



ADHERE: a toolkit for retaining PWID living with hepatitis C in healthcare systems

Ricardo Baptista-Leite^{1,2} · Henrique Lopes¹ · Diogo Franco¹ · Catarina Hermenegildo¹ · Timo Clemens² · Helmut Brand²

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Abstract

Aim Despite advancements in hepatitis C care, significant gaps remain, particularly in retaining people who inject drugs (PWID) in treatment, which hinders progress toward achieving the World Health Organization's (WHO) hepatitis C elimination goals. The ADHERE (Attract pwiD Hepatitis hEalthcaRE) toolkit was developed to address these challenges by optimizing linkage-to-care services for PWID, focusing on the critical steps within the care cascade (CC) where losses are most likely to occur.

Subject and methods Retaining PWID through the entire treatment process until the achievement of sustained virologic response (SVR) remains a formidable challenge. The ADHERE toolkit interconnects micro-ecosystemic conditions with public health policy implementation, offering a structured approach to enhancing PWID retention in healthcare systems. This toolkit was developed through an extensive literature review and consultations with key opinion leaders (KOL) from seven countries, ensuring its relevance and applicability across diverse settings.

Results The ADHERE toolkit provides a comprehensive framework and strategy for public health interventions, focusing on the later stages of the CC for hepatitis C. By facilitating continuous quality improvement and enabling the integration of various public health policies, the toolkit aims to minimize treatment dropouts and maximize the chances of achieving a cure among PWID.

Conclusion The ADHERE toolkit aims to aid in advancing the management of hepatitis C among PWID, offering a feasible and auditable approach to improving patient retention and treatment outcomes. By establishing a robust network of health policy management processes, the toolkit is expected to contribute to the global effort to eliminate hepatitis C.

Keywords Public health policies · People who inject drugs · Hepatitis C · Healthcare management · Care cascade

Background

Globally, hepatitis C virus (HCV) remains a significant public health challenge, particularly among populations with high HCV prevalence, such as people who inject drugs

(PWID). Despite the availability of highly effective direct-acting antiviral (DAA) treatments, the uptake among PWID has been suboptimal due to a range of barriers including stigma, inadequate access to healthcare, and insufficient linkage-to-care strategies. The World Health Organization

✉ Ricardo Baptista-Leite
r.guerreirobaptistaleite@maastrichtuniversity.nl

Henrique Lopes
hlopes@novaims.unl.pt

Diogo Franco
dfranco@novaims.unl.pt

Catarina Hermenegildo
chermenegildo@novaims.unl.pt

Timo Clemens
timo.clemens@maastrichtuniversity.nl

Helmut Brand
helmut.brand@maastrichtuniversity.nl

¹ NOVA Center for Global Health, NOVA-IMS, Universidade Nova de Lisboa, 1099-085 Lisbon, Portugal

² Department of International Health, Care and Public Health Research Institute - CAPHRI, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands

(WHO) has set an ambitious goal to eliminate hepatitis C as a public health threat by 2030. However, reaching this target is contingent upon improving treatment access and retention, especially within vulnerable populations such as PWID. Estimates on the HCV prevalence among the PWID population indicate rates over 60% worldwide (ECDC 2021). Risk behaviours such as drug injection are linked to around 9% of HCV infections (Grebely et al. 2019a, b), with anti-HCV antibodies prevalence rates differing significantly at the national and international levels (ECDC 2021; EMCDDA 2019). However, PWID epidemiological data may not reflect reality as this population is often difficult to reach by health systems, which is partly due to the social impact between hepatitis C and aspects of the PWID lifestyle (Goodyear et al. 2021), thus hindering the identification and diagnosis of individuals living with HCV infection.

To achieve the elimination of the disease, it is vital to provide treatment to the highest possible number of individuals living with HCV (Cornberg and Manns 2022), which means that the greatest efforts must be applied to those population segments which have not only a high prevalence of hepatitis C cases but also represent a high potential of contamination to third parties.

As social determinants of health influence one's global health state, to efficiently combat hepatitis C in PWID populations it is necessary to address lifestyle contexts and behaviours in an ecosystem context where problems identified by the scientific literature occur, but where solutions already exist that can be put into practice in a structured and quantifiable way. Only by addressing issues related to patient abandonment and improving retention processes after diagnosis of individuals living with HCV infection will it be possible to proceed with the remaining disease CC steps, namely treatment success, and rehabilitation (Valencia et al. 2021).

Problems such as drug addiction, HCV/HIV co-infections, mental health conditions, sex work, and crime, among others, aggravate the health condition of PWID who live with hepatitis C (EMCDDA 2021; Larney et al. 2020; Molinaro et al. 2019) and create difficulties in adherence to the disease treatment (Pericot-Valverde et al. 2022). This constitutes a global health issue requiring urgent development and strengthening of public health strategies to control hepatitis C in the PWID population and to integrate the different components of healthcare systems' contributions that have to manage this issue.

Data shows that over half of the individuals with a lifetime history of substance abuse were also affected by another mental disorder or psychotic situation (Adams et al. 2020). Compared to the general population, PWID are more likely to develop major depression and, from this, there is a significant likelihood of developing substance use disorders (Pericot-Valverde et al. 2022). A growing number of studies demonstrate that untreated mental illness, especially

depression and alcohol/substance use disorders, is associated with hepatitis C-related risk behaviours, contraction of HCV infection, failure to access HCV care and treatment, failure to adhere to HCV care and treatment, and increased morbidity and mortality from HCV-related diseases and comorbidities (Pericot-Valverde et al. 2022; Pericot-Valverde et al. 2020a, b; Reddon et al. 2017). The strengthening of policies to control this disease must address finding and diagnosing individuals living with hepatitis C and subsequently guaranteeing all the resources for adequate linkage-to-care and treatment to prevent losses in the CC follow-up (Grebely et al. 2017a, b, c, d; Krekulova et al. 2022).

Despite advancements in hepatitis C treatment, significant gaps persist in retaining PWID in the healthcare system through to treatment completion and achieving sustained virologic response (SVR). Existing strategies often fall short in addressing the complex needs of PWID, who face multiple intersecting challenges such as mental health issues, substance use, and social stigma. These barriers lead to high rates of treatment discontinuation, compromising efforts to control and eventually eliminate HCV within this population. Moreover, current public health approaches frequently lack the flexibility to adapt to the unique circumstances of PWID, resulting in a one-size-fits-all approach that fails to achieve optimal outcomes.

In response to these challenges, the ADHERE toolkit was developed to provide a tailored, ecosystem-based approach to retaining PWID in care. By focusing on the critical linkage-to-care steps of the CC, the "ADHERE" (Attract pwiD Hepatitis hEalthcaRE) toolkit addresses these gaps by offering a structured yet adaptable framework that integrates public health policies (PHP) with on-the-ground realities. This toolkit is designed to enhance the capacity of healthcare systems to engage and retain PWID in treatment, ultimately improving health outcomes and contributing to the broader goal of hepatitis C elimination.

This paper is thus produced as a complement to the article describing the "APPEAL" toolkit, centered on attracting PWID to healthcare systems, and comprises a proposal of a second approach which seeks an integrated and ecosystemic response to the problem of PWID abandoning treatment processes. We found that the response to improving the quality of service to PWID has to go through these two independent but interconnected tools to support healthcare services management and health decision-makers, as well as hepatitis C patient advocacy stakeholders.

Worldwide, the patient is progressively set at the centre of healthcare systems, converging with public health interests and goals (Harm Reduction International 2022; Moretta Tartaglione et al. 2018). This conjoint actuation can be witnessed in the increasing number of healthcare plans and clinical services addressing different population groups, including PWID. Therefore, the healthcare

system's approach to public health issues is fundamental in providing adequate healthcare aligned with disease best practices. Key stakeholders are developing hepatitis C programmes on the disease, which must be supported by scientific evidence to its greatest possible extent (EMCDDA 2019, 2021).

This toolkit seeks to reduce PWID abandonment during the treatment period, so that the highest possible percentage of patients reaches the end of the 8–12 weeks cured. It is, therefore, a linkage-to-care optimization tool, also aiming to increase the economic efficiency of the investment made in programs to combat hepatitis C. It was designed within a public health reading towards the continuous quality improvement of hepatitis C care in PWID, being centered on the linkage-to-care step of the CC and resorting to different PHP (partial hospitalization programs) and other procedures expressed as “process procedures” (PPs). The tool is presented openly, that is, without rules for applying quality processes to avoid the rigidity of conduct in the management of processes that this would imply. Thus, it enables its use both by small organizations of local action such as NGOs, and also by more formal systems such as health authorities acting regionally in the PWID segment. The tool's philosophy is, therefore, closer to a checklist for conducting action and responding to problems than to a quality system, being supported by available scientific evidence. This last condition means that if there is a structural change in the scientific bibliography that feeds each of the 19 PPs, their implications and organizational experiences must be reorganized according to what is the new scientific evidence. As a result, the ADHERE toolkit becomes alive, being interactive with scientific development. It is therefore suggested that communities of practice be created that use the tool, so that not only the scientific component is incorporated, but also the experience that comes permanently from the field of the diversity of cultures and legislation can be debated and thought about.

Although PWID represent most individuals living with hepatitis C in developed countries, their treatment uptake was generally low in the Interferon era (Karasz et al. 2022). This was due to the treatment's side-effects (compared to withdrawal from drugs, depression, and suicidal ideation, among others), low efficacy, and fear of needles from therapy and liver biopsy (Karasz et al. 2022; Rich et al. 2016). The introduction of DAA therapies dramatically changed the perception and prevalence of HCV infection among PWID: the treatment timeline was reduced drastically (8 weeks for the majority of treatment durations) (Sandmann et al. 2019); sustained virologic cure rates are over 95% (Schutz et al. 2018); it is a simple oral treatment, taken once a day, that comprises nearly no psychiatric and side effects; and it proves to be cost-effective (Grebely et al. 2017a, b, c, d; Verma et al. 2021), among other aspects (Cornberg and Manns 2022).

Similarly to the HIV/AIDS strategy, preventive medication for HCV infection is also used as a tool for prevalence reduction in high-risk patients, such as PWID. DAA treatments in this population are crucial in preventing HCV transmission and reducing prevalence rates while improving health-related quality of life, reducing liver disease progression, and reducing advanced liver disease mortality due to decompensated cirrhosis or hepatocellular carcinoma (Cacoub and Comarmond 2018; Grebely et al. 2017a, b, c, d; Pawlotsky et al. 2018). As a better-tolerated and painless treatment, PWID adherence rates have also improved, similar to non-PWID patients living with hepatitis C (Alimohammadi et al. 2018; Elsherif et al. 2017; Kanwal et al. 2017; WHO 2017).

Adherence to DAA treatment has the potential of leading to other health counselling programs (WHO 2018). This is especially relevant, knowing that HCV infection has very common overlapping populations with common risk factors (e.g., PWID, prisoners, etc.), with individuals infected by the human immunodeficiency virus (HIV) who share closely related transmission networks (Alipour 2022; Boeke et al. 2020). This not only increases the risk of liver damage, but can also accelerate the onset of liver damage following infection (Liu et al. 2022).

The typical PWID patient living with hepatitis C is one with multi-addictions (alcohol, tobacco, drug consumption, among others) (Pericot-Valverde et al. 2020a, b). Concerning this dimension, a study (Barré et al. 2020) identified three obstacles that may affect the treatment of PWID on an individual level and act as predictors of exclusion for the antiviral therapy — continued injecting drug use, alcohol use, and pre-existing mental disorders (Conway et al. 2020). These obstacles may hinder clinicians' investment with regard to assistance to PWID compared with non-PWID when infected with HCV (Broady et al. 2020; Muncan et al. 2020).

Until recently, most HCV treatment guidelines excluded PWID due to concerns about poor adherence, adverse events, and reinfection (Graf et al. 2020; Murdock et al. 2019). Nonetheless, the conditions mentioned above are no longer a contraindication if patients comply with prescribed medication under health professional supervision (Murdock et al. 2019).

There is still a lack of evidence supporting the above-mentioned exclusions, which partially explains the differences between the hepatitis C burden among PWID and non-PWID (Graf et al. 2020; Murdock et al. 2019). Moreover, continued injecting behaviour places the user at reinfection risk even if SVR₀ is achieved after treatment completion, despite reinfection rates being generally low (Grebely et al. 2022). Considering the higher risk of HCV infection among PWID populations due to lifestyle-associated risk behaviours, reducing prevalence and incidence rates is even more

urgent, due to single patients representing a high-risk vector for all the remaining drug users (Grebely et al. 2019a, b).

As stated above, in the pre-DAA period, only a residual percentage of people who were aware of their HCV condition, including PWID, received treatment (Grebely et al. 2017a, b, c, d). Studies (Buchanan et al. 2020; Silano et al. 2022; Teti 2020) have shown PWID attendance of support groups for HCV infection to be effective in minimizing the impact of drug use on HCV burden when patients interact at different treatment levels, increasing attendance rates and subsequently improving treatment results.

Successful HCV treatment studies among PWID, providing evidence of high uptake levels, improved adherence to treatment, and treatment outcomes (including diverse quality of life aspects, both physical and mental) (Graf et al. 2020; Guggisberg et al. 2022; OECD/European Union 2020; Pedlar and Sandhu 2020). It is also important to destigmatize and prepare physicians (GP and others) and other healthcare professionals to deal with the reality of how difficult it is for PWID to abandon consumption while accepting and receiving the best treatment.

Clinicians can adopt a harm-reduction approach and tolerate illicit drug use during treatment as long as there is adherence to the therapeutic regime (Graf et al. 2020). Also, the combination of opioid substitution treatment (OST) and high-coverage needle and syringe programs (NSP) can contribute to achieving these goals (Day et al. 2019a, b; Palmateer et al. 2022). Rehab programmes, such as methadone use, allow the implementation of prevention interventions while treating patients with DAA at the point of care (Bartlett et al. 2022).

Another critical obstacle is the lack of appropriate national policy or treatment guidelines (ECDC and EMCDDA 2018; Harm Reduction International 2022) that include PWID. In a survey with data from 33 European countries, only a third included PWID in their national strategies or plans (Maticic et al. 2019). HCV elimination is an ambitious target that may not be achieved unless actions toward controlling hepatitis C in the PWID population are strengthened and prioritized, especially if PWID exclusion from treatments is still a reality (Grebely et al. 2017a, b, c, d; Krekulova et al. 2022).

Possible approaches

Primary care-based model

There are several care-based models for managing hepatitis C among PWID, of which the ‘primary care-based model’ (Radley et al. 2019) is one of the most promising approaches. According to Grebely et al. (2017c), the expansion of HCV care to general practitioners and other non-hospital settings

is essential in providing linkage to HCV care and treatments for PWID, with a higher likelihood of attendance and willingness to be tested and treated (Wade et al. 2019). Overall, this model creates a multidisciplinary environment for diagnosing and treating HCV, determining its success or failure. It implies PWID attendance to a community clinic or mobile unit rather than a hospital, including antiviral therapy availability. It comprises a large team: a clinical nurse specialist on hepatitis C, a physician in infection and immunity, pharmaceutical professionals, social workers, peers, and a general clinician who is responsible for PWID and for the professionals who assist this group. There are, however, countries where there is a strong reaction against this model for historical reasons, which consider hepatitis C as the exclusive responsibility of one or two medical specialties. This will potentially be an element that limits the legal and cultural application of ADHERE.

Peer-support model

The ‘peer-support model’ has a crucial role in the treatment and, ultimately, the well-being of the PWID population. This model has been implemented in various settings, with those including OST being more common (Bonnington and Harris 2017; Day et al. 2019a, b). Peer-support models can be grouped and divided into two categories: community-controlled and service-generated models (EMCDDA 2019). The former are usually implemented by peer-based drug group organizations, the affected community, and local service providers. These one-to-one models are entirely controlled and based around the OST clinics in which peer-support workers offer extensive and ongoing support and education during the assessment and treatment of HCV. The latter can overcome mistrust from potential users and provide intensive support for people with multiple issues. There is also potential cultural and legal interference in the application of this model in various parts of the world, especially outside westernized countries, which must be taken into account in the application of ADHERE.

Service-generated model

Another type of peer professional support model (paid or without salary) is the ‘service-generated model’ created by the service or healthcare centre in which PWID receive HCV treatment. This model’s approaches include self-help groups, peer interventions, and therapeutic communities, supported by the service itself (Dillon et al. 2016; Falade-Nwulia et al. 2020). These models are highly effective at managing a large number of patients and are well-accepted by those who are ready for a sharing and group model approach. Peer support models are a practical approach to overcoming the low treatment and assessment rates of PWID affected by HCV

(Jugnarain et al. 2021). For this to be viable, it is necessary for the healthcare provider structure to recognize peers as potential partners, which can be complex where there is resistance to PWID, which, as seen before, even involves low clinical investment in this type of treatment. However, its simple consideration obliges the most conservative healthcare organizations to take a conceptual leap that will end up having repercussions in multiple areas for the benefit of patients.

Materials and methods

The scoping review was conducted utilizing the “Pubmed”, “Google Scholar” and “Scopus” databases. The inclusion criteria for scientific works comprised academic papers published from 2014, obtained through the search of the keywords “hepatitis C”, “drug users” and “PWID” applied for each of the latter CC steps. This database search resulted in 10,130 initial hits. Following this identification, the results were screened for titles and abstracts focusing on hepatitis C linkage-to-care, treatment, and rehabilitation, eliminating duplicates and inaccessible works, resulting in 357 eligible works. From the latter, 114 were initially included by applying the inclusion and exclusion criteria as presented in Table 1.

Contextual information from the “Let’s End HepC” (LEHC) European project developed by the same team of authors was also used, based on the discussion and interviews with 57 experts from national advisory boards (NAB) of seven countries, to complement recommendations for hepatitis C care in PWID in the latter stages of the CC. Four additional works were added as contributions from the NAB members of the Let’s End HepC project, representing 119 scientific works in total.

In the final step, the articles that did not contain quantitative information or were applied in samples with specific populations were not considered for the final synthesis of this article. As a result, 67 bibliographic elements were included in the review as presented in Fig. 1.

Given that the action will potentially be different in each location when applying the process procedure to a specific context, the quantitative information provided by the

supporting articles is not presented as something directly transposable to the context. Application is therefore presented as a sense of action that has already been measured as valid. If when applying the tool it is understood that contexts can be transposed, some potentially interesting information will be surely found in the presented bibliography. However, it must be warned that the transposition of elements that differ in the target populations, in the moments and forms of measurement, in legislations, languages, and other determinant cultural elements, is a huge risk as seeking a positive or negative meaning is quite different from tracing objective and subjective conditions.

As previously stated, this article focuses only on the creation of a conceptual tool that helps the linkage-to-care of PWID. However, we argue that there should be a greater articulation of this phase with rehabilitation, the later phase of the CC. The bonds are deep, and whatever is done well or badly in the linkage-to-care will necessarily be reflected in the rehabilitation. We mentioned some aspects that we believe should be considered in the linkage-to-care phase. PWID rehabilitation is a subject of enormous complexity, as it must involve the coordination of health services with social services and often also those linked to justice (Masarone et al. 2020; Phillips et al. 2020).

The vastness and complexity of this subject oblige us to only refer to the need for treatment plans for PWID, considering from the first moment the presence of elements as simple as the alignment between judges and the recovery and treatment team of the PWID living with hepatitis C, the articulation between social support teams for PWID with the hepatitis C team, employment services, and social reintegration, among others. We believe that voluntary not-integrated efforts will only obtain suboptimal results (Olgin et al. 2020).

Production of the ADHERE toolkit

Following the literature review and identification of the main challenges in retaining PWID living with hepatitis C in healthcare systems, below follows a proposal for a toolkit to control the disease in this population, focusing on the CC steps of linkage-to-care.

Table 1 Inclusion and exclusion criteria for scientific works included in the article

Inclusion criteria:

- Study samples must focus on current drug users or individuals with history of IDU or general drugs
- Scientific works and data published after the introduction of DAA therapies in the market, by 2014
- The aim of the scientific works should focus on linkage-to-care, treatment and/or rehabilitation

Exclusion criteria:

- Scientific works and data published prior to 2014
- Articles in languages other than English

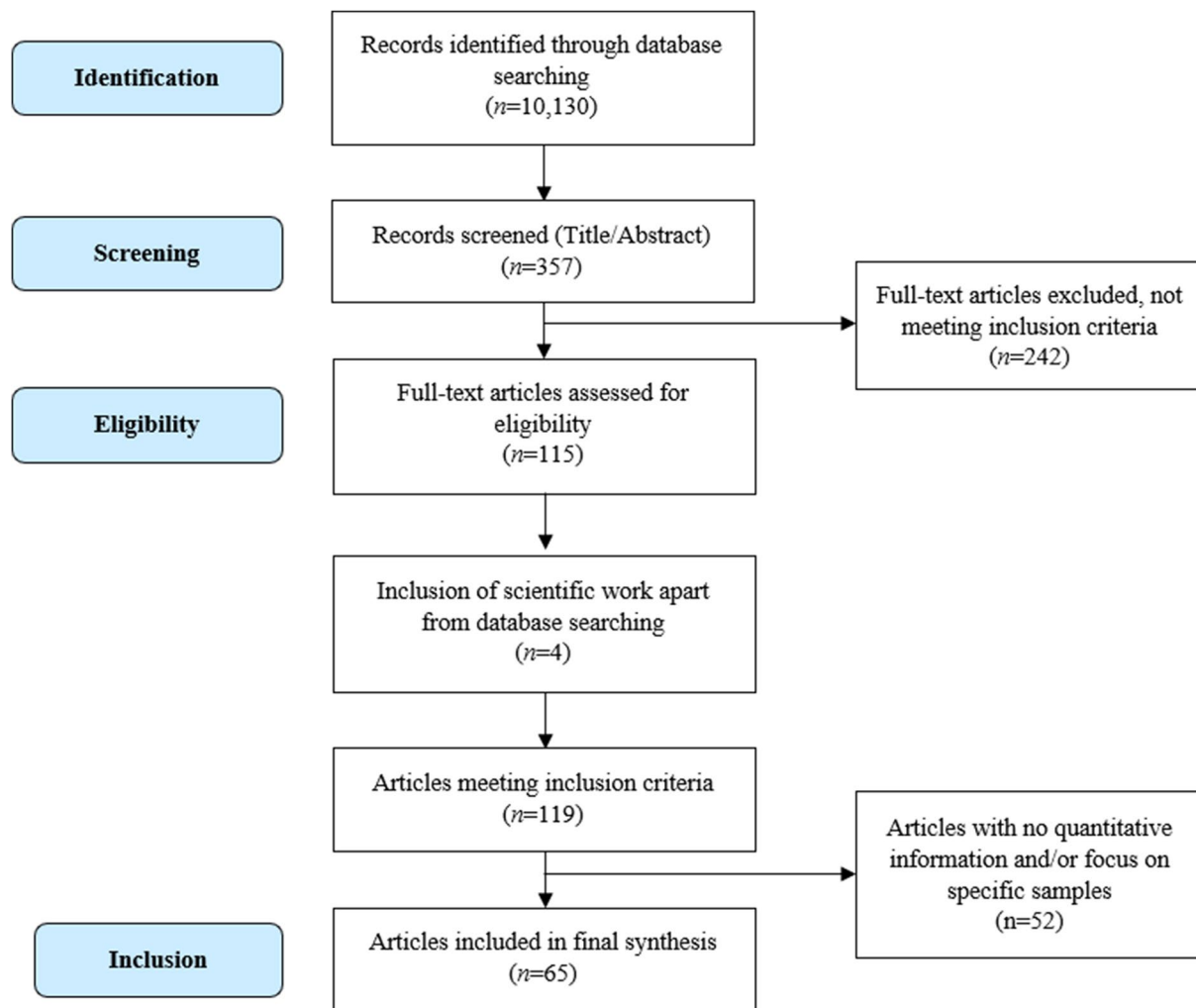


Fig. 1 Fluxogram of scientific work selection criteria for inclusion in the article

The toolkit is organized into three axes: problems, solutions, and the respective outputs, each containing a set of key elements deemed most relevant by both the authors and the National Advisory Board (NAB). Nineteen process procedures (PPs) were proposed, each supported by bibliographical references. While Fig. 2 provides an overview of these PPs, detailed bibliographical support is available in the supplementary file, which should be consulted as a companion to Fig. 2.

The toolkit was created from an ecosystem perspective, including the economic context in which it occurs that will be decisive for making many of the decisions, the national social context that includes the cultural, sociological, and anthropological components, as well as vulnerable groups, and also the legislative context.

A number of outcomes result from the interaction between problem, solutions, and outputs, which are organized by five levels of social grouping, from the individual to the economic life of the region considered. This type of

organization allows each context to obtain unique results, specific to its existence and adapted to the health care and economic conditions of each given moment.

In our reading, any PHP intervention toolkit should aim to be intelligent. This means that it must have a system for collecting, processing, and storing data. This accountability element means the ability to reflect on these data and generate new solutions for PHP and for procedures in a cycle approach, either by correcting deviations (gap analysis) or by generating new paths that prove to be important for the ecosystem under analysis. As such, in view of the framework we propose (Fig. 2), each organization must produce a written procedure adapted to its reality for each of the 19 PPs (represented by the arrows). This procedure should include the following items: (1) implementation of the procedure in the organization duly adapted to its ecosystem of action and legal framework in force, (2) coordination defined through the structure of hierarchies of responsibility and inherent mandates inserted in the organization's organizational chart,

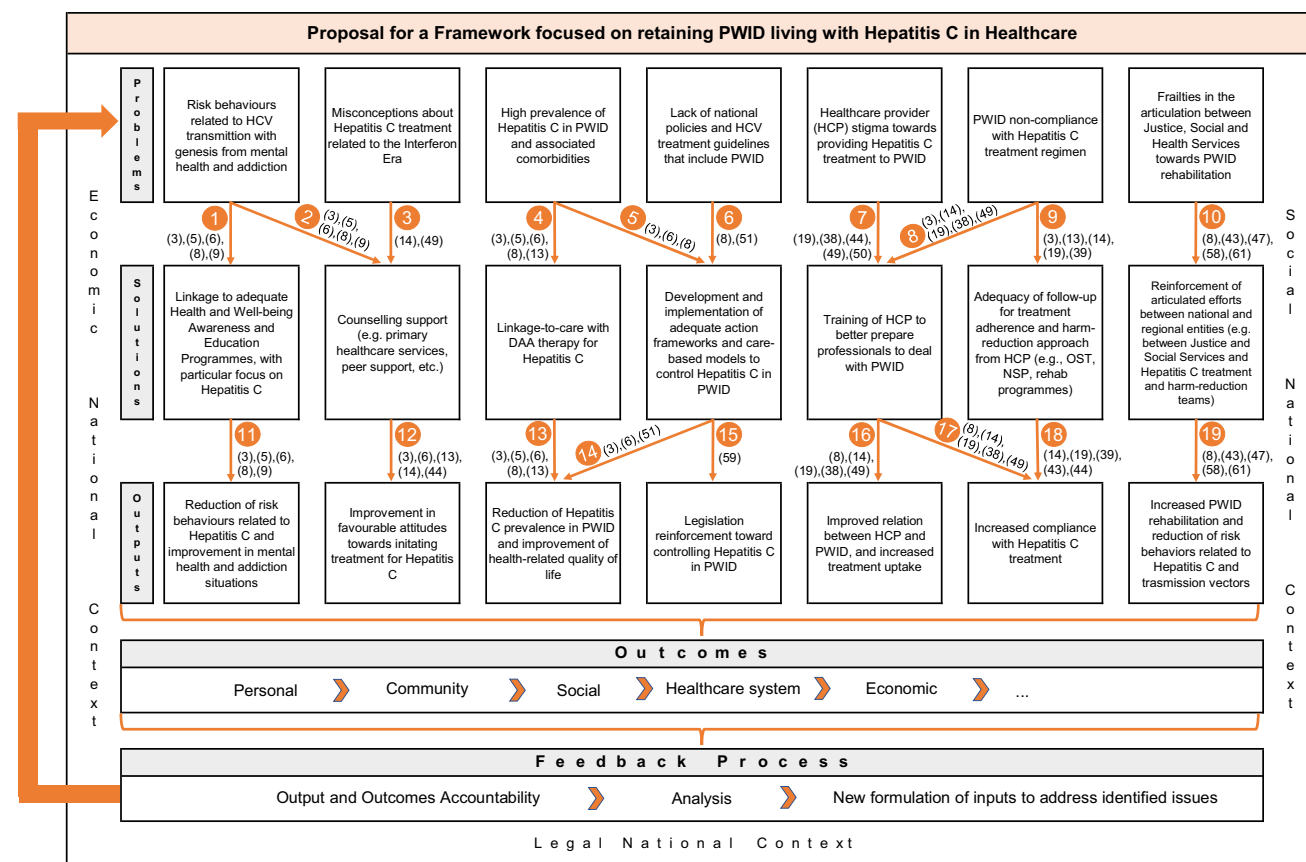


Fig. 2 Proposal for a toolkit focused on retaining PWID living with hepatitis C in healthcare – ADHERE, with bibliographical references

(3) the quantification system for each activity developed, their respective metrics and ways of collecting information, and (4) the audit system (included in quality seals or outside of them), which verifies where there are deviations, their intensity, and defines the necessary steps to recover what is necessary.

Results

All the efforts made towards achieving the WHO's HCV elimination target have defined great progress in the approaches of healthcare systems to the disease, thus diminishing the HCV prevalence rates. It is fundamental to subsequently retain every newly diagnosed patient in healthcare systems, which is especially important in vulnerable populations that live on the fringe of healthcare systems. Therefore, we propose the ADHERE toolkit to address and reinforce the CC steps from linkage-to-care to treatment and rehabilitation, aiming to reduce the loss of follow-up in the PWID population throughout these steps

until a cure is achieved. Once diagnosed, assuring a high retaining rate throughout the remaining CC is fundamental to maximizing the efforts and benefits from the early stages.

In the ADHERE toolkit, education and training must also be provided to empower and improve PWID engagement with treatment until the achievement of SVR_0 , while preventing re-infections and supporting rehabilitation. Also, one of the best tools to achieve these goals is primary healthcare services due to its close action with the population and point-of-care where possible, given approved clinical practices and current legislation. With the short duration of DAA treatments and their oral administration, primary healthcare is equipped with the resources for a close follow-up with patients during all the HCV CC steps. This action would be a fundamental element in a national framework of healthcare action towards eliminating hepatitis C, raising the system's efficiency and efficacy by retaining patients in healthcare systems. Ultimately, this action is fundamental to reducing disease prevalence while providing PWID with tools to prevent risk behaviours.

Discussion and conclusions

The ADHERE toolkit presents a critical advancement in the effort to retain PWID in hepatitis C treatment, addressing the persistent gaps that have hindered global progress towards eliminating hepatitis C. The COVID-19 pandemic has exacerbated these challenges, diverting resources and attention away from hepatitis C and other public health priorities. As healthcare systems worldwide grapple with the ongoing repercussions of the pandemic, it is more urgent than ever to implement robust, adaptable strategies such as the ADHERE toolkit.

This toolkit not only offers a structured framework for improving PWID retention across the CC but also fosters a culture of continuous quality improvement within healthcare systems. By adopting the ADHERE toolkit, healthcare providers and policymakers can strengthen their response to hepatitis C, ensuring that vulnerable populations receive the comprehensive care they need to achieve SVR.

In this critical moment, the adoption of toolkits such as ADHERE may not be just an option but a necessity. The global community must act swiftly to integrate such tools into public health strategies, safeguarding the progress made thus far and accelerating the journey towards the elimination of hepatitis C. Failure to do so risks losing ground on the gains achieved and could result in prolonged suffering and increased transmission rates among PWID. The time to act is now — by implementing the ADHERE toolkit, we can move closer to a future where hepatitis C is no longer a public health threat.

Note: The mentions of PWID in this paper are related to individuals with current/ “active” injection drug use and ex-PWID with active non-injection drug use.

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Declarations

Conflict of interest None to declare.

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