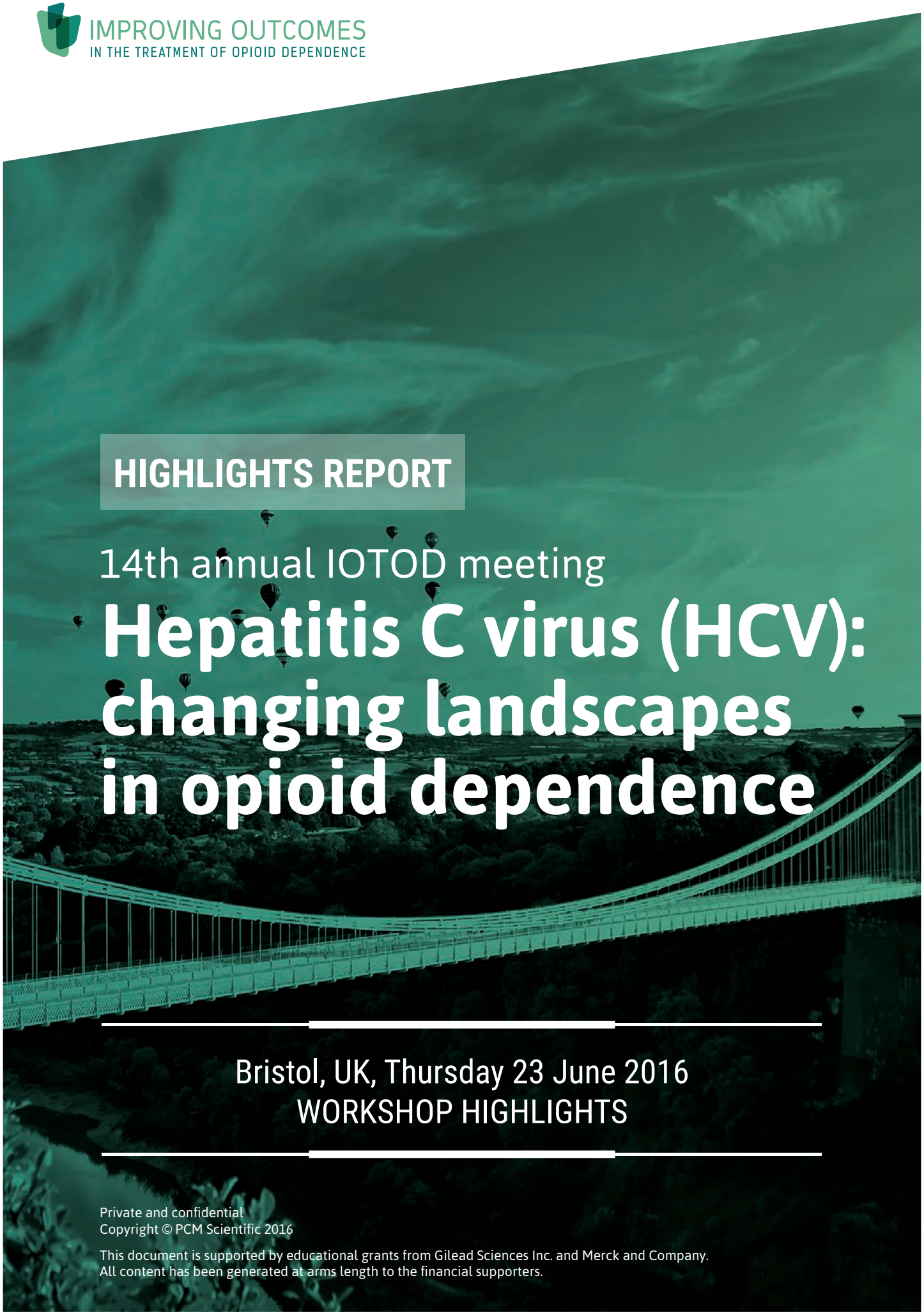
IMPROVING OUTCOMES
IN THE TREATMENT OF OPIOID DEPENDENCE



HIGHLIGHTS REPORT

14th annual IOTOD meeting

Hepatitis C virus (HCV): changing landscapes in opioid dependence

Bristol, UK, Thursday 23 June 2016
WORKSHOP HIGHLIGHTS

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Introduction

The 14th annual 'Improving Outcomes in the Treatment of Opioid Dependence' (IOTOD) meeting took place at the Bristol Marriott Hotel City Centre on 21–23 June 2016. European clinicians and international experts gathered to present and discuss new developments in the field of addictions medicine, with a particular focus on new opportunities to improve population health in opioid dependence.

A key topic discussed this year was the hepatitis C virus (HCV); although far from an emerging population, new developments in the treatment of HCV present a new frontier, allowing clinicians to help address this public health issue. In order to educate delegates and facilitate discussion, a 2.5-hour HCV workshop was designed and held on the morning of the third day. Four international experts in the field presented on the topic, before culminating in an expert Q&A panel.

The workshop was tremendously well received by delegates. Among glowing feedback and genuine enjoyment of the morning was an honest desire to improve outcomes for this patient population, with over **80% of delegates committing to change their clinical practice to better support HCV-positive patients in addictions services**.

This report summarises the content and feedback for this HCV workshop, with a focus on the opportunities and educative highlights that will impact the delegates' clinical practice.

"Best hep C presentation I have seen"

"Best session of the conference by far. Very practical and informative"

"Worth coming to the conference for this session"

International clinicians' commitment to change

WORKSHOP 2 – Hepatitis C virus (HCV): changing landscapes in opioid dependence	
As a result of IOTOD 2016, I pledge to:	
1. Screen 100% of new patients for HCV	90.5%
2. Ensure all seropositive patients receive viral load and genotyping tests	96.6%
3. Discuss treatment options with all patients diagnosed with HCV	95.8%
4. Lobby appropriate authorities for increased access to all-oral HCV therapies	80.9%
5. Liaise with local HCV treatment providers to provide community-based treatment	86.2%
6. Educate HCV-positive patients on the new treatment options available	96.9%

Mr Charles Gore
Chief Executive of the Hepatitis C Trust, UK

THE TIME IS NOW: NEW IMPERATIVES AND OPPORTUNITIES FOR THE ADDICTIONS CLINIC IN HCV MANAGEMENT

A call to action for addiction clinicians

Opening the morning session with a powerful summarisation of the current HCV landscape, Mr Gore leapt straight at the core issues underlining current treatment. Asking clinicians to provide frank, honest reflections of their own practice, he provided genuine insight into the barriers that stand between patients and treatment – many either constructed or perpetuated by healthcare professionals themselves.

Challenging clinicians to do more, Mr Gore's brutally honest evaluation of current practice resonated with the audience and captured delegates' interest for the remainder of the workshop.

Key highlights

Mr Gore opened the session with a clear statement of purpose: "The key thing is that uncured hepatitis C… can be transmitted, and if we want to do something about the amount of hepatitis C in people who inject drugs, we need to treat them." However, in order to do so, it is clear that common barriers to treatment must be addressed.

When asked what happened to their patients following a positive screening test, the results were very telling: **27% of delegates didn't know what happened** to patients who were provided a referral, and **less than a third of RNA-positive patients would have received a liver assessment.**

Of your last 5 referrals to relevant hepatitis C services, how many successfully completed the referral?
Please enter a number between 0 and 5. If you don't know, enter '6'.

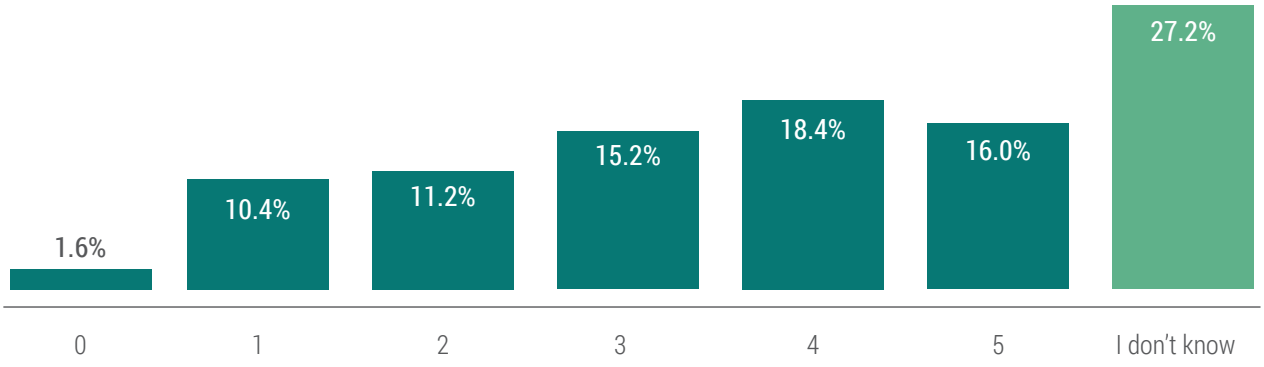


Figure 1 – Outcomes of delegates' referrals

Among your patients who screened positive for HCV antibodies, which of the following is true?

Please select one of the following options:

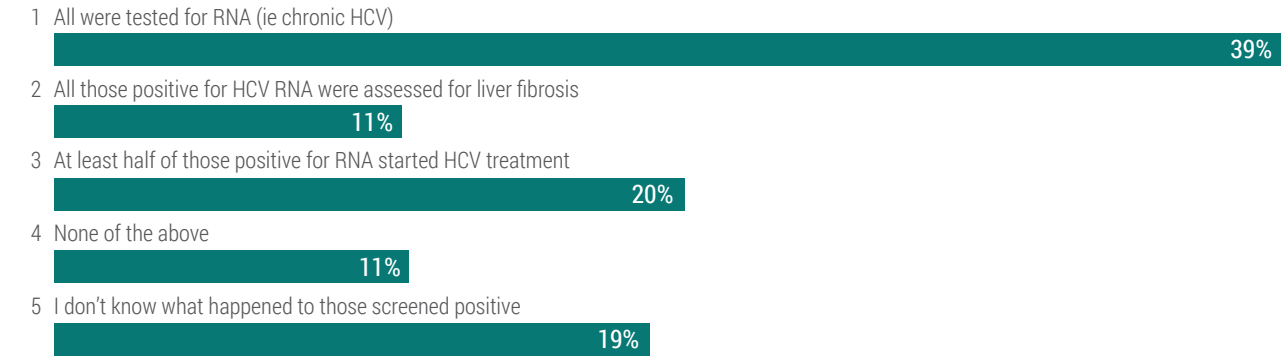


Figure 2 – Outcomes for delegates' HCV+ patients

A large component of disparity between screening and treatment is the length of the referral pathway – beyond the sheer number of tests and appointments between diagnosis and treatment, there can also be a lack of understanding between services and the patients they aim to treat. "Sometimes, people in second/tertiary care, in their ivory towers, think it's perfectly reasonable to ask people who inject drugs to turn up at 8 o'clock in the morning for appointments, and then complain about do-not-attend rates, rather than thinking 'how can we make this convenient?'."

However, Mr Gore emphasised the importance of seeking solutions. "Today is about making commitments to doing things better, so I hope you are thinking very much about how we can change… we are happily in a new era, and that means that we have the opportunity to change [current practice]." The new treatments and principles discussed throughout the rest of the workshop provide the tools delegates need to treat this invisible epidemic.

One key reason to treat is the fact that "the more people we cure, the less chance there is that a new injector will get infected." This is supported by statisticians such as Dr Natasha Martin, whose models were referred to throughout the workshop. By increasing treatment to just 10% of people who inject drugs (PWID) annually, prevalence could be reduced by three-quarters within 15 years (Martin NK, et al. Hepatology 2013).

Concluding with a final call to action, Mr Gore reiterated once more that elimination of HCV is entirely possible, and it is imperative that addictions clinicians seize the opportunity.

Delegate feedback

I found the talk:

Clear **92%** Useful **90%** Informative **90%** Engaging **91%**

Based on the talk:

I might make some changes to my clinical practice **25%**

I will definitely make changes to my clinical practice **57%**

"Can't beat personal experience… Chaired this really well. Worth coming to the conference for this session"

"Educative, useful, structureful"

"Excellent talk"

Professor Graham Foster

Professor of Hepatology, Queen Mary University of London, and Honorary Consultant Physician, Bart's Health NHS Trust, UK

NEW DEVELOPMENTS IN HCV TREATMENT

New drugs, new opportunities

The realm of hepatitis C antivirals is a rapidly changing environment, which Professor Foster spared no time in pointing out – "most of what I tell you now is going to be redundant in 6 to 12 months." However, it is important to consider some key principles in what new direct-acting antiviral (DAA) therapies are and how they can be used to transform the lives of patients living with HCV.

Focusing in on genotypes 1 and 3, due to their increased prevalence in the UK and EU, Professor Foster outlined the new combination DAA therapies now available and how they can be of immediate benefit to patients. Importantly, he noted, the single-tablet-per-day formulations of antiviral therapy allow treatment to be provided by any practitioner, from any office, with cure rates as high as 98% and courses as short as 8 weeks. The talk concluded with an analysis of the cost-effectiveness of providing treatment and a call for clinicians to champion their patients' right to treatment among their local services.

This engaging plenary was praised by delegates for its rigorous pace and crisp, clear delivery. Professor Foster's emphatic yet informative style of presentation helped to precipitate a clear understanding of the new treatments, allowing clinicians to educate patients in turn.

Key highlights

Beginning with a brief recap of previous therapies, Professor Foster described the pegylated interferon-based therapy as a "wretched" compound, remarking that often "you are not surprised that patients turn it down – in fact, the surprise to me is that anyone ever takes it up." However, there is now a new wave of antivirals available that act directly on specific sites of viral replication within a host cell (Figure 3).

This has led to dramatic new therapeutics with astounding cure rates. For example, in genotype 1 HCV, a combination of two or more DAAs results in an all-oral, once-daily therapy with a 95% cure rate. "Doesn't matter what you do, doesn't matter where you do it … take a tablet, you get cured, done."

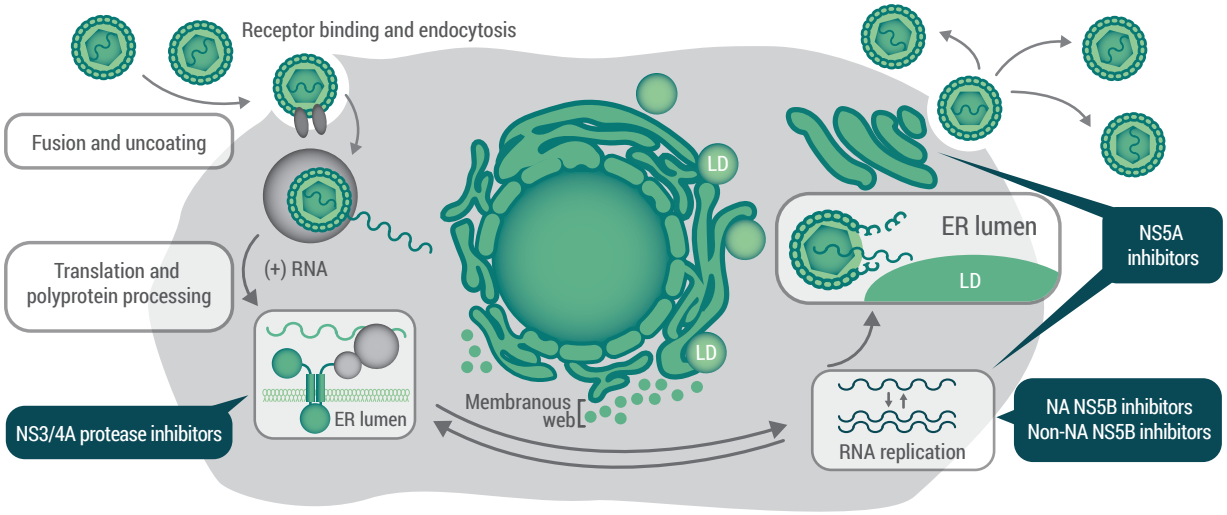


Figure 3 – DAAs and their sites of action
ER: endoplasmic reticulum; LD: luminal domain; NA: nucleo(s/t)ide analogue; NS: non-structural protein.

Unfortunately, "it's not all roses." In genotype 3, "old-fashioned interferon" sees 80% cure rates in non-cirrhotic patients after 24 weeks of therapy. As this is much more cost-efficient, "it's going to be very hard to persuade payers… to pay for genotype 3… That is an issue we need to recognise and a problem we've got to deal with."

Presenting the results of the BOSON trial (Foster GR, et al. Gastroenterology 2015), Professor Foster discussed the possibility of combining the DAA sofosbuvir with conventional interferon-based therapy. "In cirrhotic genotype 3 patients… I can cure nearly 90% with 3 months' peg-ribavirin and sofosbuvir and, in my view, that is still the preferred treatment… most likely to get rid of the virus and most likely to live and be cured." While it is understandably unpopular with patients, 12 weeks of interferon is well-tolerated and, as noted in the BOSON study, "most found it was manageable and they were able to cope with the treatment."

Moving on from the drugs available, Professor Foster turned to the patients and their specific needs. "The patients, of course, are a complex, heterogeneous group," which currently need prioritising based on urgent risk of death (ie those who already have cirrhosis). "I don't care whether that's an injecting drug user with cirrhosis, or a [non-user], they're all priorities if they have cirrhosis, and we need to make sure [they] are treated now." It's critical to treat these patients in a matter of months, as this will allow clinicians to shift focus to those with ongoing drug use, who may otherwise transmit the virus. "For every drug user I treat, that's 3 or 4 of his friends who will not get infected."

To conclude: "today we need to set up the infrastructure; tomorrow we need to wrap-up the treatment." However, acknowledging the political and practical hurdles to face in doing this, "it's our job to put [PWID] on the political agenda and make sure they're not forgotten."

Delegate feedback

I found the talk:

Clear **96%** Useful **96%** Informative **96%** Engaging **96%**

Based on the talk:

I might make some changes to my clinical practice **22%**

I will definitely make changes to my clinical practice **58%**

"Fantastic, challenging talk"

"I feel better informed to discuss newer treatments with patients and encourage them to follow up on positive diagnosis"

"Helped me to refocus about Hep C to push uptake to testing & engagement to Rx"

Dr Ashley Brown

Consultant Hepatologist, St Mary's and Hammersmith Hospitals, and Honorary Senior Lecturer at Imperial College London, UK

NURSE-LED HEPATITIS CARE IN ADDICTIONS CENTRES AND OTHER MODELS OF INTEGRATED CARE: A LONDON CASE STUDY

Bringing the medic to the mountain

While it's all very well and good to know what treatments are now available, it is important to recognise the challenges that lie in their implementation. Drawing on his experiences in West London, Dr Brown looked to provide delegates with creative solutions to systems-level barriers: "What we actually need to do is be collaborative… I'm not suggesting [our model] is going to fit everybody, but hopefully you can identify some issues you can take back to your own services."

Delivering practical solutions through tongue-in-cheek anecdotes, Dr Brown's approach resonated with the audience, leading to **over 85% committing to liaise with their local HCV services to provide community-based treatment.**

Key highlights

Although injecting drug use is by far the most common route of transmission, it is important to recognise other populations and their overlap with PWID. "A significant number of our injectors at any one time may be in the criminal justice system; people will move in and out, often several times a year," which has obvious implications on the ability to treat these individuals. Similarly, injecting drug use among men who have sex with men (MSM) "is on the increase – we're not talking about opioids here, we're talking about recreational sexual enhancing drugs (chemsex), and what we forget is that a lot of the information that we put out there may not be reaching that particular group of individuals." In addition, "reinfection among [injecting MSM] is a significant risk."

All things considered, however, community-based care still represents a vast opportunity to treat the epidemic. However, there are still significant barriers to HCV treatment in the community – "one of the problems I face when I go out into the drug treatment unit is that many of the clients, and in fact many of the key workers, are still disseminating information on [interferon-based therapies], rather than [DAAs]." This leads to the first challenge of community-based care: education and upskilling of key workers so that they can propagate knowledge throughout the community.

Systems-level barriers, too, are an issue, with HCPs blaming patients for poor engagement and unwillingness to treat. However, this is far from true – citing work by Grebely and Dore, Dr Brown estimated that as many as 80% of PWID are willing to receive treatment, if you offer treatment in the right way.

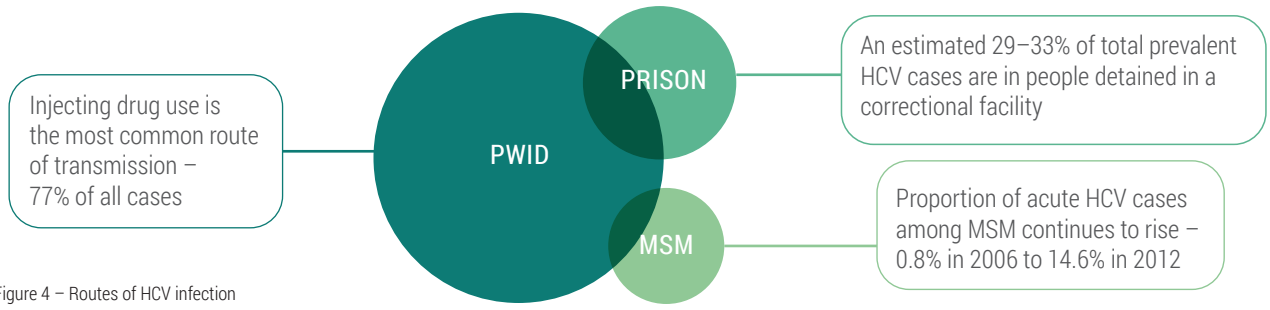


Figure 4 – Routes of HCV infection

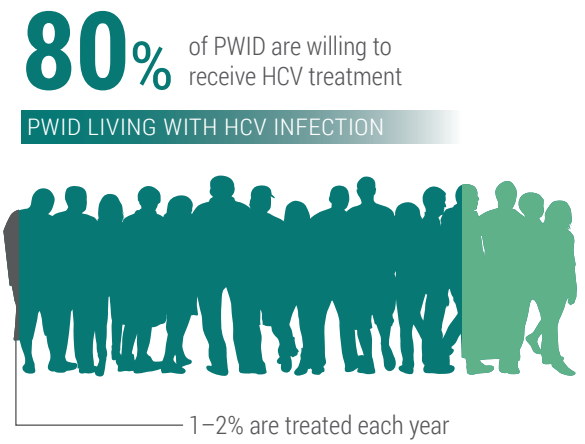
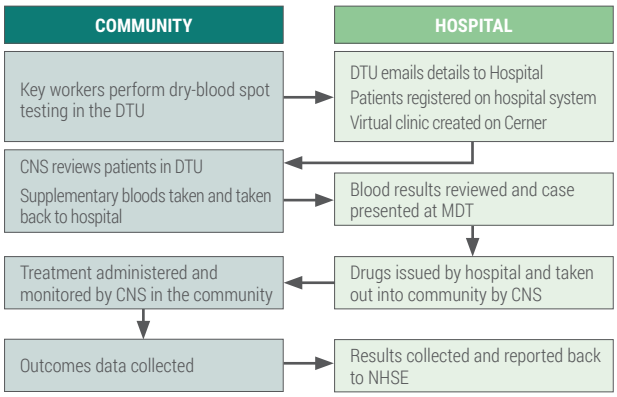


Figure 5 – PWID and HCV treatment

However, the issue lies in the "mountain of people who need treatment out there; the current system clearly does not work… the reality is we've actually got to go out there and treat these individuals in their own environment in a way that is acceptable to them… we've got to adapt." In order to do just that, Dr Brown sat with local colleagues in mental health and addiction services to decide how to provide treatment out in the community. While everybody shared the same goal, an important issue lay in funding and who would be able to fund the venture. This led to the development of the Imperial Model, in which treatment was coordinated and funded by the local hospital department, but largely delivered by key workers in the community (Figure 6).



DTU: drug treatment unit; CNS: clinical nurse specialist;
MDT: multidisciplinary team; NHSE: NHS England.

Figure 6 – The Imperial model of community-based treatment

This involved upskilling key workers in the field. This led to numerous hurdles being identified, the first of which was their terror of giving positive results. "They felt they did not have the background knowledge – they weren't able to answer their clients' questions, and that put them in a very vulnerable position." As such, it needed to be made clear that the clinical nurse specialists (CNS) would be answering questions for them. Another issue was the variability in uptake of HCV testing, which lay in how opt-out testing was framed.

Ultimately, the initiative led to 216 patients being screened; of these, 66 were HCV RNA-positive and 29 went on to receive treatment. Importantly, **approximately 25% of these patients had severe liver disease but would otherwise have remained untreated** – Dr Brown "was actually finding patients with decompensated cirrhosis who hadn't seen a GP in over a year."

Despite challenges in setting up community-based care, the schemes are "incredibly cost-effective," and engage patients who would otherwise go undiagnosed. If we are to eliminate HCV, it is essential to implement innovative, community-based schemes that can and will save lives.

Delegate feedback

I found the talk:

Clear **93%** Useful **92%** Informative **93%** Engaging **92%**

Based on the talk:

I might make some changes to my clinical practice **25%**

I will definitely make changes to my clinical practice **47%**

"Great way of delivering third level care at first level localisation"

"Excellent delivery plus educative plus understandable"

"Fantastic model"

Dr Hemant Shah

Clinic and Education Director, Francis Family Liver Clinic, Canada

FUNDAMENTAL HCV MANAGEMENT SKILLS FOR ADDICTIONS TREATERS: LIVE PATIENT JOURNEY INTERACTIVE ROLE PLAY

Demonstrating best practice, live

Rounding off the session was a highly interactive, half-plenary/half-role play hosted by Dr Hemant Shah and designed to tie together all of the concepts introduced throughout the workshop. Following a model patient from diagnosis to cure, the live patient journey focused on providing back-to-basics understanding of HCV and its clinical treatment, phrased in a manner that patients can understand and delivered alongside motivation to continue on and receive the treatment they need.

The patient in this illustrative case study, as played by Mr Duncan Cairns, was an intravenous drug user since adolescence. Having entered addictions treatment services 3 years prior, 'James' screened positive for anti-HCV antibodies on arrival; however, he did not pursue the referral offer for further testing. Now, having achieved some level of stability, James' doctor has convinced him to take the necessary diagnostic blood tests to confirm whether he has an active infection.

Picking up from this first diagnostic appointment, Dr Shah demonstrated key communication skills in patient management, managing fears where they arose and addressing common myths surrounding the condition. Interactive questions were interspersed throughout these sections, allowing the audience to reveal how they would approach treatment themselves. This revealed clear areas of misconception and suboptimal practice, which Dr Shah addressed in accompanying plenary segments.

Delegates found the session highly engaging, with the scenario modelling behaviours seen throughout the world.

Key highlights

While a great deal of knowledge was imparted throughout the hour-long session, perhaps the most striking moments were where Dr Shah challenged the audience's perceptions of HCV.

When asked what lifestyle advice they would give to James, the audience mainly focused on 'standard' advice, such as a complete abstinence from alcohol and avoiding sharing needles. Less than half correctly identified that smoking cannabis or tobacco products should be avoided, and fewer than 30% offered a more relaxed alcohol limit. More worryingly, 25% of the audience would have advised James to avoid sharing drinks, demonstrating a clear lack of understanding surrounding the routes of transmission of the virus.

As was subsequently discussed with James, the virus is only transmitted by contact with infected blood. This means that while patients should avoid sharing needles and personal products (eg toothbrushes, razors, nail cutters, etc.), there is no need to avoid sharing items such as cutlery or glasses, and there is very little risk of sexual transmission of the virus in practices that do not typically incur mucosal tearing.

Beyond considerations of transmission, Dr Shah recommended making healthy lifestyle choices, such as a balanced diet and exercise, in addition to reducing drinking and smoking due to their synergistic effect on liver disease.

Regarding liver assessments, Dr Shah posed that there are three questions to be answered in order to treat HCV: how active is the virus? how much damage has been done? and are there extrahepatic manifestations present? When asked what tests they would order for James, the audience's general consensus demonstrated good practice, with only 6% referring directly for invasive tests such as liver biopsy. However, only 6% would have referred for an abdominal ultrasound, which Dr Shah recommended alongside routine blood tests, viral tests and either Fibroscan or Fibrotest. "An abdominal ultrasound can occasionally be that tool that helps you determine someone has cirrhosis."

Dr Shah also recommended to "remember the W" (see fig 4.1). This diagram describes the pattern that happens to blood test results as someone becomes cirrhotic – identifying a drop in platelet count or increase in INR can help identify cirrhosis in individuals earlier, whereas "waiting for their bilirubin to go up before you're going to call them cirrhotic [will] miss a lot of individuals you could have diagnosed earlier, even with these very simple blood tests."

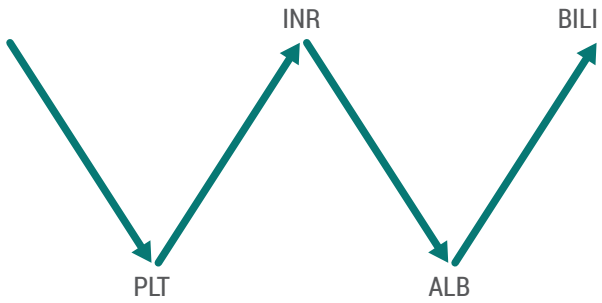


Figure 7 – "Remember the W". A useful reminder on cirrhotic blood test results

After presenting James' test results, Dr Shah resumed the patient journey, and provided a diagnosis of advanced fibrosis. James reacted with concern and asked when he could expect to have cirrhosis; at this point, the audience was asked what factors are associated with a faster progression of fibrosis. The level of knowledge in the room was mixed: **29% incorrectly identified heroin/opioid use as an exacerbatory factor, and fewer than 50% identified factors such as diabetes, cannabis use and male gender.**

Following this, James raised the question of whether his fibrosis would affect what medication he can take, due to frequent headaches. This was subsequently posed to the audience, of whom **73% mistakenly identified paracetamol as a contraindicated drug** in advanced liver fibrosis, and only **32% correctly identified NSAIDs** as "not recommended."

Dr Shah then addressed these common misconceptions: "paracetamol… is the medication we would recommend for people with the most advanced liver disease, even decompensated cirrhosis – it's quite safe in prescribed doses… The problem with [NSAIDs] with people who have more advanced liver disease [is] it can actually precipitate or cause a kidney injury." This was clarified further in the interview segment: "There is no doubt that paracetamol, by overdose, is the number one cause of drug-induced liver injury and death, but that's really only in overdose. If you understand the biochemistry around how paracetamol causes liver injury, you'd recognise that for prescribed doses, there's actually no risk of liver damage, and that's true even for people with the most advanced liver disease."

Delegate feedback

I found the talk:

Clear **95%** Useful **94%** Informative **94%** Engaging **95%**

Based on the talk:

I might make some changes to my clinical practice **27%**

I will definitely make changes to my clinical practice **68%**

"Absolutely inspiring presentation – a practical and empathetic way of dealing with this problem"

"Excellent session. The role plays illustrated issues I face as a D&A psychiatrist"

"Very useful info, very informative and useful to present information to clients"

This document is supported by educational grants from Gilead Sciences Inc. and Merck and Company.
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