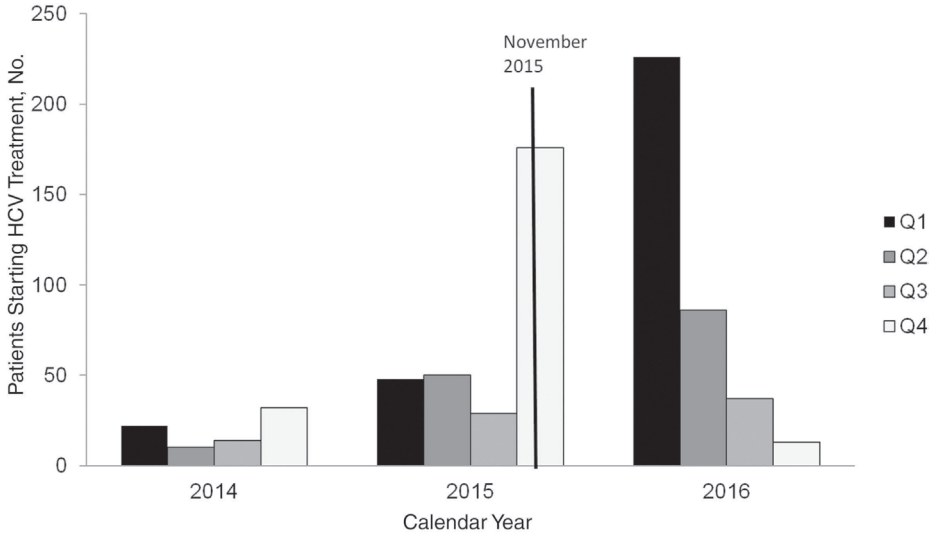

Figure 4. Hepatitis C virus (HCV) treatment uptake per quarter in 2014, 2015, and 2016
Q1, quarter 1; Q2, quarter 2; Q3, quarter 3; Q4, quarter 4.

cART during last HCV treatment

The cART regimens at the time of HCV treatment initiation are listed in Table 1. Of the 702 patients who were treated with a currently used DAA regimen, 191 (27%) had switched cART regimen in the 3 months before HCV treatment initiation. For 130 of those patients, "start of HCV treatment" was recorded in the database as reason for the cART switch; for the other 61, the reason was not explicitly recorded. Of 582 patients who were treated with an old HCV treatment regimen, 109 (19%) had switched cART regimen in the 3 months before HCV treatment initiation. For 54 of those patients, "start of HCV treatment" was recorded in the database as reason for the cART switch.

Stratification by liver fibrosis stage F3-F4

Of the 244 patients classified with liver fibrosis stage F3 or higher and retained in care on 1 February 2017, 79% (192 of 244) had achieved SVR and 5% (13 of 244) were still undergoing DAA treatment. Thirty-nine patients with severe liver disease remain to be treated (previous treatment failed in 14 patients, and 25 were never treated).

Stratification by HIV transmission route

Findings in MSM

A total of 1022 HIV/HCV-coinfected patients identified as being MSM were retained in care as of 1 February 2017. SVR was achieved in 83% (844 of 1022), significantly higher than the 76% with SVR in the overall population (P <0.001). In 6% (66 of 1022), DAA treatment was still ongoing or treatment results were pending. Thus, only 112 MSM remain to be treated.

Findings in persons who injected drugs

Of the 224 HIV/HCV-coinfected patients retained in care as of 1 February 2017 and classified as persons who (formerly) injected drugs (PWID), 57% (127 of 224) reached SVR, which was significantly lower than in the overall population (P <0.001). In 8% (18 of 224), DAA treatment was still ongoing or treatment results were pending.

Characteristics of patients who never started treatment

In the patients who never started treatment (n=187), the proportion of women was significantly higher than the proportion among patients who ever received treatment (n=1284) (20% vs 8%; P <0.001). The proportion of MSM was lower (39% vs 74%; P <0.001) and the proportion of PWID was higher (35% vs 12%; P <0.001). Four percent of patients untreated for HCV never received cART, compared with 1% in the group treated for HCV (P <0.001). Region of origin differed significantly between the 2 groups (overall P <0.001), with a higher proportion of patients from the Netherlands among the treated patients (69% vs 55%) and a lower proportion from the Caribbean and Latin America (6% vs 11%). Furthermore, HCV genotype differed significantly between the 2 groups (overall P <0.001), with a higher proportion of genotype 1 (62% vs 51%) and a lower proportion of genotype 3 (8% vs 14%) among the treated than among the untreated patients (51% and 14%). The presence of severe liver fibrosis (METAVIR score F3 or higher) did not differ significantly between these 2 groups.

Characteristics of patients who failed treatment

Overall, treatment failed in 68 patients, DAAs in 14 and a pegylated interferon-alfa–based regimen in 54. Compared with the patients who achieved SVR (n=1124), the proportion of PWID was higher in the patients with failed treatment (21% vs 11%; P =0.02), and the proportion of MSM was lower (59% vs 75%; P =0.003). Furthermore, 3% of the patients with failed HCV treatment never received cART, compared with 1% in the group who achieved SVR (P =0.02). Other variables did not differ significantly between the 2 groups.

Of the patients in whom DAAs failed (n=14), 9 were MSM, 2 were PWID, and 3 had another HIV transmission route. Seven patients were infected with genotype 1a, 5 with genotype 4, and 2 with another HCV genotype. Three patients had severe liver fibrosis (METAVIR score F3 or higher).

Discussion

As of 1 February 2017 and only 15 months after DAAs were made available to all patients with chronic HCV in the Netherlands, 76% of the Dutch HIV/HCV-coinfected patients in care had been successfully treated for HCV. Another 6% are still undergoing DAA treatment or have completed treatment but are awaiting SVR12. The majority of this 6% can be expected to also have their HCV infection cured, because real-world SVR rates after DAA treatment in HIV/HCV-coinfected patients are well above 90% [5–8]. Our results demonstrate that in resource-unconstrained settings, a very high treatment uptake is possible in HIV/HCV-coinfected patients within only 15 months after unrestricted availability of DAAs.

Treatment uptake and HCV cure rates were highest in MSM and significantly higher than in other categories of coinfected patients. Only 112 HIV/HCV-coinfected MSM remain to be treated. In the Netherlands, in contrast to other countries, ongoing HCV transmission occurs mainly among HIV-infected MSM [9]; transmission among PWID is nearly nonexistent as a result of successful harm reduction policies [10]. Therefore, it is promising that treatment uptake is highest among MSM, which may help reduce ongoing HCV transmission in the Netherlands. However, the fact that treatment uptake in HIV/HCV-coinfected PWID in care was significantly lower when than in the overall population of HIV/HCV-coinfected patients is an important signal that might reflect social, medical, psychiatric and/or substance use-associated factors or barriers perceived by practitioners, as reviewed extensively by Grebely et al [11].

Our study has several strengths. The data we analyzed were derived from the longstanding ATHENA cohort of HIV-infected patients and include data on HCV status and treatment. This cohort is representative of all HIV-infected patients in the Netherlands, because it captures data from > 98% of all HIV-infected patients in care. In addition, for this study an extra query was performed by contacting each HIV treatment center with a list of HCV-coinfected patients whose treatment status remained uncertain or whose SVR12 results were pending in February 2017. As a result of this query we have made the data of this study as up to date as possible. To our best knowledge, this is the first study that provides truly nationwide data on HCV treatment uptake and cure rates after unrestricted DAA availability for chronic hepatitis C in HIV/HCV-coinfected patients. If this rapid treatment scale up is continued, it may contribute to the future elimination of HCV among HIV/HCV-coinfected patients in the Netherlands. Of note however, additional harm reduction strategies and scaling up of HCV testing will probably be necessary to eventually reach elimination [2, 3].

Our study also has some limitations. First, only the patients who were retained in care could be analyzed and therefore we were unable to provide data on the 114 patients who were

lost to follow-up. However, these 114 patients represent only 6% (114 of 1989) of the HIV/HCV-coinfected patients overall. Collaboration between different stakeholders could possibly lead to (re)identification of these patients and further elimination of HCV from the HIV/HCV-coinfected population. Second, a certain proportion of HCV infections in this population will remain undiagnosed, because alanine aminotransferase levels may occasionally remain within normal limits after HCV infection [12]. However, 99% of HIV-infected patients currently in care in the Netherlands have been tested for HCV at least once [4]. A third limitation is that only the most recent treatment and its outcome was included in the cascade. This is an appropriate method to visualize the overall treatment uptake, but in the calculation of the SVR rate it may have led to an overestimation, because for patients in whom the first DAA treatment failed the second was successful, the calculation took only the second result into account. Real-world SVR rates found in other studies in HIV/HCV-coinfected patients are indeed lower than the 98% that we report [5-8]. Furthermore, owing to the cross-sectional design of our analysis, HCV reinfections after DAA treatment could not be taken into account. Because HCV reinfections are common in HIV-infected MSM [13, 14], a certain proportion of the population will become reinfected with HCV and therefore again be in need of effective treatment.

Although treatment uptake and HCV cure rates are high, the group of patients that remains to be treated will be the most challenging. To target this remaining subgroup of HIV/HCV-coinfected patients, we provided each HIV treatment center with a coded list of patients who, according to the information available in the ATHENA database, remain in need of curative treatment, in order to facilitate their identification and reevaluation.

In conclusion, we demonstrate a very high treatment uptake among HIV/HCV-coinfected patients. Fifteen months after unrestricted availability of DAAs, 76% of Dutch HIV/HCV-coinfected patients overall have had their HCV infection cured and an additional 6% are either still being treated with DAAs or awaiting their treatment result.

Funding

A.N. was financially supported by the "Aidsfonds" Netherlands (grant 2013.037). The ATHENA database is maintained by Stichting HIV Monitoring and supported by a grant from the Dutch Ministry of Health, Welfare and Sport through the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment.

Athena HIV observational cohort

Academic Medical Centre of the University of Amsterdam (AMC-UvA): *HIV treating physicians:* M. van der Valk*, S.E. Geerlings, M.H. Godfried, A. Goorhuis, J.W. Hovius, J.T.M. van der Meer, T.W. Kuijpers, F.J.B. Nellen, DT. van der Poll, J.M. Prins, P. Reiss, H.J. M. van Vugt, W.J. Wiersinga, F.W.M.N. Wit. *HIV nurse consultants:* M. van Duinen, J. van Eden, A.M.H. van Hes, M. Mutschelknauss, H.E. Nobel, F.J.J. Pijnappel, A.M. Weijsenfeld. *HIV clinical virologists/chemists:* S. Jurriaans, N.K.T. Back, H.L. Zaaijer, B. Berkhout, M.T.E. Cornelissen, C.J. Schinkel, K.C. Wolthers. **Admiraal De Ruyter Ziekenhuis, Goes:** *HIV treating physicians:* M. van den Berge, A. Stegeman. *HIV nurse consultants:* S. Baas, L. Hage de Looff. *HIV clinical virologists/chemists:* B Wintermans, J Veenemans. **Catharina Ziekenhuis, Eindhoven:** *HIV treating physicians:* M.J.H. Pronk*, H.S.M. Ammerlaan. *HIV nurse consultants:* E.S. de Munnik. *HIV clinical virologists/chemists:* A.R. Jansz, J. Tjhie, M.C.A. Wegdam, B. Deiman, V. Scharnhorst. **DC AMC Hiv Behandelcentrum:** *HIV treating physicians:* A. van Eeden*, M. van der Valk. *HIV nurse consultants:* W. Brokking, M. Groot, L.J.M. Elsenburg. *HIV clinical virologists/chemists:* M. Damen, I.S. Kwa. **Elisabeth-TweeSteden Ziekenhuis, Tilburg:** *HIV treating physicians:* M.E.E. van Kasteren*, A.E. Brouwer. *HIV nurse consultants:* R. van Erve, B.A.F.M. de Kruijf-van de Wiel, S.Keelan-Pfaf, B. van der Ven. *Data collection:* B.A.F.M. de Kruijf-van de Wiel, B. van der Ven. *HIV clinical virologists/chemists:* A.G.M. Buiting, P.J. Kabel, D.Versteeg. **Erasmus MC, Rotterdam:** *HIV treating physicians:* M.E. van der Ende*, H.I. Bax, E.C.M. van Gorp, J.L. Nouwen, B.J.A. Rijnders, C.A.M. Schurink, A. Verbon, T.E.M.S. de Vries-Sluijs, N.C. de Jong-Peltenburg. *HIV nurse consultants:* N. Bassant, J.E.A. van Beek, M. Vriesde, L.M. van Zonneveld. *Data collection:* H.J. van den Berg-Cameron, J. de Groot, M. de Zeeuw-de Man. *HIV clinical virologists/chemists:* C.A.B. Boucher, M.P.G Koopmans, J.J.A van Kampen, S.D. Pas. **Flevoziekenhuis, Almere:** *HIV treating physicians:* J. Branger*, A. Rijkeboer-Mes. *HIV nurse consultant:* C.J.H.M. Duijf-van de Ven. **HagaZiekenhuis, Den Haag:** *HIV treating physicians:* E.F. Schippers*, C. van Nieuwkoop. *HIV nurse consultants:* J.M. van IJperen, J. Geilings. *Data collection:* G. van der Hut. *HIV clinical virologist/chemist:* N.D. van Burgel. **HMC (Haaglanden Medisch Centrum), Den Haag:** *HIV treating physicians:* E.M.S. Leyten*, L.B.S. Gelinck. *HIV nurse consultants:* A.Y. van Hartingsveld, C. Meerkerk, G.S. Wildenbeest. *HIV clinical virologists/chemists:* E. Heikens. **Isala, Zwolle:** *HIV treating physicians:* P.H.P. Groeneveld*, J.W. Bouwhuis, A.J.J. Lammers. *HIV nurse consultants:* S. Kraan, A.G.W. van Hulzen. *Data collection:* G.L. van der Bliek, P.C.J. Bor. *HIV clinical virologists/chemists:* P. Bloembergen, M.J.H.M. Wolfhagen, G.J.H.M. Ruijs. **Leids Universitair Medisch Centrum, Leiden:** *HIV treating physicians:* F.P. Kroon*, M.G.J. de Boer, H. Scheper, H. Jolink, A.M. Vollaard. *HIV nurse consultants:* W. Dorama, N. van Holten. *HIV clinical virologists/chemists:* E.C.J. Claas, E. Wessels. **Maasstad Ziekenhuis, Rotterdam:** *HIV treating physicians:* J.G. den Hollander*, K. Pogany, A. Roukens. *HIV nurse consultants:* M. Kastelijns, J.V. Smit, E. Smit, D. Struik-Kalkman, C. Tearno. *Data collection:* T. van Niekerk. *HIV clinical virologists/chemists:* O. Pontesilli. **Maastricht UMC+, Maastricht:** *HIV treating physicians:*

S.H. Lowe*, A.M.L. Oude Lashof, D. Posthouwer. *HIV nurse consultants:* R.P. Ackens, K. Burgers, J. Schippers. *Data collection:* B. Weijenberg-Maes. *HIV clinical virologists/chemists:* I.H.M. van Loo, T.R.A. Havenith. **MC Slotervaart, Amsterdam:** *HIV treating physicians:* J.W. Mulder*, S.M.E. Vrouenraets, F.N. Lauw. *HIV nurse consultants:* M.C. van Broekhuizen, D.J. Vlasblom. *HIV clinical virologists/chemists:* P.H.M. Smits. **MC Zuiderzee, Lelystad:** *HIV treating physicians:* S. Weijer*, R. El Moussaoui. *HIV nurse consultant:* A.S. Bosma. **Medisch Centrum Leeuwarden, Leeuwarden:** *HIV treating physicians:* M.G.A.van Vonderen*, D.P.F. van Houte, L.M. Kampschreur. *HIV nurse consultants:* K. Dijkstra, S. Faber. *HIV clinical virologists/chemists:* J Weel. **Medisch Spectrum Twente, Enschede:** *HIV treating physicians:* G.J. Kootstra*, C.E. Delsing. *HIV nurse consultants:* M. van der Burg-van de Plas, H. Heins. *Data collection:* E. Lucas. **Noordwest Ziekenhuisgroep, Alkmaar:** *HIV treating physicians:* W. Kortmann*, G. van Twillert*, R. Renckens. *HIV nurse consultant and data collection:* D. Ruiter-Pronk, F.A. van Truijen-Oud. *HIV clinical virologists/chemists:* J.W.T. Cohen Stuart, E.P. IJzerman, R. Jansen, W. Rozemeijer W. A. van der Reijden. **OLVG, Amsterdam:** *HIV treating physicians:* K. Brinkman*, G.E.L. van den Berk, W.L. Blok, P.H.J. Frissen, K.D. Lettinga W.E.M. Schouten, J. Veenstra. *HIV nurse consultants:* C.J. Brouwer, G.F. Geerders, K. Hoeksema, M.J. Kleene, I.B. van der Meché, M. Spelbrink, A.J.M. Toonen, S. Wijnands. *HIV clinical virologists:* D. Kwa. *Data collection:* R. Regez (coordinator). **Radboudumc, Nijmegen:** *HIV treating physicians:* R. van Crevel*, M. Keuter, A.J.A.M. van der Ven, H.J.M. ter Hofstede, A.S.M. Dofferhoff, J. Hoogerwerf. *HIV nurse consultants:* K.J.T. Grintjes-Huisman, M. de Haan, M. Marneef, A. Hairwassers. *HIV clinical virologists/chemists:* J. Rahamat-Langendoen, F.F. Stelma. *HIV clinical pharmacology consultant:* D. Burger. **Rijnstate, Arnhem:** *HIV treating physicians:* E.H. Gisolf*, R.J. Hassing, M. Claassen. *HIV nurse consultants:* G. ter Beest, P.H.M. van Bentum, N. Langebeek. *HIV clinical virologists/chemists:* R. Tiemessen, C.M.A. Swanink. **Spaarne Gasthuis, Haarlem:** *HIV treating physicians:* S.F.L. van Lelyveld*, R. Soetekouw. *HIV nurse consultants:* L.M.M. van der Prijt, J. van der Swaluw. *Data collection:* N. Bermon. *HIV clinical virologists/chemists:* W.A. van der Reijden, R. Jansen, B.L. Herpers, D.Veenendaal. **Medisch Centrum Jan van Goyen, Amsterdam:** *HIV treating physicians:* D.W.M. Verhagen. *HIV nurse consultants:* M. van Wijk. **Universitair Medisch Centrum Groningen, Groningen:** *HIV treating physicians:* W.F.W. Bierman*, M. Bakker, J. Kleinnijenhuis, E. Kloeze, Y. Stienstra, K.R. Wilting, M. Wouthuyzen-Bakker. *HIV nurse consultants:* A. Boonstra, P.A. van der Meulen, D.A. de Weerd. *HIV clinical virologists/chemists:* H.G.M. Niesters, C.C. van Leer-Buter, M. Knoester. **Universitair Medisch Centrum Utrecht, Utrecht:** *HIV treating physicians:* A.I.M. Hoepelman*, J.E. Arends, R.E. Barth, A.H.W. Bruns, P.M. Ellerbroek, T. Mudrikova, J.J. Oosterheert, E.M. Schadd, M.W.M. Wassenberg, M.A.D. van Zoelen. *HIV nurse consultants:* K. Aarsman, D.H.M. van Elst-Laurijssen, I. de Kroon, C.S.A.M. van Rooijen. *Data collection:* M. van Berkel, C.S.A.M. van Rooijen. *HIV clinical virologists/chemists:* R. Schuurman, F. Verduyn-Lunel, A.M.J. Wensing. **VUmc, Amsterdam:** *HIV treating physicians:* E.J.G. Peters*, M.A. van Agtmael, M. Bomers. *HIV nurse consultants:* M. Heitmuller, L.M.

Laan. *HIV clinical virologists/chemists:* C.W. Ang, R. van Houdt, A.M. Pettersson, C.M.J.E. Vandenbroucke-Grauls.

Coordinating centre: *Director:* P. Reiss. *Data analysis:* D.O. Bezemer, A.I. van Sighem, C. Smit, F.W.M.N. Wit, T.S. Boender. *Data management and quality control:* S. Zaheri, M. Hillebregt, A. de Jong. *Data monitoring:* D. Bergsma, S. Grivell, A. Jansen, M. Raethke, R. Meijering, T. Rutkens. *Data collection:* L. de Groot, M. van den Akker, Y. Bakker, M. Bezemer, E. Claessen, A. El Berkaoui, J. Geerlinks, J. Koops, E. Kruijne, C. Lodewijk, R. van der Meer, L. Munjishvili, F. Paling, B. Peeck, C. Ree, R. Regtop, Y. Ruijs, M. Schoorl, A. Timmerman, E. Tuijn, L. Veenenberg, S. van der Vliet, A. Wisse, E.C. de Witte, T. Woudstra. *Patient registration:* B. Tuk.

** denotes site coordinating physician*

References

1. Arends JE, Kracht PA, Hoepelman AI, European Study Group for Viral Hepatitis. Performance of hepatitis C virus (HCV) direct-acting antivirals in clinical trials and daily practice. *Clin Microbiol Infect* 2016; 22(10):846-852.
2. Salazar-Vizcaya L, Kouyos RD, Zahnd C, Wandeler G, Battegay M, Darling KE, et al. Hepatitis C virus transmission among human immunodeficiency virus-infected men who have sex with men: Modeling the effect of behavioral and treatment interventions. *Hepatology* 2016; 64(6):1856-1869.
3. Martin NK, Thornton A, Hickman M, Sabin C, Nelson M, Cooke GS, et al. Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights. *Clin Infect Dis* 2016; 62(9):1072-1080.
4. van Sighem AI, Boender TS, Wit FWNM, Smit C, Matser A, Reiss P. Monitoring Report 2016. Human Immunodeficiency Virus (HIV) Infection in the Netherlands. *Stichting HIV Monitoring*; Available at: www.hiv-monitoring.nl. Accessed 14 July 2017.
5. Ingiliz P, Christensen S, Kimhofer T, Hueppe D, Lutz T, Schewe K, et al. Sofosbuvir and Ledipasvir for 8 Weeks for the Treatment of Chronic Hepatitis C Virus (HCV) Infection in HCV-Monoinfected and HIV-HCV-Coinfected Individuals: Results From the German Hepatitis C Cohort (GECCO-01). *Clin Infect Dis* 2016; 63(10):1320-1324.
6. Piroth L, Wittkop L, Lacombe K, Rosenthal E, Gilbert C, Miailhes P, et al. Efficacy and safety of direct-acting antiviral regimens in HIV/HCV-co-infected patients - French ANRS CO13 HEPAVIH cohort. *J Hepatol* 2017.
7. Menard A, Colson P, Catherine D, Isabelle R, Christelle T, Meddeb L, et al. First Real Life Evidence of New Direct-acting Antivirals (DAA) in Co-infected HIV HCV Patients: Better than Ever. *Clin Infect Dis* 2016; 62(7):947-949.
8. Milazzo L, Lai A, Calvi E, Ronzi P, Micheli V, Binda F, et al. Direct-acting antivirals in hepatitis C virus (HCV)-infected and HCV/HIV-coinfected patients: real-life safety and efficacy. *HIV Med* 2017; 18(4):284-291.
9. Vanhommerig JW, Stolte IG, Lambers FA, Geskus RB, van de Laar TJ, Bruisten SM, et al. Stabilizing incidence of hepatitis C virus infection among men who have sex with men in Amsterdam. *J Acquir Immune Defic Syndr* 2014; 66(5):e111-115.
10. de Vos AS, van der Helm JJ, Matser A, Prins M, Kretzschmar ME. Decline in incidence of HIV and hepatitis C virus infection among injecting drug users in Amsterdam; evidence for harm reduction? *Addiction* 2013; 108(6):1070-1081.
11. Grebely J, Oser M, Taylor LE, Dore GJ. Breaking down the barriers to hepatitis C virus (HCV) treatment among individuals with HCV/HIV coinfection: action required at the system, provider, and patient levels. *J Infect Dis* 2013; 207 Suppl 1:S19-25.
12. Vanhommerig JW, Schinkel J, van der Valk M. Seven years of chronic hepatitis C virus infection in an HIV-infected man without detectable antibodies. *AIDS* 2015; 29(3):389-390.
13. Lambers FA, Prins M, Thomas X, Molenkamp R, Kwa D, Brinkman K, et al. Alarming incidence of hepatitis C virus re-infection after treatment of sexually acquired acute hepatitis C virus infection in HIV-infected MSM. *AIDS* 2011; 25(17):F21-27.
14. Ingiliz P, Martin TC, Rodger A, Stellbrink HJ, Mauss S, Boesecke C, et al. HCV reinfection incidence and spontaneous clearance rates in HIV-positive men who have sex with men in Western Europe. *J Hepatol* 2017; 66(2):282-287.