HepCare Europe: a new user-friendly hepatitis C care service model. What have we learned? What are the remaining challenges?

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Introduction to HepCare Europe

In 2011, the first two direct-acting antiviral agents (DAAs) for treatment of hepatitis C were introduced.^{1,2} Since then, a rapid introduction of safe and effective all-oral HCV treatment combinations (promising HCV cure in more than 97% of all treated patients in shortened-duration treatments of 8-12 weeks) has followed. This has allowed the dream of HCV elimination to become a worldwide goal.^{3,4} Nevertheless, the WHO report from 2017 clearly describes some significant obstacles that need to be overcome in order to achieve HCV exlimination.⁵ The first major obstacle is underdiagnosis, with only 20% of people with HCV worldwide having been diagnosed so far.⁵ Equally disturbing is that while approximately 71 million people were thought to be infected with HCV in 2015, only 1.76 million people received HCV treatment in 2016 despite the remarkable advances in HCV therapy.⁵ Therefore, new strategies of HCV diagnosis, linkage to care, and treatment are urgently needed to meet the newly defined ambitious time-bound targets for eliminating HCV as a public health threat by 2030. The key targets for countries worldwide are by 2030 to diagnose 90% of HCVinfected individuals and initiate HCV therapy in 80%, thereby reducing new HCV cases by 80% and reducing HCV-related deaths by 65% by 2030.⁶ Clearly, this will only become feasible with new models of care. The European Commission has realized this need and therefore funded a project named HepCare, which aims to investigate models of HCV care that are more user-friendly. The HepCare Europe project is a €1.8 million 3 year EU-supported project in four member states from northern, southern and eastern Europe (Ireland, UK, Romania and Spain) that focuses on providing an 'integrated care' model for HCV treatment based on the joint participation of primary and specialty care practitioners, NGOs, community services and peers in particular, to allow the more efficient use of limited specialist resources. It aims to improve access to HCV testing, linkage to care, treatment, and retention in care among key risk groups, including people who inject drugs (PWID) and the homeless, through outreach to the community and intearation of primary and secondary care services. The use of rapid HCV testing is promoted to implement community-based

screening strategies, to identify those not accessing care. Peer support (using community-based organizations) is provided to assist those identified with HCV to access care. Nurse liaison links are being developed so that the secondary caregivers go to the patients, rather than the patients going to the secondary caregivers. Moreover, in addition to being tested in the community, patients have their HCV evaluated in the community by means of the recently established non-invasive FibroScan test, which has replaced liver biopsy, to assess the degree of hepatic impairment caused by HCV. Finally, community-based HCV treatment projects are being piloted. Other support to patients includes interventions to help reduce or cease alcohol consumption, which remains a significant problem among these vulnerable individuals. In addition to outreach, the HepCare project involves education of caregivers and patient groups about HCV and the new curative treatments available. It also conducts cost-effectiveness evaluations of the interventions performed to guide public authorities in the reassessment of the hepatitis C models of care. This Supplement to the Journal of Antimicrobial Chemotherapy aims to highlight the ongoing research efforts in the different work packages of HepCare Europe and gives a first overview of lessons learned and remaining challenges to overcome.

HepCheck

HepCheck represents a multisite feasibility study of an intensified HCV screening intervention for vulnerable patient populations. The study recruited patients through their points of contact with community services, including drug addiction services, night shelters, homeless day services and prisons. Participants were offered HCV screening via blood tests, oral swabs or dried blood spot testing. The number of new HCV cases identified varied by participating country but was on average high, with the proportion of new HCV cases among those tested ranging from 4% (in the UK) to 8% (in Romania).⁷ A recent meta-analysis comparing targeted HCV testing interventions (targeting individuals or groups at increased risk of HCV) with non-targeted interventions demonstrated that targeted testing strategies were far more effective in diagnosing

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cases and increasing treatment uptake,⁸ although to achieve elimination it is probable that multiple testing strategies (and not just one) should be implemented. In order to target at-risk groups, outreach screening initiatives must be well planned, use adequate tools, and involve collaboration between NGOs, community services and healthcare providers. In addition to recruiting patients at community points of contact, other interventions such as screening individuals through active case-finding approaches, for example mobile units, should be also evaluated.⁹ Although within each country there are different healthcare structures and pathways to care, the principles of HepCheck screening can be applied effectively in different EU countries, including countries with lower GDP, such as Romania, through outreach initiatives. The overall evidence on HCV testing has considerable gaps in terms of the countries and populations represented and the validity of testinguptake data. More research is needed throughout Europe to guide efforts to provide testing to certain key populations.¹⁰

HepLink

The burden of hepatitis C infection is considerable among PWID, with an estimated prevalence of greater than 40%, representing an estimated 5.6 million people who have recently injected drugs and who are living with hepatitis C infection.¹¹ As such, PWID are a priority population for enhancing prevention, testing, linkage to care, treatment and follow-up care in order to meet WHO hepatitis C elimination goals by 2030. In this research project HCV prevalence and management among PWID attending primary care and community-based services at four European sites (Dublin, London, Seville and Bucharest) are described.¹² Lifetime RNA testing among HCV antibody-positive patients ranged from 13.2% to 87.1%, with rates of RNA positivity among those tested ranging from 60% to 89%. Among HCV antibody-positive patients, the proportion of those who attended hepatology/infectious disease services (6%-53%) and initiated HCV treatment initiation (3%-34%) were low and widely heterogeneous. Clearly, this study outlines considerable differences in the current management of HCV across these four European sites, with substantial variability in HCV screening, linkage to care and treatment rates among PWID. It is paramount that effective interventional strategies are developed and rolled out to primary and community care settings in order to facilitate linkage to HCV treatment among PWID and to achieve the WHO goal of HCV elimination. Recently, strategies for eliminating hepatitis C as a major public health threat among PWID have been published by an expert panel organized by the International Network of Hepatitis in Substance Users (INHSU), which outlines future priorities for action within a health systems framework.¹¹

HepEd

Within the HepEd work package a multidisciplinary educational masterclass series was developed for healthcare professionals working in primary care in Ireland and Romania.¹³ Healthcare professionals from local general practice, NGOs and addiction treatment services were invited to eight 1 day symposia (HCV Masterclass series) examining the burden of HCV, how to prevent new infections, why and how to screen, new approaches to diagnosis and treatment, management of HIV/HCV coinfection in PWID, and treating coexisting problematic alcohol use. Peer-

support sessions as training day programmes and flyers were offered to homeless people and PWID. The majority of the over 200 participants, involved in HCV care in the community, emphasized the value of educational programmes in increasing HCV management skills. Prior studies evaluating the impact of formal HCV patient education on primary provider-specialist HCV comanagement and treatment also demonstrated that formal HCV education expedites HCV therapy and improves virological response rates.¹⁴ As primary care provider attitude plays a significant role in referral to HCV education classes, improving provider knowledge will likely enhance access to HCV specialty services in the vulnerable populations. With regard to making an integrated model of care happen in practice, 100% of participants also indicated the importance of a 'designated nurse to liaise with hospital services' and 88%–92% of 'computerized decision making'. Incorporating computerized behavioural interventions into existing prevention services is currently under evaluation by others; for example in syringe exchange programmes that aim to increase HCV screening and decrease risky drug use behaviour among PWID.¹⁵ The outcome of the HepEd project highlights the importance of integrated approaches to healthcare and addressing the educational level of the patients in optimizing hepatitis C care in the community.

HepFriend

The HepFriend work package aims to utilize peer support in the community to increase awareness of the risk of HCV, the importance of testing and disease severity assessment, and provide treatment support.¹⁶ Indeed, various educational interventions, such as HCV peer education, have been previously demonstrated to enhance HCV treatment initiation and engagement within opioid substitution programmes.¹⁷ Peers in the HepFriend project were trained and instructed to hold HCV awareness sessions for individuals at risk of HCV, test for HCV using point-of-care tests (POCTs) use the Orasure HCV Ab mouth swab test and dried blood spot (DBS) testing for HCV RNA, assess liver fibrosis using a portable FibroScan, accompany HCV-infected patients to clinical appointments following referral to reduce loss to follow-up, and support individuals through treatment to improve treatment completion and success. Peers were successful in engaging newly diagnosed HCV-infected individuals with specialist care services, with 104 out of 197 individuals (52.8%) chronically infected with HCV and having no follow-up receiving approval to start treatment. Over 50% of participants were homeless and over 90% had a history of IVDU, highlighting that this programme was able to engage underserved vulnerable patient groups. Highly trained peer support workers working as part of a specialist outreach clinical team can help to identify a high proportion of individuals exposed to HCV, achieve high rates of engagement with treatment services and maintain high rates of treatment success amongst a population with complex needs. Clearly, peers can serve as a powerful resource to empower patients to access treatment, which is vital if we are to eliminate HCV as a public health concern, where traditional medical models have failed. However, as demonstrated in the past, one should consider that the efficacy of peer involvement can be constrained by organizational structures and boundaries, especially regarding who is deemed to be a 'peer', and this should be defined.18

HepCost

The HepCost study aims to assess the cost-effectiveness of combining HCV outreach screening, treatment and peer support (i.e. the HepCare service) in London from a healthcare perspective in comparison with current care pathways; namely, testing in locations such as drug treatment centres, and linkage to secondary care.¹⁹ Clearly, this study is extremely important as payers will need to be convinced that new models of care are cost-effective in order to promote widespread implementation. Interestingly, for a willingness-to-pay threshold of £20000 per quality-adjusted life year (QALY) gained, the HepCare service in London was costeffective [incremental cost effectiveness ratio (ICER) of £8614 per QALY gained, with a net monetary benefit of £5175024]. Therefore, increasing the levels of support offered to marginalized and vulnerable groups, via peer support and active case-finding and treatment in outreach locations, can be a cost-effective and progressive model of care. Other studies in the HCV field illustrated the high effectiveness, and cost-effectiveness, of a faster diagnosis/linkage to care together with treatment with DAAs starting from no fibrosis at all, highlighting that cost-effectiveness studies can play an important role in improving and especially helping to implement new HCV care models.²⁰

Conclusions

HCV infection is a major public health problem in the European Union. An estimated 5.6 million Europeans are chronically infected, with a wide range of variation in prevalence across European Union countries. In order to improve HCV diagnosis rates and treatment uptake in Europe, new integrated models of care are urgently needed that can help to meet the WHO hepatitis C elimination goal by 2030. The HepCare Europe project delivers promising results and strategies to better establish HCV diagnosis in vulnerable patient populations and to improve linkage to care and treatment uptake. The models and integrated approaches to healthcare it proposes involve primary and specialty care practitioners, NGOs, community services and peers. Through the costeffectiveness studies it proposes, decision makers and policymakers are targeted, which should facilitate the implementation of these models. Beyond new care models, however, many other barriers to enhancing hepatitis C prevention and care exist, including poor global coverage of harm-reduction services, restrictive drug policies and criminalization of drug use and the lack of national strategies and government investment to support WHO elimination goals. Only strengthened combined efforts of all stakeholders will eventually make HCV elimination more than a dream.

Transparency declarations

None to declare.

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References

1 Zeuzem S, Andreone P, Pol S *et al.*; REALIZE Study Team. Telaprevir for retreatment of HCV infection. *N Engl J Med* 2011; **364**: 2417–28.

2 Poordad F, McCone J Jr, Bacon BR *et al.*; SPRINT-2 Investigators. Boceprevir for untreated chronic HCV genotype 1 infection. *N Engl J Med* 2011; **364**: 1195–206.

3 Zeuzem S, Foster GR, Wang S *et al*. Glecaprevir-pibrentasvir for 8 or 12 weeks in HCV genotype 1 or 3 infection. *N Engl J Med* 2018; **378**: 354–69.

4 Feld JJ, Jacobson IM, Hézode C *et al.*; ASTRAL-1 Investigators. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. *N Engl J Med* 2015; **373**: 2599–607.

5 World Health Organization. *Global Hepatitis Report,* 2017. http://apps.who. int/iris/bitstream/10665/255016/1/9789241565455-eng.pdf.

6 World Health Organization. *Global Health Sector Strategy on Viral Hepatitis,* 2016–2021: Towards Ending Viral Hepatitis. http://apps.who.int/iris/bitstream/ 10665/246177/1/WHO-HIV-2016.06-eng.pdf.

7 Barror S, Avramovic G, Oprea C *et al.* HepCare Europe: a service innovation project. HepCheck: enhancing HCV identification and linkage to care for vulnerable populations through intensified outreach screening. A prospective multisite feasibility study. *J Antimicrob Chemother* 2019; **74** Suppl 5: v39–46.

8 Aspinall EJ, Doyle JS, Corson S *et al.* Targeted hepatitis C antibody testing interventions: a systematic review and meta-analysis. *Eur J Epidemiol* 2015; **30**: 115–29.

9 Kakalou E, Papastamopoulos V, Ioannidis P *et al*. Early HIV diagnosis through use of rapid diagnosis test (RDT) in the community and direct link to HIV care: a pilot project for vulnerable populations in Athens, Greece. *J Int AIDS Soc* 2014; **17** Suppl 3: 19619.

10 Lazarus JV, Sperle I, Spina A *et al*. Are the testing needs of key European populations affected by hepatitis B and hepatitis C being addressed? A scoping review of testing studies in Europe. *Croat Med J* 2016; **57**: 442–56.

11 Day E, Hellard M, Treloar C *et al.*; International Network on Hepatitis in Substance Users (INHSU). Hepatitis C elimination among people who inject drugs: challenges and recommendations for action within a health systems framework. *Liver Int* 2019; **39**: 20–30.

12 Nic An Riogh E, Swan D, McCombe G *et al*. Integrating hepatitis C care for at-risk groups (HepLink): baseline data from a multicentre feasibility study in primary and community care. *J Antimicrob Chemother* 2019; **74** Suppl 5: v31–38.

13 McCombe G, Almaazmi B, Cullen W *et al.* Integrating primary and secondary care to optimize hepatitis C treatment: development and evaluation of a multidisciplinary educational Masterclass series. *J Antimicrob Chemother* 2019; **74** Suppl 5: v24–30.

14 Lubega S, Agbim U, Surjadi M *et al.* Formal hepatitis C education enhances HCV care coordination, expedites HCV treatment and improves antiviral response. *Liver Int* 2013; **33**: 999–1007.

15 Westergaard RP, Hull SJ, Merkow A *et al*. Computerized tailored interventions to enhance prevention and screening for hepatitis C virus among people who inject drugs: protocol for a randomized pilot study. *JMIR Res Protoc* 2016; **5**: e15.

16 Surey J, Menezes D, Francis M *et al.* From peer-based to peer-led: redefining the role of peers across the hepatitis C care pathway: HepCare Europe. *J Antimicrob Chemother* 2019; **74** Suppl 5: v17–23.

17 Batchelder AW, Cockerham-Colas L, Peyser D *et al*. Perceived benefits of the hepatitis C peer educators: a qualitative investigation. *Harm Reduct* J 2017; **14**: 67.

18 Bonnington O, Harris M. Tensions in relation: how peer support is experienced and received in a hepatitis C treatment intervention. *Int J Drug Policy* 2017; **47**: 221–9.

19 Ward Z, Campbell L, Surey J *et al*. The cost-effectiveness of an HCV outreach intervention for at-risk populations in London, UK. J Antimicrob Chemother 2019; **74** Suppl 5: v5–16.

20 Cousien A, Tran VC, Deuffic-Burban S *et al.* Effectiveness and costeffectiveness of interventions targeting harm reduction and chronic hepatitis C cascade of care in people who inject drugs: the case of France. *J Viral Hepat* 2018; **25**: 1197–207.