Home Office

THE PRIMARY PREVENTION OF HEPATITIS C AMONG INJECTING DRUG USERS

Advisory Council
on the Misuse of Drugs

ACMD
Advisory Council on the Misuse of Drugs

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Dear Minister,

I have pleasure in enclosing our report on The Primary Prevention of Hepatitis C among Injecting Drug Users.

Hepatitis C is a significant public health issue. It has been estimated that in 2003 in England and Wales there were around 190,000 individuals infected with the hepatitis C virus (HCV). It is likely that over 80 per cent of current HCV infections are due to injecting drugs and that around 50 per cent of injecting drug users (IDU) in the UK are infected with HCV. Moreover, of those IDU who are infected, approximately half may be unaware that they are HCV positive. It is likely that HCV prevalence fell during the early and mid 1990s, but the trends have now reversed and among recent IDU HCV prevalence almost doubled between 1998 and 2007.

In light of these trends the ACMD believed that it would be expedient to review the prevention of hepatitis C and what actions could be taken to reduce its transmission and improve knowledge and awareness, particularly among at-risk groups. The report therefore focuses on HCV prevention among injecting drug users.

These statistics are set against a backdrop of an expansion of diagnostic and treatment services as part of the HCV Strategy and HCV Action Plan in England and the HCV Action Plan in Scotland.

In reviewing the evidence, we conclude that a single intervention may not, alone, be sufficient to prevent the spread of the hepatitis C virus. The evidence suggests that the most effective way of reducing HCV incidence among active IDUs is through a combination of Opiate Substitution Therapy (OST) and the provision of Needle and Syringe Programmes (NSP).

This finding has important implications for future policy in relation to both HCV prevention and harm reduction services.

We also make further recommendations around gathering data on HCV regarding epidemiology, testing and treatment referrals. Such information will provide more robust evidence upon which decisions underpinning policy can be made.

This report is being published concurrently with and complementary to, public health guidance from the National Institute for Health and Clinical Excellence (NICE) on *Needle and syringe programmes: providing people who inject drugs with injecting equipment*. We are most grateful to NICE for their sharing of review level evidence. We are further indebted to Health Protection Scotland for their collaboration that allowed us to undertake a review of reviews of the evidence of interventions to prevent HCV.

In producing this report, the ACMD is especially grateful for the valuable knowledge and expertise provided by co-opted specialists and service users and providers.

Yours sincerely,

Dr Matthew Hickman
Chair, ACMD Hepatitis C Prevention Working Group

Professor David Nutt FMedSci
ACMD Chairman

Contents

Glossary of acronyms, organisations and terms

BBVs: Blood-borne viruses

95 per cent Confidence Interval (95% CI): A measure of precision – telling us that we are 95 per cent certain that the true population value lies between the upper and lower range of the interval.

DAAT: Drug and Alcohol Action Team.

HCV: Hepatitis C virus.

HIV: Human Immunodeficiency Virus.

HPA: Health Protection Agency.

HPS: Health Protection Scotland.

IDU: Injecting drug user.

IEC: Information, Education and Counselling.

Incidence: Number of new occurrences of disease over a specified time period.

NICE: National Institute for Health and Clinical Excellence.

NSP: Needle and Syringe Programmes.

NTA: National Treatment Agency for Substance Misuse.

OST: Opiate substitution therapy.

PCT: Primary Care Trust.

PIED: Performance and image-enhancing drugs.

Prevalence: Total number of people with disease in the population at a given time.

Primary prevention: Actions to prevent transmission or disease onset.

Recent initiate: An injector who had injected for the first time during the preceding three years.

Turning Point: A UK based social care organisation providing services for people with complex needs including drug and alcohol misuse.

1. Background

1.1 The Advisory Council on the Misuse of Drugs (ACMD) is established under the Misuse of Drugs Act 1971. The Council's current membership is shown in Annex A. The Council is required under the Act "*to keep under review the situation in the United Kingdom with respect to drugs which appear to them likely to be misused and of which the misuse is having or appears to them of having effects sufficient to constitute a social problem*".

1.2 The ACMD's Prevention Working Group aims to provide advice and recommendations on the health and social problems connected with substance misuse. In this report we examine issues concerning the primary prevention of the hepatitis C virus (HCV) among injecting drug users (IDUs).

1.3 The Prevention Working Group is particularly grateful to the valued assistance of experts who contributed evidence to the ACMD's meetings for the preparation of this report (Annex A).

1.4 In the course of our examination of HCV prevention we invited and considered a range of evidence, including an invitation to service users and providers to give their views on current and past experience of HCV prevention. We are indebted to collaborations with Health Protection Scotland that allowed us to undertake a review of reviews of the evidence of interventions to prevent HCV (Palmateer *et al.*, 2008). We are also grateful to the National Institute of Health and Clinical Excellence (NICE), which allowed us to use reviews of needle and syringe programmes (NSP) (Cattan *et al.*, 2008; Jones *et al.*, 2008) and cost-effectiveness modelling (Vickerman *et al.*, 2008) that they commissioned to inform NICE guidance on NSPs (NICE, 2009).

2. Introduction

2.1 The hepatitis C virus (HCV) is a substantial public health problem. Globally, two per cent of the population may be infected (Shepard, 2005). In the UK, HCV is one of the commonest chronic viral infections, predominantly spread via injecting drug use (Department of Health, 2002). It is likely that between 120,000 to 300,000 (mid estimate 190,000) people are infected with HCV in England and Wales and about 50,000 in Scotland – 85-90 per cent acquired through injecting drug use. Approximately one in five people recover with the rest becoming chronically infected. There is no vaccine against hepatitis C.

2.2 Previous Advisory Council on the Misuse of Drugs (ACMD) prevention reports concerning infection (ACMD, 1988; ACMD, 1993), examined the prevention of HIV infections, acquired by the practice of injecting. Many of the findings of these earlier reports have important parallels to the present inquiry regarding HCV prevention.

2.3 The ACMD's AIDS and Drug Misuse report (ACMD, 1988) was highly influential in two ways. First, it emphasised the importance of secondary prevention or harm reduction i.e. that preventing the serious health consequences of addiction (in this case the prevention of HIV transmission through injecting drug use) was a legitimate and as important public health goal as primary drug prevention. The ACMD advised the Government that the "*threat to individual and public health posed by HIV and AIDS was much greater than the threat posed by drug misuse*".

2.4 Second, the ACMD emphasised the importance of investing in a range of harm reduction services, needle and syringe programmes (NSP), opiate substitution therapy (OST), outreach, health education and other interventions aimed at reducing injecting risk and HIV transmission. The ACMD concluded that "*the benefit to be gained from oral methadone… has been clearly demonstrated* [and that] *the comprehensive range of advice and treatment options… must remain a key dimension of overall HIV and drug misuse prevention*".

2.5 It was welcome that the publication of the ACMD report coincided with strategies in government that led to the expansion of OST and the establishment of NSP. These early interventions were later attributed as the primary reason the UK averted an HIV epidemic among injecting drug users (Stimson, 1995).

2.6 Current surveillance data suggest that the overall prevalence of HIV infection among IDU (recruited from the community, NSPs and low threshold drug agencies) in the UK has been around one per cent for over a decade (Health Protection Agency (HPA), 2008a).

2.7 Compared to many other countries (including in Europe), HIV infection among IDUs in the UK is low, and can be considered an important public health and policy success. However, the threat of HIV infection and potential for new outbreaks of HIV among IDUs remain an important public health priority, given the levels of injecting risk and HCV infection in some areas in the UK (Vickerman *et al.*, in review).

2.8 The picture for HCV and the success of harm reduction interventions in preventing HCV transmission among IDUs is less clear; this is also the case internationally. It is appropriate, therefore, that the ACMD consider HCV prevention and the actions that could be taken to reduce HCV transmission and improve knowledge and awareness in this area.

2.9 In this report we focus on the primary prevention of HCV among IDUs. We note that expanding access to treatment services (secondary prevention) to all people infected with HCV is critically important. However, this issue is being addressed as the prime focus of the HCV Strategy and HCV Action Plan in England (Department of Health, 2004), and has also been addressed by the recent HCV Action Plan in Scotland (Scottish Government, 2008). In this report we do discuss the potential for HCV treatment as a component of prevention; and the importance of HCV testing to promote prevention and improve epidemiological evidence.

2.10 In addition to the risks of HCV and HIV, IDUs are at risk of other infections including hepatitis B and bacterial infections at the injecting site (HPA, 2008a). However, this report does not specifically consider these other related infections.

2.11 It is also important to recognise the potential risk of HCV transmission among people that inject performance and image-enhancing drugs (PIEDs) such as anabolic steroids, and the significant number of this group that access needle and syringe programmes (NSP) (McVeigh *et al.*, 2003). However, there is little published information on the size of the risk to this group or on their contribution to overall numbers of HCV cases. Clearly, HCV infection is not confined exclusively to current and ex-injecting drug users and it is important to obtain better information on the scale and size of HCV risk among other sub-groups (such as people born in India, Pakistan and Bangladesh) (D'Souza *et al.*, 2005; Bajwa, 2005). Nonetheless, it is likely that over 80 per cent of current HCV infections are due to injecting. Reducing HCV incidence among IDUs is critical to the prevention of HCV in the general population.

2.12 In this report we do not specifically consider the risk of sexual transmission of HCV; which is considered to be low, except in some specific instances and among some specific populations (e.g. men who have sex with men) (Giraudon, 2008).

2.13 In the report we summarise the evidence on the epidemiology of HCV and the effectiveness of interventions to prevent HCV. We make recommendations to address gaps in the evidence and current practice in order to improve our understanding of: a) HCV epidemiology and injecting risk where this information will be important to policy-makers; b) of what interventions work to prevent HCV; and c) most importantly, what actions will reduce the risk of HCV infection.

3. HCV infection and injecting drug use

3.1 Chronic HCV infection can lead to severe liver disease, liver cancer and death. Rates of progression, though initially slow, increase over time. For example, after 20 to 40 years approximately 20 per cent of those infected will develop cirrhosis of whom approximately three per cent annually will die from decompensated cirrhosis or liver cancer. Chronic HCV can be successfully cleared in at least half of patients that are treated (Department of Health, 2002; Irving, presentation to ACMD, 2008).

3.2 Based on the Health Protection Agency's (HPA) analysis of the Office for National Statistics (ONS) death certificates, the numbers of deaths from liver cancer in people diagnosed with HCV has increased threefold from 25 in 1996 to 75 in 2004. Provisional data suggest that this rising trend is continuing with 104 such deaths recorded in 2007. This number is likely to be a substantial under-estimate of the total number of HCV-related deaths because HCV is not always identified on the death certificate. The true number of people with severe liver disease is uncertain. Nonetheless, projections in the UK and other European countries suggest that the number of deaths and number with severe liver disease will increase (Sweeting *et al.*, 2007). In addition, the number of people at risk of dying from liver cancer will continue to increase in the medium to long term unless the number of new infections is reduced (Sweeting *et al.*, 2007; Sypsa *et al.*, 2004).

3.3 There is no available HCV vaccine, unlike for hepatitis B (HBV) and hepatitis A. IDU are a major risk group for HBV infection and vaccinating IDU (and other "at-risk populations") is the key public health strategy to prevent HBV transmission in the UK[1]. Other countries have introduced HBV vaccination into childhood immunisation programmes (Van Damme *et al.*, 1997). Routine surveillance data suggest that the number of IDUs who report HBV vaccination has increased, with around two-thirds reporting at least one dose (HPA, 2008a; Health Protection Scotland/University of the West of Scotland, 2008; Hope *et al.*, 2007), and that the prison vaccination scheme has made a substantial contribution to the increased uptake (Hutchinson *et al.*, 2004; Hope *et al.*, 2007; HPA, 2008a).

3.4 Information on the prevalence and risk of injecting site infections and the potential effectiveness of different interventions to prevent serious consequences is at an early stage (Hope *et al.*, 2008).

1 http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079917

4. Epidemiology and surveillance

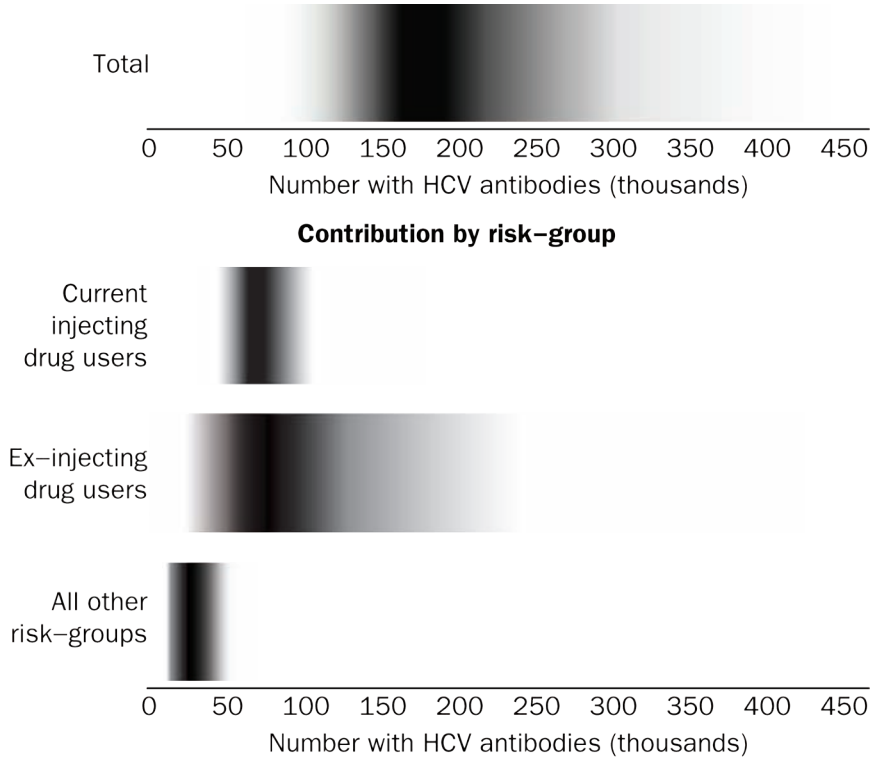
4.1 In this section we report mostly on HCV epidemiology in England and Wales. Key epidemiological data for Scotland have also been reported in the Hepatitis C Action Plan for Scotland (Scottish Government, 2008) and for Northern Ireland (HPA, 2008b).

Prevalence and geographical variation

4.2 Prevalence data are critical for diagnostic and treatment service planning and informing estimates of HCV morbidity.

4.3 The best current estimates of the number of people infected with HCV (including people who are chronically infected or have cleared the virus) obtained by combining information on HCV prevalence and the size of the 'at-risk' populations in England and Wales are shown in Figure 1 (Sweeting *et al.*, 2008a; De Angelis *et al.*, 2008). It is likely that between 120,000 to 300,000 (mid estimate 190,000) people are infected with HCV; and that of these, 50,000 to 100,000 are among current IDUs; 40,000 to 190,000 among ex-IDUs; and 14,000 to 50,000 in the rest of the population. The figure shows the uncertainty surrounding the estimates, especially in relation to ex-IDUs since information on the size of the ex-injecting population is scarce (Sweeting 2008b). This implies that the population prevalence of HCV in England and Wales in those aged 15–59 is between 0.4 per cent and one per cent (mid estimate 0.6 per cent). It is estimated also that there are about 50,000 (one per cent) people infected with HCV in Scotland (Scottish Government, 2008) of whom around 90 per cent acquired their virus through injecting drug use. There are no equivalent data yet for Northern Ireland (Department of Health, Social Services and Public Safety, 2007).

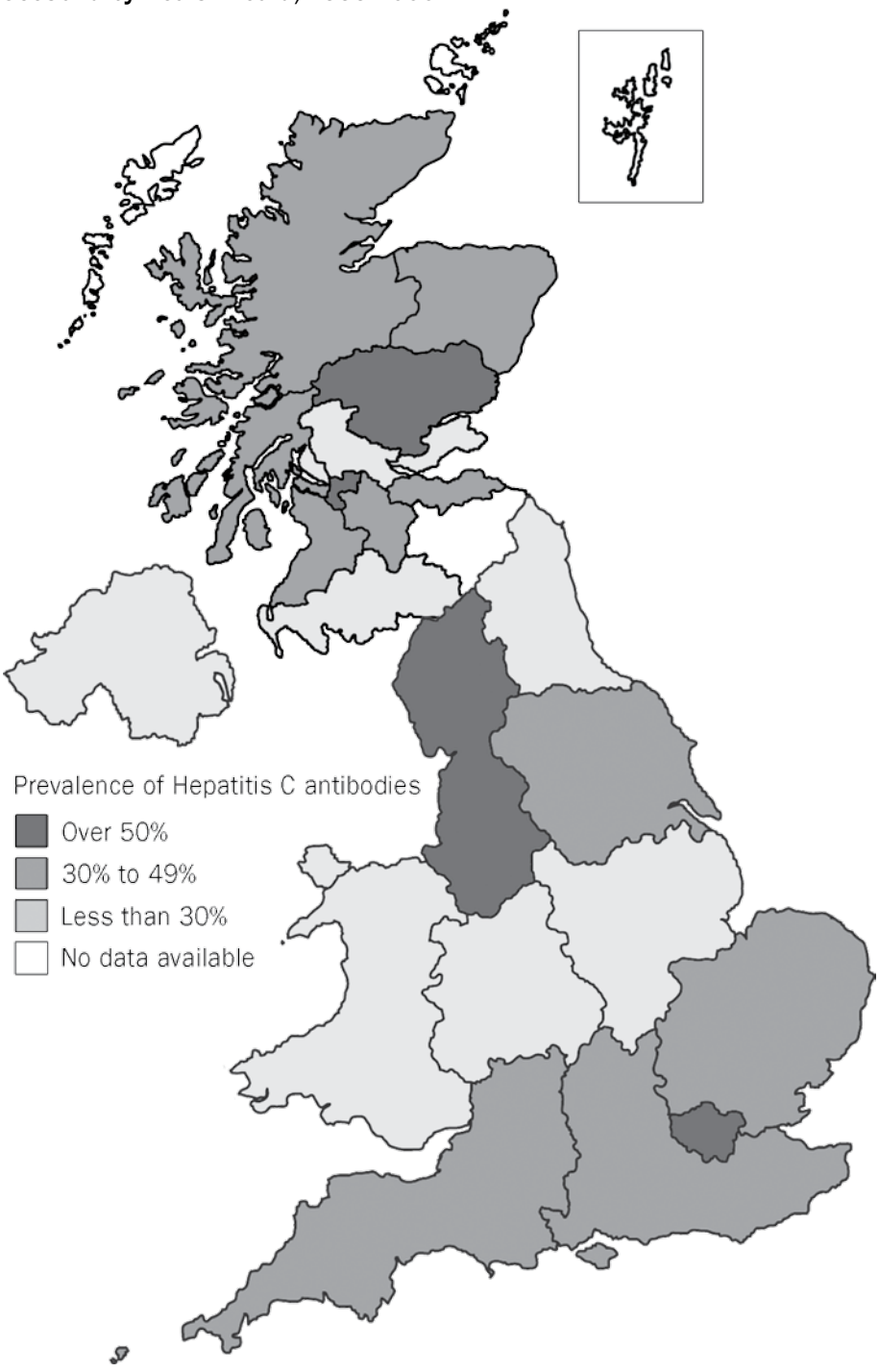
Figure 1. Estimated number of people with anti-HCV antibodies in England and Wales



The shading shows the 95% confidence interval (95% CI) for the number of people who are HCV positive. The darker area shows the median and the values which are the most likely within the 95% CI.

4.4 Best estimates suggest that, overall, approximately half of IDUs in the UK are infected with HCV (HPA, 2008a). However, high prevalence and incidence rates of HCV infection among IDUs are not inevitable. There are substantial geographical differences in HCV prevalence, with a greater than threefold difference between different geographical areas. The geographical variations in antibody prevalence in England, Wales, Northern Ireland and Scotland (Hutchinson *et al.*, 2006a) are shown in Figure 2.

Figure 2. Percentage hepatitis C antibody prevalence among a sample of current and former injecting drug users in England, Wales, Northern Ireland and Scotland by Health Board, 1999-2000.



Data Source: Unlinked anonymous anti-HCV testing of specimens taken for voluntary confidential (named) anti-HIV testing

4.5 In some cities (such as London, Manchester, Glasgow, Bristol and Brighton), often with large and long-established populations of IDUs, over 60 per cent will be infected with HCV (Judd *et al.*, 2005a; Hickman *et al.*, 2007). Whereas, in other sites (such as in South Wales and Teesside), less than 20 per cent of IDUs are infected with HCV (Craine *et al.*, in press; HPA, 2008a). However, there remain many areas in the UK where information on HCV prevalence is very limited.

Incidence

4.6 Information on incidence is important because it tells us more about the current risk of HCV infection and provides evidence on the impact of prevention.

4.7 There is less evidence on the incidence of HCV as, until recently, it has been more difficult to collect (involving the longitudinal follow-up of IDUs or analysis of serial cross-sectional data). Nonetheless, available estimates also show great geographical variation: from 30 to 40 per 100 person years (that is annually 30 to 40 per cent of people who are not already infected becoming HCV infected) in Glasgow, London and Bristol to less than 10 per 100 person years in South Wales, and even lower in some rural communities in Wales (Craine *et al.*, in press; Hope *et al.*, in review; Judd *et al.*, 2005b; Roy *et al.*, 2007).

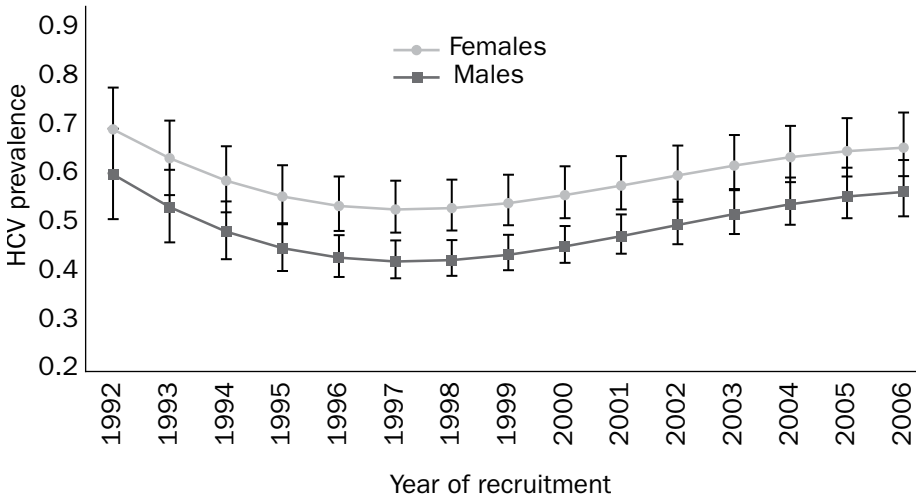
4.8 A novel technique for estimating HCV incidence has been developed that uses information on very recent infections (i.e. samples that are HCV RNA positive but HCV antibody negative) and the "window period" between when HCV RNA is detectable and HCV antibodies are detectable (Hope *et al.*, in review). The method has been piloted in Bristol and is being used in other sites in the UK. However, the length of the window period and therefore the estimates of incidence obtained from information on recent infections remains uncertain. Nonetheless we believe this technique could be used to evaluate the effectiveness of interventions.

Time trends

4.9 Preliminary analysis of HCV surveillance data based on recent testing of stored specimens suggests that HCV risk may have fallen during the early 1990s and increased again since 1998 (Hutchinson *et al.*, 2002). In some sites and for some IDUs the risk may have returned to the same level as that at the beginning of the 1990s (Sweeting *et al.*, in review). It is therefore likely that the overall prevalence of HCV among IDUs has increased in recent years (HPA, 2008a; Sweeting, in review; Sutton *et al.*, 2006). HCV infection among recently initiated injectors has almost doubled from 12 per cent in 1998 to 21 per cent in 2007 (HPA, 2008a).

4.10 Figure 3 shows the estimated HCV prevalence for men and women in England and Wales, after controlling for differences in age, injecting duration, and geographical region over time (Sweeting *et al.*, in review).

Figure 3. Estimated HCV prevalence among IDUs in England and Wales by gender and over time[2]



4.11 The absolute values in Figure 3 should not be interpreted directly as the levels of HCV prevalence in all IDU. This is because the estimates are based on routine surveillance data obtained from non-random samples; and because the analysis has controlled for differences in sample selection over time. However, the results seem to suggest that:

- HCV can be prevented and that public health action and policies in the early 1990s may have reduced HCV risk;
- HCV risk among women (after adjustment for differences in injecting duration) is higher than for men; and
- the public health challenge now is to halt the upward rise in HCV risk and the loss of the benefit achieved earlier in the 1990s.

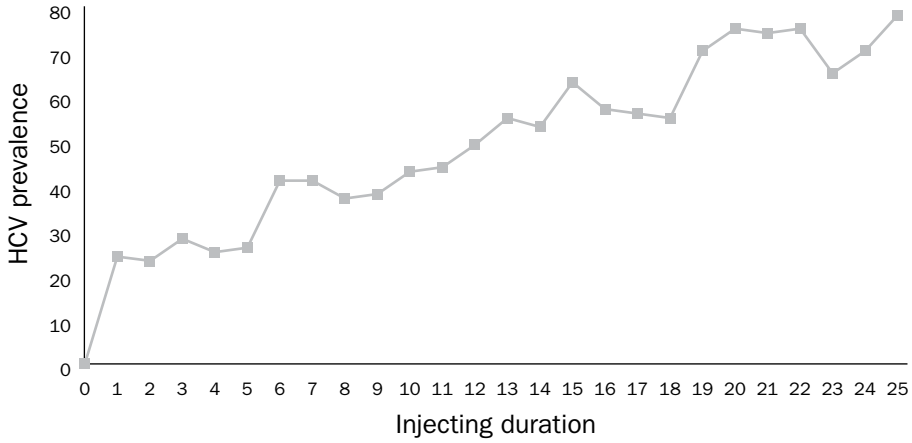
2 After controlling for differences in age, injecting duration and geographical region over time.

5. Injecting risk and HCV

5.1 HCV infection in IDUs is acquired primarily through injecting with an infected needle and syringe, which has been used by someone else who is infected with HCV or possibly has become contaminated through contact with other contaminated injecting paraphernalia. The probability of becoming infected after using an infected syringe ranges from 1.5 to 5 per cent for HCV, in contrast to 0.34 to 1.4 per cent for HIV (Vickerman *et al.*, in press).

5.2 The prevalence of HCV in a given population typically increases with duration of injecting as shown in Figure 4. Persistent IDUs and IDUs with long durations of injecting are increasingly likely to become infected with HCV. However, one of the periods of greatest risk (where risk of transmission may be at its highest) is very early on, in the first year of injecting (Sutton *et al.*, 2006; Sweeting *et al.*, in review; Vickerman *et al.*, 2007). Currently, a fifth of IDUs in the UK become infected with HCV within three years of starting to inject (HPA, 2008). Estimates of HCV risk over time suggest the risk has shown a return to early 1990 levels (see Figure 3; Sweeting *et al.*, in review). Projections from a mathematical model of the impact of reductions in syringe sharing on HCV suggest that the greatest impact of such an intervention is achieved if the reductions in sharing occur in the first year of injecting. (Vickerman *et al.*, 2007).

Figure 4. Prevalence of hepatitis C infection among current and former injecting drug users in England, Wales and Northern Ireland by number of years injecting



Data Source: Unlinked Anonymous Prevalence Monitoring Programme survey of injectors in contact with drug agencies. The sensitivity of the test used for antibodies to hepatitis C is approximately 92%.

5.3 Other important factors and key risks associated with HCV include homelessness and crack cocaine injecting. For example, Table 1 shows crude data from an English multiple city study and South Wales cohort study, on HCV prevalence by whether people inject crack cocaine and/or were recently homeless (Hickman *et al.*, 2007). Part of the reason for the increased risk associated with crack cocaine use and homelessness is that both are associated with factors that increase injecting risk behaviour, such as greater injecting frequency, larger and less stable networks of IDUs, and more frequent reported sharing. The cohort study in South Wales (Table 1) reported approximately four times greater incidence of HCV amongst IDUs who were homeless compared to those who were housed (Craine *et al.*, 2006).

Table 1. England (7 cities)* and South Wales study of HCV prevalence (%) and the variables of homelessness in year and/or crack cocaine use*** (unadjusted data)**

	HCV prevalence (%)	
Housing status and injecting behaviour	**England**	**South Wales****
Never homeless and non-crack cocaine	28	17
Never homeless and crack cocaine	44	32
Recent homeless and non-crack cocaine	44	23
Recent homeless and crack cocaine	71	46

* (Hickman *et al*., 2007)
** in Wales study never homeless in last 12 months (never homeless) or homeless in last 12 months (recent homeless).
***Crack cocaine injection refers to ever injecting crack.

5.4 Associations between homelessness (including hostels) and drug use are complex and mutually reinforcing. Qualitative studies have suggested that hostels may act as a 'safe haven' from street-based drug use, but may sometimes act as 'risk environments' for initiation into higher-risk networks of injecting (Briggs *et al.*, in press). Indeed it has been suggested that large homeless shelters may have increased the risk of HCV (Wadd *et al.*, 2006a). It is uncertain how or whether policies to tackle homelessness and improvements to hostels (such as closure of large-scale old-style homeless hostels) have contributed to reducing HCV risk (Neale, 2008; Neale, oral evidence, 2007).

5.5 Several surveys of IDUs in the UK suggest that people with a history of imprisonment have a higher risk of HCV (Hickman, *et al.*, 2007, Judd, *et al.*, 2005a; Taylor *et al.*, 2000). There have been outbreaks of HIV and evidence of ongoing transmission of HCV in UK prisons. Equally, injecting frequency is substantially reduced in prison and some estimates of HCV incidence are lower than those occurring in the community (Champion *et al.*, 2004; Gore *et al.*, 1995; Weild *et al.*, 2000). Prison is, and can be, a setting for effective public health interventions – such as hepatitis B vaccination, HCV testing and management (Hope *et al.*, 2007; Tan *et al.*, 2008; Hickman, *et al.*, 2008; Horne *et al.*, 2004). There are several potential explanations for the higher risk of HCV among IDUs with a prison history that need further investigation. It could be that IDUs with a prison history in general have greater injecting risk behaviour than IDUs without a prison history; experience greater risk during imprisonment; or experience a period of increased injecting risk immediately after leaving prison i.e. that people may be more vulnerable and less able to control their injecting risk if and when they relapse and continue injecting after leaving prison. The latter would be similar to the increased risk of drug overdose in the period immediately following prison release (Farrell *et al.*, 2008, Bird *et al.*, 2003). Unfortunately, there is a lack of good quality UK research on the effectiveness of prison-based harm reduction interventions (Cattan *et al.*, 2008).

5.6 The results from analysis of surveillance data in Figure 3 suggest that there is a higher prevalence of female IDUs with HCV (after adjustment for injecting duration and other factors). The reason for this is not yet clear. It may be related to women's different injecting patterns and differential exposure to HCV. For example, women tend to inject with older men with longer injecting duration who may be more likely to be infected with HCV. There is also evidence

that women are more likely than men to share needles, receive previously used injecting equipment, be injected by someone else (rather than inject themselves) and have a sexual partner who is also a drug user (Barnard, 1993; Becker and Duffy, 2002; Powis *et al.*, 1996; Wright *et al.*, 2007).

5.7 One of the key problems with the epidemiological and behavioural information on HCV is how to interpret the evidence on needle/syringe and paraphernalia sharing. Epidemiological surveys that analyse the strength of association between reported sharing and HCV infection are inconsistent. In some studies reported sharing is not predictive of HCV infection; and in many studies HCV prevalence remains high, even among people that report never having shared a syringe. Cross-sectional surveys of IDUs in several countries have reported HCV prevalence of over 40 per cent in IDUs who report "never having shared" (Hickman, *et al.*, 2007). Equally, high rates of incidence have also been found in IDUs who report never sharing syringes between baseline and follow-up measures.

5.8 Three potential explanations for the absence of a strong association are: misclassification i.e. a bias against reporting of socially undesirable behaviours such as sharing syringes; that HCV is being transmitted in other ways, perhaps through the sharing of injecting paraphernalia or participation in behaviours where the user is unaware that they are sharing. Qualitative ethnographic studies have shown that drug injectors' interpretations of 'syringe sharing' may differ from those presumed by epidemiological surveys, and that syringe sharing may be under-reported (Rhodes *et al.*, 2004, 2008a; Bourgois, 1998). Sharing behaviour is important when considering the outcomes and the interpretation of outcomes in the evaluation of interventions. We note also that the evidence in support of the validation of self-reported behaviour by problem drug users does not necessarily extend to sharing behaviour (Darke, 1998).

5.9 Paraphernalia sharing, which involves the sharing of water, filters, cookers or spoons used in the preparation of drugs for injection, is more common than the direct sharing of syringes (HPA, 2008a; Health Protection Scotland/ University of the West of Scotland, 2008). Some epidemiological studies have reported paraphernalia sharing as an independent risk factor for HCV (e.g. Hagan *et al.*, 2001). A recent systematic review found limited evidence on whether HCV transmission occurs through sharing of paraphernalia or on the size of any potential risk (De *et al.*, 2008). Inadvertent sharing of equipment, where people mistakenly use another person's equipment, may also be an important, as well as difficult to measure, risk (Taylor *et al.*, 2004). This has prompted the design of syringes with different coloured plungers[3], which are also recommended for use and distribution by NICE.

5.10 It is important to note, however, that it is not just behavioural data that are uncertain. Mathematical models of the transmission of HCV also highlight uncertainty in key biological measures (Hutchinson *et al.*, 2006b). These include: the HCV transmission probability (see 5.1); probability of recovery after exposure to HCV (18 to 50 per cent, Micallef *et al.*, 2006); immunity or reduction in probability of re-infection after clearing the virus (0 to 100 per cent); as well as the window period between detection of RNA and antibodies mentioned above (60 to 90 days). Additional uncertainty exists as to the extent that exposure to HCV may result in a cell mediated immune response that does not produce detectable levels of anti-HCV antibody (Elliot *et al.*, 2006).

3 http://www.exchangesupplies.org/needle_exchange_supplies/never_share_syringe/never_share_syringe_intro.html

5.11 In the UK, overall measures of reported injecting risk behaviour do not appear to differ greatly between IDUs in different geographical areas and are unlikely to be sufficient alone to explain such large geographical differences in estimated HCV prevalence. Equally, the proportion and number of homeless and crack cocaine injectors, though higher in some areas with high HCV prevalence, offers an insufficient explanation. There is likely to be a complex interplay of individual, social, and environmental factors linked to area differences in HCV prevalence. These include the size, mobility, mixing and turnover within drug-injector networks, and historical patterns of local drug injecting and risk practices. Understanding these differences is of interest, but more important is to intervene and to collect epidemiological data in order to assess HCV prevention impact and effectiveness.

5.12 A recent review of published qualitative research on drug injectors' perceptions of HCV risk highlighted a lack of awareness concerning the health implications of HCV as well as uncertainty regarding HCV transmission, especially that linked to the sharing of injecting paraphernalia (Rhodes *et al.*, 2008b). Qualitative data have suggested a tendency for some drug injecting networks in the UK to perceive HCV as an ubiquitous, inevitable, and thus difficult to avoid, consequence of injecting (Rhodes *et al.*, 2004). Other studies show that HCV risk may be 'normalised' as part of everyday injecting lifestyles, wherein multiple other risk priorities compete for a user's attention (Rhodes *et al.*, 2008b). While UK qualitative research on HCV risk and IDU is in need of updating, these studies emphasise how local social contexts and risk perceptions may shape HCV prevention. Evidence given by user representatives to the ACMD likewise expressed a tension between the competing everyday priorities of consuming/injecting drugs and being in situations where this can be done safely to avoid infection, with the latter usually losing (oral evidence from user representatives, 2008).

5.13 What is clear from quantitative and qualitative evidence is that persistent injecting is the key risk factor for HCV, and that reducing frequency and duration of injecting may be critical to HCV prevention. This is because occasional sharing among novice IDUs and/or during a period of chaotic injecting among those that become dependent may be inevitable, even if advice is provided. In those areas with a high background prevalence of HCV even small lapses in unsafe injection pose a high risk of transmission.

5.14 In some needle and syringe programmes ten per cent or more of their clients are people who use performance and image-enhancing drugs (PIEDs) such as anabolic steroids. Clearly, this group of people may be at risk of HCV and other blood-borne infections if they share syringes, and share with people who are infected with HCV. However, information on HCV prevalence and risk among PIED users is unknown and needs to be investigated[4].

4 The ACMD have convened a Working Group to review PIEDs, including their misuse and harms. The Working Group is scheduled to report to Ministers in 2009.

6. HCV morbidity, testing, and intervention coverage

6.1 HCV diagnostic testing has increased, but uptake and frequency is generally inadequate among current IDUs. Routine surveillance data in England and Wales suggest that at least 7,500 people were reported as diagnosed in 2007, a greater than 60 per cent increase on the number reported as HCV positive in 2000 (HPA, 2008a). Because of under-reporting the true number of diagnoses is likely to be larger. Injecting drug use is the attributed cause in 90 per cent of these diagnoses, where information is available. In England and Wales there may be 100,000 undiagnosed people with HCV, though this number has a high degree of uncertainty. In Scotland, a further 30,000 individuals estimated to be infected with HCV have not been diagnosed with the virus (Scottish Government, 2008).

6.2. Anonymous surveys of IDUs show that at least three-quarters of participants report that they have been tested at some time for HCV. These same surveys also show that less than half are aware that they are HCV positive (i.e. by comparing the number with HCV antibodies detected with self-reported HCV status). (Hickman, *et al.*, 2007; HPA 2008; Health Protection Scotland/ University of the West of Scotland, 2008). In addition, the frequency of testing by specialist drug agencies and prisons has been poor, and may be less than 15 per cent of their caseload (Hickman, *et al.*, 2008). Dried blood spot (DBS) testing can now be offered which addresses part of the problem in relation to the difficulty of taking blood from injectors with poor venous access (Judd *et al.*, 2003; Hickman, 2008). Establishing competence and building confidence among drug workers in dealing with HCV also may need to be addressed.

6.3 We undertook a mapping exercise of the coverage of HCV interventions, which highlighted the lack of robust data (C Beynon, presented evidence to ACMD, 2008). First, estimates of the number of IDUs (the denominator) are inconsistent. Home Office estimates suggest that there may be around 137,000 IDUs in England (Hay *et al.*, 2006), whereas estimates of IDUs used in the work shown in Figure 1 above were between 150,000 to 300,000. Second, surveys of IDUs suggest that the majority are in contact with a Needle and Syringe Programme. However, there are no reliable data for England and Wales on the number of syringes distributed. A Turning Point report (*At The Sharp End*, 2007), estimated that there were around 23 million syringes distributed in England and Wales in 2005. This estimate is similar to a previous survey conducted in 1997 (Parsons *et al.*, 1997), whereas the number of IDUs is likely to have increased over the same period. The number of people and IDU diagnosed with HCV is also uncertain because of under-reporting. In contrast, data on the number of people receiving opiate substitution therapy (OST), if delivered through specialist drug treatment agencies or shared care arrangements with primary care, are more robust. One of the great successes of the recent drug policy was the investment in and increase in specialist drug treatment. In 2006/07 over 100,000 people received OST, and the amount of methadone prescribed has increased threefold since the mid-1990s (Morgan *et al.*, 2006). However, the combination of uncertainties in both denominator (number of IDU) and some of the numerators (interventions) means that to date accurate estimates of intervention coverage have been difficult to obtain.

6.4 We have highlighted the large geographical variation in HCV prevalence above. This information was derived from a wide-ranging surveillance programme including detailed studies of HCV and injecting risk in IDUs in selected studies, routine surveillance of HCV at over 50 sampling sites in England and Wales, and multiple surveys in Scotland (HPA, 2008a; Roy *et al.*, 2007; Scottish Government, 2008). The UK HCV surveillance programme is one of the most developed in Europe and worldwide. However, it is also limited as the survey can only operate in a comparatively small number of sites in the whole of the UK. Ideally, reliable information on the likely prevalence of HCV and the number of people infected should be provided to local policy-makers. Data have been provided, but the current methods are unsatisfactory and the estimates themselves are at best only indicative (NTA unpublished estimates).

6.5 In contrast, estimates of the total number of people infected with HIV are more robust (Goubar *et al.*, 2008). Part of the reason is that information on the number of people diagnosed with HIV is more complete and the proportion of people infected with HIV that have been tested is higher than for HCV. Better information on HCV diagnoses, more frequent testing among current and ex-IDU, and more consistent estimates of the IDU population (Academy of Medical Sciences, 2008) will provide the platform to reduce the uncertainty surrounding current estimates of the number of HCV infections nationally and provide more reliable estimates for local areas.

6.6 It is important to recognise several notable and very successful aspects of recent policy. All Primary Care Trusts (PCTs) and health boards in Great Britain have some form of needle and syringe provision. Specialist drug treatment and opiate substitution therapy have been expanded markedly and new HCV, safer injecting, and other health education campaigns for IDU have been launched: (http://www.harmreductionworks.org.uk/). The HCV Action Plan Scotland has secured significant new resources allied to a clear set of objectives and recommendations that will increase health education, HCV diagnosis and treatment, and NSP activity in order to prevent HCV infection and morbidity (Scottish Government, 2008). Selected PCTs in England have also joined together to develop local HCV plans to increase treatment services (e.g. Manchester HCV strategy (http://www.greatermanchesterhepc.com/)). In Wales a blood-borne viral Action Plan has been produced and is currently under consideration by the Welsh Assembly Government. Northern Ireland has published an HCV action plan (Department of Health, Social Services and Public Safety, 2007). However, to date investment in new surveillance data or intervention evaluation has lagged behind policy and service development leading to the many uncertainties in the evidence.

7. Intervention and prevention

7.1 There is a fundamental disconnect between the strength of the evidence on the effectiveness of interventions to reduce HCV infection and what many concerned parties, including policy-makers, services, service users, and policy advocates, would like to see put in place. Submissions from services and user representatives has emphasised the need to:

- make greater investment in needle exchange and the distribution of all injecting paraphernalia;
- increase the number of NSP sites and their opening hours;
- make NSP available in prisons;
- pilot drug consumption rooms;
- invest in outreach and peer education programmes to promote safer injecting;
- introduce contingency management to promote blood-borne virus testing;
- and provide greater access to HCV diagnosis and treatment.

(Joseph Rowntree Foundation, 2006; Wadd *et al.*, 2006b; oral evidence from user representatives, 2008).

Review of reviews: strength of evidence

7.2 In collaboration with Health Protection Scotland we undertook a "review of reviews" which was a complete and systematic search of the English language literature to identify reviews of the impact of interventions on HCV transmission, HIV transmission, and injecting risk behaviour. The executive summary is available at http://www.hepcscotland.co.uk/action-plan.html. The key conclusion from the review is that the strength of the evidence for the effectiveness of many interventions in reducing HCV and HIV transmission among IDUs is weaker than we expected, and is weaker than often given credit for by many of the reviews in the literature.

Lack of evidence of intervention effect does not mean no intervention effect

7.3 The absence of evidence for many of the interventions discussed above probably reflects a corresponding lack of primary studies investigating these interventions. That is: a lack of or insufficient review-level evidence of an effect does not imply no evidence of an effect; and certainly does not imply that other interventions may be more effective or that policy-makers should reconsider funding of these interventions.

7.4 Much of the evidence for harm reduction interventions, with the exception of OST, is based on observational study designs. These are study designs that recruit IDUs and record whether they have been exposed to a specific intervention under investigation (retrospectively or prospectively) and relate this information to different outcomes (HIV, HCV, injecting risk behaviour). These are sub-optimal designs when trying to test questions of whether an intervention is effective. This is because apparent effects of the intervention are often confounded by factors associated with receipt of the intervention. That is, the characteristics of IDUs exposed and unexposed to the intervention can be very different and this can dilute, exaggerate or reverse the true relationship between intervention and outcome. A further problem is that the level or 'dose' of intervention exposure is rarely measured in the same way between studies, and few reviews, except those looking at OST, were able to assess the impact of different levels of exposure on HCV or HIV incidence (Cattan *et al.*, 2008;

Palmateer *et al.*, 2008; Tilson *et al.*, 2007). An infamous example in this field is an assessment of NSP effectiveness in Vancouver. The initial report seemed to suggest that IDUs in contact with the NSP were more likely to become infected with HIV. However, IDUs in contact with the NSP were also found to have greater injecting risk behaviour than IDUs not in contact with the NSP and only after controlling for these differences were the counter intuitive findings removed (Schecter *et al.*, 1999; Strathdee *et al.*, 1997; Wood *et al.*, 2007).

7.5 Some concern has been expressed that a systematic review methodology of these interventions may disadvantage NSP and other harm reduction interventions, as they may not take account of subtleties in measuring a complex behavioural change or in how services are delivered. We reject this criticism. But we do agree that NSP and other harm reduction measures are complex interventions (i.e. that they are likely to involve more than one 'active ingredient') and evaluation should be developed appropriately (Medical Research Council, 2000). Moreover, there is a lack of UK specific data in general, and it is unclear whether the findings from many assessments of NSP are applicable to the UK given the differences in the political acceptance of NSPs and wider harm reduction services for IDUs.

Needle and syringe exchange programmes

7.6 The balance of evidence from primary studies, identified by the reviews in the literature, led to the conclusion that there is insufficient evidence to either support or discount the effectiveness of NSP in preventing HCV transmission. A further review commissioned by the National Institute for Health and Clinical Excellence (NICE) also concluded that there was insufficient evidence "to determine the impact of NSPs on HCV infection in IDUs" (Jones *et al.*, 2008). In contrast, as noted by NICE, indirect evidence supports NSPs, such as: ecological studies reporting that cities with NSPs have a lower HCV prevalence than those without NSPs; and, dynamic modelling which suggests that if NSPs can reduce injecting risk they can reduce HCV transmission. There is also a lack of published evidence assessing the cost-effectiveness of NSP for preventing HCV. This prompted the development of new HCV models that are summarised below.

7.7 Our review of reviews (Palmateer *et al.* 2008) found discrepancies in the reporting of primary studies between reviews and could only tentatively conclude that NSP are effective in reducing HIV incidence. A review commissioned by NICE (Jones *et al.*, 2008) also highlighted conflicting evidence: two 'good quality' reviews supported the effectiveness of NSPs in reducing HIV infection among IDUs but two other reviews (including one 'good quality') "suggest that the evidence may be less convincing".

7.8 It has been suggested that NSPs can have wider benefits through secondary distribution to IDUs who are not in direct regular contact with NSPs. However, evidence on injecting risk of IDUs obtaining syringes through secondary distribution (compared to IDUs in direct contact with NSPs) is inconsistent and there is little evidence on the impact of secondary distribution on HCV infection. Equally, there has been considerable debate on the strengths and limitations of agency-based and pharmacy-based NSPs (HPA, 2008; Healthcare Commission, 2008). While there is some evidence that IDUs report benefits of both forms of provision (e.g. anonymity of pharmacy NSP and access to other services from agency NSP), there is no evidence of any difference in intervention effect on HCV transmission.

Opiate substitution therapy (OST)

7.9 The review of reviews (Palmateer *et al.*, 2008) tentatively concluded that OST has a small impact in reducing HCV incidence. This impact is greatest among those in continuous treatment and those with longer duration of treatment and may be most apparent in areas of currently low prevalence. There was sufficient review-level evidence that continuous OST at higher doses is effective in reducing HIV incidence. There was also sufficient evidence in support of the cost-effectiveness of NSP and OST in preventing HIV transmission among IDUs (Jones *et al.*, 2008, Palmateer *et al.*, 2008; Tilson *et al.*, 2007).

Other harm reduction interventions

7.10 The review of reviews by Palmateer *et al.*, (2008) identified no or insufficient review-level evidence to either support or discount the effectiveness or cost-effectiveness of any of the following in relation to HCV or HIV prevention:

- needle/syringe vending machines;
- the provision of sterile drug preparation equipment;
- bleach disinfection;
- information, education and counselling (IEC);
- behavioural outreach;
- HCV screening;
- drug consumption rooms (DCRs); or,
- the promotion of non-injecting routes of administration (NIROA).

Behavioural outcomes

NSPs (reported sharing vs. HCV incidence)

7.11 The strength of evidence is much greater for behavioural measures (i.e. self-reported injecting risk behaviour) than for biological measures (incidence). There is good evidence that participation in NSPs reduces injection risk behaviours among injecting drug users (IDUs), in particular self-reported sharing of needles and syringes. For example, Table 2a below summarises studies investigating the relationship between NSPs and sharing behaviour – with each row showing a different study design and the columns reporting the finding as positive (a reduction in self-reported injecting risk), negative (an increase in self-reported injecting risk) or no change. Among 43 studies the overwhelming majority suggested that NSPs were effective, and most of these are cohort studies which are higher in the hierarchy of evidence than the other designs. In contrast, Table 2b summarises studies investigating the relationship between NSP and HCV infection – showing both that there are fewer studies in total (n=14) and fewer studies, especially among the better study designs, that report positive findings. Table 2c summarises studies investigating the relationship between NSP and HIV infection (n=16). There were more positive findings as compared with Table 2b, although there were notably mixed results among the more robust study designs – cohort and case-control (Palmateer *et al.*, 2008; Tilson *et al.*, 2007).

Tables 2 a–c Studies (from Palmateer *et al*., 2008) showing the association between:
a) NSP and syringe-sharing behaviour
b) NSP and HCV transmission
c) NSP and HIV transmission

a) Review of Reviews: studies showing association between NSP and sharing behaviour

	Finding		
Study Design	**Positive**	**Negative**	**No/equivocal association**
Cohort	20	0	1
Ecological	1	0	0
Serial cross-sectional	7	0	0
Cross-sectional	11	1	2
Total	**39**	**1**	**3**

b) Review of Reviews: studies showing association between NSP and HCV transmission Other interventions

	Finding		
Study Design	**Positive**	**Negative**	**No/equivocal association**
Cohort	0	2	2
Case-control	1	0	0
Ecological	1	0	0
Serial cross-sectional	2	1	1
Cross-sectional	3	0	1
Total	**7**	**3**	**4**

c) Review of Reviews: studies showing association between NSP and HIV transmission

	Finding		
Study Design	**Positive**	**Negative**	**No/equivocal association**
Cohort	2	2	2
Case-control	0	0	2
Ecological	4	0	0
Serial cross-sectional	2	0	0
Cross-sectional	2	0	0
Total	**10**	**2**	**4**

7.12 There is good evidence also to support the effectiveness of OST in reducing self-reported injecting risk behaviour: specifically on decreasing frequency of injection.

7.13 There is tentative review-level evidence to support the effectiveness of information, education and counselling (IEC) in reducing injecting risk behaviour, which also involves HCV and other BBV testing. In addition, there is tentative review level evidence to support pharmacy access to sterile needles/syringes, behavioural outreach, and drug consumption rooms (DCRs) in reducing injecting risk behaviour (Palmateer *et al*., 2008; Tilson *et al*., 2007).

Paraphernalia distribution and sharing

7.14 Both the review of reviews and the NICE review found little evidence that exposure to NSPs reduced the sharing of paraphernalia (such as cookers, filters or water for injection), primarily because few studies have examined these outcomes (Palmateer *et al.*, 2008, Jones *et al.*, 2008). A small qualitative study of injecting risk in two cities in Scotland (one of which distributed paraphernalia and one that did not) found little difference in injecting risk behaviour (Scott, 2008). The most recent surveys suggest that most needle exchanges (NEX) distributed syringes and some form of paraphernalia with wide variation in the number of syringes and range of paraphernalia distributed (Abdulrahim *et al.*, 2007; Griesbach *et al.*, 2006).

Bleach

7.15 There is consistent evidence from laboratory studies that bleach disinfection is effective in deactivating HIV. However, the evidence suggests that IDUs' practices in cleaning their syringes are too inconsistent to represent an effective stand-alone intervention (Palmateer *et al.*, 2008; Tilson *et al.*, 2007). New evidence is also likely to suggest that bleach is effective in deactivating HCV as reported in new health education material[5]. Therefore, syringe cleaning and improving IDUs' practice could become an important harm reduction intervention and target.

Prison populations

7.16 There was insufficient evidence to assess the effectiveness of NSP or other interventions in preventing HCV or HIV transmission in prison settings (Palmateer *et al.*, 2008).

Recent IDU

7.17 We found no review-level evidence for any of the interventions in relation to prevention of HCV or HIV transmission among young IDUs (Palmateer *et al.*, 2008; Tilson *et al.*, 2007).

HCV Interventions

7.18 On balance we consider NSP to be an effective intervention which needs to be delivered within a comprehensive prevention programme including OST (Tilson *et al.*; 2007). However, there is no question that the evidence base

5 http://www.harmreductionworks.org.uk/2_films/viral_survival_in_syringes.html)

needs to be improved; as information on the intervention effect (especially the combination of OST and NSP) needs to be strengthened in order to address uncertainty over the most effective level and mix of interventions for reducing HCV infection.

7.19 We agree with NICE guidance and recommendations (NICE, 2009) that local DA(A)Ts and others e.g. LSPs, PCTs consult with people who inject drugs and others in the local community to assess the need for, and the planning of, needle and syringe programmes (NSP). In particular, the consultation needs to identify potentially inadequate provision in relation to site, situation or occasion, and type of IDUs (e.g. hostels, out of hours, commercial sex workers); this is in accordance with the Department of Health HCV strategy and action plan (Department of Health, 2002 and 2004). These also recommended that prevention efforts may need to be intensified, and that local Primary Care Trusts (PCTs) may need to review their local harm reduction services. The Healthcare Commission and the NTA (2008) have already noted that there was a clear national shortfall in the provision of out-of-hours needle exchange. It is now time for PCTs and Local Health Boards to do both: review and intensify their HCV intervention effort. Equally, this time, policy-makers and scientists need to ensure that the impact of changes and increases in intervention provision is evaluated properly and rigorously. This is particularly important given that both evidence reviews noted the lack of UK studies.

7.20 We endorse the NICE recommendations (NICE, 2009) that local policy-makers should be encouraged to commission a range of services to ensure the widest possible availability of needles and syringes within the local strategic partnership area – with a particular focus on opening hours and availability and that there should be no arbitrary limit set on the number of syringes/packs distributed. In addition, we need to emphasise that NSPs on their own will be insufficient to prevent HCV, and that they should be seen and commissioned as a component part of a comprehensive service.

7.21 NSPs need to provide or ensure access to a range of other services including HBV vaccination, referral to OST, BBV antibody testing, and referral for HCV treatment (see below).

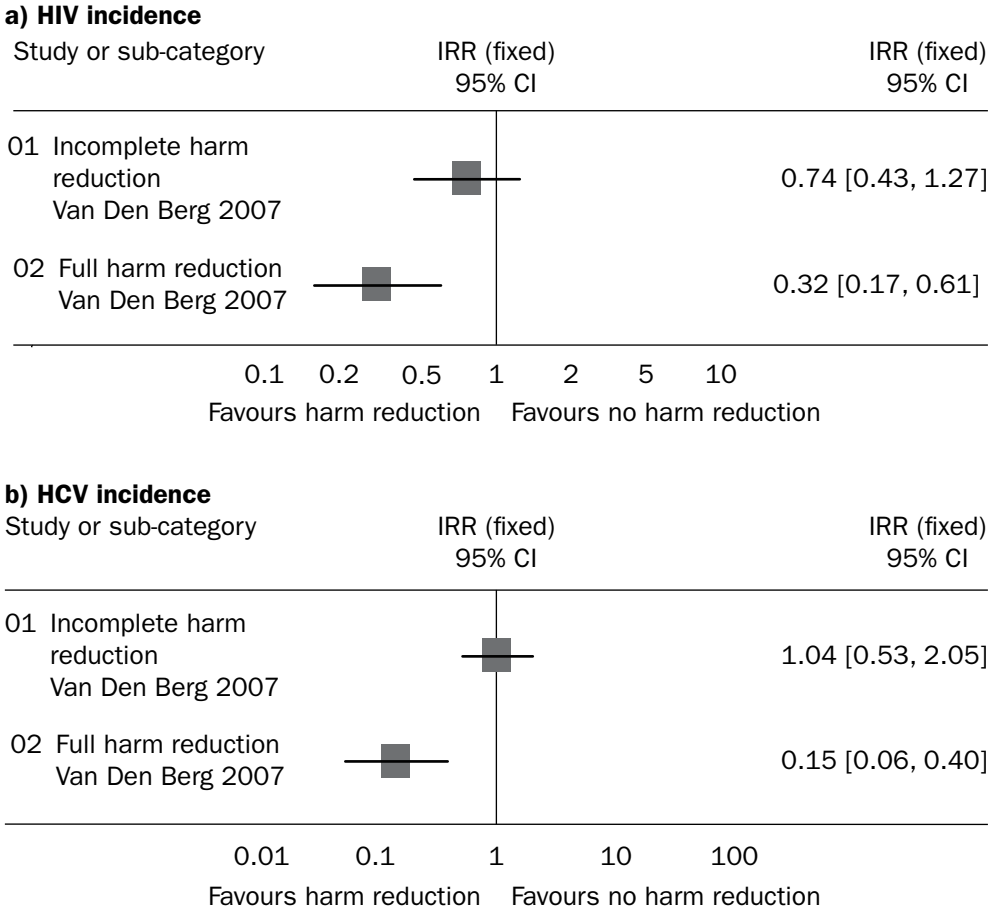
7.22 We concur with the NICE guidance (NICE, 2009) that local PCTs and DA(A)Ts need to commission services in relation to the level of risk (such as disease prevalence).

Modelling intervention effect

7.23 New modelling work commissioned by NICE (Vickerman *et al.*, 2008) sought to assess the impact and cost-effectiveness of NSPs and selected interventions to reduce HCV (see www.nice.org.uk/ph018). Clearly, this is a challenge given the lack of direct evidence of an intervention effect as summarised above. However, one published study (see Figure 5) of a cohort study in the Netherlands suggests that the combination of OST and full participation in NSPs may reduce the incidence of HIV and HCV among IDUs (Van Den Berg *et al.*, 2007). Van Den Berg and colleagues assessed harm reduction in the six months prior to incident infection on the basis of whether the person reported: no use of NSP and OST; incomplete participation (either irregular use of NSP or low dose methadone); or full participation (defined

as high or optimal methadone dose and always use NSP to provide syringes for injection). The figure compares no harm reduction to incomplete or full participation in harm reduction for HIV incidence in the top graph and HCV incidence in the bottom figure. Measures to the left favour the intervention, suggesting a lower incidence expressed as an Incidence Rate Ratio (IRR) and vice versa to the right. Thus, compared to no harm reduction: incomplete harm reduction slightly reduced HIV incidence (though the confidence interval also crossed 1, suggesting that evidence is not strong enough to reject the null hypothesis of no effect) and had no impact on HCV incidence. Full or complete harm reduction reduced HIV incidence by one-third and HCV incidence by six times.

Figure 5 a) and b) Amsterdam addiction cohort showing the impact of interventions (NSP and OST) on HIV and HCV incidence (Van Den Berg *et al.*, 2007)[6]



6 IRR – Incidence rate ratio.

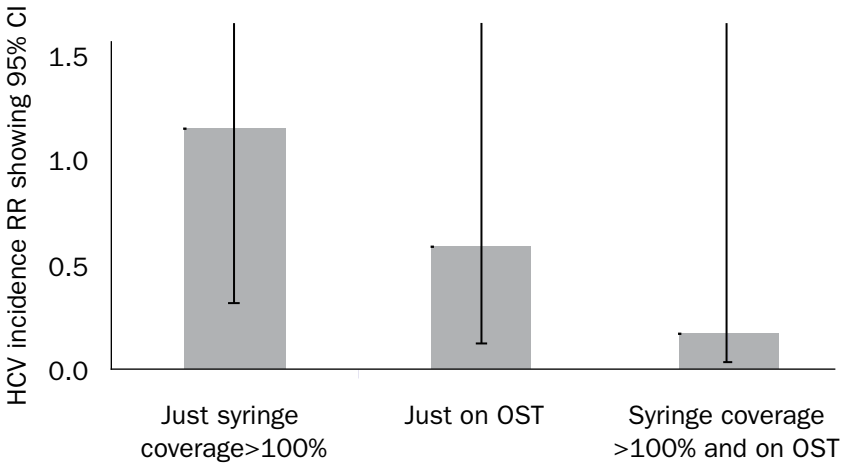
Interpretation of these findings to the UK must be cautious. The Amsterdam cohort had a high background prevalence of HIV and HCV (26 per cent and 82 per cent respectively at study entry). Nonetheless, there are preliminary findings in the UK that also suggest that the combination of OST and NSP may be more effective in reducing HCV than either intervention alone (Hope in review; Vickerman *et al.*, 2008). In this case NSP participation was measured in terms of whether an estimated 100 per cent or less of injections could be covered by syringes obtained through NSPs. For instance, Table 3 shows that in a follow-up study in South Wales HCV incidence was less than two per cent among IDUs in OST and who received 100 per cent NSP coverage compared to approximately ten per cent among IDUs receiving less than 100 per cent coverage and who were not on OST. In a cross-sectional study of active IDUs in Bristol, HCV incidence, measured using HCV PCR and antibody tests, was 16 per cent among IDUs in OST and 100 per cent NSP coverage compared to over 50 per cent in IDUs receiving less than 100 per cent NSP coverage and who were not on OST. The studies, however, are comparatively small and uncertain as can be seen in the figure which shows wide 95 per cent confidence interval around IRR estimates of IDU with different levels of intervention coverage compared against those with < 100% NSP and no OST. But the key message is that combined or comprehensive harm reduction intervention may be the most effective at reducing HCV incidence, and that a single intervention – be it NSPs or OST may not, on its own, be sufficient.

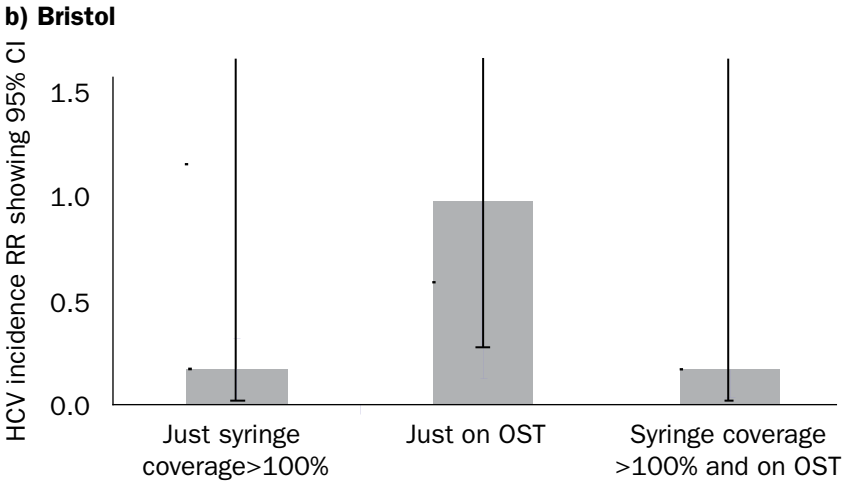
Table 3. UK results regarding the impact of interventions (preliminary findings) showing incidence of HCV per 100 person years

Coverage	South Wales	Bristol
<100% NSP no OST	9.7%	55%
100% NSP no OST	11.1%	13%
<100% NSP OST	5.7%	45%
100% NSP OST	1.6%	16%

Figure 6. Incidence Rate Ratio of NSP and OST coverage – compared against <100% NSP and no OST

a) Wales





Intervention effect and cost-effectiveness modelling

7.24 The above findings and other biological and behavioural information that govern HIV and HCV transmission were used to adapt and modify existing infectious disease models in order to assess the potential impact of interventions on HCV transmission (Vickerman *et al.*, 2008). The models were fitted to HCV prevalence data from two areas indicative of a high and low HCV prevalence. The new model adopts a slightly different measure of the NSP coverage. Previous models and some definitions of coverage used by the World Health Organisation and the NTA have examined the average number of injections covered by a sterile syringe (Vickerman *et al.*, 2007; WHO, 2009). In contrast, the new model considers the proportion of IDUs that are in receipt of an estimated 100 per cent coverage (i.e. a syringe for every injection) (Vickerman *et al.*, 2008). The principle remains the same i.e. what level of intervention is likely to lead to sufficient behaviour change to minimise the number of new infections[7].

7.25 The models investigated whether changes in intervention coverage were likely to be cost-effective and found that overall there is a strong likelihood that NSP and other interventions are cost-effective. We summarise the findings below.

7.26 First, increasing the number of IDUs receiving full NSP coverage may be cost-effective if the costs of delivering the increased intervention are not too high and the intervention achieves a moderate decrease in syringe sharing (Vickerman *et al.*, 2008). Results suggest, however, that the impact and the cost-effectiveness of NSP alone are likely to be greater in lower HCV prevalence settings.

Second, increasing the number of people receiving OST will be cost-effective, primarily because of other benefits such as reductions in drug-related crime and overdose, while its impact alone on blood-borne viruses may only be modest.

Third, the models suggest that increasing the referral and participation of active IDUs into HCV treatment may be a cost-effective intervention to reduce population levels of HCV incidence and prevalence.

7 We note as with NICE that there is no accepted or standard definition of NSP coverage. Indeed the concept is borrowed by analogy from vaccine preventable diseases (such as smallpox or measles) where there is a theoretical level of vaccine "coverage" which once achieved will eradicate the disease.

Fourth, model projections suggest that increasing the coverage of syringe distribution or the recruitment rate onto OST may be sufficient for controlling HIV, but large reductions in HCV infection rates may only be achieved through the combination of interventions.

7.27 The need for a combination of interventions is illustrated in Table 4 below, which suggests that the greatest impact may be achieved by a strategy that seeks to increase the number and proportion of IDUs in receipt of 100 per cent of their required syringes, on OST, and entered into HCV treatment. It is important to note that these projections are indicative of the relative impact of increasing the recruitment of IDUs onto OST or high syringe coverage rather than estimates of the absolute impact of current levels of OST recruitment or syringe distribution. In addition, all projections are approximate because they are based on a model, which, although it fitted well the available information in two UK sites also contains a number of assumptions (outlined in full in Vickerman *et al.*, 2008). A key limitation is the paucity of good quality (and UK specific) evidence on intervention effects. Other limitations include a lack of cost data and quality-of-life indicators, and uncertainty on any potential immunity or the likelihood of re-infection following successful HCV treatment. The lack of data also meant that it was not possible to consider which types of NSP or which configuration of NSPs and OST may be more cost-effective.

Table 4. Impact projections of interventions on HCV incidence (%) and prevalence (%) over 20 years[8]

Single focus interventions	**Decrease HCV incidence**	**Decrease HCV prevalence**
Increase OST recruitment rate (doubling in OST recruit rate)	10.1	6.0
Increase 100% syringe coverage recruitment (doubling in IDU on 100% syringe coverage)	7.3	4.7
Increase HCV treatment recruitment rate (doubling of chronic HCV IDUs treated a year from 5% to 10%)	20.4	13.0
Multi-faceted interventions		
Increase OST and 100% syringe coverage recruit rates	22.7	14.3
Increase OST, 100% syringe coverage and HCV treatment	42.1	27.7

7.28 There are distinct advantages to identifying and treating early HCV infection – within the first year of infection, though after the period by which viral clearance may happen automatically. Treatment success of those with acute/early infection can be higher than for people with chronic HCV infection, and treatment length can be shorter (Jaeckel, 2001; Kamal *et al.*, 2004; Blackard *et al.*, 2008).

7.29 Despite the caveats and uncertainties in the evidence, which are important to note (and address), we believe that HCV infection can only be reduced by further investment in interventions and by adopting a comprehensive multi-faceted strategy.

8 The decreases in prevalence and incidence are relative. Increase in coverage is a doubling of rate of IDUs on OST, receiving 100% syringe coverage, or HCV treatment.

8. Conclusions and Recommendations

8.1 Overall, approximately half of IDUs in the UK are infected with HCV. However, there is a greater than threefold difference in HCV prevalence between individual sites in the UK. There is some evidence that HCV prevalence among IDUs may have fallen during the early 1990s even in areas with a high prevalence of HCV. However, it is likely that the overall prevalence of HCV infection among IDUs has increased from the mid 1990s. HCV infection among recent initiates has almost doubled from 1998 to 2007. We note that harm reduction and other services to prevent HCV are being provided in local areas. The public health challenge in the UK now is to increase action and effective prevention in order to stem the upward rise in HCV prevalence. We endorse the recommendations by the National Institute for Health and Clinical Excellence (NICE) set out in http://www.nice.org.uk/ph18 (NICE, 2009) and commend the HCV Action Plan in Scotland which has already started the process of expanding HCV prevention (HCV Action Plan Scotland, http://www.scotland.gov.uk/Publications/2008/05/13103055/0).

Recommendation 1. Local service planners need to review local needle and syringe services (and be supported in this work) in order to take steps to increase access and availability to sterile injecting equipment and to increase the proportion of injectors who receive 100 per cent coverage of sterile injecting equipment in relation to their injecting frequency.

8.2 We note that the strength of the evidence for the effectiveness of many interventions in reducing HCV transmission among IDUs is weaker than we expected. However, there is positive emerging epidemiological evidence (supported by preliminary studies in the UK) that the *combination* of opiate substitution therapy (OST) and NSP is the most effective way of reducing HCV (and HIV) incidence among active IDUs. NSP or OST alone may not be sufficient to prevent HCV. A comprehensive HCV prevention and harm reduction service needs to ensure that both NSP and OST are being provided and working together, and that services and drug workers focus on reducing injecting frequency and duration.

Recommendation 2. Local services need to provide a comprehensive intervention so that those offering OST also provide access to sterile injecting equipment and those providing sterile injecting equipment facilitate entry into OST.

8.3 The frequency of HCV testing by prisons, specialist drug agencies, and other agencies managing current IDUs, has been poor. Anonymous surveys suggest that approximately half of IDUs are unaware they are HCV positive. This needs to change. Dried blood spot tests, which are non-invasive and easy to learn, provide part of the solution. HCV testing and knowledge of HCV status provides an opportunity to initiate further health education advice and harm reduction interventions that will be of benefit: to the patient (such as managing alcohol use if HCV infected), to other IDUs and society (in relation to reducing injecting risk behaviour), and potentially to both the patient and society (by referral for HCV treatment, see recommendation 7). Information on HCV testing also may be used to improve local and national estimates of the number of people infected with HCV.

Recommendation 3. All services (especially specialist drug clinics, low threshold agencies, and prisons) in regular contact with IDUs need to increase the frequency of HCV diagnostic testing among their clients.

Recommendation 4. Review workforce and training needs of NSP and other drug workers and if necessary develop further training in order to ensure that staff are competent and confident in providing HCV and other BBV antibody testing.

Recommendation 5. Establish a monitoring programme to measure success against recommendations 3 and 4 such as: the proportion of specific agency caseloads tested for HCV and other BBV (including prisons, specialist drug clinics, and patients in OST shared care) and the proportion of IDU tested anonymously that are unaware of their HCV status.

8.4 There is an urgent need for UK-based research on the effectiveness and cost-effectiveness of NSP, OST, and other interventions to reduce HCV incidence. The lack of evidence reflects the lack of large-scale studies and the difficulty of recruiting and retaining IDUs. Primarily we need better evidence on the "intervention effect" of OST and NSP; though improving the evidence on certain biological and behavioural factors that determine HCV transmission is also important. This will enable researchers and modellers to provide service planners with clearer recommendations on the optimal provision of intervention services in relation to their different epidemics. The expansion of services and development of novel techniques to estimate HCV incidence provide an ideal opportunity to generate better evidence. Cost-effectiveness modelling presented to the working group and to NICE suggested that HCV treatment of active injectors could have a primary prevention role (i.e. reducing HCV transmission in the population) as well as secondary prevention (i.e. preventing HCV morbidity). The cost-effectiveness models suggested that the combination of OST, NSP and HCV treatment had the greatest impact on HCV. However, assumptions on the level of immunity and re-infection rates following successful HCV treatment need to be tested.

Recommendation 6. Studies are required that directly test the effectiveness of OST and NSP on reducing HCV incidence (i.e. that generate evidence on the intervention effect).

Recommendation 7. A study is required to measure the re-infection rate of injectors who have been treated for HCV and to evaluate the effectiveness of providing HCV treatment to current injectors in order to reduce HCV incidence.

8.5 Though there was a lack of review level evidence on the effectiveness for many of the interventions proposed by expert witnesses to the ACMD, there has been much innovation of prevention initiatives in the UK (such as the provision of injecting paraphernalia and coloured syringes) and most recently the "harm reduction works" health education programme. Innovation and development need continued support, but more attention needs to be given to evaluation and to modelling the potential impact and cost-effectiveness of new interventions. We know that recent injectors (perhaps in the first six months or year) have an elevated risk of HCV infection; but have no review level evidence on which interventions successfully target and reduce HCV incidence among recent injectors. People with a prison history have a greater

risk of HCV infection but we cannot explain fully why; and have no good quality review level evidence or UK research on the effectiveness of prison-based harm reduction interventions. Homelessness also increases the risk of HCV infection.

Recommendation 8. Evaluate whether new health education messages have changed the perception and views of IDUs about the risk and inevitability of HCV; and whether campaigns to teach and encourage IDUs to use bleach to clean injecting equipment (when sterile equipment is not available) have resulted in safer re-use of equipment.

Recommendation 9. Studies are required to determine why IDUs with a prison history are at greater risk of HCV, and to develop and trial appropriate harm reduction interventions within the prison service and in the community to reduce the risk.

Recommendation 10. Develop and promote effective strategies to target and reduce HCV risk among recent injectors.

Recommendation 11. A study is required to investigate HCV risk and prevalence among people that use performance and image-enhancing drugs.

8.6 Finally, we recognise that compared to many other countries the UK has a well developed public health surveillance system for measuring the prevalence of HCV. Though there is a need to improve some of the epidemiological evidence (including recruitment and coverage of routine surveillance, and risk of HCV among some groups e.g. see recommendations 3, 9 and 11), we think that greater priority should be given to supporting and monitoring the impact of interventions to reduce HCV infection.

Recommendation 12. The public health surveillance of HCV needs to be developed and extended so that it can monitor and provide evidence on the impact of interventions on HCV risk; and if required the roles and responsibilities of public health scientists and public health agencies need to be extended in order to support the development and evaluation of HCV interventions.

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District Judge Justin Phillips	District Judge, Drugs Court
Mr Richard Phillips	Director of Services, Phoenix Futures
Dr Ian Ragan	Pharmaceutical Industry consultant
DCC Howard Roberts	Deputy Chief Constable, Nottinghamshire Police
Dr Mary Rowlands	Consultant Psychiatrist in Substance Misuse, Exeter
Dr Polly Taylor	Veterinary Surgeon, Cambridgeshire
Ms Monique Tomlinson	Freelance Consultant in Substance Misuse
Mrs Marion Walker	Pharmacist, Berkshire Healthcare NHS Trust
Mr Arthur Wing	Assistant Chief Officer – Sussex Probation Area

Annex C: Experts submitting evidence to the ACMD at its Prevention Working Group meeting in April 2008

Oral evidence was submitted from representatives from the following organisations:

Addaction

Black Poppy

National Treatment Agency for Substance Misuse

Reading User Forum

Turning Point

Written submissions were received from:

Janet Catt

Dr Ross Coomber

Jon Derricott

Hepatitis C Trust

Imelda O'Mahony

Release

Sefton Service User Forum

Annex D: Other evidence considered by the ACMD in addition to the items cited under References

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