

Economist Intelligence Unit

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THE SILENT PANDEMIC

**TACKLING HEPATITIS C
WITH POLICY INNOVATION**

A report from the Economist Intelligence Unit.

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Executive summary

Hepatitis C may be the serious disease that most combines widespread prevalence with widespread ignorance. According to the World Health Organisation (WHO), this urgent public health problem kills 350,000 people per year, and 150 million have the chronic form of the hepatitis C virus (HCV). The incidence of new infections is simply not known at the global level. Yet, HCV is entirely preventable and largely curable.

A disease spread through blood-to-blood contact, HCV is usually symptomless for decades, all the while slowly damaging the liver. It is already one of the world's leading causes of cirrhosis and primary liver cancer – a form of the disease with especially low survival rates. HCV is also the biggest reason for liver transplants globally, an operation which runs into hundreds of thousands of dollars, provided there actually is a replacement organ available. Worse still, the transplant is only a temporary fix – reinfection is universal. The recurrence of HCV infection after liver transplantation leads to the development of chronic hepatitis in at least 50% of grafts after one year, and in up to 100% of all cases after five years.¹

The impact of HCV looks set to grow as increasing numbers of people who were infected before the discovery of the virus in 1989 suffer from

so-called end-stage conditions. In the US, for example, HCV now accounts for more deaths than HIV, and 82% of those with the former disease are among those born between 1945 and 1965. Experts agree, however, that typically only a minority of those with HCV have been diagnosed, and even in developed countries only a small number of these are treated.

In order to investigate the extent of the health challenge posed by HCV, the Economist Intelligence Unit, on behalf of Janssen, conducted 16 in-depth interviews with experts, including global and national health officials, activists, researchers and medical personnel, as well as extensive desk research.

The key findings of this research include the following:

The scope of the problem is unknown because epidemiological data remain incomplete.

As one official interviewed for this study noted, “we don’t have a real understanding of the magnitude” of the challenge HCV presents. Too few countries – developed or developing – have recently conducted the epidemiological studies necessary for good policymaking at a national, let alone a local level. According to the World Hepatitis Alliance, a patient group, within the

¹ Claudio Augusto Marroni, “Treatment of recurrent hepatitis C post-liver transplantation”, *Annals of Hepatology*, 2010.

European Union (EU) only the Netherlands has good data on hepatitis C, while in 16 EU countries the data are either poor or non-existent.

Significant barriers to addressing the disease exist, including a lack of scientific knowledge, poor public awareness and delay of treatment owing to cost and side effects.

Despite substantial scientific progress since the discovery of HCV in 1989 and the availability of increasingly effective treatments with improving cure rates, some basic elements of its biology remain a mystery, such as why some people develop end-stage conditions and others do not. At the same time, the public remains largely ill-informed about HCV: a survey by the European Liver Patients Association found that only 20% of those diagnosed had heard of hepatitis C before being told they had it. Policymakers also need to learn more, as some still tend to confuse HCV with hepatitis B. Meanwhile, treatments are increasingly effective, but they are also expensive and frequently have substantial side effects. Activists complain that this may lead doctors and patients to wait, hoping that something better will come along before end-stage conditions kick in.

For too many developing countries, the healthcare system itself remains a leading vector of transmission for HCV.

In developing countries the major transmission route of HCV is through the health system, via injections with unsterilised equipment or the transfusion of infected blood. In 2008 the WHO found that for those low-income countries where data are available, only 53% of blood was screened for the virus in a quality-assured manner, and that in 39 countries donated blood was not routinely screened at all. Older WHO data

suggest that the use of unsterilised medical equipment is behind much of the global incidence of the disease.

The high incidence and prevalence of HCV among people who inject drugs in developed countries presents prevention and treatment problems and has stigmatised the disease.

In these countries the vast majority of new cases are among people who inject drugs (PWIDs). Since 1996, for example, 90% of new cases in England have been among these individuals. This presents a series of related problems in addressing HCV: PWIDs often exhibit little concern for their own health, so may not seek treatment or testing; the treatment is difficult for those with the co-morbidities or lack of social and financial support common among PWIDs; and there are often high levels of mistrust between these individuals and healthcare professionals. More broadly, the stigma which the association with drug use has attached to the disease may lead those who previously engaged in high-risk activity or acquired the disease through other means to be unwilling to be tested.

Facing up to the challenges posed by HCV requires a co-ordinated strategy covering a range of areas.

HCV will not go away on its own. Countries which have had the most success so far have tended to focus on the problem in a co-ordinated way, rather than on one individual aspect. Each country will have different needs and resources, but all should consider obtaining strong data, raising awareness of the disease and focusing on prevention. Those with healthcare systems that have the resources and sophistication necessary to deliver current treatments should also look at the most effective ways of doing so (see Conclusion for a detailed list of actions).

About this report

The silent pandemic: Tackling hepatitis C with policy innovation is an Economist Intelligence Unit report, supported through an educational grant by Janssen, which investigates the health challenge posed by the hepatitis C virus (HCV), and how systemic innovation can minimise its impact. The findings of this white paper are based on desk research and interviews with a range of healthcare experts.

Our thanks are due to the following for their time and insight (listed alphabetically):

- Dr Ruth Bastable, GP, UK
- Dr Sylvie Briand, co-ordinator of the Influenza, Respiratory Diseases, Hepatitis and PIP framework unit at the World Health Organisation
- Luis Gerardo Castellanos, senior advisor for the prevention and control of infectious diseases at the United Nations' Pan American Health Organisation
- F DeWolfe Miller, professor of epidemiology at Hawaii University
- Dr Ivan Gardini, president of the Italian Liver Patient Association
- Professor David Goldberg, head of the Scottish Hepatitis C programme
- Charles Gore, president of the World Hepatitis Alliance
- Achim Kautz, manager at Deutsche Leberhilfe
- Dr James Morrow, GP, UK
- Saroj Nazareth, RN, BHLth Sc, MSc, MN, nurse practitioner, liver service, Western Australia
- Maria Prins, head of the research department, cluster infectious diseases, Public Health Service of Amsterdam; professor of public health and the epidemiology of infectious diseases at the Academic Medical Centre in Amsterdam
- Professor Walter Ricciardi, president of the European Public Health Association
- Marita van de Laar, head of the programme on STI, HIV/AIDS and blood-borne viruses at the European Centre for Disease Prevention and Control
- Jack Wallace, research fellow at the Faculty of Health Sciences, La Trobe University; executive member of the Coalition for the Eradication of Viral Hepatitis in Asia and the Pacific
- Dr John Ward, director of the division of viral hepatitis, US Centers for Disease Control and Prevention
- Freke Zuure, co-ordinator of the Hepatitis C project at the Amsterdam Public Health Service

The report was written by Dr Paul Kielstra and edited by Monica Woodley and Zoe Tabary.

1

An iceberg looming in a fog of uncertainty

A big problem...

Hepatitis C is often called “the silent pandemic”, in part because the virus takes so long to manifest itself in those infected. Spread largely by blood-to-blood contact, in about 15-30% of cases the body’s natural defences can eliminate the disease. The rest of those infected develop the chronic form of HCV. For most, however, this initially has no discernible symptoms, or non-specific ones such as general fatigue.

This apparently benign situation can last for decades before turning decidedly worse. Most patients – about 60-70% of those with HCV – develop chronic liver disease. A minority – estimated at 20-30%, although for people infected when younger and healthier it can be as low as 10% – develop cirrhosis of the liver, which typically appears after two or three decades. Those patients also suffer from a higher than normal risk of developing hepatocellular carcinoma (HCC), the most common type of liver cancer.

The healthcare costs of these “end-stage conditions” of HCV can be substantial. They are the leading cause of liver transplants worldwide, including in Europe, the US and Japan. A recent study looking at countries other than the US put the average cost of a transplant at US\$139,000, although in some places it topped US\$400,000. A similar investigation found that the average cost in the US was US\$200,000, but warned that many of the data were old.² Worse still, there are not enough livers to go around: there are roughly 30,000 people on waiting lists in Europe and the US, but only about 12,000 procedures per year.

Some 20% of people awaiting a transplant die. Nor is the transplant even a cure, it merely buys time. Infection of the new livers of patients with HCV is inevitable, leading to the need for yet another transplant.

At worst, then, HCV is catastrophic physically and very expensive. On the other hand, a large number with the condition may end up suffering few recognisable ill effects. What makes the disease, in the words of Dr John Ward, director of the division of viral hepatitis at the US Centers for Disease Control (CDC), “an urgent public health issue” is that the sheer scale of the infection will inevitably produce a substantial number of end-stage patients. The WHO estimates that globally 150m people have chronic HCV and 350,000 die from related liver complications each year – roughly 1% of all deaths worldwide. Globally, approximately 27% of all cirrhosis and 25% of primary liver cancer cases trace back to hepatitis C.

As map 1 shows, disease prevalence tends to be higher in developing countries, especially in North Africa. In Egypt, which has the worst-affected national population, about one in five people have the virus (see case study page 9).

This is not, however, simply another developing-world health issue. Even wealthier countries, such as Taiwan and Japan, have a worrying prevalence, and the impact can be dramatic. In the developed countries of the Asia-Pacific region, HCV is responsible for 62% of all cirrhosis and 66% of all primary liver cancer cases. In Western Europe, the virus accounts for 38% of all cirrhosis and 44% of primary liver cancer.³

Most patients – about 60-70% of those with HCV – develop chronic liver disease.

² Antoine C El Khoury, Carolyn Wallace, William K Klimack and Homie Razavi, “Economic burden of hepatitis C-associated diseases: Europe, Asia Pacific, and the Americas”, *Journal of Medical Economics*, 2012; Antoine C El Khoury, William K Klimack, Carolyn Wallace and Homie Razavi, “Economic burden of hepatitis C-associated diseases in the US”, *Journal of Viral Hepatitis*, 2012.

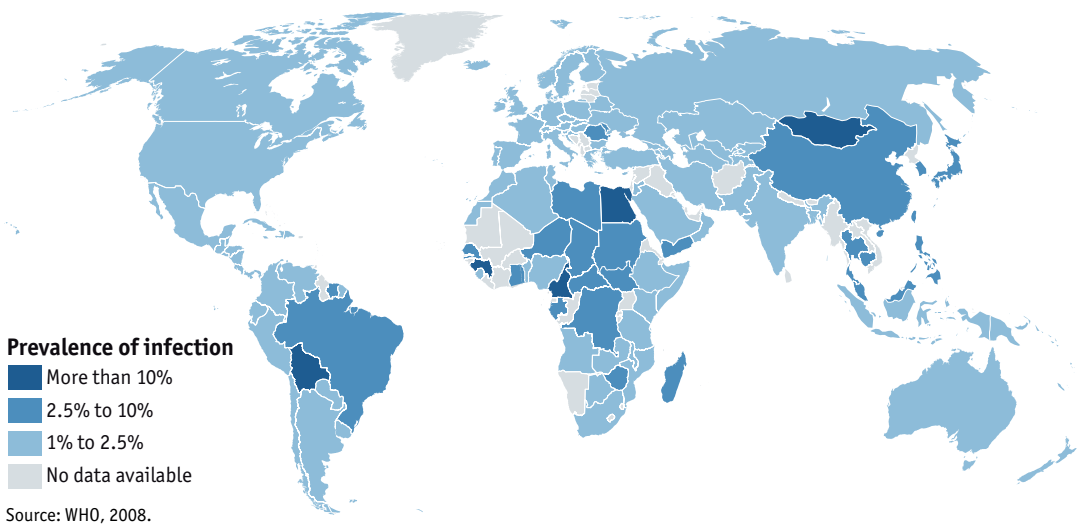
³ Joseph F Perz, Gregory L Armstrong, Leigh A Farrington, Yvan JF Hutin, Beth P Bell, “The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide”, *Journal of Hepatology*, 2006.

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HCV is a time bomb.
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Dr Sylvie Briand, co-ordinator of the Influenza, Respiratory Diseases, Hepatitis and PIP framework unit at the World Health Organisation

Map 1

Hepatitis C, 2007
Prevalence of infection by country

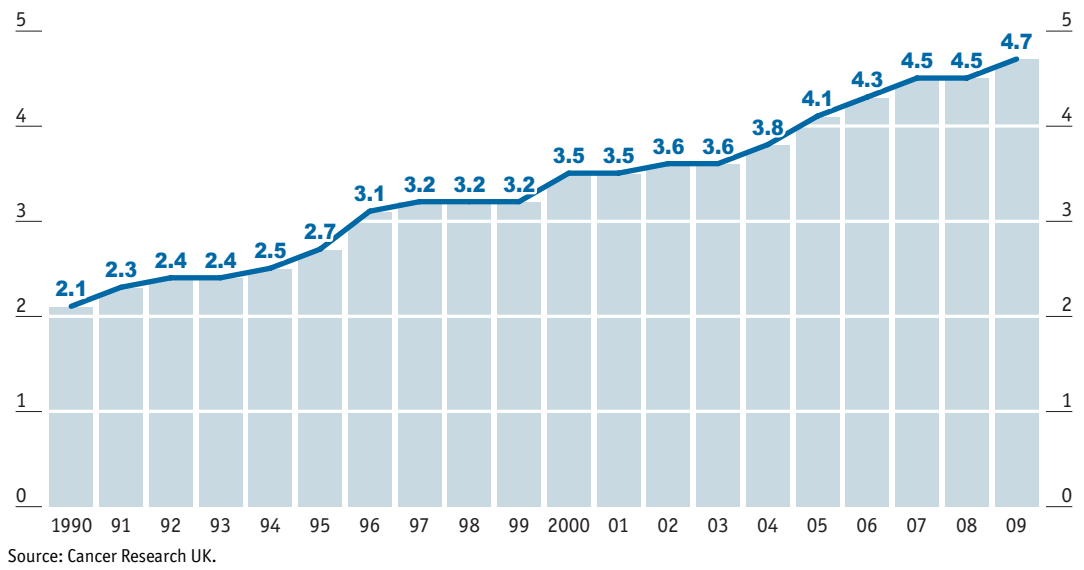


The rapid spread of the disease before the virus was identified in 1989, combined with the time it takes for end-stage conditions to appear, means that these conditions will become more common in the near future. A recent analysis of the likely progression of the disease in the US, for example,

found that although the total number of HCV cases was expected to drop by 24% between 2005 and 2021, the overall number of deaths would rise because of an increase in the mortality rate of those infected.⁴ As Sylvie Briand, co-ordinator of the Influenza, Respiratory Diseases, Hepatitis

Chart 1

Liver cancer
(incidence per 100,000 people; Great Britain)

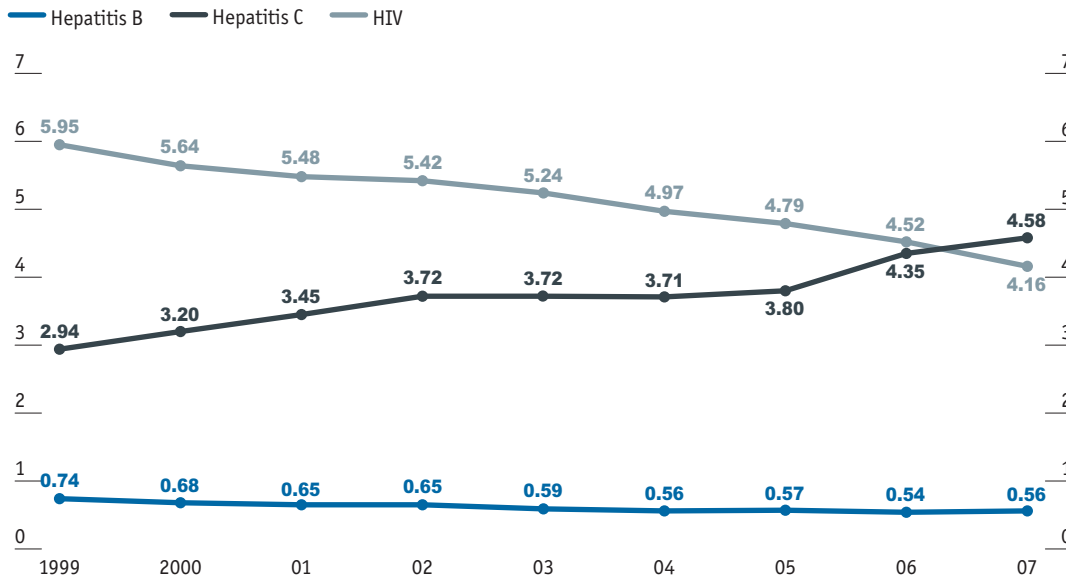


⁴ David Kershenovich *et al*, “Applying a system approach to forecast the total hepatitis C virus infected population size: model validation using US data”, *Liver International*, 2011.

Chart 2

Annual age-adjusted mortality rates from hepatitis B and hepatitis C virus and HIV infections listed as causes of death in the US between 1999 and 2007

(incidence per 100,000 people)



Source: Ly *et al.*, "The Increasing Burden of Mortality From Viral Hepatitis in the US Between 1999 and 2007", *Annals of Internal Medicine*, 2012.

and PIP framework unit at the WHO, puts it, HCV is "a time bomb".

The effects are already becoming apparent in the spread of liver cancer. In Egypt, the number of deaths attributable to liver cancer rose from 4% to 11% between 1993 and 2009. In the developed world, where HCV causes a much greater proportion of such cancer, the data are also worrying (see chart 1). In the UK, for example, the incidence of HCV has more than doubled in the last two decades. Cancer rates are an imperfect proxy for the impact of HCV, but a recent study of US death certificates filed between 1999 and 2007 found that deaths attributable to HCV rose by over 50% in that period (see chart 2). It is now a bigger killer in America than HIV. Nor are forecasts comforting. Achim Kautz, manager of Deutsche Leberhilfe, a German patient support group, says: "For hepatitis C in Europe, we expect a peak of those who develop end-stage status in 10 to 15 years."

...of undetermined size

More alarming still, current data on HCV are poor and probably understate the problem. Charles Gore, chair of the World Hepatitis Alliance, says: "Estimates of world prevalence and incidence are not a lot more than informed guesses." Dr Briand adds: "We don't have a real understanding of the magnitude [of the problem]." The silent nature of the disease makes it hard to gather data. Dr Briand estimates that mandatory reporting of those showing symptoms uncovers only about 5% of the problem. More complex tests that rely on the presence of antibodies to the disease are much more accurate, but also much more expensive.

HCV's long period of relative dormancy adds to data inaccuracy, because sometimes forgotten activities have left behind an unfortunate, unsuspected legacy. For example, in southern Italy the prevalence of the virus is among Europe's highest, in part because decades

Within the EU only the Netherlands has good data on hepatitis B and C, while in 16 EU countries the data are either poor or non-existent.

ago nurses there often reused unsterilised syringes. In some specific parts of the region the prevalence among those over 60 years old is 33%, but among those under 30 years old it is just 1.3%. Ivan Gardini, president of the Italian Liver Patient Association, explains: "These problems ended many years ago, but have left their mark on levels of advanced liver disease, much still undiagnosed."

The biggest data issue, however, is how few countries have tried to obtain even the most basic prevalence information. The World Hepatitis Alliance, which publishes a World Hepatitis Atlas, found that within the EU only the Netherlands has good data on hepatitis B and C, while in 16 EU countries the data are either poor or non-existent. The situation is worse in Latin America and Africa. In the Asia-Pacific region the picture is more mixed: China, Australia and India have reasonable data, but most small countries do not. According to Jack Wallace, an executive member of the Coalition for the Eradication of Viral Hepatitis in Asia and the Pacific (CEVHAP): "In Asia there are countries where we don't even have estimates of how many people are infected."

Good news and bad news

Faced with a serious medical issue of uncertain proportions, there is at least some good news. Treatments for HCV do exist. Combination therapies using interferon and new drugs have, in the last decade, steadily improved the rate of sustained virologic response (SVR) – or cure – including for those with genotype 1 (the most common in Europe and North America). Such treatments can now cure the disease in up to 80% of cases, although this depends on factors including the genotype, how far the disease has progressed, how soon after infection treatment occurs, and the existence of any co-morbidities.

The therapy, however, is both expensive and complex, making it a far less viable option for many developing nations. Nevertheless, in wealthier countries with health systems that have the necessary expertise and resources the current therapies are cost-effective, even for use on patients likely to be re-infected and, in some cases, on those with advanced cases of HCV.⁵ Moreover, looking ahead, trials of new drugs, which may be less difficult to administer, show great promise, in some cases achieving SVR rates of 100%.

The bad news is that these therapies are frequently not used, even where healthcare providers can do so. Dr Ward says of the US: "Many, if not most [individuals with HCV] are unaware of their status and are not benefiting from any care and treatment that could prevent end-stage outcomes." Part of this is owing to a lack of diagnosis, but a 2005 study in Nottingham (UK) found that of 256 people who tested positive for HCV antibodies, over 20% were not even told of the result, only 25% had the follow-on HCV RNA test to confirm the diagnosis, and just 10% received treatment.⁶ This will bring economic costs to healthcare systems in the long term as they face expensive treatments for chronic liver disease, cirrhosis and HCC.

It will also presumably bring a broader economic burden in terms of lost work years for employees and employers, although the general paucity of data makes this difficult to estimate. A 2010 study drawing on US employment records found that the cost of sick days and lower productivity per HCV-infected employee was US\$8,352 per year, indicating that HCV begins to exact a cost on the economically active before end-stage conditions kick in.⁷

⁵ J Shepherd, "Interferon alpha (pegylated and non-pegylated) and ribavirin for the treatment of mild chronic hepatitis C: a systematic review and economic evaluation", *Health Technology Assessment*, 2007; Natasha K Martin *et al*, "Cost-Effectiveness of Hepatitis C Virus Antiviral Treatment for Injection Drug User Populations", *Hepatology* 2012.

⁶ W Irving *et al*, "Clinical pathways for patients with newly diagnosed hepatitis C – What actually happens", *Journal of Viral Hepatitis*, 2006.

⁷ Jun Su *et al*, "The Impact of Hepatitis C Virus Infection on Work Absence, Productivity, and Healthcare Benefit Costs", *Hepatology*, 2010.

Case study

HCV in the developing world: Close-up on Egypt

Egypt's HCV problem is at least four times greater than that of any other country. Anything between one in ten and one in five of the country's 80m people are unwitting carriers, the legacy of a disastrous public health programme launched in the 1950s to vaccinate the population against the river-borne parasite bilharzia. Recent epidemiological studies of individual communities have demonstrated a close link between the advent of the vaccine – presumably delivered in unsterilised syringes – and the subsequent arrival of HCV.

Although Egypt now has the world's largest HCV treatment programme – and in October 2012 launched what will be the world's most comprehensive national HCV patient registry – every year at least 500,000 new HCV infections occur. For F DeWolfe Miller, professor of epidemiology at Hawaii University and an

expert on Egyptian public health and the HCV pandemic, the spread of the disease there is "nothing short of a scandal". He believes that the effects of the anti-bilharzia campaign are much less significant than the attitudes of healthcare professionals in explaining the ongoing record levels of infection. "This disease is being continuously spread by poor medical care," he says. "Almost every pharmacy, doctor and dental office in the country needs to clean up its act."

Professor Miller adds: "Egypt has one of the oldest and largest medical education systems in the world. They have all heard of Semmelweis, the Hungarian doctor who discovered that hand-washing reduces mortality, but they don't seem to have made the connection. Unless that message is taken on board, it is going to be a long time before anything changes there." ■

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This disease is being continuously spread by poor medical care.

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*F DeWolfe Miller,
professor of
epidemiology at
Hawaii University*

Case study

HCV in the developing world: Close-up on Latin America

The scale of HCV's presence in Latin America is only just becoming known. It is believed to have arrived in the region during the second half of the 20th century, but in countries such as Chile, Brazil, Argentina and Mexico, experts insist that the spread had less to do with unhygienic healthcare and more with the unhygienic injection of street drugs and unprotected sex with multiple partners.

Luis Gerardo Castellanos, senior advisor for the prevention and control of infectious diseases at the UN's Pan American Health Organisation, admits that reliable HCV data are still hard to come by, particularly when looking at country data. A majority of countries in the region began to implement prevention and control policies only after the WHO recognised Viral Hepatitis (including HCV) as a major public health issue in 2010. Countries such as Argentina, Brazil and Cuba have successfully developed comprehensive prevention and control strategies against hepatitis A, B and C.

In Brazil for example, a test is available to anyone who wants it and drug treatment for HCV is offered if needed. Dr Castellanos acknowledges that the take-up of the exercise has been relatively slow, albeit consistent, with around 12,000 cases a year detected since the programme began in 2009. With Brazil's population standing at around 200m and HCV drug treatment expensive, it is currently unclear, even with the nation's rapidly increasing income, how many of those infected can receive therapy.

According to Dr Castellanos, elsewhere the picture is even bleaker. "Most countries in our region have until now not had structured programmes to take care of HCV patients. Incidence has continued to grow because there is no vaccine, and even if some of the cases could be cured, access to treatment is generally very poor." ■

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Barriers to tackling HCV

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Hepatitis C is still very much an emergent, unrecognised disease, and there remain aspects of it that are not fully understood.

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Marita van de Laar, head of the programme on STI, HIV/AIDS and blood-borne viruses at the European Centre for Disease Prevention and Control

Part of the problem in addressing the challenge of HCV is the relative novelty of the disease: it takes time for medical science to understand and develop treatments for a new condition, for healthcare systems to adjust, and for the general public to become aware of the danger. At least as big a difficulty is that, for a variety of reasons and for many stakeholders, when it comes to the silent pandemic, it is often simply “a lot easier to deny that there is a problem”, to quote CEVHAP’s Mr Wallace.

Still much to learn

Despite definite progress, Marita van de Laar, head of the programme on STI, HIV/AIDS and blood-borne viruses at the European Centre for Disease Prevention and Control (ECDC), notes: “Hepatitis C is still very much an emergent, unrecognised disease, and there remain aspects of it that are not fully understood.” After all, it was discovered as late as 1989, a screening test was only available in 1991, and it was not until early 2012 that a team announced it could explain exactly how the virus uses the liver to replicate itself. Still unclear are some basic elements of the disease’s biology and crucial issues, such as why some patients reach end-stage conditions and others do not develop chronic HCV at all.

Drug development also takes time, typically at least a decade, to go from identification of a promising molecule to drug approval. The relative novelty of treatments with reasonable, if imperfect, success rates helps explain why

medical professionals have begun to react to the disease only recently, according to Professor Walter Ricciardi, president of the European Public Health Association. As cure rates improve, this trend is likely to continue.

Healthcare systems, meanwhile, change notoriously slowly, and healthcare professionals frequently lack the ability to treat, or sometimes even recognise, HCV. A 2010 literature review by the US Institute of Medicine found that “healthcare providers’ knowledge about hepatitis C appears to be insufficient”, citing one study in which 31% of family physicians were uncertain what to do in the event of a positive test, or would have to refer the patient to another doctor. It takes time for up-to-date knowledge now being taught in medical schools to feed through the system: the review found that physicians with more than 20 years of experience were the worst-informed and that those with fewer than five years had the best understanding.⁸

There is no reason to believe that America is exceptional in this regard. Mr Gore of the World Hepatitis Alliance, speaking of Britain, cites a lack of knowledge among primary care physicians as perhaps the biggest problem in addressing HCV. “GPs are critical,” he says, “but you have endless stories of people going to them for years being tested for all sorts of other things.” Primary care providers are not in a position to pass the problem on to experts. Interviewees in Australia, Germany and the US all speak of a lack of trained specialists who can administer treatments.

⁸ Heather Colvin and Abigail Mitchell, eds, *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*, 2010.

While healthcare professionals are still learning the ropes, non-specialists sometimes even conflate HCV with other forms of hepatitis. Dr Briand and Professor Ricciardi both point out that success against hepatitis B in the 1990s can lead to complacency among some policymakers about HCV. This is also a problem for the general public, adds Maria Prins from the Public Health Service of Amsterdam and professor of public health and the epidemiology of infectious diseases at the Academic Medical Centre in Amsterdam: “People confuse hepatitis A, B, C and D. They think that they are vaccinated [for HCV] when you can’t be.”

Indeed, basic information about HCV has yet to filter down to the public at large. The CDC’s Dr Ward describes “a general lack of awareness and concern about the infection”. A survey by Hepatitis Australia in 2011 found that only 20% of the public believed that HCV could cause cancer. Similarly, a survey for the European Liver Patients Association found that only 20% of those diagnosed with hepatitis B or C had previously heard of the condition. As Mr Wallace points out, the silent pandemic simply does not grab “attention as an infection” the way others might, making it less likely to gain press coverage.

Playing the odds in a dangerous game

Novelty can explain a lack of knowledge and awareness surrounding HCV, but is less helpful in understanding why, once some patients are diagnosed, so few are treated. Here, says Dr Ruth Bastable, a British GP whose practice specialises in providing care for the homeless, “at every possible level within the system, there is a barrier.”

The first is the current therapy available. The regimen is complex – involving a combination of injections and pills at different times – and can induce substantial side effects, both physical and psychological. This increases the level of expertise needed to administer and monitor the treatment. It also makes immediate therapy less

attractive to patients. “It’s not something you embrace,” says Mr Wallace.

The other difficulty with current therapies is the expense. Although cost-effective, they require a significant initial outlay for benefits which may not accrue for decades – or not at all in cases where end-stage conditions would not develop. The exact cost depends on a variety of factors but puts therapy out of the reach of many developing-world health systems, whatever the longer-term benefits. Even in wealthier societies “the cost has to be considered”, according to Dr Ward, especially when facing the potential need to treat millions of patients.

Ironically, for patients in particular, the speed of scientific developments is also contributing to delays. As Mr Kautz of Deutsche Leberhilfe points out: “A lot of patients are still waiting for one pill a day for a month with no side effects.” They are taking a calculated risk based on news reports of upcoming drugs, worries about current ones, and the time it frequently takes for serious complications to develop.

Representatives of patient groups are also concerned that cost and the inability to determine who will develop complications are restricting the use of medication. Dr Gardini notes that, in Italy, care is delayed for those deemed to be currently at lower risk of cirrhosis or liver cancer because of limited resources. He adds there is evidence that some doctors will ask patients with lower risks to wait for better therapy with fewer side effects, which they think likely to appear soon. If such “parking” of patients has occurred, it would not be the first time. Mr Kautz recalls that it took eight years of campaigning before German guidelines were changed so that HCV patients who wanted treatment could not be denied access by physicians who believed that it was not yet necessary.

Such thinking represents a high-stakes gamble. Existing treatment works better in the early

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A lot of patients are still waiting for one pill a day for a month with no side effects.

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Achim Kautz, manager at Deutsche Leberhilfe

63% of the world's roughly 16m PWIDs have HCV.

“Health systems are often the worst at discriminating against people who they think will be tricky.”

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Charles Gore,
president of the World
Hepatitis Alliance

⁹ Paul Nelson *et al*, “Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews”, *The Lancet*, August 2011.

stages of the disease. The strategy is also short-sighted on economic grounds. As Dr Gardini says of Italy: “The country has a very large number of people with HCV – diagnosed and undiagnosed – and therefore the costs associated with screening and treatment for all are supposedly unsustainable. But the clinical and social costs associated with the disease will be even higher if patients are not diagnosed and treated.”

See no evil

Although regrettable, if the barriers described so far were the only ones, they would probably disappear with time. Knowledge spreads and costs come down, either through further discoveries or the disappearance of patents. A more difficult set of problems arises from perceptions about the disease. Although in most developing countries the main route for the infection to spread is still through the medical system, in the developed world effective prevention has largely addressed this. Instead, in these countries HCV transmission now tends to take place mostly among socially marginalised groups, especially people who inject drugs (PWIDs). These individuals often have troubled relationships with healthcare providers, and their link to the disease has also attached a stigma to HCV, which impedes progress against it in a variety of ways.

PWIDs who share needles face a huge risk, but some who share paraphernalia when taking drugs nasally are also susceptible to infection. In 2011 *The Lancet*, a medical journal, estimated that about 63% of the world's roughly 16m PWIDs have HCV. It also found that in 25 countries HCV prevalence among PWIDs was between 60% and 80%, and that it topped 80% in a further 12. For Europe, the highest rates were in the Netherlands (86%), Portugal (83%), Italy (81%) and Spain (80%).⁹

This link between drug use and HCV transmission complicates efforts to deal with the disease in various ways. While PWIDs are not a monolithic group, statistically they are more likely than

the average population to be homeless or live in sub-standard housing, have other physical or psychological conditions and be economically worse off. Also, as Mr Kautz says: “it is not normal for people who take drugs to care for their health.”

They may simply not wish to know if they are infected or, if they do know, not want to do anything about it. Dr Bastable's practice offers HCV testing regularly to anyone in a high-risk group, but based on the number of PWIDs on its register, she estimates that there should be about 50% more identified cases among them. The living conditions and overall physical state of PWIDs also make them imperfect patients for physically demanding, complex therapies. Dr Bastable explains that 40% of her patients have psychiatric problems, and the treatment can also be psychologically destabilising. She reports that, unlike the Nottingham figure of 10% receiving treatment cited earlier, in her practice, where those found with HCV antibodies are largely PWIDs, only about 1% get treatment. Saroj Nazareth, a nurse practitioner at Western Australia's Liver Service, adds that her specialist HCV programme ends up treating relatively few PWIDs because patients need to be willing and able to comply with the therapy regimen.

Making matters worse, PWIDs and healthcare professionals frequently mistrust each other. According to Mr Gore, “Health systems are often the worst at discriminating against people who they think will be tricky.” How the system operates can also “put people right off. You have to come to us, travel 50 miles and you don't like how we behaved to you the last time,” he adds. PWIDs therefore are often unwilling to engage at all, especially on the health system's terms. Ms Prins believes that one key piece of research needed in efforts against HCV is to define integrated care models for such patients that are effective in terms of uptake and outcome.

Another major impediment to dealing with HCV that arises from its link to drug use is the

undeniable stigma it attaches to the condition. Mr Kautz explains: “If you have a liver disease, the general public thinks you are guilty. You did not take care in your past.” This has implications at the governmental level. Mr Kautz has found that “sometimes it is better to insert hepatitis C [activities] into existing programmes. Some politicians feel more comfortable with that.” The difficulties, though, reach down to patients themselves, including those who are not PWIDs. Mr Gore explains that for former drug users this “may be a part of their life they don’t want to

revisit. Also, even if people don’t get HCV that way but think that it is a very stigmatised drug users’ disease, they might not want to get a test.”

Such attitudes are especially problematic because, although it is easy to identify high-risk behaviours for transmission, the long time it takes for complications to develop can mean that this identification does not really help all that much in predicting where the worst health problems will appear.



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Finding a way forward

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Countries need a systematic approach. You have the virus, the doctor, the health system. If you address just one [aspect of the issue], it's unlikely that you will be successful.

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Dr Sylvie Briand, co-ordinator of the Influenza, Respiratory Diseases, Hepatitis and PIP framework unit at the World Health Organisation

Presenting a single, detailed solution for HCV would be of little practical use. As CEVHAP's Mr Wallace says: "We are living with multiple epidemics, different ones in different countries." Leading transmission routes, resources available and even disease genotypes vary. Rather than providing a pat prescription, this section will discuss areas which policymakers should consider, illustrated by specific initiatives with broader resonance.

A universal starting point is that HCV will not go away on its own. "Countries need a systematic approach," says the WHO's Dr Briand. "You have the virus, the doctor, the health system. If you address just one [aspect of the issue], it's unlikely that you will be successful."

The WHO's recently released *Framework for Global Action* on viral hepatitis, although fashioned as a global strategy, provides a useful delineation of some of the specific areas which such a comprehensive approach needs to encompass: obtaining data for evidence-based policy, raising awareness and creating partnerships, prevention, care and treatment.

Piercing the fog

The ECDC's Dr van de Laar describes the lack of good epidemiological data on HCV, even in developed countries, as a major challenge: "Without accurate epidemiological information it is difficult to plan and monitor services effectively." Accordingly, the ECDC has rolled out enhanced surveillance on HCV and will publish the first full report with comparable European results early in 2013. Understanding the scope of

the problem is an essential first step to dealing with it.

The US is taking a slightly different tack which, although more expensive, has direct clinical utility. Like many countries, the US had originally followed a risk-based approach to screening for HCV. The growing burden of the disease, however, brought this policy into question. Dr Ward explains that especially for the generation born between 1945 and 1965 (the so-called baby boomers) infected by the medical system before the 1990s, a risk-based strategy was just not working. Many were infected so long ago that they might not even recall any relevant activity when asked.

The CDC therefore recommended in August 2012 that all Americans born between 1945 and 1965 be tested once. This group accounts for 82% of all HCV infections in the country. Widespread adoption of this advice, and appropriate treatment when the disease is found, would alleviate much of the disease burden HCV represents. The CDC also calculates that it would be cost-effective in the long term.

Such an approach may not be best for every country. Dr Ward notes: "You need to look at the data that profile a country's problem. We looked at the epidemiological information, laboratory capacity, strategy, what we were already doing elsewhere. It was clear that this represents good value." Other countries are taking note. Public health authorities in Canada, which has a similar demographic profile, are planning to issue a review of HCV strategy in March 2013.

Dr Ward adds that the new recommendation has had positive effects beyond screening. The media coverage has been wide and positive. Moreover, the policy review has allowed his organisation to engage with leading professional societies “so that public health officials and clinicians can work together to develop models of care that make sense”. That said, he realises that issuing a recommendation does not bring change on its own: “You don’t just set the policy and walk away. You have to see it through.”

Raising public (and political) awareness

In 2010 a WHO resolution designated July 28th as an annual World Hepatitis Day “to provide an opportunity for education and greater understanding of viral hepatitis as a global public health problem, and to stimulate the strengthening of preventive and control measures of this disease”.

Such resolutions are not made lightly. Hepatitis is one of only four diseases with a “WHO day” – along with malaria, tuberculosis and HIV – although the UN General Assembly designated an annual World Diabetes Day as well. How well, though, do such days deliver on their stated goals?

Mr Gore of the World Hepatitis Alliance thinks that initiatives such as World Hepatitis Day are critical, although he believes that in many countries campaigners fail to make proper use of them. Their primary use is not simple awareness-raising. “I see them largely as a way of engaging governments,” he says. “Getting countries to do something is difficult, and this is a really good rallying point. You can say ‘you signed up to this’. It is about pushing them.” Other activists agree: Deutsche Leberhilfe’s Mr Kautz calls the day “useful as a door opener”. From a public health perspective, Professor Ricciardi of the European Public Health Association calls activist efforts surrounding such occasions “important, particularly in a time of financial crisis. You have to decide how to allocate resources. The fact that

policymakers are aware that this is an important problem helps a lot.”

Prevention: Healthier than treatment

Prevention needs to be a core component of any HCV strategy. Its potential effectiveness is substantial. Although HCV incidence before the virus was discovered obviously could not be measured, an analysis of American data was able to derive approximate figures for the 1980s. It found that the incidence dropped by about 85% after the blood supply began to be screened in the early 1990s. Similarly, studies from the middle of that decade show that, after 1991, the incidence of HCV in European patients receiving blood transfusions dropped to below 1%.¹⁰

Prevention strategies are not perfect in developed countries: Dr Ward reports that in the last decade the US has seen 32 outbreaks related to poor infection control practices. Meanwhile, in Europe, the ECDC reports that, as of 2010, Luxembourg and Liechtenstein still did not screen blood or organ donors for HCV.

Nevertheless, the issue is particularly important for the developing world, where in many countries, as Dr Ward notes, unsafe health practices are the most common cause of the disease. These problems overwhelm efforts to address the disease. Mr Gore points out: “In Egypt they are treating tens of thousands of people, but may have more than a hundred thousand new infections per year. This is great for the patients receiving treatment but from a public health point of view, it’s going the wrong way. They need to tighten up on blood safety and the reuse of equipment.”

Prevention is also an area where cash-strapped governments can take effective action. Dr Briand explains: “There are things we can do that are not expensive. We are telling governments that, if they cannot treat people because it is expensive, they can still do something about reducing transmissions.” The most obvious step is improving the training and compliance

In the last decade the US has seen 32 outbreaks related to poor infection control practices.

¹⁰ I Williams, “Epidemiology of hepatitis C in the US”, *American Journal of Medicine*, 1999; S Touzet et al, “Epidemiology of hepatitis C virus infection in seven European Union countries: a critical analysis of the literature”, *European Journal of Gastroenterology & Hepatology*, 2000.

of healthcare workers, as well as introducing stricter policies on the reuse of medical supplies. The use of auto-destruct syringes, for example, which are impossible to use more than once, is cost-effective even though they are more expensive than traditional needles. The screening of blood donations is a more difficult case, as the necessary tests are relatively costly. Even here, though, in at least some developing-world contexts, screening for HCV is worth the money. It is certainly cheaper than treatment, which many of these countries simply cannot afford.

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*Dr Ruth Bastable,
GP, UK*

Primary prevention, however, is not the only kind. Current therapies are not universally effective. Although there is hope for improvement, a significant minority of those infected still have to learn to live with the condition for an indeterminate period in both the developing and the developed world. Ms Nazareth of Western Australia's Liver Service points out that it is important for them to be put on a chronic liver disease management plan. This does not involve medication so much as information on lifestyle choices. It also keeps them in touch with health providers as new treatments are developed.

The impact can be dramatic. Even low alcohol use increases the likelihood of HCV patients developing cirrhosis or HCC, and high usage more than doubles those risks. It also brings on these conditions much more quickly than would normally be the case. A recent Scottish study estimated that over one-third of cirrhosis among HCV patients was attributable to the fact that they had been heavy drinkers at some stage in their lives.¹¹ With alcohol abuse commonly found among HCV patients, behaviour change alone, while by no means a solution, could do much to reduce the burden of the disease.

Reaching and caring for patients where they are

If developing-country health systems have to address weaknesses in infection control, developed ones have to face up to their poor

record of being able to find and treat HCV patients, especially current and former PWIDs. Doing so will require innovation as much as money. Professor Ricciardi explains: "Healthcare services people tend to wait for patients to come to them. With those engaging in high-risk behaviour, you have to go there. We need to find new ways of interaction." Dr Bastable, a GP with extensive experience in this area, adds: "What doesn't work is just giving patients an appointment. You have to manage hepatitis C in the context of someone who needs an integrated, multi-agency approach."

Two initiatives from different continents show promising innovation in that direction.

In the Netherlands, researchers set up a website, promoted by a mass media campaign, which provided an interactive questionnaire to identify individuals at risk of HCV. Those judged at risk could then download a letter offering them a free, anonymous blood test, done in a non-clinical setting, for HCV antibodies. Between April 2007 and December 2008, while the project ran, nearly 10,000 individuals completed the questionnaire and 1,480 qualified for the test, of whom 28% chose to take it. Those who tested positive were then offered a HCV RNA test to confirm the diagnosis, and individuals diagnosed with chronic HCV were offered treatment. The project was judged very successful because it was low-cost, had a high take-up rate for such an initiative, and all the newly identified chronic HCV-infected individuals were from hard-to-reach populations.

Freke Zuure from Amsterdam's Public Health Service, who co-ordinated the internet effort, says that it has several advantages specific to HCV beyond low cost. In particular, because of the disease's stigma, "people may not come forward. The web provides an anonymous way to facilitate testing and, because the risk assessment questionnaire can be interactive, it can give personalised advice." Ms Prins, who also worked on the project, adds that the internet is

¹¹ H A Innes *et al*, "Quantifying the fraction of cirrhosis attributable to alcohol among chronic HCV patients: Implications for treatment cost-effectiveness", *Hepatology*, 2012.

where many people are already getting medical information and advice, so it would be natural for them to use such a web-based tool for HCV. The project therefore offered care in an environment where many potential patients were already present and comfortable, and did so in a way that circumvented the effects of stigma.

In Western Australia, health professionals are trying to access remote populations and overcome stigma in a different way. The state is half the size of Europe but sparsely populated. Last decade it instituted a broad HCV prevention and treatment strategy, which included more clinics in rural locations as well as greater training of, and co-operation with, GPs around treatment. But even after these changes, patients still faced long waiting lists to see experts.

Therefore, in 2005, the state modified legislation to create the position of hepatology nurse practitioner (HNP) within the liver service. Unlike a traditional nurse, this practitioner can, within strict clinical protocols, order tests, give diagnoses, prescribe drugs and refer patients to other medical practitioners, as well as monitor treatment and adjust it in light of any side effects. Ms Nazareth, the state's first HNP, explains that the initiative has streamlined care – an important consideration for a population where seeing a healthcare professional can involve substantial travel. "It provides a one-stop shop for the patient, who can get seen and get

medication. It is both time- and cost-effective, because you don't have to see the specialist." It also allows greater contact with the population, especially those who value discretion. The HNP is able to go out into the community rather than rely on patients to come to clinics in public places, which is difficult for some because of the ongoing stigma of HCV.

The results have been positive. Waiting times are down and faster attention to side effects has led to fewer complications, freeing up specialists to concentrate on more difficult cases. A survey of patients found that 98% were satisfied with the HNP service. Best of all, within a year of the creation of the role the number of new patients accessing treatment had doubled from 60 to 120 without an increase in medical personnel. Moreover, a shift to greater use of telemedicine has made care for those in the most rural areas even easier. Since the pilot in Western Australia, a second HNP has been hired there and Queensland and New South Wales have both created such positions.

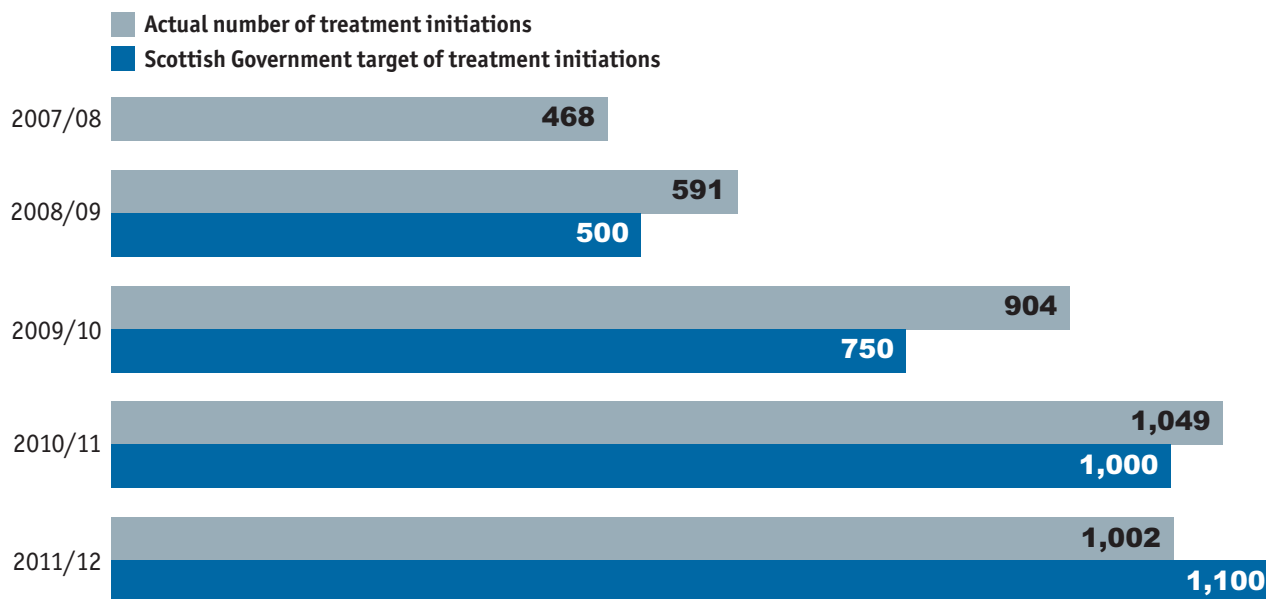
Although very different in many aspects, these Dutch and Australian examples demonstrate the benefits of finding new ways to reach populations which are potentially reluctant to interact with traditional health services and to streamline care in a patient-centred way. On their own, neither of these approaches is a complete solution to engaging with HCV patients, but they both show the kind of thinking that is needed. ■

Case study

Bringing it all together: The Scottish Action Plan

Chart 3

The actual number, and the Scottish Government's target of chronically infected people initiated on hepatitis C antiviral therapy in Scotland for the financial years, 2007/08 - 2011/12



Note. Data for 2011/12 are provisional.

Source: Health Protection Scotland, using data supplied by hepatitis C treatment centres.

Scotland's Hepatitis C Action Plan is often cited as a leading example of good practice. The active phase of the plan, which ran between 2008 and 2011, made significant progress (see chart 3). Between 2007 and 2010 the number of people tested by the four largest Scottish health boards rose from about 34,000 to around 44,000. Meanwhile, the number of diagnoses rose from just over 1,500 in 2007 to more than 2,100 in 2011. Most important, the number of people being treated more than doubled, exceeding plan targets. The slight drop in 2011-12 seems related to a number of patients waiting for the introduction of protease inhibitor-based treatment, promised by the Scottish health authorities for 2013.

At the heart of the Scottish plan was a comprehensive and co-ordinated approach. It had integrated initiatives and goals covering awareness-raising, prevention, diagnosis and treatment, as well as co-ordination. Each local health board had, or was affiliated to, a local treatment and care network, as well as a local prevention network. These were, and still

are, responsible for the implementation of policies, but they also come together in national networks which share best practice. Professor David Goldberg, chair of the Hepatitis C Action Plan governance board from 2008 to 2011, points out that such an overarching plan involving both prevention and treatment is relatively unusual.

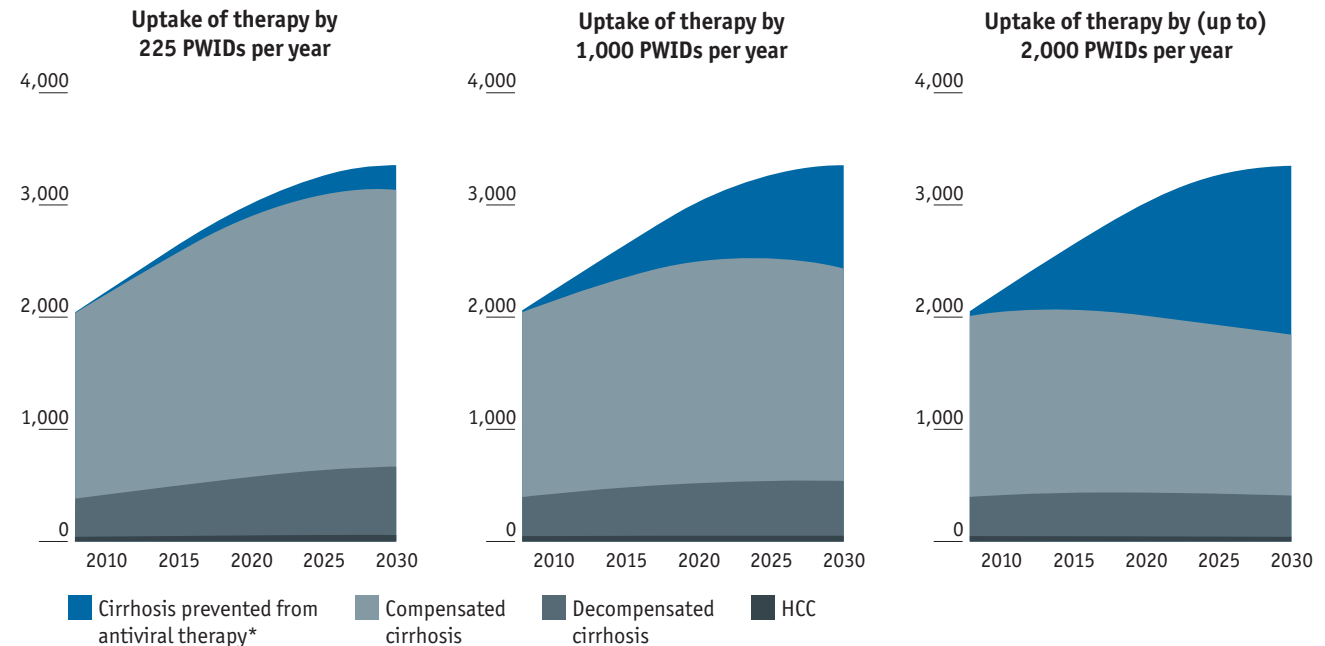
Professor Goldberg believes that a number of factors came together to allow the plan to be launched, including a growing realisation based on epidemiological data that Scotland faced an above-average problem with HCV, heightened awareness among the public and politicians driven by effective activists, good clinical and public health leadership, and the appearance of cost-effective therapies around the start of the decade.

The government was interested, but before acting it required a thought-out strategy. This request proved beneficial. Interested parties spent the next year-and-a-half gathering new information and working in various ways on a detailed

Chart 4

Modelled number of PWIDs with cirrhosis in Scotland by different uptake rates of HCV antiviral therapy, 2008-30

(number of living PWIDs with cirrhosis)



* Excludes those prevented from antiviral therapy prior to 2008.

Source: Health Protection Scotland, 2009.

scheme. These efforts also allowed the development of links with stakeholders, which proved essential to the effective co-ordination of activities later.

According to Professor Goldberg, the keys to success were proper funding – stakeholders had little time for an earlier, poorly funded HCV strategy – as well as co-ordination. He notes: “It was a very complex business, covering the whole of the country, the whole spectrum of service, all the way from educating school children to giving HCV-infected individuals anti-viral treatments. It was essential that there was a co-ordinated approach.” (see chart 4). Accordingly, while most of the funding went to prevention and treatment, a sizeable proportion was allocated to co-ordination and further information-gathering to better inform policy. Also very important, says Professor Goldberg, were transparency and accountability. The plan had built in clear goals, which it by and large achieved.

Much work remains to be done. Health Protection Scotland estimates that approximately half of those with HCV remain undiagnosed. Rather than simply being renewed in 2011, efforts to combat the disease have evolved further. They are being integrated into the Sexual Health and Blood Borne Virus Framework, which takes a comprehensive approach to dealing with hepatitis B and C, as well as HIV. This makes strategic sense, given the overlap in at-risk populations and potential means of transmission. Specific HCV prevention initiatives, including general education and a new peer-to-peer counselling initiative for PWIDs, will continue, and Professor Goldberg and his team will continue to monitor the effectiveness of these. Meanwhile, the ongoing national networks for treatment and prevention are developing indicators to measure the quality of HCV care. Perhaps the longest-lasting legacy of the action plan will be that it has helped to make the prevention and treatment of HCV a mainstream healthcare matter.

Conclusion

The silent pandemic is already starting to make a noise, which will grow much louder in the years to come. Even developed countries with a relatively low HCV incidence face a wave of liver disease with a potentially huge human cost. Given the number of people affected, the economic impact is also likely to be substantial. Currently, though, saying anything more concrete is difficult because impeding efforts to address HCV are a lack of knowledge – sometimes basic – about the virus and its prevalence, problematic treatment options, the difficulties of treating PWIDs, and the stigma attached to the disease, let alone broader issues, such as its total cost to society.

Whatever the obstacles, healthcare policymakers have no choice but to confront the issue more aggressively. Each country faces a different set of circumstances, but there are some common elements all should think about.

- **Adopting a comprehensive approach:** The various difficulties involved in addressing HCV require a co-ordinated strategy. Fixing just one set of problems may only reveal other difficulties. Initiatives such as the recently launched Euro Hepatitis Index, which rates and compares the hepatitis care performance of 30 European nations, can help countries see where they need to make improvements.

- **Obtaining good data:** Even among developed countries with sufficient resources, too few have good information on the extent of the challenge HCV represents for healthcare systems. Without it, devising policies appropriate to local conditions – such as initiatives designed to reach the entire population and raise health system standards where medical transmission is a major issue, or measures focused on reaching high risk groups such as PWIDs where they are the main locus of infection – may not be possible.

- **Awareness:** Although good public information may not stop all high-risk behaviour, its absence will leave those at risk much more vulnerable. Moreover, understanding of the disease may help overcome the stigma that impedes treatment.

- **Prevention:** Ultimately, HCV is an entirely preventable disease. Some awareness-raising may on its own reduce its incidence, but most of the focus of prevention worldwide still needs to be on healthcare systems, which are themselves too often the means through which the disease spreads. Secondary prevention is also crucial, both in parts of the world where treatment is unaffordable and for patients who do not respond to drugs.

● How to reach patients most in need:

Those with HCV may either have forgotten the events which infected them, such as blood transfusions decades earlier, or may wish to forget, such as experiments with drugs. Meanwhile, PWIDs and health systems have a strained relationship. Finding innovative ways to reach out to patients, rather than relying on traditional healthcare structures, will be essential if those needing treatment are to receive it before end-stage conditions develop.

Above all, in considering how to address HCV effectively, policymakers should remember that these changes can bring wider benefits and are often best integrated into wider initiatives. At a basic level, early treatment for HCV will greatly

diminish the level of cirrhosis and primary liver cancer in many countries. Moreover, the same steps which help prevent the spread of the virus – whether improvements in health system protocols or efforts directed at reducing transmission among PWIDs – help reduce the transmission of other diseases as well, such as hepatitis B or HIV, and new emergent diseases. More patient-centred care protocols are applicable for a host of areas: nurse practitioners, for example, are effective in providing care for a range of chronic diseases. Efforts to combat HCV, then, will not only help countries to deal with a looming threat, but they will also leave healthcare systems stronger in the face of other challenges.

The following provide helpful information on HCV and issues surrounding it:

-World Health Organisation Hepatitis Page
<http://www.who.int/topics/hepatitis/en/>

-Centres for Disease Control and Prevention Viral Hepatitis Home Page
<http://www.cdc.gov/hepatitis/>

-European Centre for Disease Prevention and Control Hepatitis C Page
http://www.ecdc.europa.eu/en/healthtopics/hepatitis_C/Pages/index.aspx

-World Hepatitis Alliance
<http://www.worldhepatitisalliance.org/Home.aspx>

-Coalition for the Eradication of Viral Hepatitis in Asia and the Pacific
<http://www.cevhap.org/index.php/en/>

-Euro Hepatitis Index
<http://www.hep-index.eu/index-map.html>

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