IOTOD

Improving Outcomes in the Treatment of Opioid Dependence

17th annual IOTOD conference
13–14 May 2019, Frankfurt, Germany

HIV and HCV: how far have we come and where are we going?

Highlights report

Contents

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HIV and HCV: how far have we come and where are we going?

Introduction

The 17th annual 'Improving Outcomes in the Treatment of Opioid Dependence' (IOTOD) conference took place at the Steigenberger Airport Hotel in Frankfurt on 13–14 May 2019. The two-day event delivered expert presentations and discussions on a wide range of issues, including novel harm reduction strategies, advances in opioid dependence therapy and the evolving challenges being faced in the field. The conference dedicated an entire session to examining human immunodeficiency virus (HIV) and hepatitis C virus (HCV) among people who inject drugs (PWID). This session, chaired by Professor Graham Foster, described the current landscape of these comorbidities among PWID and provided pragmatic, evidence-based recommendations for how to optimally manage these comorbidities. A message reiterated by experts throughout the entire session was the importance of being proactive and not settling for second-rate care for this population now that simplified testing pathways and effective treatment options are widely available.

This report summarises the key educational messages and recommendations discussed during the IOTOD 2019 HIV and HCV session.

Educational impact

Commitments to change pledged by audience during this session

Following IOTOD 2019, I will...
Encourage regular screening for HIV and/or HCV infection in all my opioid-dependent patients
Discuss treatment options with HIV- and HCV-infected opioid-dependent patients and provide treatment/linkage to treatment as necessary
Recognise and refer complex HCV-infected patients as appropriate

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Dr Vana Sypsa
National and Kapodistrian University of Athens, Greece

HIV among PWID: how far has Europe come?

Dr Sypsa provided an overview of HIV in Europe over recent decades indicating advances such as the emergence of new treatments and tests. She also highlighted fluctuations in reported HIV cases, noting that they have remained relatively stable with a slight decline over recent years, but with contrasting trends at national levels.[1]

After providing an overview, Dr Sypsa focused specifically on HIV among PWID, a group which has experienced many changes over recent years. Overall, in Europe, the number of HIV diagnoses among PWID has been declining over the past decade.[2] However, when one looks at the situation in more depth, a worrying trend emerges. Despite overall decreases, outbreaks of HIV among PWID continue to occur – as highlighted by the chair Professor Foster, "if you take your eye off the ball, you lose very quickly".

Within the last eight years, Athens, Bucharest, Luxembourg, Dublin and Glasgow have all experienced significant outbreaks. In Athens alone, 1100 new HIV cases occurred among PWID between 2011 and 2013 while Bucharest experienced 1195 new cases between 2011 and 2016. Of particular concern, are the highly vulnerable groups that appear to be involved in these outbreaks including homeless, migrant and young, female PWID.[3]

'Seek, test and treat': an approach to managing HIV outbreaks

Potential solutions to tackle outbreaks were provided, with the ARISTOTLE programme used as an example. This programme responded to the Athens outbreak and involved a 'seek, test and treat' approach. High-risk PWID were identified, engaged in HIV testing and subsequently linked to antiretroviral therapy (ART) and opioid substitution therapy (OST) if appropriate. To optimise identification, individuals were given monetary incentives to participate and recruit peers. Five rounds of this innovative respondent-driven sampling were undertaken and resulted in the recruitment of 3320 PWID, equating to a remarkable 88% of the target population. Additionally, ARISTOTLE resulted in an increased number of PWID in Athens who received OST, were aware of their HIV status and initiated ART if required.[4,5]

Preventing future HIV outbreaks

While this response is both impressive and encouraging, why these outbreaks occur in the first place must be considered. The audience were reminded of the crucial harm reduction measures necessary to reduce HIV transmission among PWID, such as needle and syringe programmes (NSP), OST, sexual health education and HIV testing and treatment. Worryingly, NSP coverage remains suboptimal in many European countries, with at least 11 countries falling below the recommended provision of 200 syringes per PWID per year. Meanwhile, OST coverage is less than 50% in at least ten countries.[2] Dr Sypsa reiterated that it is not enough to merely have harm reduction measures present – they need to also have adequate coverage to prevent HIV transmission.

Following on from this, the issue of late HIV

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diagnosis (CD4 <350 cells/mm^3) in PWID was raised. In 2017, more than half of HIV diagnoses in PWID occurred in the late stage.[6] This is a concerning trend as early diagnosis and treatment initiation reduces morbidity and mortality, in addition to benefiting public health by reducing HIV transmission.[7]

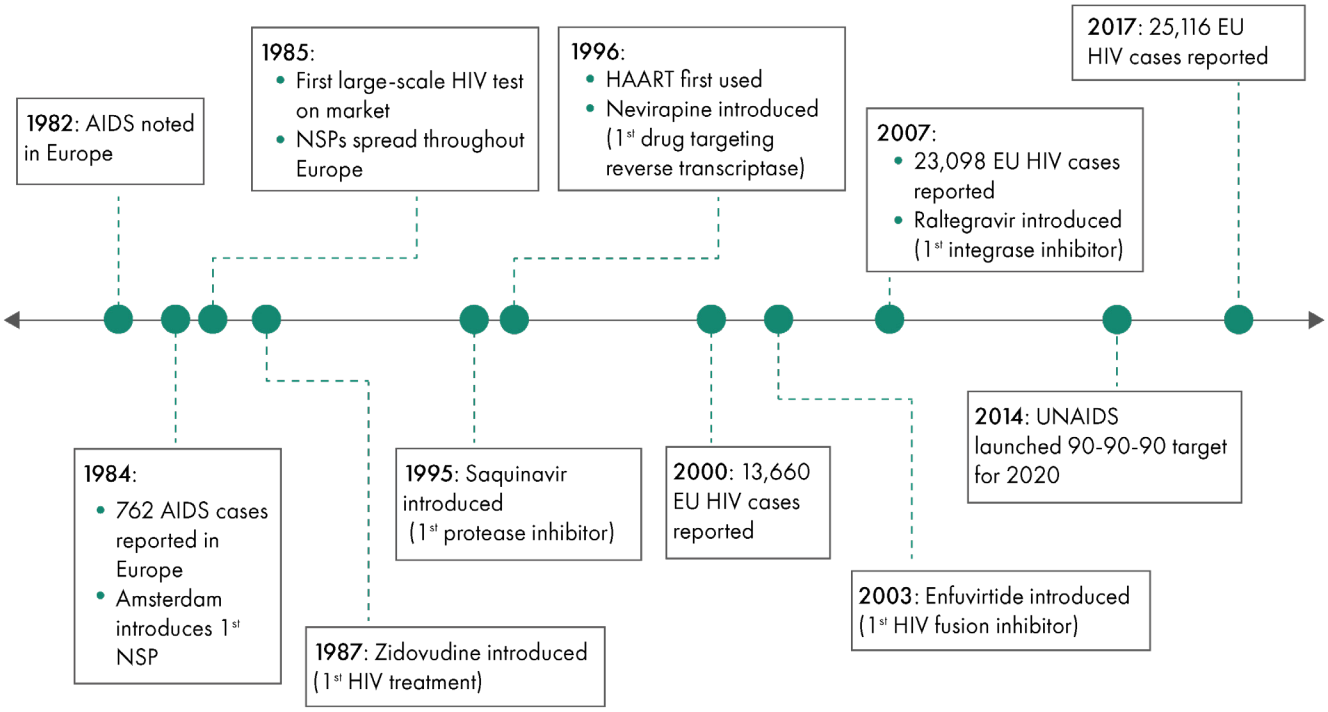
Meeting the 90-90-90 targets

Created by UNAIDS, the aim of the '90-90-90' targets is that, by 2020, 90% of people living with HIV will know their status, 90% of those diagnosed will receive ART and 90% of those receiving ART will have viral suppression. Unfortunately, data are limited with regard to PWID but current data demonstrate that this group are falling below the targets.[8]

Dr Sypsa concluded with a powerful take-home message: HIV has decreased massively among PWID in Europe, but the occurrence of multiple outbreaks in vulnerable groups demonstrates that ongoing vigilance is crucial. High-coverage NSP and OST, earlier detection of HIV, and efficient management of outbreaks are essential if HIV elimination is to be achieved.

Conference feedback revealed that 95% of delegates appreciated this content and found it helpful

HIV in Europe – a timeline[1,8,9,10,11]



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Professor Graham Foster
Queen Mary University of London and Barts Health NHS Trust, London, UK

HCV: innovations in treatment

Professor Foster provided invaluable insights into HCV treatment among PWID. He began by reminding the audience of the 'bad old days' of invasive testing and interferon treatment (with its many side effects and suboptimal efficacy). While many people are aware that those days are in the past and effective tablet-only treatments with fewer side effects are widely available, this knowledge is not universal.[1–4] Professor Foster provided a concerning example of a drug worker, whom he recently encountered, who believed interferon was the current HCV treatment choice. More worrying still, this individual was passing on this information to everyone in their drug service. Professor Foster was quick to emphasise that the audience should not assume everyone is aware of the HCV treatment options available – their job is to tell them.

"Let's get people informed of their treatment options. We have great treatment options, but they don't work if people don't know about them."

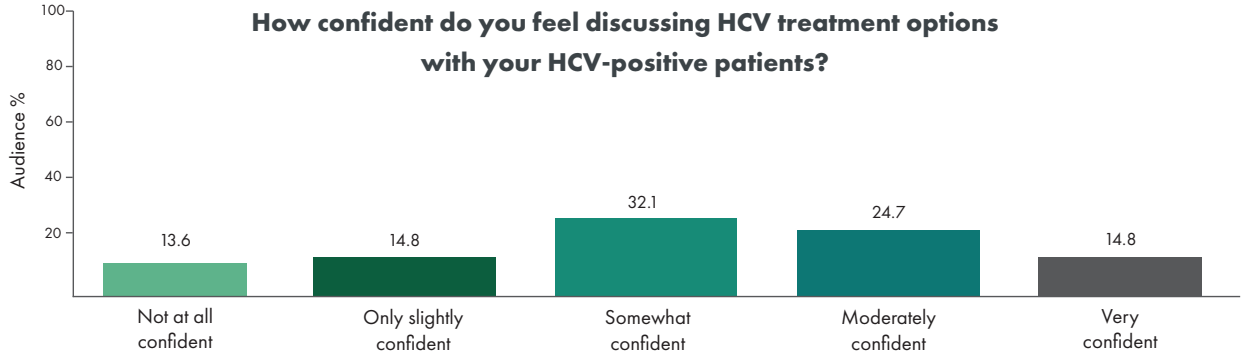
An interactive question to the audience quickly established that many were still not entirely comfortable discussing HCV treatment, with only 40% considering themselves moderately or very confident. Professor Foster simplified the mechanism of HCV treatment through a single diagram highlighting the 'weak spots' of the hepatitis C viral life cycle – the targets of current treatments.[5,6] He explained that a combination of these drugs, targeting at least two of these weak spots, is required to prevent viral replication.

What about suboptimal compliance to HCV treatment? Professor Foster discussed the SIMPLIFY study, which demonstrated that HCV treatment adherence among PWID was not perfect but a fantastic treatment response was still seen among this population.[7]

HCV treatment approaches

He summarised the treatment options into two approaches: nucleotide analogue inhibitor-based therapies and protease inhibitor-based therapies.

Within the nucleotide analogue inhibitor-based therapies, sofosbuvir/ledipasvir (genotype 1) or sofosbuvir/velpatasvir (pangenotypic) are available. These therapies demonstrated impressive treatment efficacy with over 94% of patients achieving a



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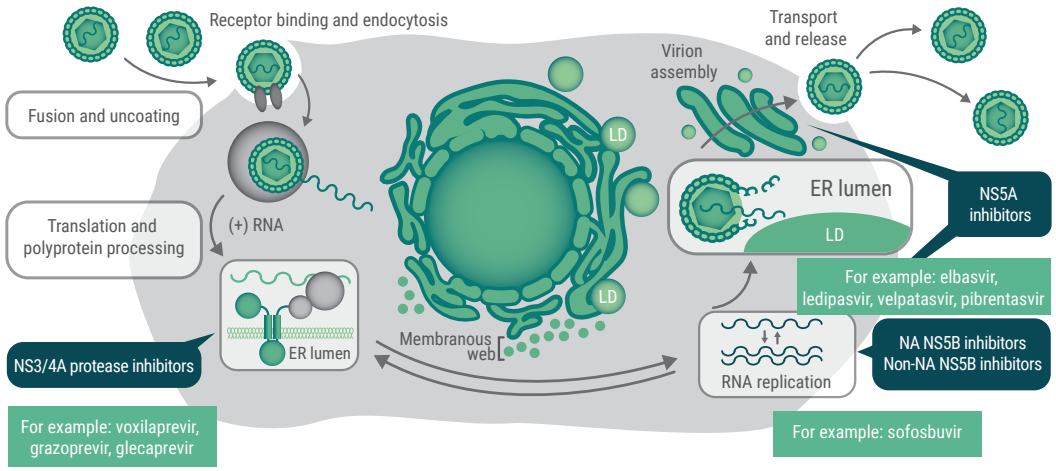
DAAs and their sites of action

ER: endoplasmic reticulum; LD: luminal domain; NA: nucleo(s/t)ide analogue; NS: non-structural protein.



sustained virologic response for 12 or more weeks after end of treatment (SVR12).[2,4]

What about the small number of patients not achieving SVR12? Are they left with no other options? It was pointed out that sofosbuvir/velpatasvir/voxilaprevir is a promising option for those who have failed previous other treatments.[8]

The second approach, protease inhibitor-based therapies, includes the elbasvir/grazoprevir (genotype 1) and glecaprevir/pibrentasvir (pangenotypic) regimens. These treatments also achieve SVR12 in more than 94% of patients.[1,3] It was noted that if elbasavir/grazoprevir is being used in the presence of NS5A resistance-associated polymorphism (a rare mutation), a longer treatment course is required along with the addition of ribavirin.[3]

While the ease of using these new treatments was highlighted, some words of caution were also issued: the importance of monitoring for cirrhosis and for drug interactions, particularly with anticonvulsants and tuberculosis medications. Additionally, if patients display decompensated cirrhosis, have been treated before or have side effects on therapy, the audience was encouraged to ask for help. Professor Foster reminded the audience of the symptoms suggesting decompensated cirrhosis "Yellow (jaundice), big belly (ascites) and vomiting blood (haematemesis)".

The role of genotyping

With the emergence of pangenotypic regimens, one point of debate has been whether genotype testing is always necessary. Professor Foster and fellow panellist Professor Brown agreed that it depends on the patient. If the patient can wait for the genotyping results, then it should be done. If, however, the delay in genotyping will cause your patient to move out of HCV treatment services, then instead consider commencing a pangenotypic regimen immediately.

Professor Foster wrapped up with a powerful question and call to action for the audience surrounding HCV treatment of PWID "Why wait?".

Conference feedback revealed that 100% of delegates appreciated this content and found it helpful

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Professor Ashley Brown
Imperial College London, UK

HCV among PWID: are we on track for elimination?

Professor Brown discussed approaches for increasing HCV testing among PWID and initiating them on HCV treatment where appropriate.

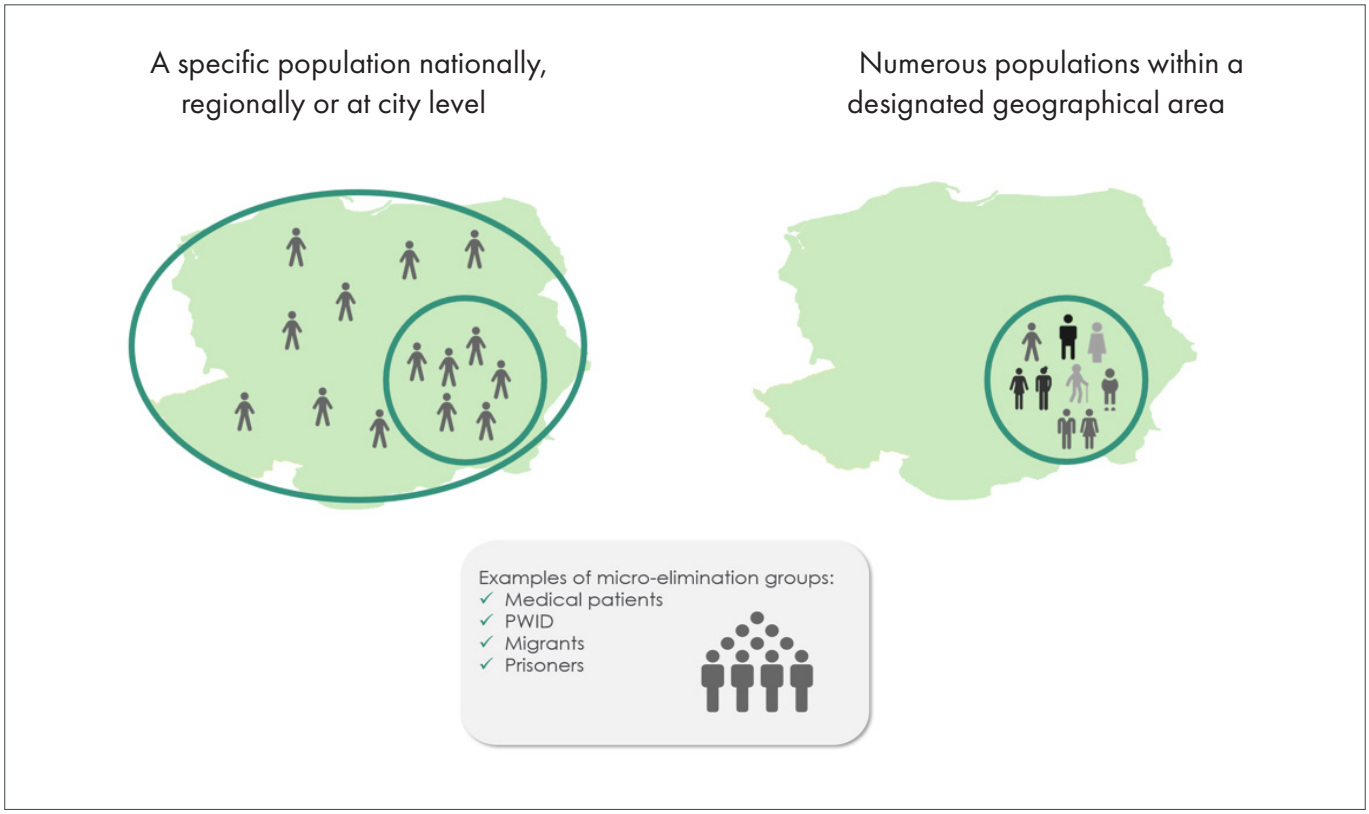
The audience was reminded of the public health implications and deadly consequences of leaving HCV untreated: chronic liver disease, cirrhosis and liver cancer, as well as extrahepatic manifestations.[1] The impact of HCV is of such significance that the World Health Organisation has created targets for its elimination, including a 90% diagnosis and 80% treatment rate by 2030.[2]

How can elimination be achieved?

One approach is 'micro-elimination', a concept whereby the elimination goals are pursued in discrete populations.[3]

Micro-elimination can be less daunting, complex and costly compared with full-scale interventions and PWID are a critical micro-elimination group due to their high HCV prevalence and transmission rates.[1,3]

Professor Brown reflected that testing levels are often low in PWID due to inadequate offerings by healthcare professionals, as well as patient



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misconceptions. He reiterated the importance of offering regular testing to patients in a positive manner to pave the way for a successful treatment programme. As noted by Professor Foster, many patients still believe interferon is the main HCV treatment used and consider the side effects more undesirable than living with HCV, which they may erroneously regard as a 'harmless disease'. Propagation of correct information is vital to address these misconceptions. A thought-provoking concept was raised that some PWID regard HCV as part of their identity and by curing it they may feel disconnected from their 'community'.[1,4]

Testing itself needs to be carried out in an appropriate manner for PWID. Drawing blood from someone with damaged veins requires significant skill and many PWID may not want this venous interference. Additionally, it may not be feasible for patients to wait long periods of time for results. Professor Brown was quick to point out that it is not only treatment that has massively advanced, so have testing options. Numerous point-of-care tests, which are easier to perform with rapid delivery of results, are now available and some allow for mass screening. In one prison, Professor Brown recalled how they tested a remarkable number of individuals (120) in one day with dried blood spot testing. This highlighted the benefit of bringing the testing to the individuals in prisons, drug treatment centres or homeless shelters, rather than waiting for individuals to present themselves.

While encouraging, there is little point in testing people if they are not suitably linked to treatment. In a study from Dublin, 547/619 (88%) homeless individuals accepted HCV screening and 206 tested positive for HCV. Of these, 51 were referred to specialist care but only one completed treatment, emphasising the need to bring treatments to PWID.[7]

It was acknowledged that the fear of re-infection is a concern for many healthcare professionals. The Co-STAR study was discussed, which involved a three-year follow-up of individuals on OST who were successfully treated for HCV, and demonstrated that less than 2% were re-infected.[8]

Professor Brown concluded with a real-life micro-elimination case example. Iceland had an HCV prevalence of 0.3% in 2014 with a prevalence of approximately 45% among PWID. During their elimination efforts, they focused on PWID as a group and tailored management accordingly, using point-of-care testing, bringing testing to PWID, providing on-treatment monitoring and travel stipends. The result was that over half of the estimated HCV-positive individuals have been identified and 94%

Point-of-care test	Results timeframe	Expertise required	Results given	Other notes
Saliva test	20–40 minutes	None	Antibody result only	Can be self-administered
Dried blood spot test	2–3 days	Minimal	Viral load	Can test for other blood borne viruses
HCV-RNA test	Within 120 minutes	Minimal	HCV-RNA	Ideal for instant linkage to care

[5,6]

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have initiated treatment.[9]

It is vital that PWID are not ignored. Professor Brown explained that if it is demonstrated to PWID that they are worth treating for HCV, it can give them a sense of self-worth. This can then translate into engagement with harm reduction and OST, as well as a complete turn-around of their lives. Moving forward, testing needs to be offered in a way that is attractive to this group, linking them closely to treatment and coupling them with harm reduction measures to benefit both PWID and public health.

Conference feedback revealed that 99% of delegates appreciated this content and found it helpful

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Discussion key highlights

One of the key issues raised was the need to target disadvantaged, marginalised populations and engage them in services to address infectious diseases, such as HIV and HCV. Professor Sypsa provided the example of how, during the Athens outbreak, migrant PWID were engaged via workers who spoke their native language. The experts agreed that a community-based service, which integrates the care of numerous infectious diseases, was lacking in many areas. The PWID population often move around and as a result may discontinue HCV treatment when they relocate. Hence, implementing a system that allows treatment histories to be accessed across multiple OST clinics for example, was deemed necessary. Additionally, the role of peer-to-peer HCV/HIV education was discussed as a potentially effective method of improving comorbidity knowledge among PWID. Some specific questions regarding HCV treatments were also raised by the audience. Professor Brown advised that some oestrogen-containing contraceptive pills may interact with HCV treatments, so monitoring concurrent medication use is important. With regard to depot HCV treatment, it was highlighted that although they might be highly useful for PWID to shorten the treatment pathway, they would not be available soon. The commitments to change were then disclosed bringing this informative and thought-provoking discussion to an end.

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