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Hepatitis C elimination among people who inject drugs: Challenges and recommendations for action within a health systems framework

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Abbreviations

DAA - direct-acting antiviral

PWID - people who inject drugs

WHO - World Health Organization

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INHSU – International Network on Hepatitis in Substance Users

OST - opioid substitution therapy

NSP - needle and syringe programmes

DBS - dried blood spot

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Abstract

The burden of hepatitis C infection is considerable among people who inject drugs (PWID), with an estimated prevalence of greater than 40%, representing an estimated 5.6 million people who have recently injected drugs living with hepatitis C infection. As such, PWID are a priority population for enhancing prevention, testing, linkage to care, treatment and follow-up care in order to meet World Health Organization (WHO) hepatitis C elimination goals by 2030. There are many barriers to enhancing hepatitis C prevention and care among PWID including; poor global coverage of harm reduction services, restrictive drug policies and criminalization of drug use, poor access to health services, low hepatitis C testing, linkage to care and treatment, restrictions for accessing DAA therapy, and the lack of national strategies and government investment to support WHO elimination goals. On 5 September 2017, the International Network of Hepatitis in Substance Users (INHSU) held a roundtable panel of international experts to discuss remaining challenges and future priorities for action from a health systems perspective. The WHO health systems framework comprises six core components; service delivery, health workforce, health information systems, medical procurement, health systems financing, and leadership and governance. Communication has been proposed as a seventh key element which promotes the central role of affected community engagement. This review paper presents recommended strategies for eliminating hepatitis C as a major public health threat among PWID and outlines future priorities for action within a health systems framework.

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Key words: elimination; health systems; people who inject drugs; viral hepatitis C

Key Points:

- PWID are a priority population in efforts to eliminate hepatitis C globally
- There are many interventions effective for hepatitis C prevention, linkage to testing, care, and treatment in PWID
- Future efforts to eliminate hepatitis C among PWID requires interventions across the six core components of a health systems framework including: service delivery, health workforce, health information systems, medical procurement, health systems financing, and leadership and governance
- Communication is a key component of the hepatitis C elimination response, promoting the central role of community engagement and ensuring dynamic interaction among the six

Introduction

Hepatitis B and hepatitis C account for approximately 1.34 million deaths globally, surpassing all chronic infectious diseases including HIV, malaria and tuberculosis⁴. It is estimated that 71 million people are living with chronic hepatitis C infection⁵. The burden of hepatitis C-related morbidity and mortality continues to rise^{4,6}. However, broad access to direct-acting antiviral (DAA) hepatitis C regimens with cure rates of over 95%⁷, provides an opportunity to reverse the rising burden of liver disease attributable to hepatitis C infection.

The burden of hepatitis C infection is considerable among people who inject drugs (PWID), with an estimated prevalence of greater than 40%, representing an estimated 6.1 million people who have recently injected drugs living with hepatitis C infection (9% of all infections globally)^{5,8,9}. There is also considerable heterogeneity in the burden of hepatitis C infection among people who have recently injected drugs (Figure 1), with half of infections from just four countries: the Russian Federation, the United States, China, and Brazil⁹. PWID are a priority population for enhancing prevention, testing, linkage to care, treatment and follow-up care.

In 2016, the World Health Organization (WHO) set an ambitious goal to eliminate hepatitis C as a major public health threat by 2030. Specific targets include increasing sterile needles/syringes distributed from 20 to 200 per person per year for PWID, reducing new hepatitis C infections by 80%, and hepatitis C -related deaths by 65%, and increasing hepatitis C diagnoses from <20% to 90%, and the number of people receiving hepatitis C treatment from <10% to 80%^{10,11}.

There are many barriers to enhancing hepatitis C prevention, diagnosis, linkage to care and treatment to achieve the WHO targets among PWID. Challenges include poor global coverage of harm reduction services, restrictive drug policies and criminalization of drug use, poor access to health services, low hepatitis C testing, linkage to care and treatment, restrictions for accessing DAA therapy, and the lack of national strategies and government investment to support WHO elimination goals^{7,12}.

However, recent advances in the simplification of hepatitis C testing, diagnosis and treatment present an opportunity to enhance hepatitis C care among PWID. On 5 September 2017, prior to the 6th International Symposium on Hepatitis in Substance Users (INHSU 2017), the International Network of Hepatitis in Substance Users (INHSU) held a roundtable panel of international experts in drug and alcohol, infectious diseases, and hepatology to discuss remaining challenges and future priorities for action from a health systems perspective. Concepts and priorities were further developed through subsequent consultation. This paper presents recommended actions based on the expert input from the roundtable, follow-up consultation and evidence from the literature. It highlights the available scientific evidence regarding strategies to enhance hepatitis C prevention, testing, linkage to care, and treatment for PWID and outlines future priorities for action within a health systems framework.

Interventions to enhance hepatitis C prevention, testing and treatment to achieve hepatitis C elimination among people who inject drugs

Hepatitis C prevention

In 2015, there were an estimated 1.7 million new hepatitis C infections globally, with 23% occurring among people who inject drugs as a result of sharing of non-sterile injecting equipment¹¹, highlighting the elevated hepatitis C incidence among PWID in many settings¹³⁻¹⁶, particularly in the initial years of injecting^{14,17}.

There is evidence of the effectiveness of combined opioid substitution therapy (OST) and high-coverage needle and syringe programmes (NSP) on reducing the risk of hepatitis C acquisition in PWID^{14,15}. OST is associated with a 50% reduction in hepatitis C acquisition risk, while combined OST and NSP are associated with a 74% reduction in hepatitis C transmissions¹⁸. NSP are also recognized as one of the most cost-effective public health interventions¹⁹. NSP and OST also have many other social, health and economic benefits beyond hepatitis C prevention, including prevention of HIV transmission and reducing death from overdose²⁰⁻²².

Increasing hepatitis C treatment among PWID also has potential prevention benefits and is cost-effective²³⁻²⁵. As per international guidelines, given PWID are at a high risk of hepatitis C transmission, and hepatitis C treatment resulting in cure eliminates infectiousness which may yield transmission reduction benefits, PWID are a high priority for treatment²⁶⁻²⁹.

However, mathematical modelling studies suggest that whilst hepatitis C treatment for PWID can lead to substantial reductions in hepatitis C prevalence and reduce transmission³⁰⁻³⁴, prevention benefits are greatest when delivered in combination with OST and NSP^{31,35,36}. Similarly, theoretical modelling

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indicates that whilst harm reduction has likely averted high HCV prevalence in some settings, scale-up of OST and NSP alone is unlikely to achieve WHO elimination incidence targets^{31,37}. Therefore, a combination prevention strategy including hepatitis C treatment as prevention and increased coverage of harm reduction interventions is critical for achieving reductions in hepatitis C prevalence/incidence among PWID²³.

Hepatitis C testing

Globally, hepatitis C testing and diagnosis remains inadequate, both in terms of numbers (<20% diagnosed) and completeness of tests offered (even fewer have been HCV RNA tested), in particular for PWID³⁸⁻⁴¹. In a systematic review of the effectiveness of interventions to improve hepatitis C testing among PWID, on-site testing with pre-test discussion and education and dried blood spot (DBS) testing were demonstrated to be effective in increasing hepatitis C testing among PWID when compared to control interventions⁴². Other strategies that have been evaluated (without any comparator intervention) include physical and electronic medical chart reminders to prompt targeted risk-based assessment and testing⁴³⁻⁴⁷, peer-delivered outreach hepatitis C testing and hepatitis C education⁴⁸, prison-based outreach testing⁴⁹, patient referral contact tracing with monetary incentive for testing⁵⁰, and point-of-care hepatitis C testing⁵¹⁻⁵⁷. Decisions on what intervention(s) to implement to enhance hepatitis C testing will depend on the setting (and prevalence of hepatitis C infection), the model of care, the local context, and healthcare system. Decisions should also be based on engagement with the affected community to assess what testing interventions are most appropriate. Interventions should be implemented in a way that is respectful of individual choice and priorities. There is a lack of quality evidence on the most effective testing strategies, as such, strategies should be trialed and implemented in a way that is consultative and responsive rather than prescriptive.

Linkage to hepatitis C care and treatment

Linkage of PWID to hepatitis C care and treatment is insufficient internationally³⁸⁻⁴⁰. In a systematic review of studies to improve linkage to hepatitis C care for PWID in the interferon-era, facilitated referral (either a nurse, peer-support worker or patient navigator) for hepatitis C assessment and scheduling of specialist appointments was associated with improved linkage to hepatitis C care⁴². Integrated hepatitis C care within drug use and psychiatric services delivered by a multidisciplinary team with case management services, with or without non-invasive liver disease assessment, was associated with improved hepatitis C treatment uptake⁴². Other strategies evaluated and shown to enhance hepatitis C linkage to care and treatment include dried blood spot testing⁵⁸, point-of-care hepatitis C testing^{54,55}, non-invasive liver disease screening using transient elastography (FibroScan®) with facilitated referral to care⁵⁹⁻⁶¹, integrated hepatitis C care^{43,62-66}, patient navigation programs^{67,68}, peer-based support⁶⁹⁻⁸¹, financial incentive programs^{82,83}, and telemedicine⁸⁴⁻⁸⁷. However, the majority of interventions that have been evaluated are specific for the interferon-era. Further research is needed to evaluate optimal interventions for linkage to hepatitis C care and treatment with interferon-free DAA therapy. Similar to efforts to increase hepatitis C testing, decisions on what intervention(s) to implement to enhance hepatitis C linkage to care and treatment will depend on the setting and prevalence of hepatitis C infection, the model of care, and the local context and healthcare system (which includes who can prescribe therapy and the reimbursement restrictions in place).

Models of hepatitis C care

There is evidence that different models of care are effective for linkage of PWID to hepatitis C care and treatment including in hospital-based specialist clinics, community health centers, drug treatment clinics, prisons, NSP, supervised consumption rooms, and primary care⁸⁸. The common theme from this spectrum of hepatitis C care models is that “one size does not fit all”⁸⁸. Models of care which provide on-site hepatitis C care in venues where PWID are already accessing services are important⁸⁸. With the availability of simple DAA therapies, the expansion of hepatitis C care to primary care,

prisons, and other non-hospital settings, as well as broadening the types of health care professionals providing care, will greatly enhance access to hepatitis C care and treatment for PWID.

Hepatitis C treatment

DAA therapy has improved the feasibility of hepatitis C treatment among PWID compared to interferon-based therapies, given DAA therapies have limited psychiatric side-effects, are simpler (oral, once-daily vs. weekly injections), and shorter in duration (8-12 weeks vs. 24-48 weeks). DAA therapy is effective among PWID receiving OST⁸⁹⁻⁹⁹, people with a history of injecting drug use^{82,100-105}, and recent PWID^{99,106-108}, including those with hepatitis C/HIV co-infection^{93-95,101,104,105,109}. There is no impact of drug use prior to or during treatment on response to DAA therapy among people receiving OST^{98,99} or people with recent injecting drug use^{99,108}. Concomitant alcohol use also has no impact on DAA treatment outcomes¹¹⁰. Hepatitis C reinfection incidence among PWID is 0.0-5.3/100 person-years¹¹¹⁻¹¹⁸, with higher rates among those with ongoing injecting (4.9-6.4/100 person-year)^{112,114,115,117}. Strategies to enhance hepatitis C prevention, such as access to high-coverage NSP and OST (>200 needle-syringes distributed per PWID and >40 OST recipients per 100 PWID) are crucial to minimize hepatitis C reinfection risk.

Remaining challenges and key recommendations for action from a health systems perspective to achieve hepatitis C elimination among people who inject drugs

Health Systems Building Blocks

A health system, as defined by WHO is all the organizations, institutions, resources and people whose primary purpose is to improve health^{1,2}. The WHO health systems framework comprises six core components, some of which underpin other components, such as leadership/governance and health information systems, others are input components to the health system (financing and the health

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workforce), or reflect the outputs of the health system (medical products and technologies and service delivery)^{1,2}. Communication has been proposed as a seventh key element. This promotes the central role of communication in the context of affected community engagement and ensures dynamic interaction among the six traditional building blocks^{1,2}.

Given the interdependent nature of health system components, barriers to hepatitis C care and treatment should be systematically addressed across all elements of the health systems framework to support sustainable improvement throughout the care cascade (Figure 2).

Communication and Engagement

A people-centered approach to the health systems framework promotes health care that is respectful of, and responsive to, the preferences, needs and values of affected communities. If communication and engagement is established as essential to the health systems framework this component provides a central tenet on which health strategies can be structured. As people who are actively involved in their own health care tend to have better outcomes¹⁹, there is potential to move beyond inefficient and inequitable health systems by focusing on patient participation and community-led health interventions.

Key actions to enhance hepatitis C care for PWID through communication and patient engagement include:

- 1) Enhancing health care worker communication through education on stigmatizing language/terminology, attitudes, practices and policies;
- 2) Providing peer-led hepatitis C, health promotion and health literacy education through drug user organisations;

- 3) Facilitating consumer participation in hepatitis service design and delivery;
- 4) Facilitating patient engagement in hepatitis C communication strategies;
- 5) Ensuring patient representation on national hepatitis C strategy planning committees/reference groups.

Service Delivery

Service delivery is the provision of healthcare to people. All inputs to the health system, for example health workforce, medical procurement and health information systems are intended to enhance service delivery. WHO categorises good service delivery as possessing the following key characteristics: comprehensiveness, accessibility, coverage, continuity, quality, person-centeredness, coordination, and accountability and efficiency¹.

As previously mentioned, there are many effective models of hepatitis C service delivery shown to successfully link PWID to care and treatment, all of which require contextual considerations such as individual diversity and culture. The same considerations need to be applied to pro-active testing outreach campaigns for those individuals not connected to any healthcare services.

New DAA therapies have simplified on-treatment monitoring and the resulting hepatitis C care pathway. This has increased the number of settings where hepatitis C services can be provided and has enabled a broader range of practitioners to be involved in prescribing (drug and alcohol specialists, general practitioners, pharmacists, nurses, and physician assistants) and supporting people through testing and care. This simplification has led to a wide spectrum of models of care that can improve hepatitis C service delivery.

Key actions to enhance hepatitis C service delivery include:

- 1) Establishing and supporting hepatitis C testing methodologies that do not require venepuncture (e.g. finger-stick and saliva) to enhance hepatitis C diagnosis, linkage to care, and treatment in a variety of settings;
- 2) Supporting the concept of task-shifting towards the continued expansion of available practitioners who can provide hepatitis C testing, linkage to care and treatment;
- 3) Delivering services to PWID in a non-judgmental and non-stigmatizing way.

Health Workforce

The health workforce is defined as ‘all people engaged in actions whose primary intent is to enhance health¹²⁰. WHO identifies human resources as clinical staff, as well as management and support staff, i.e. those who do not deliver services directly but are essential to the performance of health systems¹.

Given the ease and lower side-effect profile of DAA therapy, it is possible to increase hepatitis C treatment through simplified models of care across a range of settings⁸⁸. Integrating hepatitis C care into new settings, for example drug and alcohol services, entails service delivery by a broader multidisciplinary health workforce not previously involved in hepatitis C management⁴².

Key actions to enhance hepatitis C care for PWID through strengthening the health workforce include:

- 1) Addressing health workforce limitations through increased hepatitis C education. Education must be contextually and culturally appropriate and provided through flexible, blended learning i.e. online and face-face. Education should focus on capacity strengthening within

health systems through ‘train the trainer’ models and include a key focus on providing non-stigmatizing care;

- 2) Developing and expanding the peer workforce. Peer-based models of care receive a high level of patient acceptability and are an effective way of creating trust between services, healthcare providers and patients^{69,121}. Health practitioner definitions should be expanded to include peer workers as valued members of the health workforce and peers should be supported through appropriate remuneration and professional support/supervision;
- 3) Encouraging and driving leadership within the workforce e.g. by reaching out to professional groups to create champions in various relevant disciplines.

Health Information Systems

Health information systems are the foundation of decision-making across the health system. They enable decision-makers to identify problems and needs, make evidence-based decisions on health policy, and allocate resources optimally¹²².

Despite epidemiological estimates relating to hepatitis C prevalence and burden of disease within PWID, there are still gaps in research and monitoring data. Addressing evidence gaps and improving methods for data collection is a priority for meeting global hepatitis C elimination goals¹².

Key actions to enhance hepatitis C care for PWID through health information systems include:

- 1) Developing systems to enable electronic health medical record alerts to enhance hepatitis C testing in people at-risk who have not previously been tested or require ongoing risk-based testing;

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- 2) Assisting clients to understand how their data will be used and how their privacy will be protected;
 - 3) Collecting minimum program information at the outset of hepatitis C treatment scale-up that can monitor the uptake of hepatitis C case-finding among PWID, including the number and proportion that enter hepatitis C treatment programs;
 - 4) Creating a hepatitis C treatment registry with linkage between laboratories and community hepatitis C treatment providers;
 - 5) Developing more efficient/flexible digital means of capturing data on hepatitis C testing and treatment among PWID (particularly in settings where no registry exists or can be established);
 - 6) Evaluating the impact of DAA treatment on hepatitis C-related morbidity and mortality, including hepatitis C prevalence and incidence, incidence of liver cancer and advanced liver disease (e.g. decompensated cirrhosis), and death among PWID.

It is noted that as less restrictive care pathways are enabled through point-of-care testing and treatment access in community settings, it may become more challenging to establish or maintain classical disease registries. This reinforces the need to create alternative, digital means of capturing data.

Medical Procurement

According to WHO, a well-functioning health system ensures equitable access to essential medical products and technologies of assured quality, safety, efficacy and cost-effectiveness¹²³.

The availability of new hepatitis C diagnostics that are highly sensitive, quick and inexpensive, has facilitated the simplification of hepatitis C testing¹²⁴⁻¹²⁹. DAA therapies have also dramatically simplified on-treatment monitoring needs¹²⁴.

Point-of-care and DBS testing have been shown to increase uptake of hepatitis C testing^{42,47,54-56,130} and linkage to hepatitis C care^{54,55,58}. Both have the potential to reduce non-attendance to off-site phlebotomy and provide more immediate results to facilitate enhanced education and linkage to care. This is particularly useful for remote/rural and outreach settings.

Point-of-care hepatitis C testing can include oral fluid rapid diagnostic testing¹²⁵⁻¹²⁹, finger-stick whole-blood rapid diagnostic testing^{126-129,131,132}, on-site venepuncture-based testing^{133,134}, and finger-stick capillary whole blood testing⁵⁷. Although DBS testing is not strictly point-of-care, the ability to collect a finger-stick sample at the point-of-care simplifies sample collection, transportation to the laboratory, and diagnosis^{130,135-137}.

Key actions to enhance hepatitis C care for PWID through medical procurement include:

- 1) Simplifying, and disinvesting from, existing clinical algorithms for testing and treatment, ensuring a focus on improvement engagement with PWID;
- 2) Increasing certification of currently available diagnostics – particularly those that do not require a venous blood draw - e.g. oral tests, finger-stick blood tests – to increase access to testing for PWID;
- 3) Developing and certifying affordable diagnostics – particularly those that focus on community-based testing and reduce phlebotomy – to increase access to testing for PWID.

Health Systems Financing

Health financing is fundamental to the functionality of the health system. It involves both revenue generation/collection and purchasing/provision of services. Optimal health care financing allows access to needed services through efficient resource utilization.

The high cost of hepatitis C treatment continues to be a topic of concern; however, given economic and population prevention benefits, scaling up hepatitis C treatment and care in PWID has been shown to be cost-effective despite high drug costs and risk of reinfection²³⁻²⁵.

Globally, there is a lack of transparency in hepatitis c treatment financing mechanisms. Greater clarity and sharing of funding mechanisms would allow for a greater coordinated and effective global response.

Exploring new funding mechanisms and ensuring the financial sustainability of hepatitis C prevention and treatment programs should be an important focus for all health systems.

Key actions for enhancing hepatitis C care through financing include:

- 1) Identifying models of hepatitis C elimination success in settings with different economic health system structures and epidemic characteristics;
- 2) Advocating for transparent sharing of successes in drug procurement and pricing;
- 3) Developing investment cases including budgetary impact, epidemic impact (general and among PWID), cost-effectiveness and optimal resource allocation strategies ensuring equity.

Leadership and Governance

Effective health system leadership and governance enables strategic policy frameworks, effective service delivery oversight, coalition-building, regulation, attention to system design and accountability¹²³. As a cross-cutting component of the health systems framework, leadership and governance is an integral part of improving health outcomes.

In the context of eliminating hepatitis C, although “early adopter” countries, and regions / sites within countries, many of whom have developed national strategies, action plans and clinical guidelines, are showing that rapid scale up of testing and treatment can be achieved through committed political leadership¹¹, not all areas have such governance guidelines. To meet elimination targets by 2030 a comprehensive and global public health approach is needed.

Key actions for enhancing hepatitis C prevention and care through leadership and governance include:

- 1) Encouraging all countries to develop a national strategy with an action plan;
- 2) Ensuring engagement of key affected populations, preferably through leadership roles, in the development of national strategies and action plans;
- 3) Developing treatment guidelines specifically noting that PWID should not be excluded from treatment and addressing primary prevention to prevent reinfection;
- 4) Ensuring a financial commitment from national and regional/state governments;
- 5) Identifying what scale-up of harm reduction interventions are required to support hepatitis C treatment as prevention strategy;
- 6) Developing mechanisms for monitoring and evaluation to be able to provide data on whether progress is being made;
- 7) Identifying champions to drive change – from the community, clinicians, public health and government.

Conclusion

People who inject drugs, one of the populations most affected by hepatitis C, should be a priority population for interventions to prevent and treat the infection. If hepatitis C elimination is to be achieved a people-centered health systems approach is required, providing a framework for action in which PWID are engaged in all components of their care, from diagnosis to treatment and follow-up care. At present, this is seldom the case. This paper presents a series of recommendations, based on expert opinion and published evidence, for how to improve care for PWID in each of the WHO six health systems building blocks. The seventh central component - ensuring adequate communication among the different parts of the health system and the PWID population - is put forth as a core element of the hepatitis C elimination response.

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Figure 1. Estimated number of people with recent injecting drug use living with HCV viraemic infection, by country. This figure has been reproduced with permission from⁹.

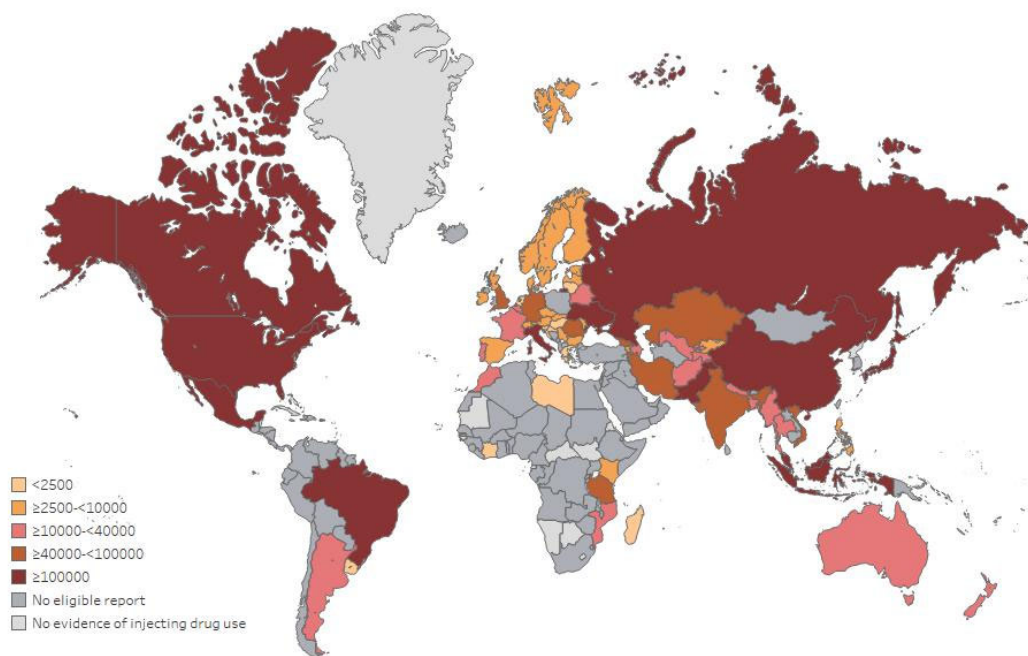


Figure 2. Proposed modified WHO Health Systems Framework for PWID. This figure has been modified from [_ENREF_3_ENREF_3](#)³.

