Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Viewpoint | Published 11 December 2017 | doi:10.4414/smw.2017.14570
Cite this as: Swiss Med Wkly. 2017;147:w14570

Access to hepatitis C treatment for patients in drug substitution programmes: the fight is far from over

Negro Francesco[ab], Maistat Liudmyla[c]

[a] Division of Gastroenterology and Hepatology, Geneva University Hospitals, Switzerland
[b] Division of Clinical Pathology, Geneva University Hospitals, Switzerland
[c] Medicines Patent Pool, Geneva, Switzerland

Hepatitis C virus (HCV) is a parenterally transmitted human pathogen of global concern. Chronic HCV infection is associated with progressive liver disease culminating in an estimated yearly toll of around 400 000 deaths, mostly due to liver failure and hepatocellular carcinoma. Thus, in 2016, the World Health Organization issued a declaration aiming at the elimination of viral hepatitis as a global public health threat by 2030 [1]. Six indicators were identified to measure the progress in this ambitious effort: infant vaccination against hepatitis B virus (HBV), prevention of mother-to-child transmission of HBV by birth dose vaccination, blood and injection safety, harm reduction measures for people who inject drugs (PWID), identification of infected patients by means of appropriate screening strategies, and treatment of patients with potent antivirals.

Transmission among PWID is currently a major driver of the persisting HCV epidemic in many countries, and a significant challenge to the HCV elimination targets set by the WHO. Switzerland pioneered the harm reduction approach as early as the 1980s, at the time of a rampant – and unprecedented – spread of illicit drug use, favoured by coercive legislation and culminating in the infamous open air drug scenes known as "needle parks". In addition to massive preventive measures targeting the youth, adequate medical management and social support, and specific law enforcement, Switzerland adopted multiple low-threshold approaches to curb the drug epidemic and to reduce the risk of infection with blood-borne pathogens. Apart from being offered opioid substitution treatment (OST) and, in 1994, the ground-breaking heroin-assisted therapy [2], PWID were enrolled in needle and syringe exchange programmes (NSPs), and allowed to inject drugs in consumption rooms specifically set up for this purpose, where sterile injection tools (including filters, water and cookers) were made available. The positive clinical impact of these preventive measures within the PWID community is well documented [3]. A later modelling study [4] incorporating the empirical evidence on the benefits of the above-mentioned interventions [3] showed that an additional reduction in the incidence and prevalence of HCV among PWID could be achieved by scaling up OST and NSPs combined with antiviral therapy, i.e., by applying the innovative concept of treatment as prevention [5]. Unfortunately, for several years both patient- and prescriber-specific barriers limited the uptake of interferon alpha-containing regimens, despite their proven efficacy among PWID [6]. It was only with the advent of interferon-free, all oral, direct-acting antiviral (DAA)-only therapies that universal access to treatment could be safely proposed to all PWID, with cure rates >90%, few side effects and virtually no contraindications [7].

A recent modelling study, now published in *Swiss Medical Weekly*, analysed the current Swiss situation among PWID actively infected with HCV, estimated at around 4200 in 2015 [8]. Based on the *status quo*, a 60% reduction in the viraemic pool would be expected by 2030, whereas to eradicate HCV from this population by the same year would require a timely treatment scale-up to 10% of the infected pool per year. The enacted robust preventive measures and the possibility of prescribing highly efficacious DAAs to all PWID irrespective of their liver fibrosis stage (as of 1 May 2017, following a decision by the Swiss regulatory authorities) make this goal within reach, but there is a glitch. These powerful approaches can be effective in the ideal situation where (i) all PWID have been accurately screened for HCV, and provided that (ii) all those found positive for anti-HCV antibodies have been tested for HCV RNA and genotype, and that (iii) all persons with active infection are linked to specialised care and (iv) treated. Indeed, the most troublesome gaps in the hepatitis C continuum of care are the poor diagnosis rate [9] and an unsatisfactory linkage to specialised care.

In an accompanying paper [10], Bregenzer and colleagues analysed in great detail the management of HCV in drug substitution programmes in the Swiss canton Aargau. In particular, they compared the cascade of care in centralised and decentralised care centres, the latter accounting for approximately 50% of enrolled cases, mostly followed up by general practitioners [11]. The most important observation of this study was the rather poor compliance with national and international recommendations for the management of patients under OST. Significant gaps in the HCV cascade

Correspondence:
Francesco Negro, MD, Divisions of Gastroenterology and Hepatology and of Clinical Pathology, Geneva University Hospitals, Rue Gabrielle-Perret-Gentil 4, CH-1211 Geneva 4, Francesco.Negro[at]hcuge.ch

of care were identified, especially in decentralised settings: as many as one fourth of patients had never been screened for HCV, around 19% of those found anti-HCV-positive had never been tested for HCV RNA, almost 20% of viraemic cases had never been genotyped for HCV, slightly more than half of them had never been evaluated for liver fibrosis stage or treated with antivirals. Provision of free rapid assays for anti-HCV in capillary blood, which has been shown to enhance the continuum of care in previous studies [12, 13], and free assessment of liver stiffness with the FibroScan™ reduced only some of these gaps. Moreover, although questionnaires were sent to all physicians prescribing OST within the canton, only one third of cases could be enrolled, for reasons that could not be identified; the possibility that compliance with guidelines might have been even worse among non-respondents cannot be excluded. Finally, despite the availability of DAAs during the second year of the survey, none of the patients had been treated with these drugs.

These results, coming from a resource-rich country, are not encouraging. As said, elimination of the HCV viraemic pool among PWID in order to comply with the WHO goals will require a substantial increase in antiviral treatment uptake. However, it seems that the system is unprepared to cope with a large increase in patients to be treated [8], in spite of the fact that the administration of DAAs is safe and requires minimal surveillance, which in principle should allow expansion of treatment capacity by shifting the task of medicine delivery to mid-level care providers. These capacity limitations have to be carefully weighed before firm recommendations can be made at the national level; possibly the ability to prescribe DAA should be extended to physicians involved in OST, ideally after a thorough case discussion with reference specialists.

For the time being, however, the major obstacle remains diagnosis and staging by general practitioners. The factors behind these gaps could not be analysed by Bregenzer and colleagues [10], but can be partly deduced from the extensive experience in the field: (i) stigma (including self-stigma) may prevent PWID from accessing proper care, especially at public hospitals; (ii) discrimination by medical and paramedical staff may be more prevalent than commonly perceived; (iii) PWID and family physicians may be totally unaware of therapeutic advances of recent years, despite the unprecedented debate on DAAs, boosted by their huge market entry price; (iv) peer support, including peer-to-peer education and debate, may be insufficient; (v) case management, ideally by social workers (rather than by doctors), including keeping track of patients' visits and missed appointments, may be erratic, aggravated by the challenges that PWID must cope with in their everyday life; and finally, (vi) there may be some misconceptions by doctors about adherence and reinfection, resulting in biased commitment.

This dismal situation is even more difficult to understand and accept given the long-standing tradition of integrating PWID services in the Swiss health system, and it is not easy to make suggestions to improve it. The level of awareness on viral hepatitis issues is lagging well behind what has been achieved in the field of human immunodeficiency virus infection; health authorities should be more sensitive to the repeated pleas of Swiss opinion leaders and advocates. Well-funded HCV awareness campaigns aiming at general practitioners and addiction medicine specialists are needed. On the other hand, the large-scale implementation of electronic medical records may help, as they may bear a red flag in the event of a missing screening assay for HCV. HCV antigen assays in the form of rapid point-of-care tests using capillary blood may help to close another gap, but the accuracy of available tests is suboptimal [14], and confirmation of active HCV infection once anti-HCV antibodies have been detected still requires retesting the patient for HCV RNA. Technological improvements may in the future rely upon isothermal amplification of viral RNA using very small amounts of blood and low power devices such as smartphones [15], although these approaches are far from being optimised and cannot at present be applied to routine diagnosis. Most importantly, more emphasis should be put on the advantages of providing HCV care for PWIDs in centralised rather than decentralised settings, possibly by expanding harm reduction programmes and integrating HCV services (prevention, social and peer support, testing, treatment and care) in these programmes. In the meanwhile, the insufficient continuum of care, especially in decentralised facilities, will keep curbing the current momentum to eliminate HCV across Switzerland.

Acknowledgments

The authors wish to thank Philip Bruggmann for advice and criticism.

Competing interests

Francesco Negro is advisor to Merck, AbbVie and Gilead, and has received research grants from AbbVie and Gilead. Liudmyla Maistat is Policy and Advocacy Manager at Medicines Patent Pool, Geneva.

References

1 http://www.who.int/mediacentre/news/releases/2016/wha69-28-may-2016/en/ (accessed November 11, 2017)

2 Uchtenhagen A. Heroin-assisted treatment in Switzerland: a case study in policy change. Addiction. 2010;105(1):29–37. doi: http://dx.doi.org/10.1111/j.1360-0443.2009.02741.x. PubMed.

3 Turner KM, Hutchinson S, Vickerman P, Hope V, Craine N, Palmateer N, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction. 2011;106(11):1978–88. doi: http://dx.doi.org/10.1111/j.1360-0443.2011.03515.x. PubMed.

4 Vickerman P, Martin N, Turner K, Hickman M. Can needle and syringe programmes and opiate substitution therapy achieve substantial reductions in hepatitis C virus prevalence? Model projections for different epidemic settings. Addiction. 2012;107(11):1984–95. doi: http://dx.doi.org/10.1111/j.1360-0443.2012.03932.x. PubMed.

5 Martin NK, Vickerman P, Hickman M. Mathematical modelling of hepatitis C treatment for injecting drug users. J Theor Biol. 2011;274(1):58–66. doi: http://dx.doi.org/10.1016/j.jtbi.2010.12.041. PubMed.

6 Bruggmann P, Falcato L, Dober S, Helbling B, Keiser O, Negro F, et al.; Swiss Hepatitis C Cohort Study. Active intravenous drug use during chronic hepatitis C therapy does not reduce sustained virological response rates in adherent patients. J Viral Hepat. 2008;15(10):747–52. doi: http://dx.doi.org/10.1111/j.1365-2893.2008.01010.x. PubMed.

7 Bruggmann P. Accessing Hepatitis C patients who are difficult to reach: it is time to overcome barriers. J Viral Hepat. 2012;19(12):829–35. doi: http://dx.doi.org/10.1111/jvh.12008. PubMed.

8 Bruggmann P, Blach S, Deltenre P, Fehr J, Kouyos R, Lavanchy D, et al. Hepatitis C virus dynamics among intravenous drug users suggest that an annual treatment uptake above 10% would eliminate the disease by 2030. Swiss Med Wkly. 2017;147:w14543. https://smw.ch/en/article/doi/smw.2017.14543/ PubMed.

9 http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/ (accessed November 11, 2017)

10 Bregenzer A, Conen A, Knuchel J, Friedl A, Eigenmann F, Näf M, et al. Management of hepatitis C in decentralised versus centralised drug substitution programs and minimally invasive point-of-care tests to close gaps in the HCV-cascade. Swiss Med Wkly. 2017;147:w14544. https://smw.ch/en/article/doi/smw.2017.14544/

11 https://www.bag.admin.ch/bag/de/home/themen/menschgesundheit/sucht/suchtberatung-therapie/substitutionsgestuetzte-behandlung.html (accessed November 11, 2017)
12 McLeod A, Weir A, Aitken C, Gunson R, Templeton K, Molyneaux P, et al. Rise in testing and diagnosis associated with Scotland's Action Plan on Hepatitis C and introduction of dried blood spot testing. J Epidemiol Community Health. 2014;68(12):1182–8. doi: http://dx.doi.org/10.1136/jech-2014-204451. PubMed.
13 Meyer JP, Moghimi Y, Marcus R, Lim JK, Litwin AH, Altice FL. Evidence-based interventions to enhance assessment, treatment, and adherence in the chronic Hepatitis C care continuum. Int J Drug Policy. 2015;26(10):922–35. doi: http://dx.doi.org/10.1016/j.drugpo.2015.05.002. PubMed.
14 Duchesne L, Njouom R, Lissock F, Tamko-Mella GF, Rallier S, Poiteau L, et al. HCV Ag quantification as a one-step procedure in diagnosing chronic hepatitis C infection in Cameroon: the ANRS 12336 study. J Int AIDS Soc. 2017;20(1):21446. doi: http://dx.doi.org/10.7448/IAS.20.1.21446. PubMed.
15 Gurrala R, Lang Z, Shepherd L, Davidson D, Harrison E, McClure M, et al. Novel pH sensing semiconductor for point-of-care detection of HIV-1 viremia. Sci Rep. 2016;6(1):36000. doi: http://dx.doi.org/10.1038/srep36000. PubMed.