Alcohol use disorder (AUD), defined as a “maladaptive pattern of alcohol use leading to clinically significant impairment or distress,” encompasses both alcohol abuse and alcohol dependence. It can be identified as the presence of at least two criteria from an 11-item list including consumption of alcohol in larger amounts or during longer periods than intended, difficulties in controlling alcohol consumption, and experiencing cravings, withdrawal syndrome, and/or important social and health-related repercussions of alcohol consumption. Globally, AUD is the most prevalent of all substance use disorders, with more than 100 million estimated cases in 2016. AUD substantially contributes to the burden of liver disease among people with chronic hepatitis C virus (HCV) infection, notably to the onset of decompensated cirrhosis and to liver transplantation and mortality. It is also associated with greater liver damage due to its interactions with immune response, cytotoxicity, and oxidative stress. People who inject drugs (PWID) are at high risk for AUD, and alcohol use accounts for more than 40% of liver associated deaths in this population. Table 1 summarizes the current guidelines for the screening of AUD.

Hepatitis C Elimination: Where Are We Now?

In 2016, the World Health Organization (WHO) set out the goal of eliminating HCV as a major public health threat by 2030, defined as an 80% reduction in new infections and a 65% reduction in deaths. Injecting drug use accounts for 23% of new HCV infections and one-third of HCV-related deaths. Current prevention efforts thus center around the population of PWID, which encompasses both individuals actively injecting drugs and those with a history of drug use and HCV.
injection. However, this population remains largely undiagnosed and untreated, and continues to drive the HCV epidemic.

According to a modelling study addressing the global timing of HCV elimination in 45 high-income countries, only 9 countries will be able to meet the deadline of the WHO’s HCV elimination target by 2030, whereas 30 are not expected to eliminate HCV before 2050. Key elements to achieve HCV elimination include the development of HCV-specific national strategies and guidelines, the decentralization of HCV screening, universal access to affordable direct-acting antiviral (DAA) treatment, and the implementation of comprehensive HCV-prevention strategies. Micro-elimination initiatives targeting key populations, such as PWID and subsets of PWID, have the potential to accelerate the HCV global elimination process while being less complex and less costly than full-scale country-level HCV initiatives. In the case of PWID, these initiatives rely notably on harm reduction services (e.g., drop-in centers, needle and syringe programs [NSPs], opioid agonist therapy [OAT] sites, and outreach services) as they are major entry points for both HCV screening and “test-and-treat” strategies. However,

### Table 1 Screening for alcohol use disorder

<table>
<thead>
<tr>
<th>Who should be screened for AUD?</th>
<th>Adults aged 18 years or older*</th>
</tr>
</thead>
<tbody>
<tr>
<td>When can AUD be screened for?</td>
<td>In the general population$^{61}$</td>
</tr>
<tr>
<td></td>
<td>During routine medical visits and visits to emergency departments</td>
</tr>
<tr>
<td></td>
<td>As part of patients’ regular checkup</td>
</tr>
<tr>
<td></td>
<td>During visits with a change in medical prescriptions</td>
</tr>
<tr>
<td></td>
<td>Particularly when new medications can interact with alcohol.</td>
</tr>
<tr>
<td></td>
<td>In HCV-infected patients$^{11,42,62}$</td>
</tr>
<tr>
<td></td>
<td>At the time of HCV diagnosis</td>
</tr>
<tr>
<td></td>
<td>To inform about AUD-related risks during liver disease.</td>
</tr>
<tr>
<td></td>
<td>Before and during HCV treatment initiation</td>
</tr>
<tr>
<td></td>
<td>To prevent non-adherence$^{b}$</td>
</tr>
<tr>
<td></td>
<td>After cure, during long-term follow-up</td>
</tr>
<tr>
<td></td>
<td>To reduce the risk of liver disease progression</td>
</tr>
</tbody>
</table>

| How to screen for AUD?         | Face-to-face interview$^{63}$ which documents in a nonjudgmental way:$^{c}$ |
|                                | Current and past alcohol use (and use of tobacco and other psychoactive substances) |
|                                | The route, quantity, and type of alcohol consumed |
|                                | The frequency and pattern of alcohol use |
|                                | The circumstances of use, including the typical setting for use |
|                                | The self-perceived benefits and consequences of use |
|                                | Use of standard questionnaires (either self-administered or face-to-face) such as AUDIT$^{50-52}$ |
|                                | Its shorter version, AUDIT-C$^{38,31,52,64}$ |
| What to do after positive screening? | Provide brief behavioral counselling interventions$^{64}$ |
|                                 | Refer patient to an addiction specialist$^{11}$ |
|                                | In HCV-infected patients$^{11,42,62}$ |
|                                | In addition to the previous two points: |
|                                | Provide access to a multidisciplinary health care team including harm reduction services |
|                                | Provide additional support for adherence in HCV-treated patients with ongoing alcohol consumption |

Abbreviations: AUD, alcohol use disorder; AUDIT, Alcohol Use Disorder Identification Test; AUDIT-C, Alcohol Use Disorder Identification Test - Consumption; HCV, hepatitis C virus.

*AUD screening is especially recommended in certain patient subgroups, such as pregnant women, women planning to conceive, young people, tobacco smokers, or people with health problems, which may be related to alcohol abuse (e.g., high blood pressure, liver disease, depression, and cardiovascular disease).$^{61}$

$^{b}$Ongoing alcohol use does not affect therapeutic outcomes among adherent direct-acting antiviral treated patients.$^{44}$

$^{c}$Patients’ self-report of certain symptoms (e.g., sleep disturbances, gastrointestinal problems, or frequent headaches after the weekend) can facilitate caregivers in opening the discussion about alcohol use.$^{61}$
access to such services remains insufficient globally and must be greatly expanded, as only 1% of PWID are living in countries with a high coverage of NSP and OAT. Micro-elimination among PWID implies scaling up HCV screening to strengthen the initial phases of the HCV continuum of care (i.e., estimating the number of PWID infected, the number of those reached by HCV prevention actions, the percentage of PWID diagnosed, and those aware of their infection) and ensuring that HCV-positive individuals can access appropriate follow-up and care. This will require multidisciplinary approaches involving, notably, physicians from different specialties, such as addiction and HCV specialists and community-based organizations (peers).

AUD and HCV: Research Needs

The availability of DAAs, which are safe and highly effective, and the promotion of novel HCV test-and-treat strategies, especially for PWID, have shifted the perspective of research toward exploring interactions between alcohol use and HCV prevention and care. These developments also highlight the need for greater and more innovative research on the impact of alcohol consumption—a modifiable risk factor—on both the effectiveness of prevention interventions and the development or progression of liver disease. Understanding how, when, and to what extent AUD affects hepatitis prevention interventions is an essential step in identifying and promoting novel approaches to reduce the impact of AUD on risk behaviors. It is also crucial to better document the effect of AUD on HCV treatment uptake and response as they represent two main steps of the HCV cascade of care. Despite the existence of review studies focusing on the interactions between alcohol and HCV or addressing global barriers to HCV care among PWID, there is a paucity of reviews specifically targeting the impact of AUD on HCV prevention and care among PWID.

Study Objectives and Search Strategy

We present here a narrative review on the effects of AUD on HCV prevention and care among PWID in the era of HCV elimination. Furthermore, we suggest recommendations to improve the assessment of AUD and to reduce its health impact in this at-risk population. Issues concerning long-term follow-up of HCV-infected PWID after hepatitis C cure have not been explored.

PubMed and the Cochrane library were searched in April 2020 for alcohol use, HCV Medical Subject Headings (MeSH), and free-text terms. We included only articles referring to alcohol use in people at risk of hepatitis C attending NSPs or on OAT (methadone or buprenorphine), people receiving educational interventions for hepatitis C prevention, or people benefiting from hepatitis C screening and linkage to care. We excluded studies that did not allow for distinguishing between alcohol and drug use and those that did not assess the effect of alcohol use on hepatitis C transmission risk or engagement in care.

Effect of AUD on HCV Prevention among People Who Inject Drugs

A variety of risk reduction interventions exist to prevent HCV in PWID, including NSP and OAT, primarily based on methadone or buprenorphine treatment, peer education interventions, and the recent implementation of test-and-treat strategies. The four primary outcomes of interest when studying the effect of alcohol use on the effectiveness of HCV prevention interventions are (1) seroconversion, (2) persistent injection, (3) sharing of needles, syringes, or other injecting equipment, and (4) unsafe sexual behaviors.

Among PWID, AUD is associated with a higher risk of engaging in unprotected sex and unsafe injecting practices, being HCV-positive, and maintaining injecting practices (Fig. 1). While the injecting of alcohol itself is rare, it also constitutes a risk behavior in PWID, especially in marginalized individuals. Within this population, alcohol injection is associated with homelessness and the sharing of cookers or filters.

Few studies have specifically investigated the influence of alcohol use on injecting behavior in PWID exposed to NSP. Indeed, in many prevention studies, information about alcohol use is embedded under the term drug and alcohol use, making it nearly impossible to distinguish the impact of AUD from that of drug use. One study that examined 196 PWID in Rhode Island showed that individuals participating in NSP and who met the criteria for alcohol abuse (according to the third version of the Diagnostic and Statistical Manual of Mental Disorders, DSM-III) had at least a twofold greater risk of needle sharing compared with nondrinkers and moderate alcohol users, even after controlling for other demographic and behavioral factors. A more recent study of 315 male PWID in rural Puerto Rico attending NSP showed that at-risk alcohol drinking compared with low-risk drinking and no drinking was associated with increased injecting-related and sexual-related risk behaviors. Another study showed that among 296 male PWID in Nepal, the unavailability of new needles and drinking alcohol were independently associated with sharing injecting equipment among PWID.

In addition to the evidence on the association between alcohol use and injecting-related risk behaviors, evidence suggests that the type of drugs injected may also have an impact on alcohol use. For example, people who inject stimulants have been shown to be significantly more likely to report AUD than people who exclusively inject opiates. As such, further investigation is required to understand whether the concomitant use of alcohol and specific classes of drugs increases the risk of parenteral transmission of HCV through a higher frequency of unsafe injections.

In high-income countries, AUD is frequent in individuals receiving methadone treatment. Several studies have shown that AUD increases HCV risk behaviors in individuals receiving OAT. A U.S. study of 386 individuals entering integrated buprenorphine/naloxone and HIV care, alcohol use during the previous 30 months (irrespective of amount) was associated with an increased risk of unprotected sex.
Another U.S. study conducted among 515 women receiving methadone maintenance treatment showed that those diagnosed with alcohol abuse or dependence disorder (according to the DSM-IV classification) had a more than twofold risk of unprotected sexual encounters and an 11-fold risk of having anal sex compared with other women. Similarly, a study conducted among 1,253 HIV-infected PWID entering detoxification or methadone maintenance treatment in New York City showed that drinking more than 14 alcohol drinks per week for males or seven alcohol drinks per week for females was associated with higher rates of injecting and sexual risk behaviors.

In France, the community-based AERLI (Accompanying [support] and Educating to the Risk Linked to Injection) intervention provided face-to-face harm reduction educational sessions to PWID to decrease HIV- and HCV-related risk practices and other injecting-related complications. More than half of the 271 study participants reported harmful alcohol consumption (AUDIT-C [Alcohol Use Disorder Identification Test - Consumption] score ≥ 3 for women and ≥ 4 for men) at enrolment, which was associated with an increased risk of unsafe HIV–HCV transmission practices. However, results showed no significant association between harmful alcohol consumption and HCV testing uptake.

**Effect of AUD on HCV Treatment Uptake**

AUD has been associated with advanced liver disease stage (i.e., compensated cirrhosis or end-stage liver disease) at HCV diagnosis. For instance, alcohol abuse was the strongest predictor of advanced liver disease at initial HCV diagnosis in three U.S. Medicare cohorts. Until the early years of DAA availability, AUD remained a barrier to HCV treatment uptake or a reason for deferring HCV treatment initiation. This was partly due to some health care providers’ concerns about heavy drinkers’ ability to adhere to treatment. According to current guidelines, HCV-infected persons should be considered for HCV therapy regardless of alcohol intake. However, the European Association for the Study of the Liver (EASL) recommends additional support for individuals who consume alcohol while on HCV treatment.

Research evidence has also supported the inclusion of alcohol users in DAA treatment. For example, a U.S. study conducted among 17,487 HCV-infected patients treated with DAA within the national Veterans Affairs health care system showed high sustained virologic response rates among all groups of patients regardless of alcohol use (assessed using the AUDIT-C).

**Efficacy of Interventions to Manage AUD in People at Risk of HCV**

Pharmacotherapy for AUD remains globally underused in primary care, whereas medications such as acamprosate and oral naltrexone have been associated with a reduction in returning to drinking. The methodological heterogeneity across studies comparing psychosocial interventions for AUD in populations at greater risk of HCV, such as PWID, makes it difficult to draw firm conclusions concerning their overall efficacy. However, some important points can be raised. First, alcohol reduction interventions may help decrease the level of consumption in HCV-infected individuals with moderate-to-high alcohol consumption. Second, brief motivational interventions can help reduce the frequency of injection-related blood-borne virus risk behaviors, as shown in hazardous drinkers in one needle exchange program. However, a systematic review did not find sufficient evidence supporting the effectiveness of brief interventions in reducing alcohol use in people with concurrent illicit drug use and AUD. Third, psychosocial therapy and participation in self-help groups are useful for patients with AUD affected by liver cirrhosis and/or hepatocellular carcinoma awaiting liver transplantation, even in the posttransplant period. Fourth, integrating harm reduction interventions for AUD in a more global health care setting for PWID, including social and support services (e.g.,

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**Fig. 1** Impact of AUD on HCV prevention and cascade of care. AUD, alcohol use disorder; HCV, hepatitis C virus; NSP, needle and syringe programs; OAT, opioid agonist therapy; PWID, people who inject drugs.
h住房、为所用的社会服务（如牙科护理、心理健康服务等）以及其他健康服务（如性健康和生殖健康服务等），是潜在的能够帮助提高可用性并促进这些干预措施的实施，尤其是如果 PWID 本身参与了这些开发的服务。

**Suggested Recommendations**

在基于这一文献综述的基础上，我们提出以下建议，以帮助减少 AUD 对 HCV 预防和护理的影响。

**Standardizing Alcohol Use Assessment to Facilitate Research on AUD and HCV**

在行为中评估饮酒量的多种方法被用于评估饮酒量，这些方法在研究中被应用出来，随后在行为中评估饮酒量的实施。在行为中评估饮酒量的实施是分析使用药物，防止行为习惯的可能影响的评估。此外，尽管使用标准问卷调查在酒精和 HCV 中的文献中存在明显差异，但尚未完全探索这一问题，需要依赖于酒精摄入量的后验测量。此外，尽管存在容易使用的 NSP 测试，但仍需要制定伤害减少和宣传活动来更有效地提高 HCV 检测率。此外，尽管由于酒精的使用限制，对宗教或文化原因可能的伤害减少和宣传活动，也需要保护他们免受大脑和肝脏损伤。这些活动需要适应到特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。此外，酒精使用可能被禁止，以适应特定的需要。

| Alcohol use in resource-limited settings: the case of Sub-Saharan Africa |  
| Emerging alcohol market | Widespread use of home-produced alcoholic beverages | AUD-related disease burden greater than that of high-resource settings | Hidden populations including people who inject drugs and people with AUD | High abstention rates, with a strong heterogeneity between countries due to economic factors, religion, ethnicity, and availability and acceptability of alcohol in society |

**Abbreviation:** AUD, alcohol use disorder.  
*Per unit of alcohol used.*

**Developing Harm Reduction Interventions**

干预旨在减少 HCV 传播，PWID 或其他高风险人群应针对自己经常饮酒的人，以及在高体积中饮酒的人，采取策略来减少有害行为。这些伤害减少的干预措施也被需要来保护他们免于脑和肝损伤。他们必须被改编到给定的文化背景，特别是在对酒精使用被禁止的宗教或文化原因。

最近对 HCV 预防/伤害减少干预措施在 179 个国家的综述中强调了需要在更多国家中增加投资。因此，这些干预措施（包括 OAT，NSP，和即决程序）不足以预防、延迟和逆转 HCV 流行。此外，具体 PWID 子群（如甲基苯丙胺注射者），可能处于更高的 NSP 覆盖率和需要护理的脆弱性。此外，除了实施伤害减少干预措施和基于社会支持的干预措施，如稳定的住房，可以加强 NSP 在 HCV 预防中的效果。

**Scaling Up HCV Testing**

HCV 检测率目前仍然不足。尽管使用点-即决的快速检测在伤害减少和宣传活动中可以大大改善对 HCV 检测的可及性，但通过这些干预手段（包括 OAT，NSP，和即决程序）仍然不足以预防、延迟和逆转 HCV 流行。此外，出台更有利于 NSP 覆盖率和需要护理的脆弱性。此外，除了实施伤害减少干预措施和基于社会支持的干预措施，如稳定的住房，可以加强 NSP 在 HCV 预防中的效果。

**Engaging HCV At-Risk Populations in Treatment Despite Alcohol Use**

建模研究表明，提高 DAA 可及性在高风险人群中，如 PWID，将实质性影响 HCV 传播的预防。然而，HCV 治疗覆盖率仍然很低。
at-risk populations, especially in eastern European countries, such as Russia.\textsuperscript{57} Expanding access to HCV treatment even among marginalized PWID will have both public health and social benefits.\textsuperscript{9,58} Engaging primary care providers/general practitioners in the screening, follow-up, and treatment of HCV infection can extend access to HCV care.\textsuperscript{59} The coordination of primary health care with addiction and HCV specialists is important to both engage and retain patients with AUD in HCV care. Evidence-based approaches of care delivery based on equity, nondiscrimination, and community engagement are needed for marginalized populations, such as PWID. Extending the use of practical tools such as service design checklists may help health policy-makers, caregivers, nongovernmental organizations, and communities to develop, update, or monitor care services for at-risk groups.\textsuperscript{49}

**Conclusion**

To achieve the WHO goal of eliminating HCV as a public health threat, interventions must address alcohol misuse in at-risk populations, especially PWID. To adequately address AUD, policy-makers and care providers must prioritize providing more information on treatment and education to reduce alcohol-related harms, promoting an expanded range of treatment options, which incorporate brief interventions, and guaranteeing adequate case management. This spectrum of interventions should be proposed even to those still engaged in alcohol use. Furthermore, interventions to reduce AUD and prevent related harms in all individuals at risk of or living with HCV must be included in future research and policy agendas.

**Main Concepts and Learning Points**

- Alcohol use disorder (AUD) negatively impacts prevention, access to, and continuity of care for hepatitis C virus (HCV) in at-risk populations, such as people who inject drugs (PWID).
- Specific interventions are required to reduce AUD and prevent related harms among PWID.
- Scaling up HCV testing and treating HCV-positive individuals despite AUD are needed to achieve micro-elimination in this key population.
- Research studies assessing AUD must use standardized measures of alcohol use to facilitate comparisons among studies.
- These measures must document, at a minimum, the number of alcohol units consumed in a given period of time.

**Author Contributions**

F.M. and P.C. drafted the manuscript. A.J., P.M., and J.V.L., contributed to the full manuscript and provided critical reviewing and suggestions throughout the different versions of this manuscript. All authors revised the manuscript and approved the final draft for submission.

Funding

F.M. and P.C. were supported by the French National Agency for Research on AIDS and Viral Hepatitis (Agence Nationale de Recherches sur le Sida et les hépatites virales, ANRS) and the French National Institute of Health and Medical Research (Institut National de la Santé et de la Recherche Médicale, INSERM). A.J. was supported by a grant from the National Cancer Institute, the Eunice Kennedy Shriver National Institute of Child Health & Human Development, the National Institute of Allergy and Infectious Diseases, and the National Institute of Drug Abuse (grant no. 5U01AI069919). P.M. is supported by the National Institute of Health (NIH)/National Institute of Alcohol Abuse and Alcoholism (P60 AA009803). J.V.L. is supported by a Spanish Ministry of Science, Innovation, and Universities Miguel Servet grant (Instituto de Salud Carlos III/ESF, European Union [CP18/00074]) and further acknowledges support to ISGlobal from the Spanish Ministry of Science, Innovation, and Universities through the “Centro de Excelencia Severo Ochoa 2019-2023” Program (CEX2018-000806-S) and from the Government of Catalonia through the CERCA Program.

Conflict of Interests

The authors have no conflict of interest to declare with regard to this work.

**References**


Jin J. Screening and counseling to reduce unhealthy alcohol use. JAMA 2018;320(18):1948


O’Keefe D, Scott N, Aitken C, Dietze P. Longitudinal analysis of change in individual-level needle and syringe coverage amongst a cohort of people who inject drugs in Melbourne, Australia. Drug Alcohol Depend 2017;176:7–13


Bazzi A, Saizt R. Screening for unhealthy alcohol use. JAMA 2018;320(18):1869–1871


