International Journal of Drug Policy 26 (2015) 1041–1049

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Policy analysis

Expansion of HCV treatment access to people who have injected drugs through effective translation of research into public health policy: Scotland's experience

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ARTICLE INFO

Article history:
Received 2 February 2015
Received in revised form 11 May 2015
Accepted 31 May 2015

Keywords:
HCV
PWID
Public health policy

ABSTRACT

Seven years have elapsed since the Scottish Government launched its Hepatitis C Action Plan – a Plan to improve services to prevent transmission of infection, particularly among people who inject drugs (PWID), identify those infected and ensure those infected receive optimal treatment. The Plan was underpinned by industrial scale funding (around £100 million, in addition to the general NHS funding, will have been invested by 2015), and a web of accountable national and local multi-disciplinary multi-agency networks responsible for the planning, development and delivery of services. Initiatives ranged from the introduction of testing in specialist drug services through finger-prick blood sampling by non-clinical staff, to the setting of government targets to ensure rapid scale-up of antiviral therapy. The Plan was informed by comprehensive national monitoring systems, indicating the extent of the problem not just in terms of numbers infected, diagnosed and treated but also the more penetrative data on the number advancing to end-stage liver disease and death, and also through compelling modelling work demonstrating the potential beneficial impact of scaling-up therapy and the mounting cost of not acting. Achievements include around 50% increase in the proportion of the infected population diagnosed (38% to 55%); a sustained near two-and-a-half fold increase in the annual number of people initiated onto therapy (470 to 1050) with more pronounced increases among PWID (300 to 840) and prisoners (20 to 140); and reversing of an upward trend in the overall number of people living with chronic infection. The Action Plan has demonstrated that a Government-backed, coordinated and invested approach can transform services and rapidly improve the lives of thousands. Cited as "an impressive example of a national strategy" by the Global Commission on Drug Policy, the Scottish Plan has also provided fundamental insights of international relevance into the management of HCV among PWID.

Introduction

In September 2006, the Scottish Government launched its Action Plan on Hepatitis C (HCV), which included three aims: (i) to prevent the spread of infection, particularly among people who inject drugs (PWID); (ii) to diagnose HCV-infected people, particularly those who would most benefit from treatment; and (iii) to ensure that those infected receive optimal treatment, care and support (Scottish Executive, 2006). The first phase of the Plan, involved gathering evidence from a combination of surveillance and research initiatives to inform proposals for the development of HCV services (described below); limited additional funding (£2 million per annum) was thus provided during this initial period to

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http://dx.doi.org/10.1016/j.drugpo.2015.05.019

support service development. The second phase (Scottish Government, 2008), launched in May 2008, saw serious commitment from Scottish Government to deliver actions designed to dramatically improve prevention, diagnosis and treatment services throughout the country; by 2015, around £100 million will have been invested in HCV, additional to that of the general National Health Service (NHS) budget, in Scotland (a country with a publicly funded healthcare system). Equating to more than £20 per capita over the period, the Plan represents one of the most financed and evidenced national policies on HCV globally. This article provides a review of the Action Plan in respect of the key evidence which informed actions, the principles and characteristics underpinning its implementation, the evidence we now have of the progress made in diagnosing and treating infection and in preventing severe liver morbidity (SLM) particularly among PWID, and the challenges and opportunities which lie ahead.

Key evidence gathered during Phase I of the Action Plan

Fig. 1 provides a summary of the HCV epidemiological landscape in Scotland during 2006, at the start of the Action Plan. An estimated 38,000 Scots (0.9% of the adult population) were living with chronic HCV (i.e. RNA positive); a further 13,000 will have been infected in the past but have since cleared their HCV either spontaneously (in the main) or through therapy. Of those chronically infected, around 90% had acquired their infection through injecting drug use, the majority (>60%) remained undiagnosed, less than 10% had attended specialist care and only 1% had been initiated on antiviral therapy during 2006 (Hutchinson, Roy, et al., 2006; Hutchinson et al., 2012; McDonald, Hutchinson, Schnier, McLeod, & Goldberg, 2014; McDonald, Innes, Hayes, et al., 2014). Serious clinical consequences of chronic HCV infection were growing rapidly: the annual number newly hospitalized with HCV-related decompensated cirrhosis (liver failure) had more than doubled and the associated bed-days more than tripled between 1996 and 2005 (McDonald, Hutchinson, & Bird, 2010).

Characterizing the topography of this landscape relied on a number of monitoring systems, without which the evidence for the Action Plan could not have been generated, including: a national HCV diagnosis database, providing data on the numbers diagnosed (Hutchinson, Roy, et al., 2006; Shaw et al., 2003); a national HCV clinical database, providing data on the numbers attending specialist care and being treated (Innes et al., 2012; McDonald, Innes, Hayes, et al., 2014); and record-linkage of these HCV databases with other national hospital and deaths registers, providing data on the numbers advancing to end-stage disease and death (McDonald et al., 2008, 2009, 2010; Palmateer, Hutchinson, McLeod, Codere, & Goldberg, 2007).

Modelling work, synthesizing data from these monitoring systems, further estimated that over 2000 HCV-infected people in Scotland (involving 1900 people who had *ever* injected drugs) were living with cirrhosis in 2005, and the annual number developing decompensated cirrhosis was projected to double between 2000 and 2020 unless treatment rates were scaled-up considerably (Hutchinson, Bird, & Goldberg, 2005). The annual health service cost of managing chronic disease (excluding HCV antiviral therapy costs) among people who had *ever* injected drugs was estimated to double between 2008 (£9.9 million) and 2030 (£20.2 million), and total £362 million during 2008–2030. Uptake of antiviral therapy (with pegylated interferon and ribavirin) needed to increase to 2000 per year, to curb the rising trend in the prevalence of cirrhosis and incidence of decompensated cirrhosis (see Figs. 2 and 3). If 2000 persons per year received HCV antiviral therapy over two decades, an estimated 5200 cases of cirrhosis and 2700 cases of decompensated cirrhosis could be prevented in the future.

On the basis of the above evidence, the key actions within the Phase II Action Plan to address these issues (see Table 1) included local NHS Boards (of which there are fourteen in Scotland, each with responsibility for provision of healthcare in their respective areas) developing services to: improve HCV testing and referral activities, particularly by GPs and other community setting practitioners, and increase the numbers of persons undergoing therapy in Scotland each year in line with Government targets.

Hallmarks of the Action Plan

The Phase II Plan was launched by Scotland's Health Minister, who described it "as an example of best practice in public policy development". It had a number of principles and characteristics worthy of mention:

(I) *Robust evidence base*: As described above, the Plan was developed on the basis of robust evidence, generated through comprehensive national monitoring systems which quantified the scale and severity of the problem, and compelling modeling work which demonstrated the potential beneficial

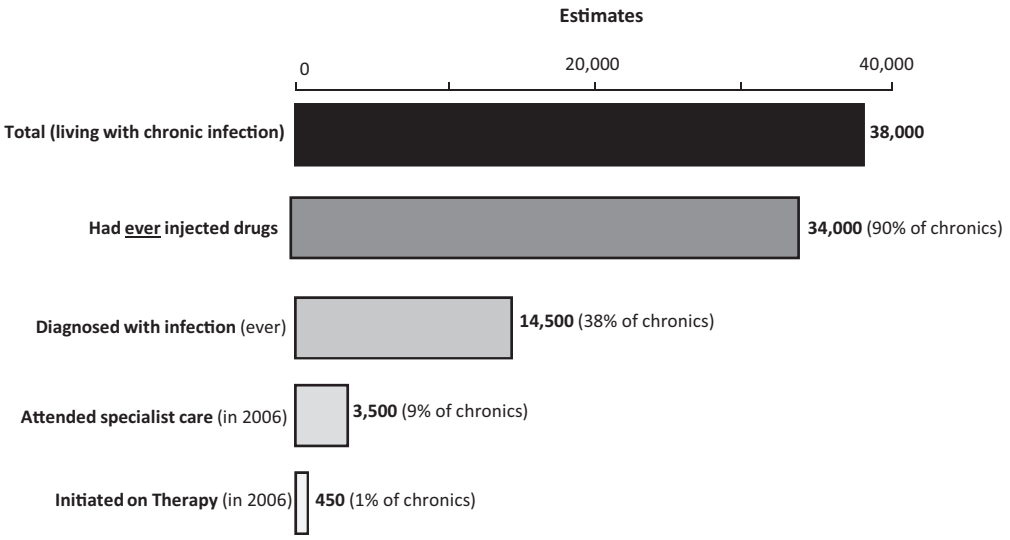

Fig. 1. Estimates of the number of people living with chronic HCV infection (i.e. HCV RNA positive) in Scotland during 2006, at the start of Scotland's Hepatitis C Action Plan.

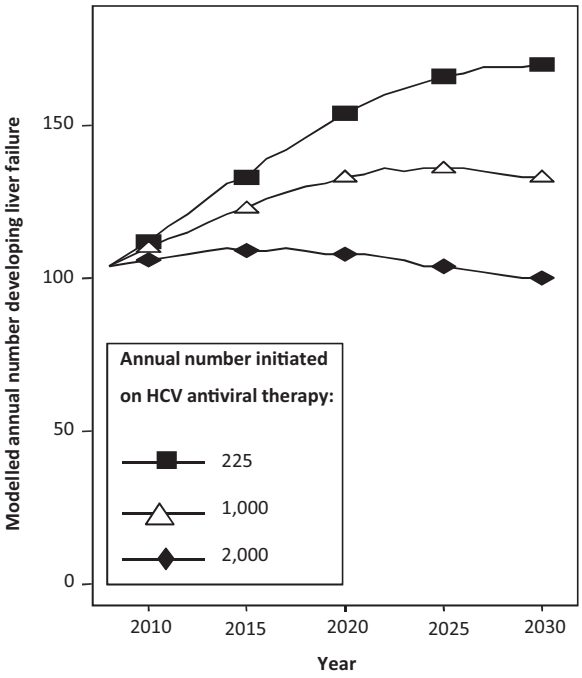

Fig. 2. Modelled incident number of chronic HCV infected people, who had *ever* injected drugs, in Scotland developing decompensated cirrhosis (liver failure) each year according to different uptake rates of HCV antiviral therapy during 2008–2030. Adapted from Hutchinson et al., 2005.

impact of scaling-up therapy and the mounting cost of not acting. Further, HCV antiviral therapy (with pegylated interferon and ribavirin) had been shown to be highly cost-effective (NICE, 2006). While this evidence relates to Scotland, much of it will be cross-transferable to other countries, particularly those with injecting drug use driven HCV epidemics.

(II) *High-level actions and extensive consultation process*: The Phase II Plan included around 30 actions geared towards developing and improving services (Scottish Government, 2008). Dedicated working groups – established during Phase I – were responsible for reviewing the evidence and translating it into proposed key issues and actions. These proposals were shared extensively, including at a consultation event held at the Royal College of Physicians of Edinburgh where nearly 200 stakeholders provided their approval through a digital voting system. The actions were high-level in nature, allowing NHS Boards the freedom to develop services in the context of existing arrangements and epidemiology of infection in their area.

(III) *Strong governance and clear accountability*: The Plan aimed to put in place mechanisms to ensure better accountability of services, and to raise awareness of HCV among those who are responsible for the planning and delivery of services in NHS boards, local authorities, community health partnerships and drug and alcohol action teams. The Plan mostly concerned the development of services by NHS Boards and other organisations, all of which received funding for this purpose. Accordingly, these lead organisations were directly accountable to the Government. To facilitate and ensure this process was consistent and managed well, a project management approach was employed in Phase II. A governance board, comprising representatives from lead organisations, and advisory board, involving independent experts in the field, was established to review progress on, and advise on issues concerning, Action Plan delivery.

(IV) *Leadership and co-ordination*: Nationally, Health Protection Scotland (the organisation which coordinates, supports and advises on health protection activities, including monitoring of health hazards, across the country) was responsible for co-ordinating the Action Plan; this involved presiding over the governance board during Phase II, establishing national networks to support other lead organisations delivering different aspects of the Plan, monitoring progress and performance to help ensure the Plan was delivered in a timely way, and communicating progress to, and seeking feedback from, stakeholders. NHS Boards, through their appointed Hepatitis C Executive Leads (mostly Directors of

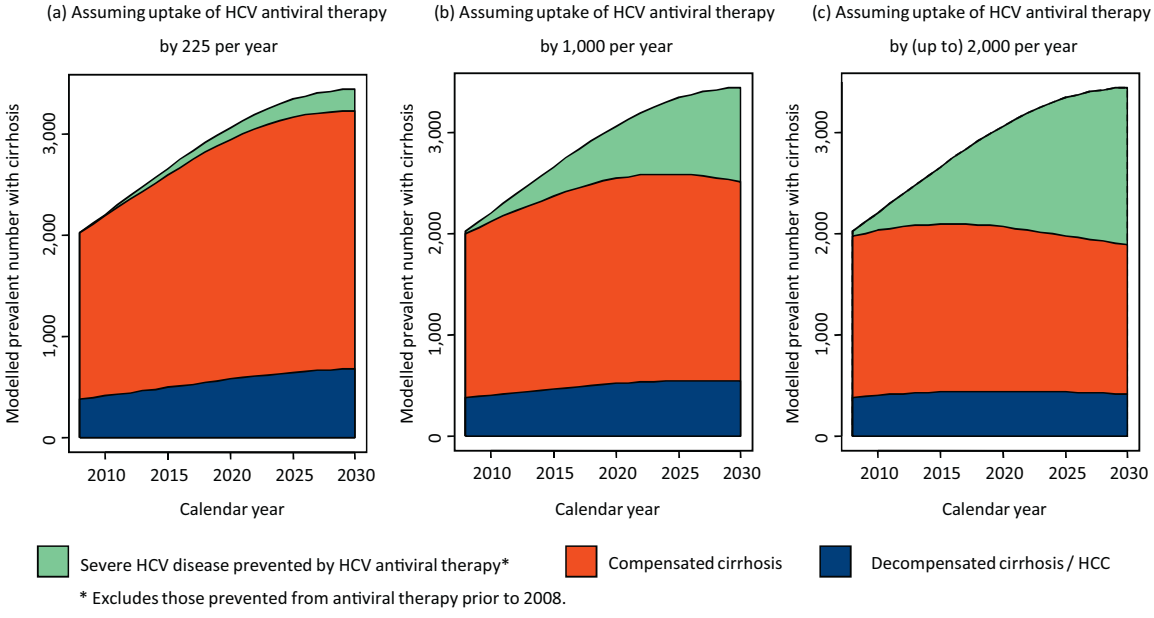

Fig. 3. Modelled prevalent number of chronic HCV infected people, who had *ever* injected drugs, with cirrhosis in Scotland according to different uptake rates of HCV antiviral therapy during 2008–2030.
Adapted from Hutchinson et al., 2005.

Table 1
Summary of the key evidence, issues stemming from the evidence, actions designed to address the issues, progress made in delivering actions and associated outcomes, in respect of testing, treatment, care and support.

Key evidence and issues	Key actions	Progress and outcomes
Key evidence (mid 2000s) • An estimated 38,000 individuals living with chronic HCV, of whom around 90% had acquired their infection through injecting drug use • Over 60% of people in Scotland living with HCV infection remained undiagnosed • Less than 10% of chronically infected individuals had attended specialist care and only 1% had been initiated on a course of antiviral therapy, during 2006 • Over 2000 HCV-infected persons were however living with cirrhosis, and over 100 HCV-infected persons were developing liver failure each year • Of 450 persons initiated on antiviral therapy each year, only 4% were prison inmates • It was estimated that if 2000 persons per year received antiviral therapy over the next two decades, 5200 cases of HCV-related cirrhosis and 2700 liver failures would be prevented in the future • Studies undertaken in Glasgow showed that a targeted approach to HCV testing in the GP setting – focusing on PWID aged over 30 years – generates a high test uptake and yield of HCV diagnoses • GPs and other service providers highlighted difficulties in taking blood from PWID as a barrier to HCV test uptake **Major issues** • The majority of persons chronically infected with HCV remain undiagnosed and many of those diagnosed fail to reach and stay within specialist care services • There are widespread variations in testing practice in the community setting • Widespread variations in the approach to the clinical management and social care of HCV-infected persons exist • Insufficient numbers of HCV-infected persons, including prisoners, receive antiviral therapy • There are insufficient links between social care/addiction/mental health services and specialist services for HCV treatment	• Each NHS Board will have, or be affiliated to, a Managed Care Network for HCV; this Network will comprise representatives of relevant specialists in healthcare and other stakeholder groups including those for the prison service, local authority, social work, the voluntary sector, mental health/addictions, and people living with and affected by HCV • Testing, treatment, care and support services within each NHS Board will be developed to increase the numbers of persons undergoing therapy in Scotland from 450/year to 1000 in 2010/11 and at least, 2000/year thereafter • Service Level Agreements (SLAs)/Memoranda of Understanding (MoU) between NHS Boards and the Scottish Prison Service, to promote the treatment of HCV infected inmates in prisons, will be developed • Awareness-raising campaigns and communications initiatives will continue to be developed, and implemented to meet the information and education needs of a range of professional audiences • An awareness-raising campaign, to promote HCV testing among those at risk of being infected, will be implemented • NHS Boards to develop and implement innovative approaches to improve HCV testing and referral activities by GPs and other community setting practitioners • A programme of work to evaluate different approaches to HCV testing/body fluid sampling (e.g. dried blood spots) will be undertaken	• All NHS boards have established multi-disciplinary Managed Care Networks • A public and professional website was launched, and public and professional awareness campaigns undertaken in 2010 • New approaches in getting people tested for HCV have been implemented; this includes the roll-out of dried blood spot (DBS) testing, allowing sampling in non-clinical settings (i.e. drug treatment services) • A 30% increase in the annual number of persons newly diagnosed with HCV between periods pre and during the Action Plan has been observed; around 20% of new diagnoses in 2011 were made in specialist drug services where DBS testing has been introduced • Around 55% of all persons in Scotland living with chronic HCV have been diagnosed (by 2013), a rise from 38% in 2006 • Clinical services – leading to more than a doubling in the numbers of HCV infected persons initiated on treatment from 468 in 2007/08 to 1049 in 2010/11 – have been developed; 80% of initiates in 2010/11 with a known risk factor had ever injected drugs • MoU, followed by SLAs, have been agreed by the majority of NHS Boards and the prisons within their areas to ensure that inmates receive optimal care and treatment; more than a eight-fold increase in the number of inmates treated between 2007/08 (17) and 2010/11 (143) has been observed • National procurement of antiviral drugs from the two key pharmaceutical companies, securing, on average, a 20% reduction in costs, has been implemented

and Consultants in Public Health), were responsible for co-ordinating the Plan locally; this involved establishing local/regional networks to support the planning, development and implementation of services, and commissioning services.

(V) *Multidisciplinary approach*: The Plan embraced all service needs and adopted a multidisciplinary approach. Local and national networks, comprising representatives from all relevant healthcare specialists and other stakeholder groups, were established so that experience, best practice and progress on the delivery of the Action Plan could be shared, and support, advice and guidance provided. Thus these networks ensured that approaches taken were effective and, where appropriate, consistent.

(VI) *Serious investment*: The Plan was supported by additional government funding (£43 million over the initial 3 years); the bulk (85%) was given to regional NHS boards to develop testing and treatment (£28.7 million) and prevention (£8 million) services.

(VII) *Monitoring and performance measures*: Each action within the Phase II Plan had a desired outcome, performance measure(s) to gauge progress in achieving the desired outcome, and timescales. For example, it was anticipated that, by 2011, actions would lead to considerable increases in the numbers of persons diagnosed with HCV and the numbers of infected persons having cleared their virus through antiviral therapy. Given significant resources were allocated for treatment, government targets were set to ensure the annual numbers of people undergoing therapy in Scotland increased. To monitor progress and the impact of actions, the maintenance/development of existing and establishment of new national surveillance systems was essential (described below).

Progress and impact

Seven years have elapsed since the launch of Phase II and a considerable amount of data, permitting evaluation of the plan's impact, are now available. Monitoring systems, and use of advanced statistical analysis/modelling techniques (involving segmented regression and multi-parameter evidence synthesis), were vital to understand the scale-up and impact of interventions. Of particular importance were national HCV diagnosis and clinical databases to inform on whether measures, to reduce the proportion of the infected population undiagnosed and increase the proportion of the infected population treated, were effective (Innes et al., 2012; McLeod, Weir, et al., 2014; PHE, 2014). During Phase II, a HCV test database, covering the four largest NHS Board areas with over 70% of the country's diagnosed population, was also established to further understand whether initiatives designed to increase test uptake and diagnosis were effective. Biennial nationwide surveys of PWID, principally involving those actively injecting drugs, were undertaken to gauge the prevalence and incidence of HCV infection in this population but also uptake of interventions, such as HCV testing (Palmateer et al., 2014; UWS,

2015). The annual linkage of the national HCV diagnosis database to morbidity/mortality records arguably generates the most important indicator data of all: on the numbers of HCV-infected people advancing to end stage liver disease and death (McDonald et al., 2010; PHE, 2014). The following three sections present the headline data from these systems and associated research initiatives, and the progress made in diagnosing and treating infection and in preventing SLM.

Diagnosing infection

From a diagnostic perspective, 2011 saw the highest annual number of new HCV diagnoses ever made in Scotland, with around a 30% rise observed in these annual numbers between the 5-year periods pre (averaging 1600) and during/post Phase II (averaging 2100) (see Fig. 4a) (McLeod, Hutchinson, & Goldberg, 2014). The proportion of people reporting injecting drug use among those newly diagnosed (and with available risk factor information) has remained high (≥90%). Further, estimates indicate that now around 55% of all persons in Scotland living with chronic HCV have been diagnosed (by 2013), a rise from 38% in 2006 (PHE, 2014).

Awareness of HCV among professionals as a consequence of a wide range of action plan initiatives, including the establishment of numerous local and national networks, is likely to have played a role in the promotion of HCV testing. However, the introduction of dried blood spot (DBS) testing in the specialist drug service setting in 2009, following laboratory evaluations demonstrating its validity (Bennett et al., 2012), has had the greatest impact on the diagnosis effort and has since been deemed cost-effective (Martin, Hickman, Miners, et al., 2013). This non-invasive approach, involving finger-prick blood spotted onto filter paper, enabled staff with minimal training to undertake an HCV test and thus permitted the roll-out in non-clinical settings (McAllister et al., 2014). The annual number of people tested for HCV in specialist drug services across Scotland increased dramatically from <100 prior to the Action Plan, to over 1000 since, with this setting now referring almost 20% of all new diagnoses (McLeod, Hutchinson, et al., 2014; McLeod, Weir, et al., 2014). The proportion of PWID in Scotland, interviewed at services providing injection equipment, who had been tested for HCV in the last year (excluding those already diagnosed) increased from 40% in 2008–09 to 52% in 2013–14 (PHE, 2014). Accordingly, there is evidence that a breakthrough has been made in getting infected PWID tested and diagnosed in Scotland. While HCV testing among PWID is advocated internationally (WHO, 2014), research conducted in Scotland underlines the need to act on a diagnosis, as awareness of one's infection status was found to be associated with a reduction in health-related quality of life (McDonald et al., 2013).

Progress has also been observed in the uptake of specialist HCV services (which remains primarily confined to secondary care) following HCV diagnosis, with approximately 60% increase in the total numbers attending between 2006 (3500) and 2013 (5700) (PHE, 2014). Also, 45% attendance was observed within 12 months of first diagnosis during Phase II compared to 32% pre-Phase II (McDonald, Hutchinson, Innes, et al., 2014). However, the attendance at specialist services (within 12 months of diagnosis) still varied considerably during Phase II, with lower rates observed among PWID (39%) compared to non-PWID (63%) and those diagnosed in drug services (40%) compared to primary care (60%). These data reflect that further efforts will be required in Scotland to ensure the vast majority of infected PWID, many of whom are now being diagnosed within drug treatment services, engage with HCV treatment and care services. The further co-localization of HCV management with addiction and other community setting services, currently confined to a few areas, is a strategy likely to result in higher treatment rates among PWID (Alavi et al., 2013; Bruggmann & Litwin, 2013; Zeremski et al., 2013).

Treating infection

From a treatment perspective, much has been achieved in developing clinical services throughout the country. The foundation of which was the establishment of managed care networks (MCNs) across Scotland, forming multi-disciplinary multi-agency networks with responsibility for the planning and delivery of HCV testing, treatment and care services. Establishing agreements with the prison service was central to that, to promote the treatment of HCV-infected inmates. Recognizing that it was not possible to manage and treat HCV-infected individuals divorced from concomitant lifestyle issues (drug, alcohol or psychiatric problems and social care needs), MCNs had to integrate specialist HCV services with those for social care and mental health/addictions. Funding from the Action Plan helped to resource specialist nurse teams enabling an expansion of nurse-led liver assessment and treatment clinics not just in the main hospital, but in prison and, in some areas, community settings such as drug treatment services (Tait, McIntyre, McLeod, Nathwani, & Dillon, 2010).

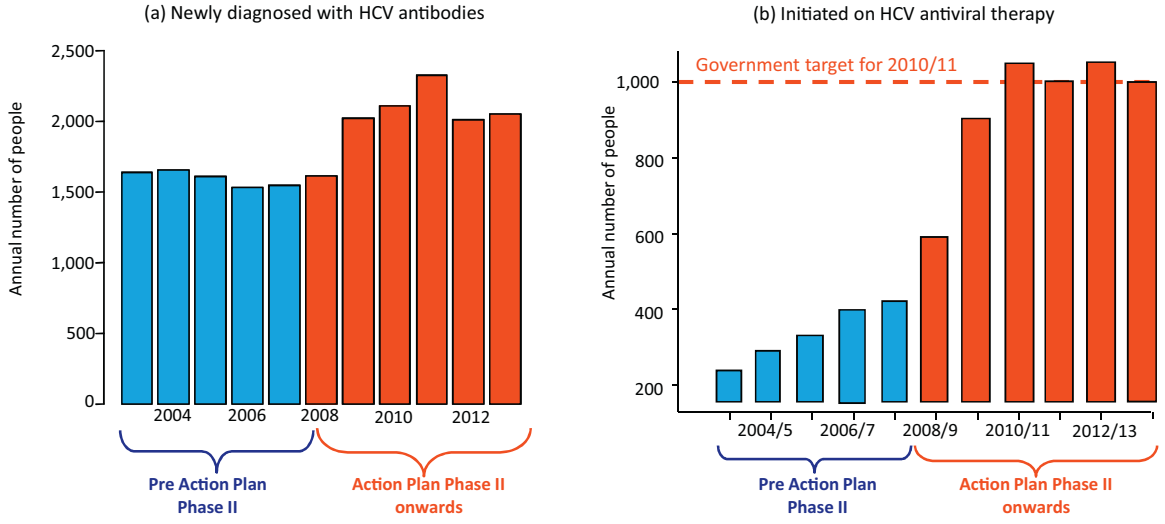

Fig. 4. Annual number of people in Scotland who were (a) newly diagnosed with HCV antibodies, and (b) initiated on HCV antiviral therapy, during 2003–2013.

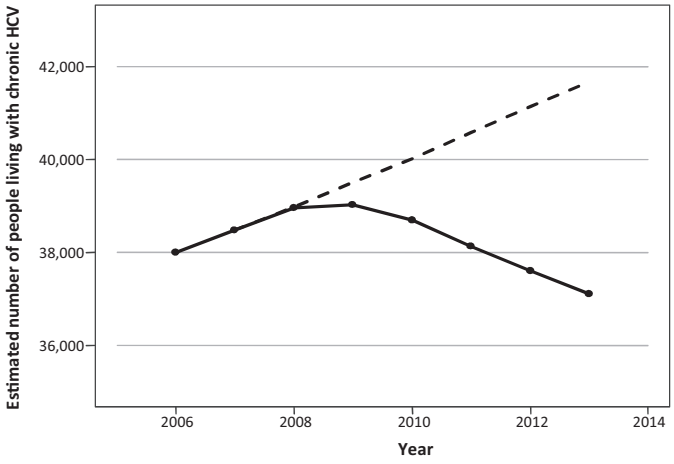

Fig. 5. Estimated number of people living with chronic HCV infection each year in Scotland during 2006–2013: (a) taking account of the impact of the national scale-up in interventions (solid line), and (b) not taking account of the impact of the national scale-up in interventions (dashed line).

During Phase II, the annual number of people initiated onto antiviral therapy had more than doubled (and increased more than eightfold among prisoners) from 468 (and 17) in 2007/08 to 1049 (and 143) in 2010/11, which exceeded Scottish Government targets during this period (PHE, 2014) (see Fig. 4b). Since then, the annual treatment numbers have remained close to 1000, which fall slightly short of Government targets but likely reflect a delay in treatment initiation for many individuals due to the prospect of more effective therapies in the near future. Of critical importance is the observation that, for the great majority of this group, injecting drug use was the principal risk factor for HCV transmission. Among people initiated on therapy across Scotland (and with available risk factor information), the proportion who had reported having *ever* injected drugs increased from 65% (300) in 2007/08 to 80% (840) in 2010/11, corresponding to around a tripling in treatment uptake in this population. Despite the country-wide scale-up in therapy – and inevitable expansion into increasingly more difficult and complex groups of patients – there was no evidence that SVR rates had been compromised in Scotland (McDonald, Hutchinson, Innes, et al., 2014). It is therefore evident that having a history of injecting drug use, per se, is no barrier to receiving, and indeed fully benefitting from, combination therapy.

An important turning point was reached during the Action Plan period, whereby the number of people living with chronic HCV infection in Scotland started to decline – an observation which contrasts sharply with the increasing trend estimated for the years leading up to Phase II (see Fig. 5). This decline stems essentially from (a) an increase in the annual number of people clearing their chronic infection from therapy, and (b) a decrease in the estimated annual number of PWID becoming newly infected. Approximately 37,000 people were estimated to be chronically infected during 2013, which is lower than the 38,000–39,000 estimated during 2006–2008, in the early phase of the Action Plan (PHE, 2014). Further, the estimated total of 37,000 by 2013 is considerably lower than a projected total of almost 42,000, assuming a continuing upward trend in the size of the chronic HCV population – and thus no change in the numbers of people clearing HCV from therapy or those newly acquiring infection – as estimated during 2006–2008 (see Fig. 5).

Preventing severe liver morbidity

The ultimate aim of the Action Plan was to reduce the numbers of infected persons who develop severe HCV-related disease. The annual numbers of persons diagnosed HCV-antibody positive who had been hospitalized for the first time with SLM (defined as either decompensated cirrhosis or hepatocellular carcinoma) had more than doubled in the decade leading up to the Action Plan, from approximately 40 in 1996 to 100 in 2005 (see Fig. 6). These numbers continued to increase, plateaued at approximately 150 cases per annum during 2009–2012, and increased again to near 190 cases in 2013. This continuing upward trend is consistent with the statistical modelling work (Hutchinson et al., 2005), which informed the Plan and highlighted that greater treatment rates (double that which has been achieved) would be required to curb the rise in SLM (see Fig. 2). All-cause and liver-related

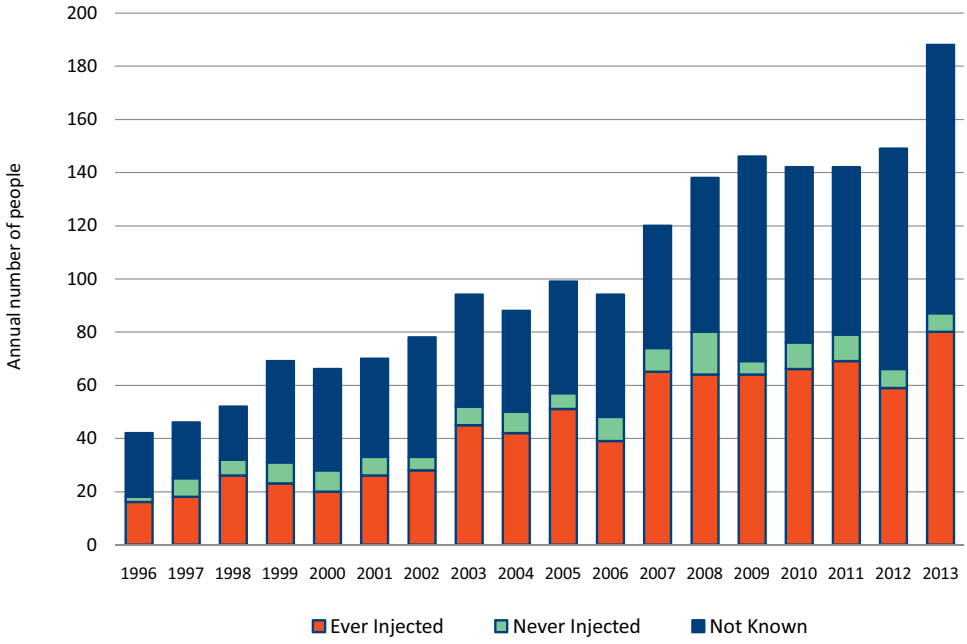

Fig. 6. Annual number of people in Scotland diagnosed HCV antibody positive and who had been hospitalised for the first time with either decompensated cirrhosis or hepatocellular carcinoma.

(age-adjusted) mortality rates have remained relatively stable among the HCV diagnosed population in Scotland during 2005–2010, a further indicator that therapy has so far had minimal impact on population level HCV-related disease (Aspinall et al., 2015). At an individual level, however, Scotland has been at the forefront internationally in demonstrating that attainment of SVR following therapy is significantly associated with a reduced risk of a broad range of outcomes: including hepatic, non-hepatic and those driven by extreme lifestyle behaviours (Innes et al., 2015).

So, while Scotland has managed to scale-up diagnosis and treatment, the continuing rise in SLM since Phase II of the Action Plan likely reflects that (i) treatment uptake – although ranking high internationally (Dore, Ward, & Thursz, 2014) – is still relatively low at around 3% per annum, (ii) SVR rates – although in keeping with what you would expect during an era dominated by pegylated interferon and ribavirin – have nevertheless been suboptimal (ranging from 39% with genotype 1 to 70% with genotype 2/3) (Innes et al., 2012), (iii) insufficient numbers of infected persons with significant fibrosis (METAVIR score F3–F4) – representing those most in need of therapy from a clinical perspective – being initiated on therapy (relating to only around 300 of the 1000 annual treatment initiates in Scotland), and (iv) the extent of excessive alcohol intake in those with HCV infection in Scotland, and limited impact of measures aimed at tackling it (an estimated 36% of all cases of cirrhosis among persons attending specialist HCV services would not have occurred if such individuals had not drank to excess (Innes et al., 2013)). Among those developing SLM in 2013, 92% of those (with available risk factor information) had reported injecting drug use (Fig. 6) and 53% were aged at least 50 years of age. These data highlight that not enough has been done to tackle HCV among those individuals who acquired their infection during the rapid rise of heroin use in Scotland in the late 1970s and early 1980s (Hutchinson, Bird, Taylor, & Goldberg, 2006); thus, as a consequence, we are now experiencing the subsequent wave of PWID-related late HCV sequelae.

Challenges and opportunities which lie ahead

The future holds much promise with the advent of highly effective therapies, eradicating the virus in the vast majority of patients. This watershed in HCV treatment however comes at a price; for Scotland, it theoretically translates to a bill of the order of £1 billion in antiviral drug costs alone (assuming an average cost of £25,000 per course of therapy), almost a tenth of the entire annual health budget, to treat all infected individuals across the country. Clearly the prohibitive cost of the new regimens represents a significant challenge, not just for Scotland but, for all countries affected by HCV. The following sections present the latest evidence on the challenges and opportunities facing Scotland in its bid to fully achieve the three aims of the action plan.

Treatment to prevent onward transmission among PWID

Considerable progress has been made in scaling up the provision of harm reduction interventions (i.e. injecting equipment provision (IEP) and opiate substitute therapy (OST)) in Scotland, known to appreciably reduce the risk of HCV infection if given at sufficient levels and in combination (Palmateer et al., 2014; Turner, Hutchinson, & Vickerman, 2011). Whilst there is evidence to suggest a reduction in the incidence of HCV infection has taken place among PWID in Scotland (from 13.3 per 100 person years during 2008–09, to 6.1 and 10.0 per 100 person years during 2011–12 and 2013–14, respectively), the prevalence of HCV still remains relatively high (at least 20%) among individuals who have commenced injecting in the last 3 years (Palmateer et al., 2014; PHE, 2014). Mathematical modelling work has suggested that substantial reductions in the prevalence of chronic HCV among PWID populations cannot be achieved with IEP and OST alone and would require the scaling up of HCV antiviral therapy, an approach which has the potential to not only eradicate the virus for the individual but also prevent the onward transmission to others (Martin, Hickman, Hutchinson, Goldberg, & Vickerman, 2013).

A meta-analysis demonstrated that acceptable treatment outcomes can be achieved in patients who report actively injecting drugs and who are eligible and committed to starting HCV therapy (Aspinall et al., 2013). Treatment uptake specifically among those actively injecting drugs in Scotland is estimated to have doubled during the Action Plan period; the numbers still constitute a minority (10–15%) of those initiated on treatment each year (Innes, Goldberg, Dillon, Hutchinson, 2014). With the introduction of interferon-free therapies (achieving typically ≥90% SVR), the annual incidence of chronic HCV is estimated to reduce to approximately 500, 300, and <50 new infections by 2025 with treatment of around 100, 300 and 600 PWID per year in Scotland, respectively (Innes, Goldberg, Dillon, et al., 2014). While these projections are consistent with previous research (Martin, Vickerman, Grebely, et al., 2013), they, nevertheless, are generated from modeling studies; accordingly, further observational or experimental studies are needed to evaluate whether treatment can indeed prevent onward transmission, and ultimately control the spread of HCV, in PWID populations.

Diagnosing the undiagnosed

With an estimated 55% of the infected population diagnosed, Scotland ranks among the highest internationally; however, a few countries, notably Australia and Sweden, report rates in excess of 80% (Dore et al., 2014). It could take another decade to achieve these high rates based on the current pace of testing/diagnosis, in Scotland. While DBS testing in drug treatment settings is effective in diagnosing PWID, its reach is limited to those still in contact with services and generally younger in age (45% aged <35 years) (McAllister et al., 2014). Recent modelling work has estimated that 27,000 people who had *ever* injected drugs remained undiagnosed (in 2009) and, of these, 71% were aged ≥35 years and 83% had not injected recently (Prevost et al., 2015). Thus, additional case-finding will be needed to identify this older population of PWID, many of whom will no longer be in contact with drug services. Birth cohort screening has been recommended in the United States on the back of an economic evaluation (Rein et al., 2012), but such an approach is not guaranteed to be cost-effective in Scotland unless perhaps targeted at areas of high HCV prevalence.

Evaluations of case-finding approaches in Glasgow have demonstrated that targeting older individuals (aged 30–54 years) with a history of injecting drug use, as indicated within primary care administrative systems, can be highly effective (Anderson et al., 2009; Cullen et al., 2012). However, the limited implementation of this systematic risk-based approach across Scotland to date likely reflects the difficulty in getting GPs fully engaged in such case-finding initiatives. It remains uncertain as to whether incentives, as adopted in the aforementioned evaluations and with so many other conditions, would appreciably increase HCV testing and diagnosis by GPs. With the potential to treat people with short, safe and easy to administer HCV therapies, case-finding and treatment in the primary care setting could however become more widely embraced.

Treatment to prevent severe liver morbidity

In an era of highly effective interferon-free therapies, the numbers of HCV-infected people developing SLM should be avoidable in the great majority of instances. Modelling work has

demonstrated that it is theoretically possible to dramatically reduce the incidence of HCV-related SLM in Scotland over the next 5 years but it will require increased uptake of therapy, particularly among those with moderate to advanced fibrosis (Innes, Goldberg, Dillon, et al., 2014). During 2009–2013, approximately 60% of treatment initiates in Scotland had mild fibrosis (Innes, Goldberg, Dillon, et al., 2014), reflecting the wider population being diagnosed and entering specialist services but also a group unlikely to progress to SLM in the short term (Huang et al., 2015; Innes, Goldberg, Dusheiko, 2014). The current high cost of regimens will likely mean that healthcare providers will now have to focus treatment, at least initially, on those with more significant fibrosis (EASL, 2014). The population impact of therapy will however not be fully realized unless heavy alcohol use and other harmful lifestyle factors, highly prevalent among HCV-infected PWID populations, are tackled (Innes et al., 2011).

Conclusion

Scotland's Hepatitis C Action Plan has been cited as "an impressive example of a national strategy" by the Global Commission on Drug Policy (GCDP, 2013). The Plan has shown that a Government-backed, coordinated and invested approach can transform services for PWID and rapidly improve the lives of thousands. The surveillance and research initiatives described here, provided the clinical and public health champions with the necessary ammunition to raise awareness and convince policy-makers of the imperative need for action on HCV, a condition which disproportionately affects those living in the most deprived parts of the country. This exceptional affinity with deprivation (with over half of the HCV diagnosed population residing in the 20% most deprived areas) was no doubt a key factor in securing Scottish Government's commitment, given its flagship mission to tackle health inequalities. The support of governments in other countries could similarly be garnered through aligning action on HCV with political agendas and aspirations.

It is evident that a considerable amount of progress has been made in expanding access to HCV treatment among PWID across Scotland, particularly among those in prison and in contact with drug treatment services. The evaluation of the Plan's impact, disseminated extensively through national/international conferences and peer-review publications, has further provided fundamental insights to the international audience on the management of HCV among PWID. Serious challenges remain, with tens of thousands – an appreciable and growing proportion with significant fibrosis – still requiring therapy and almost half remaining undiagnosed. Going forward, Scottish Government has further endorsed its commitment to tackle HCV, with new targets, informed by the latest modelling work (Innes, Goldberg, Dillon, et al., 2014), set to reduce the number of people developing HCV-related SLM to 50 by 2020 (a near 75% reduction within 5 years) and an associated uplift in funding. Scotland's strategy on HCV will continue to be closely monitored – as should be the case for other countries – and judged ultimately according to its ability to prevent HCV-related SLM.

Acknowledgements

The authors are grateful to the Scottish Government for funding the hepatitis C information generating initiatives presented here. The authors would also like to thank and acknowledge the following: the Hepatitis C Clinical Database Monitoring Committee, the clinics and staff supporting the Hepatitis C Clinical Database; the laboratories and staff supporting the Hepatitis C diagnosis and test databases; Information Services Division Scotland for undertaking the linkage of hepatitis C databases with other national registries; and the services, staff and respondents who participated in the Needle Exchange Surveillance Initiative.

Conflict of interest statement: We wish to draw the attention of the Editor to the following facts which may be considered as potential conflicts of interest

- SH reports personal fees from Abbvie, Gilead, Janssen, MSD, Roche, grants from Janssen, outside the submitted work.
- HI reports personal fees from Janssen, outside the submitted work.
- DG reports personal fees from MSD, Janssen, Abbvie, BMS and Gilead, outside the submitted work.
- JD reports grants and personal fees from Roche, grants and personal fees from MSD, grants and personal fees from Janssen, grants and personal fees from Gilead, personal fees from BMS, grants from GSK, grants and personal fees from Abbvie, outside the submitted work.
- RF reports personal fees from Gilead, Janssen, BMS, Abbvie, outside the submitted work.

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