Health Protection Scotland

The Scottish Government

# The Scottish Government

# Hepatitis C Treatment & Therapies

# Group Report

## Revised February 2017

**Revisions**

**(See Strategy p7, Prioritisation for Therapy p8 and**

**Treatment Targets p11)**

## Hepatitis C Treatment and Therapies Group

With the imminent availability of highly effective, safe and easy to administer therapies for Hepatitis C infection, the Scottish Government asked HPS in late 2013 to lead a group, accountable to the Minister for Public Health, to generate a set of guiding principles for service providers and users to ensure that Scotland maintained its global leadership and investment in Hepatitis C service provision and secured the greatest benefit from these outstanding therapeutic advances.

The membership of the group is listed in appendix 1. The group convened on five occasions during 2014-15. Proposed principles were shared with approximately 150 Hepatitis C service users and providers at the Royal College of Physicians & Surgeons in Glasgow in September 2014. This consultation, together with feedback from Scotland's National Sexual Health and Bloodborne Virus Advisory Committee (chaired by the Minister for Public Health), the Sexual Health and Bloodborne Virus Executive Leads, the Viral Hepatitis Clinical Leads Group and a number of NHS Board medical directors, informed the development of the principles.

## Background

### *Hepatitis C: Key facts*

*General*

- Between 100 and 200 million people worldwide are infected with Hepatitis C. In the EU the figure is around 6 million; in the UK 214,000 and in Scotland 37,000.
- In resource-rich countries, injecting drug use is the principal route of Hepatitis C transmission while in resource-poor ones, sub-optimal infection control associated with healthcare procedures is the main cause.
- 8-16% of people infected with Hepatitis C for 20 years have cirrhosis of the liver. Disease progression is accelerated by, in particular, excessive alcohol consumption and HIV co-infection.
- Hepatitis C's role in causing serious illness and death from cancer or liver failure is well recognised but infection is also associated with non-liver related disease and psycho-social morbidity.
- Prevention of Hepatitis C is dependent on interrupting routes of transmission. A vaccine is unavailable and is unlikely to become available in the near future.
- Diagnosis of Hepatitis C is imperative to allow people to be assessed for treatment but also provides an opportunity to drive home behavioural change messages in terms of preventing onward transmission of infection (especially among PWID) and reducing the risk of disease progression (e.g. warnings about the dangers of excessive alcohol consumption).

- The efficacy of antiviral treatments which eradicate HCV infection has increased dramatically over the last 20 years. (Pawlotsky et al)

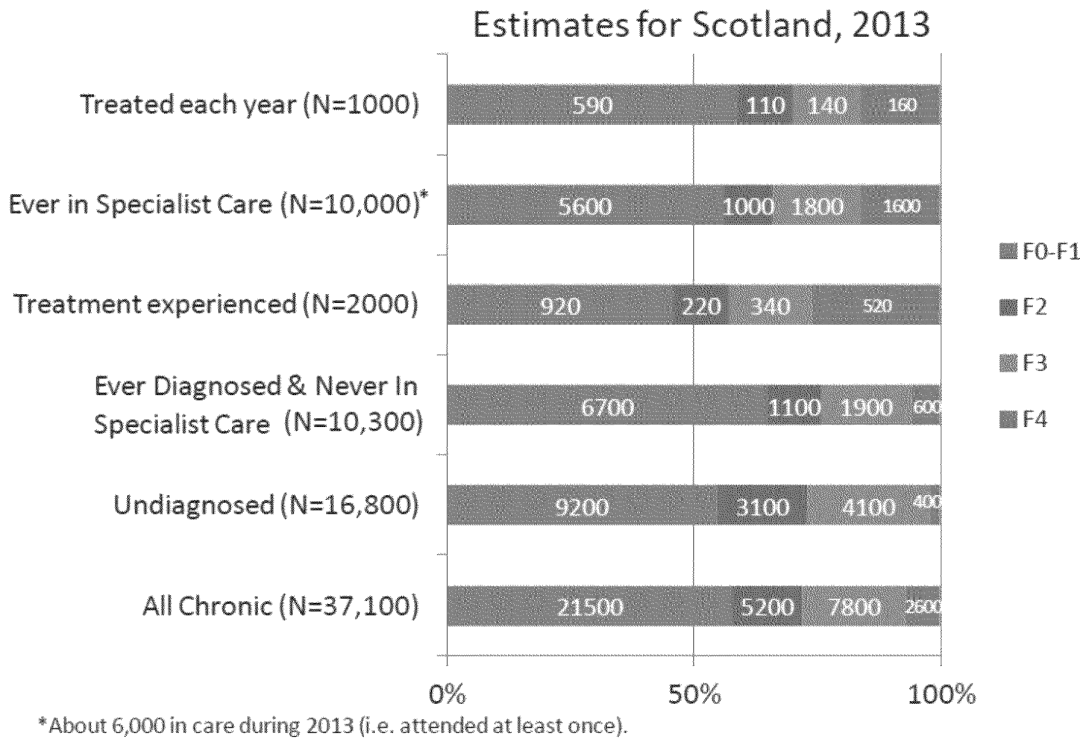
| Year | Treatment | Sustained Viral Response % (Genotype 1)* |
|---|---|---|
| 1994 | Interferon | 7-11 |
| 1998 | Interferon + Ribavirin | 28-31 |
| 2001 | Pegylated Interferon + Ribavirin | 42-46<br>(note 70-80% for G3) |
| 2011 | Pegylated Interferon + Ribavirin + 1st Generation Direct Acting Antivirals | 67-75 |
| 2014/15 | Interferon-free Direct Acting Antiviral Therapy (especially for genotype 1 but increasingly for other genotypes) | 93-100 |

***Clinical Trial Data**

- The new all-oral Direct Acting Antiviral therapeutic regimes are safe, relatively short duration and highly effective. Those approved by the Scotland Medicines Consortium are deemed cost-effective in general terms. It should be acknowledged that studies have demonstrated that treating people with no or mild liver disease are not cost-effective (at costs greater than £12 - 18,000/course) when compared to the alternative approach of waiting till moderate disease develops before administering therapy. (Leidner et al)

*Scotland*

- *Estimates for Scotland's HCV Chronic Population by Disease Stage:*




*About 6,000 in care during 2013 (i.e. attended at least once).

***Scottish Government Response to Hepatitis C***

2006: Launch of Scotland's Hepatitis C Action Plan Phase I: Development of a case for investment in Hepatitis C service provision.

2008: Launch of Scotland's Hepatitis C Action Plan Phase II: Investment of £43 million for Hepatitis C prevention, diagnosis and care services during 2008-11.[Scottish Government, 2008]

2011: Launch of Scotland's Sexual Health & Bloodborne Virus Framework (Phase I) incorporating continued investment in Hepatitis C services and adopting an outcome indicator approach to monitoring the impact of the investment.

2014: The establishment of Scotland's HCV Treatment & Therapies Group to generate guiding principles for service providers and users in the era of new highly effective antiviral therapies.

2015 Launch of Scotland's Sexual Health & Bloodborne Virus Framework (Phase II) incorporating continued Hepatitis C service investment, the employment of which is to be steered by the principles generated by the Hepatitis C Treatment & Therapies Group.

***Impact of Scotland's Response to Hepatitis C and the Challenges Ahead*** (Hutchison et al; PHE)

During 2006/7-13:

- An estimated 50% reduction in the annual number of new HCV infections from 1,500 to 750.
- An increase in the proportion of the total estimated infected population who are diagnosed, from 38% to 55%.
- A two and a half fold increase in the number of new initiates onto antiviral therapy annually from 450 to approximately 1100.
- An overall reduction in the estimated number of people infected from 38,000 to 37,000; the figure, likely, would have been 42,000 if there had been no response.

However, very considerable challenges exist:

- The annual number of new presentations of HCV related liver failure/HCC increased from 138 to 180; approximately 50% occurred in people who had been HCV diagnosed within five years of presentation.
- 16,800 infected people, a high proportion of whom are older, former PWID with moderate or severe liver disease, remain undiagnosed.
- Most (75%) diagnosed HCV infected people are either not now, or have never been, in specialist care.
- Nearly 11,000 infected people have either cirrhosis of the liver (stage F4) or are in the pre-cirrhotic stage (F3) and, thus, are in urgent need of therapy; most are undiagnosed or are not in specialist care.
- Optimal therapies, while highly cost-effective for those with F3/F4 liver disease, are costly, particularly in the context of large numbers of such individuals being eligible for therapy now.

See Appendix 2 for a report on the impact of Scotland's Hepatitis C Response (Diagnosis & Treatment perspective) Hutchinson et al.

***Why Scotland Is Ready to Take Its Hepatitis C Response to the Next Level***

The Interferon-based therapies with their sub-optimal cure rates, long duration and adverse effects, have restricted the impact of Scotland's response to Hepatitis C. However, with the

availability of highly effective, short duration, safe and easy to administer treatment, Scotland is in an outstanding position to take advantage of this remarkable therapeutic breakthrough.

The Action Plan has established an infrastructure which is the envy of the world - one which comprises a highly trained workforce, with specialist nurses at its heart, and a web of multi-disciplinary/ multi-agency local and national networks to ensure an integrated and efficient approach to service development and operation throughout the country.

Accordingly, Scotland is cited by WHO and WHA (World Hepatitis Alliance - the umbrella organisation for Hepatitis patient representative groups throughout the world) as a model country in terms of concerted national action and response to the Hepatitis C challenge.

## Hepatitis C Treatment and Therapies Group: The Principles

### *Strategy*

The key aim of investing in Hepatitis C services in Scotland is to reduce severe morbidity and mortality caused by infection. As predicted, the numbers of cases of Hepatitis C related liver failure and hepatocellular carcinoma (HCC) have risen year on year over the last two decades to approximately 170 and 30, respectively, in 2013; with the availability of highly effective direct acting antiviral therapies which can prevent liver disease progression even in those who already have advanced disease, there is the potential to effect a dramatic reduction in the incidence of such severe morbidity and mortality in a similar way to that achieved with AIDS cases and deaths following the introduction of HIV combination antiviral therapy in 1996.

- **Scotland should reduce the number of people who develop HCV related liver failure, hepatocellular carcinoma (HCC) and the number of people who die from HCV related disease, and thus make progress towards the elimination of Hepatitis C as a serious public health concern. This strategy is consistent with WHO's strategy on Hepatitis, May 2016, and the Glasgow Declaration on Hepatitis, World Hepatitis Summit, September 2015.**

### *Therapy: Decision Making* (Innes et al (4 papers) and Huang et al)

It is essential that principles regarding decision making around the administration of Hepatitis C antiviral therapy should be equitable, made by both patient and attending clinician, and be driven principally by the patient's need and the effectiveness and safety of available drugs. How a patient acquires his/ her Hepatitis C infection should never influence therapy decision making.

Compelling evidence, based on Scottish and international data, indicates that the liver disease stage of the Hepatitis C infected patient strongly determines the short to medium term risk of developing severe HCV related liver disease; those with no or mild disease, for example, are very unlikely to progress to severe disease for many years. Nevertheless there is also compelling evidence that Hepatitis C can cause serious non-liver related conditions and can have major psycho-social effects even in the presence of mild, or absence of, liver disease.

In the context of this evidence and the current high cost of the optimal therapies, prioritisation of such treatment - in terms of its timing - should be given to people at risk (imminently or in the next few years) of developing severe life threatening or seriously debilitating liver and/or non-liver Hepatitis C related disease. This approach, coupled with

the rigorous clinical monitoring of people not being offered therapy, is consistent with European Association for the Study of Liver (EASL) 2015 guidelines on the management of Hepatitis C [(EASL)].

It must be emphasised, however, that the ultimate goal should be the offer, as soon as practically possible, of therapy to all people with chronic Hepatitis C. Early treatment is likely to convey population benefits in terms of the prevention of onward transmission of infection (particularly among active PWID) and reduces the risk of infected people - lost to clinical monitoring (a common occurrence among those who have ever injected drugs) - presenting years later "out of the blue" with end stage liver disease.

The prioritisation of the timing of optimal therapy - in both absolute and relative terms - will be reviewed frequently.

- **Scotland's approach to HCV therapy should be consistent with the ambitions of the NHS Scotland Healthcare Quality Strategy: "the most appropriate treatments, interventions, support and services will be provided at the right time to everyone who will benefit, with no wasteful or harmful variation".**
- **Therapeutic decision making should be determined principally by the potential benefits and risks of therapy as judged by both the patient and the attending clinician.**
- **HCV infected patients should be offered optimal SMC approved therapies judged by effectiveness (SVR at least 90%) and adverse effect profile (minimal); thereafter, the cost of therapy becomes an important consideration.**
- **All HCV infected individuals are eligible for treatment with optimal SMC accepted regimens which have an SVR of at least 90%. However, in view of the current high cost of these regimens and the high number of individuals infected in Scotland*, priority, in terms of the timing of treatment, should be initially given to those patients with the highest need**. Because the availability of new treatments and their pricing is changing rapidly, this position will be reviewed in an ongoing way.**

  ***Est. 37,000 (20,000 diagnosed and 17,000 undiagnosed)**
  ****As a minimum:**
  **- patients with F2-F4 hepatic fibrosis;**
  **- and/or patients with severe extra-hepatic manifestations of hepatitis C;**
  **- and/or patients with significant psychosocial morbidity as a consequence of hepatitis C**
  **- and/or patients with HIV/HCV co-infection**
  **- and/or patients who have had a liver transplant**

***Therapy: Delivery***

Scotland's Hepatitis C Action Plan achieved a rapid scale-up of therapy from 450 to approximately 1,100 initiates between 2007 and 2010; thereafter the numbers plateaued. The principal barriers to getting people treated have been sub-optimal effectiveness, adverse effects and the duration of Interferon-based therapeutic regimens. A further barrier has been the practice, in most instances for logistical reasons, administering Interferon containing therapy in the hospital setting. With the availability of easy to administer, safe, highly effective, short duration therapies, it is now practical to deliver treatment in community settings (e.g. general practice and prison).

- **Scotland should aim to deliver HCV therapy for most infected people in "community settings" (including prisons); such an approach must be overseen by the NHS Board Managed Care Network responsible for HCV.**
- **This strategic change in service delivery should not preclude certain people receiving all or some of their management in a secondary care setting if their clinical status merits this.**

***Diagnosis***

Since the implementation of Scotland's Hepatitis C Action Plan, incorporating several initiatives to improve case finding, much has been achieved. However, with an estimated 45% of infected people remaining undiagnosed and thousands of already diagnosed people (a large proportion with advanced disease) never having been or not now in specialist care, the diagnostic and "re-diagnostic" challenge is very considerable.

Prioritising initiatives to (re) identify and then assess for treatment individuals likely to have moderate to severe disease - i.e. infected people who are older and /or have a history of excessive alcohol consumption - is essential. Data, generated during the Action Plan period, indicate that the (re) identification of such individuals can be achieved in the general practice setting through systems which flag up indicators of infection risk (especially those pointing to previous injecting drug use) or previous Hepatitis C diagnosis.

Such prioritisation should not diminish the importance of diagnosing everyone who has chronic Hepatitis C but it should be recognised that making someone aware of their Hepatitis C positive status - which, per se, conveys a reduction in quality of life - must be followed up with assessment for, and then (where appropriate) administration of, optimal treatment.

While a targeted risk factor-based approach is likely to result in the diagnosis of the great majority of infected individuals it will not permit the detection of a small but appreciable

number of people; such individuals may have acquired their infection through (i) sub-optimal infection control measures associated with health care procedures within or outwith the UK, (ii) a risk event many years before for which they have no recall or (iii) birth to an HCV infected mother. Accordingly, the cost-effectiveness of restricted (e.g. within an age range/birth cohort or high Hepatitis C prevalence geographical area) general population screening approaches should be evaluated.

- **Hepatitis C Managed Care Networks should identify and prioritise initiatives to diagnose or re-diagnose those most likely to (i) have moderate to severe disease, or (ii) progress rapidly to severe disease.**
- **To identify undiagnosed individuals, a population–based case finding approach, focusing on people belonging to a certain age group (to be agreed) and living in higher HCV prevalence areas, should be considered if deemed cost effective; this should complement existing initiatives involving a targeted, risk factor based approach.**
- **An intensive effort to re-diagnose individuals lost to, or never in, specialist care - particularly those older and thus more likely to have advanced disease - should be made.**

***Monitoring and Targets***

The success of Scotland's Hepatitis C Action Plan has been achieved in part through the ability of service providers to monitor performance through a range of outcome indicators including numbers of people diagnosed, getting into specialist care, undergoing treatment and eliminating their infection. Accordingly, it is essential that outcome indicator data continue to be collected and made available to NHS Board providers through Scotland's Sexual Health & Bloodborne Virus Framework Data Portal, populated and hosted by Health Protection Scotland.

A single Scottish Government target - the number of people initiated onto antiviral therapy (changing year on year) - has been in operation since the launch of the Action Plan Phase II in 2008 when substantial additional earmarked funding was made available to NHS Boards. Generally, targets have been met and stakeholders, unanimously, support the continuation of the treatment initiation target.

An additional target is proposed - the number of infected people presenting with liver failure and/or HCC. The context for this new target is (i) the year on year increase in the number of cases of Hepatitis C related liver failure and/or HCC, (ii) the potential for the new direct antiviral therapies to prevent people at all stages of HCV disease progressing to these end points and (iii) the need for the Hepatitis C workforce to prioritise the identification and

offer of therapy to infected people with moderate to severe disease who are diagnosed but have been lost to/ never been in specialist care and those who are still undiagnosed.

The principal goal of the Scottish Government's commitment to Hepatitis C service development is the prevention of serious morbidity and mortality. This new target will complement the treatment initiate one and, effectively, will be aligned to it.

Modelling work undertaken by GCU/HPS estimates that a minimum of 1500 treatment initiates per year during 2015-2020 is required to stand a chance of reducing the number of new liver failure/ cancer presentations from the current level of nearly 200 to 50 by 2020.

- **Scotland should continue to assess the impact of its investment in HCV infection and disease prevention through the monitoring of key outcome indicators.**
- **Scottish Government HCV targets are as follows:**
  - **The annual number of people initiated onto antiviral therapy: 1500/year, during 2016/17, rising to 1800 during 2017/18; of the 1800, 1500, or as near to that figure as possible, should belong to the F2-F4 liver fibrosis category at time of treatment, to ensure that the 2020 target associated with morbidity reduction (as below) is met.**
  - **The annual number of people developing HCV-related liver failure and/or HCC: 74% reduction from 194 in 2013 to 50 in 2020.**

  **Note: these are all-Scotland targets; for NHS Boards targets will be set according to population based criteria.**

***Research***

The research dividend of Scotland's Hepatitis C Action Plan and investment has been spectacular. Reports published in the world's leading liver disease journals have not only informed and evaluated policy and practice in Scotland but internationally. Three priority areas of research have been identified.

In the context of the scale and potential cost of managing Hepatitis C infection and disease in Scotland, further health economic work focussing on the cost-effectiveness of different models of diagnosis, assessment, treatment and care, needs to be undertaken.

Much ground-breaking work has been done to demonstrate the contribution of excessive alcohol consumption to Hepatitis C disease development and antiviral treatment impact; further work is required to (i) understand better the drivers of and (ii) evaluate interventions to combat such consumption in individuals know to be Hepatitis C infected.

The concept of treating infected people (especially people continuing to inject drugs) who are at a high risk of transmitting infection - to secure a population as well as an individual benefit - stemmed from Scotland's Hepatitis C Action Plan and was progressed through a collaboration with a statistical modelling team at Bristol University (Martin et al). The concept, now internationally recognised, has evolved into an EASL 2015 Hepatitis C treatment policy recommendation. The effectiveness of this intervention, however, is still to be evaluated. Accordingly, it is proposed that Scotland continues its leadership role in this sphere by determining whether or not treating a population of active PWID with high HCV prevalence can reduce it to a very low level (less than 10%) and sustain that reduction.

**Research should focus on:**

- **Cost, effectiveness and cost-effectiveness of different models of diagnosing, assessing and delivering of therapy to HCV infected people**
- **Assessing the drivers and impact of alcohol consumption on HCV case management and evaluating interventions to address the adverse impact of such consumption**
- **Evaluating the concept of the administration of antiviral treatment to people who actively inject drugs (PWID) to prevent onward transmission of infection.**

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## Appendix 1: Membership of the Hepatitis C Treatment & Therapies Group

| Member | Organisation | Role/ Representation |
|---|---|---|
| Professor David Goldberg (Chair) | NHS NSS Health Protection Scotland | Consultant Epidemiologist & Chair of National Monitoring & Assurance Group (NMAG), SHBBV Framework |
| Mr Gareth Brown | Scottish Government | Head of Heath Protection |
| Dr Nicola Steedman | Scottish Government | Senior Medical Officer |
| Ms Marjorie Marshall | Scottish Government | Economic Advisor<br>Public Health Analytical Services, Heath & Social Care Directorate |
| Professor Sharon Hutchinson | Glasgow Caledonian University | Professor of Epidemiology and Population Health |
| Mr Hamish Innes | Glasgow Caledonian University | Epidemiologist |
| Ms Lindsay McClure | National Procurement | Pharmaceutical Advisor |
| Ms Ainsley Ritchie | National Procurement | Senior Commodity Manager |
| Mr Andrew Stewart | National Procurement | Pharmaceutical Advisor (replaced Ainsley Ritchie at final meeting on 31/3/15) |
| Dr Ray Fox | NHS Greater Glasgow & Clyde | Consultant in Infectious Diseases & Co-Chair of the National Viral Hepatitis Clinical Leads & MCN Coordinators Network |
| Dr Ken Oates | NHS Highland | Consultant in Public Health Medicine |
| Dr John Logan | NHS Lanarkshire | Consultant in Public Health Medicine |
| Dr Ewen Stewart | NHS Lothian | General Practitioner & Clinical Lead Lothian Hepatitis MCN |
| Dr John Dillon | NHS Tayside | Consultant Gastroenterologist and Hepatologist & Co-Chair of the National Viral Hepatitis Clinical Leads & MCN Coordinators Network |
| Dr Brian Kidd | NHS Tayside | Clinical Senior Lecturer in Addiction Psychiatry |
| Mr Charles Gore | Hepatitis C Trust | Chief Executive, Hepatitis C Trust. |
| Mr Leon Wylie | Hepatitis Scotland | Lead Officer, Hepatitis Scotland |
| Ms Ailsa Brown | Health Improvement Scotland | Lead Health Economist, Scottish Medicines Consortium |
| Ms Roberta James | Health Improvement Scotland | SIGN Programme Lead, Scottish Intercollegiate Guidelines Network |

**Appendix 2: Report on the Impact of Scotland's Hepatitis C Response (Diagnosis & Treatment Perspective)** [Hutchison et al IJDP 2015 (in press)].

*(This paper will be incorporated in the report via Appendix 2, subject to approval from the Journal).*