

Update on envisaged next steps: HCV prevention in key populations

The Hepatitis C Disease Narrative, published February 2020, identified prevention of HCV among key populations as a high priority for the HCV response that Unitaid can contribute to. Improved prevention of HCV among key populations will contribute to achieving both the WHO goal of elimination of HCV as a public health problem by 2030 and the health-related Sustainable Development Goals (SDGs)¹. The Unitaid Secretariat has therefore explored options related to HCV prevention. This document provides a summary of this opportunity.

Hepatitis C remains an important public health problem, despite progress made; gains in HCV treatment resulting in people being cured is largely offset by new infections, in particular among key populations. Reducing HCV infection among key populations is therefore essential to achieve elimination targets, and scored highly on both impact potential and ability for Unitaid to make a difference during the recently concluded prioritization exercise.

Unitaid has played a leadership role in HCV, and Unitaid investments are recognized for having created many of the tools that have enabled this progress. These tools make HCV elimination feasible. In addition, several innovative and under-used products have been identified that can contribute to prevention of HCV, in particular among key populations. These will be the basis for a Call for Proposals targeting a holistic approach for HCV prevention.

Hepatitis C remains an important public health problem

Hepatitis C virus (HCV) infection is a major cause of liver diseases (including liver cancer) that lead to approximately 300,000 deaths annually. An estimated 58 million persons are chronically infected, with a disproportionately high burden in low- and middle-income countries (LMICs). People living with HIV are six times more likely to be infected with HCV than people who are HIV-negative, and chronic HCV infection rates can be particularly high in key populations.

Unitaid contributed to significant progress in HCV

Despite the relatively limited financing, significant progress has been made with regard to HCV elimination since the introduction of curative, short-course direct acting antiviral (DAA) therapy in 2014. Notably, WHO estimates that the number of people cured from HCV has increased from 1 million in 2015 to 9.4 million in 2019 (latest available estimate). The estimated number of people with chronic HCV has reduced from 71 million in 2017 to 58 million.

Unitaid started investing in HCV in 2015 and is widely seen as having played a key role in putting HCV on the map. Unitaid's investments have been credited for having made important contributions by creating conditions and tools to facilitate wider access to HCV testing and treatment². In particular:

- The project “Ensuring access to HCV treatment revolution for HCV/HIV co-infected patients in low and middle-income countries” with Médecins Sans Frontières (MSF) (2015-2018, US\$8 million)

¹ SDG target 3.3 includes viral hepatitis.

² HCV portfolio evaluation, available https://unitaid.org/assets/Final_Report_HCVEvaluation_CEPA.pdf

demonstrated the feasibility of HCV treatment in resource limited settings. It also developed simpler and more affordable HCV treatment and care models, and generated evidence on their effectiveness and cost-effectiveness in order to promote uptake at national and global level.

- The project with Coalition PLUS (2015-2021, US\$10.1 million) raised awareness on HCV, including on the fact that it can be cured. It also advocated for increased uptake of affordable HCV treatments, greater investment in and prioritization of HCV elimination.
- The “Hepatitis C Elimination through Access to Diagnostics” (HEAD-Start) project with FIND (2016-2020, US\$27.4 million) supported the development of new, simpler HCV diagnostic products. It has also generated evidence for simplification of HCV screening and testing algorithms, on decentralization and on integration of HCV testing and treatment in other programmes or settings.

These three projects dedicated to HCV are now closed. They have mostly achieved what they set out to do³ (though some work related to new diagnostics is still ongoing).

Progress in HCV treatment is largely offset by new infections

Despite these successes, challenges remain; there has been insufficient progress on HCV testing and there has been no progress on prevention of HCV among key populations. Both need to be scaled up in order to meet the 2030 elimination targets. This has become particularly urgent as COVID-19 has diverted funding away from other diseases, including viral hepatitis; according to WHO, viral hepatitis services are among the most frequently disrupted services due to COVID-19⁴.

The lack of prevention of HCV among key populations is a priority as it undermines progress made; every year, 1.5 million people become newly infected with HCV⁴.

Prevention among key populations is essential to achieve targets

Key populations for HCV include people who inject drugs (PWID), prisoners and PLHIV.

There are an estimated 11 million people who inject drugs globally, and PWID are a key population for both HCV and HIV transmission. Around 1.4 million PWID are living with HIV, and injecting drug use accounts for approximately 10% of HIV infections globally. Injecting drug use also accounts for 23-39% of new HCV infections. The estimated global prevalence of hepatitis C in people who inject drugs is 39%, with a higher prevalence in some settings. Approximately 2.3 million people are co-infected with HIV and HCV, and more than half of them inject drugs⁵.

³ For more details, see: Unitaid. [Impact story. Paving the way for hepatitis C elimination](#), 2021.

⁴ WHO. Progress report on HIV, viral hepatitis and sexually transmitted infections, 2021.

⁵ WHO. People who inject drugs. <https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/populations/people-who-inject-drugs> (accessed 8 Dec. 2021).

More than 11 million people are in prison on any day⁶, while around 30 million people pass through prisons every year (globally)⁷. The estimated HCV prevalence is around 26%⁸.

Reaching these key – and often very marginalized and vulnerable – populations with treatment and prevention services will be essential to achieving both HCV elimination and contribute to achieving HIV targets. It is also an essential step toward more equitable access to HCV care and cure. It has been estimated that elimination of HCV transmission among PWIDs would be able to prevent 40% of new HCV infections⁹.

Services for key populations can contribute to closing the diagnostic gap

Testing and treating key populations is another important step toward elimination of HCV. It has multiple benefits: the individual will be cured, it reduces transmission and it helps close the diagnostic gap. Moreover, this is an effective way of identifying people with chronic HCV (due to the high HCV prevalence in key populations).

Access to innovative and under-used products for HCV prevention in key populations is limited

Innovative and existing but under-used tools have been identified that could provide additional options and choices to affected communities, and that may increase uptake and/or effectiveness of harm reduction:

- Long-acting buprenorphine: several formulations are on the market for subcutaneous injection of buprenorphine. They require weekly or monthly injection. In addition, a 6 monthly implant exists.
- Low dead-space syringes: design features reduce the amount of liquid (or blood) that is left in the syringe after use, thus reducing the risk of bloodborne diseases in case of sharing of syringes.
- Curative HCV treatment: direct acting antivirals can cure HCV infection in 8-12 weeks, and a person who is cured will not infect others ('treatment-as-prevention').

Combining these interventions in a holistic and person-centered approach would enhance and accelerate impact.

Access challenges for long-acting buprenorphine relate to the lack of availability in LMICs, questions on uptake and feasibility of use in resource-limited settings, and costs. Access challenges for low dead-space syringes include lack of awareness, questions on uptake, costs and potentially supply-side challenges. Tests and treatments for HCV are on the market, but their availability and cost varies among countries. Moreover, HCV treatment is often not available to key populations, despite their higher risk of chronic HCV infection, and at times PWIDs are excluded from treatment (contrary to WHO guidance).

Alignment with Unitaid expertise and strategic principles

⁶ Walmsley R. World Prison Population List. 12th edition.

⁷ WHO. People in prisons and other closed settings. <https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/populations/people-in-prisons> (accessed 8 Dec. 2021).

⁸ Larney S. et al. Incidence and Prevalence of Hepatitis C in Prisons and Other Closed Settings: Results of a Systematic Review and Meta-Analysis. *Hepatology*, 2013.

⁹ WHO. Progress report on HIV, viral hepatitis and sexually transmitted infections, 2021

The work envisaged involves the introduction of innovative products that reduce the risk of both HCV and HIV infection, facilitate adherence to ART and reduce HCV prevalence in key populations. These products, especially used in combination, will not only reduce HCV in key populations, but can also enable simplification of care, facilitate decentralization and integration of services, and increase people's autonomy and choices.

Future options: Accelerating introduction of products currently under development

Two additional innovative products whose (ongoing) development is or has been supported by Unitaid are relevant in this context:

- a core-antigen rapid diagnostic test (cAg RDT) for HCV: the HEAD-Start project successfully completed the development of a cAg RDT; technology transfer to a commercial partner is ongoing. An HCV cAg RDT is widely considered to be a game-changing product; it would enable confirmation of chronic HCV infection in those screened positive in approximately one hour, and without the need for laboratory infrastructure.
- a long-acting HCV treatment: the LONGEVITY project envisages developing a long-acting formulation of a hepatitis C treatment. Ideally, it will be a single injection that releases the medicines over 12 weeks and result in cure (a 'one-shot cure').

Both products would be particularly suitable for key populations. If used in combination (and assuming their development will be successful), they would make it possible to diagnose and cure HCV infection in a single visit or patient contact, which would be important for hard-to-reach key populations, such as for instance a subset of PWIDs.

As these products are still being developed and their launch dates are not yet known, proposals under the current Call for Proposals should not include these products.