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TECHNICAL
REPORT

Hepatitis C

A projection of the healthcare and economic burden in the UK

Bhanu Patruni, Ellen Nolte

Prepared for the Hepatitis C Trust

RAND EUROPE

The research described in this document was prepared for the Hepatitis C Trust.

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Preface

Work presented in this report sought to assess the healthcare and economic burden of the hepatitis C virus (HCV) infection in the United Kingdom. It used a cohort simulation model to estimate the prevalence of HCV infection in the UK, including the number of persons who live with HCV infection at different disease stages, and the number of deaths that can be attributed to HCV infection through to 2035. It further assessed the healthcare and societal costs that are associated with HCV infection under different scenarios of diagnosis and treatment rates.

This report will be of interest to researchers and policy makers alike. We present estimates for different treatment scenarios that may usefully inform decision making on hepatitis C infection. At the same time we highlight the need for further work to enable better understanding of current trends in the prevalence and incidence of HCV infection. This will be important not only to monitor the impact of interventions on the HCV-related burden of disease but also to inform the development and test the validity of existing models aimed at projecting the health and social burden associated with HCV infection.

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Summary

Hepatitis C is a leading cause of chronic liver disease, end-stage cirrhosis and liver cancer. Because of the slow progression and asymptomatic character of the infection, many people are unaware of having it. The UK has been found to lag behind a number of European countries with respect to disease detection and treatment. At the same time, relatively little is known about the healthcare and economic burden associated with hepatitis C in the UK.

This study sought to contribute to better understanding of the burden associated with HCV infection in the UK through estimating the prevalence and the number of deaths that can be attributed to HCV-infection and through assessing the healthcare and societal costs that are associated with HCV infection under different scenarios of diagnosis and treatment rates.

Using a cohort simulation model, we projected that, under current treatment patterns, the overall prevalence of HCV infection would increase from 0.44 per cent in 2010 to 0.61 per cent in 2035. This equates to an increase in the number of persons living with HCV infection from around 265,000 in 2010 to 370,000 in 2035. We estimated that this rise in prevalence would be associated with an increase in healthcare costs, from £82.7m in 2012 to £115m in 2035. Productivity losses were estimated to rise from £184–367m in 2010 to £210–427m in 2035, depending on whether we assumed minimum wage (lower estimate) or median income (upper estimate) for the productive population.

We explored different scenarios projecting the impact of providing antiviral treatment to a larger proportion of persons with HCV infection from 2012 onwards. Quadrupling treatment rates would halt the rise in projected prevalence, with the estimated number of chronically infected individuals falling from 265,000 in 2010 to 262,000 by 2035. While much of this reversal of trend would be among those with mild to moderate HCV infection, increasing treatment rates would also reduce the number of those with decompensated cirrhosis and hepatocellular carcinoma, from an estimated 17,000 under the current treatment assumption to 12,000 in the increased treatment assumption (2035).

Increasing antiviral treatment is associated with an increase in healthcare costs overall, with the projected total increase amounting to four per centage points (or £4.8m) by 2035 compared to the baseline scenario. Much of the increase in healthcare cost was estimated to be attributable to the costs associated with antiviral treatment, which we found to be part compensated for by a fall in the costs of treatment of the long-term sequelae of (untreated) HCV at the early stages of disease progression. The average additional cost of antiviral treatment per annum between 2012 and 2035 is estimated at £43.8m.

Productivity losses associated with HCV infection were estimated to range from £184–380m in 2012, set to increase to £209.7–427m in 2035, based on our median incidence assumption. Increasing the proportion of antiviral treatment would lead to a reduction in HCV-related productivity losses of £59–122m (28 per cent), quadrupling the proportion of those receiving antiviral treatment.

Cumulatively, using the median wage assumption, the average gain in productivity per annum is estimated at £73.3m per annum. This estimated gain would outweigh the additional investment required to cover the additional cost of antiviral treatment if treatment rates are quadrupled, at £43.8 million.

In conclusion, our findings suggests that increasing treatment rates of those with HCV infection is associated with a gain in productivity because of a decline in the overall number of persons carrying the infection and, as a consequence, the number of those progressing to advanced disease stages. However, the impacts will be long-term and immediate impacts in terms of benefits to society as measured by productivity are likely to be counterweighted by additional investments required to make antiviral treatment more widely available. At the same time, our estimates illustrate that the current pattern of treating only a very small proportion of persons infected with HCV will have little impact on the future burden associated with HCV-related disease.

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The views expressed in this report are those of the authors alone and do not necessarily represent those of the Hepatitis C Trust. The authors are fully responsible for any errors.

CHAPTER 1 Introduction

1.1 Background

Hepatitis C is a leading cause of chronic liver disease, end-stage cirrhosis and liver cancer.[1] An estimated 75–85 per cent of acute disease cases progress to become chronic because of the protracted course of the infection and because disease complications may only appear decades after contracting the hepatitis C virus.[2] As a consequence, the infection is often diagnosed at a late stage when treatment options are limited. Because of the slow progression and asymptomatic character of the infection, many persons are unaware of having it. Recent work has suggested that about 86 per cent of those infected with hepatitis C in the UK do not know about their infection.[3]

Hepatitis C is a blood-borne virus (HCV) that is largely restricted to injecting drug users (present and past), recipients of blood transfusion (before September 1991) or blood or blood products (before 1986) in the UK, and migrants to the UK from countries where hepatitis C is common. Testing for hepatitis is by means of a blood test for HCV antibodies, which can be detected in the blood of 90 per cent of patients within five months post infection. However, earlier testing for exposure to HCV, within one to two weeks post infection, is possible within the period before the appearance of HCV antibodies, by means of a blood test for the presence of HCV RNA.[4]

The number of individuals chronically infected with hepatitis C in the UK is estimated to be 216,000.[5] In 2010, there were just over 10,380 new diagnoses of HCV infection across the UK, of which 7,830 (75 per cent) were in England and 2,130 in Scotland (20 per cent).[6] For England and Wales, diagnostic testing of non-randomly selected blood samples between the mid-1980s and 2000s provides prevalence estimates in the range of 0.6–1.2 per cent of the population[7-9], with evidence of some decline between the mid-1980s and early 1990s, followed by an increase thereafter. A study applying Bayesian analysis techniques to a combination of group-specific prevalence data arrived at an overall prevalence in 2003 of 0.44 per cent (95 per cent CrI 0.29, 0.72) among those aged 15–59, or between 90,000 and 213,000 chronically infected in England and Wales.[10] A recent update of this analysis for England in 2005 estimated the number of people aged 15–59 with chronic HCV infection to be 150,000 (95 per cent CrI 113,000–226,000).[11]

Given the specific risk profile of HCV transmission, much of the prevalent infection is concentrated in marginalised populations, mostly injecting drug users. Despite investment in community drug treatment and improved needle exchange programmes, in England, the observed prevalence of hepatitis C in this group has remained fairly stable over recent

years, at 45 per cent in 2011,[5] with other estimates ranging between 30 per cent and 60 per cent.[4, 12–14]

Deaths certified as HCV-related end-stage liver disease or hepatocellular carcinoma in the UK have risen from 98 in 1996 to 323 in 2010,[5] with the number of related deaths projected to continue to rise substantially over the coming decade.[15]

The UK has been found to lag behind a number of European countries with respect to disease detection and treatment, with one report estimating the proportion of those with HCV infection to be identified and receive treatment at only one to two per cent.[16] By contrast, approximately 13 per cent of infected individuals in France receive treatment. This has been supported by work by Lettmeier and colleagues (2008) who examined the market uptake of peginterferons for the treatment of hepatitis C in 21 European countries during 2000–5.[17] It estimated the number of those ever treated to range between a high of 16 per 100 prevalent cases in France to less than one per cent of cases in countries such as Greece, Poland and Romania. The UK was among the countries with a relatively low number of patients treated, at around 3.5 per cent (the average rate across 21 countries). Lettmeier et al. (2008) highlighted the role of under-detection of prevalent cases, citing evidence that in France, which operates an active screening policy for hepatitis C, about 40 per cent of cases remain undetected whereas in Spain, for example, this figure is estimated at 80 per cent. High uptake of treatment in France has been attributed to a government-led campaign and investment in hepatitis C services, with detection rates doubling since 1994 and awareness levels rising from 24 per cent to 56 per cent during the same period, a figure that is four times higher than in the UK.[16]

A 2010 report to the Secretary of State for Health by Professor Sir Mike Richards on International Variation in Drug Usage found the uptake of treatment of hepatitis C in the UK (peginterferon) to be lower than in 14 comparator countries, at just over 50 per cent of the all-country average.[18] This is despite positive guidance by the National Institute for Health and Clinical Excellence and evidence that drug treatment of hepatitis C is effective, on average, in more than half of those treated.[19] The report suggested that lower than expected uptake of treatment in the UK might be attributable to a higher prevalence of HCV genotype 3 compared with other countries; HCV genotype 3 requires a slightly different treatment regime. However, similar to the work by the Hepatitis C Trust (2006)[16] and Lettmeier et al. (2008),[17] it suggested that the UK lags behind other countries, and France in particular, with regard to the development and implementation of a national strategy to address hepatitis C, including promoting higher rates of diagnosis and treatment.

Relatively little is known about the social and economic burden associated with hepatitis C in the UK. A small number of studies has attempted to estimate the HCV-related burden of disease, projecting the cost to the NHS associated with failure to treat existing patients at around £4–13 billion over the next 30 years.[3, 16] The added societal cost of not providing treatment has been determined to be £6–14 billion over the same period.[3] This report aims to revisit some of these estimates and so contribute to better understanding of the burden associated with HCV infection in the UK.

1.2 Aims and objectives

The work presented in this report sought to assess the social and economic burden of HCV infection in the United Kingdom through:

- estimating the prevalence of HCV infection, including the number of persons who live with HCV infection at different disease stages by year (2012–35)
- estimating the number of deaths that can be attributed to HCV infection by year (2012–35)
- assessing the healthcare and societal costs that are associated with HCV infection if diagnosis and treatment rates remain at present (2010) levels through to 2035
- assessing the impact on healthcare and societal costs of increasing the proportion of persons with HCV infection receiving antiviral treatment through to 2035.

This report is structured as follows. Following this introductory chapter, chapter 2 sets out in detail the model and the underlying assumptions that are used to estimate the healthcare and economic burden associated with HCV infection in the UK. Chapter 3 describes findings for three scenarios that explore different assumptions related to the proportion of HCV-infected persons receiving antiviral treatment. Chapter 4 concludes the report with a discussion of our findings.

CHAPTER 2 Methodological approach

2.1 Structure of the model and model output indicators

We used a cohort simulation model that follows cohorts of infected individuals as they age. A cohort simulation model allows for tracking infected cohorts over time as they move from one age and year to another. This permits simulation of events in a population as they occur and an understanding of how infected cohorts progress over time. It also allows characterisation of the infected population as a whole over a specific period of time.

At the core of the model is a cohort of infected individuals (men or women), whose size is equal to the number of persons who contract the infection in a specific year (ie incidence). The size of the cohort is reduced every year by applying age-, year- and sex-specific rates of mortality, calculated as a multiple of the mortality in the general population of the same sex for a specific age and year. At the same time, the population of those infected with HCV is joined by a new cohort of infected every year.

Figure 2.1 presents a simplified model of the natural history of HCV infection, describing how the infected cohort progresses through different stages of the disease, adapted from Sweeting et al. (2007).[15] Accordingly, a newly infected individual can follow different trajectories, including progressing to chronic (mild) infection (stage 2), spontaneous resolution of the infection (stage 7) or indeed death because of reasons unrelated to the infection (stage 8).

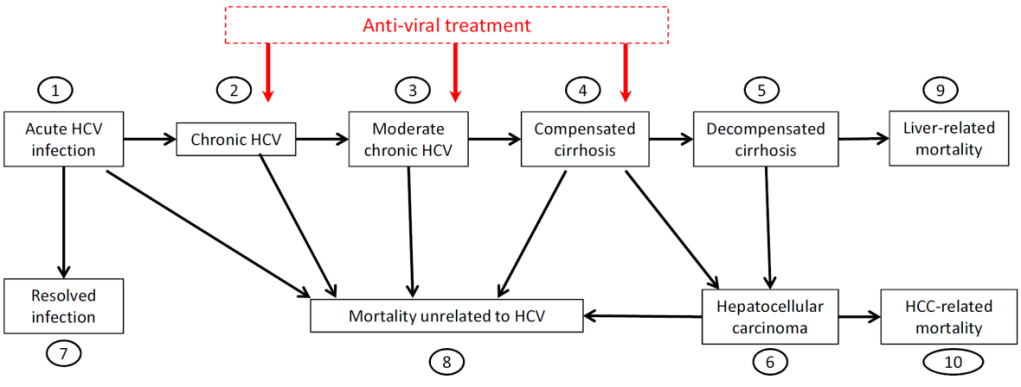

Figure 2.1 Schematic outline of the natural history of HCV infection and antiviral treatment

SOURCE: Adapted from Sweeting et al. (2007)[15]

The annual probabilities from progressing through various disease stages used in our model are given in Table 2.1. Transition probabilities were derived from the literature and, in accordance with Sweeting et al. (2007), we applied age-specific probabilities to some stages. The model considers women and men separately, as men are more likely to contract the virus.[6]

Table 2.1 Annual progression probabilities between disease stages

Transition (disease stages)	**Age group** (years)	**Annual probability**	**(95 per cent Confidence interval)**	**Reference**
Spontaneous viral clearance (1 ⇨ 7)		0.26	(0.22; 0.29)	Micallef et al. (2006)[20]
Acute to chronic HCV (1 ⇨ 2)		0.74	(0.37; 1.00)*	Micallef et al. (2006)[20]
Chronic HCV to moderate chronic HCV (2 ⇨ 3)				
	0–29	0.017	(0.01; 0.028)	Posttransfusion cohort, UK
	20–39	0.01	(0.005; 0.025)	Sweeting et al. (2006)[21]
	40–49	0.016	(0.007; 0.035)	
	50+	0.054	(0.036; 0.08)	
Moderate HCV to compensated cirrhosis (3 ⇨ 4)				
	0–29	0.008	(0.003; 0.026)	Posttransfusion cohort, UK
	20–39	0.005	(0.001; 0.02)	Sweeting et al. (2006)[21]
	40–49	0.008	(0.002; 0.029)	
	50+	0.029	(0.01; 0.079)	
Compensated cirrhosis to decompensated cirrhosis (4 ⇨ 5)		0.065	(0.04; 0.092)	Hutchinson et al. (2006)[22]
Compensated cirrhosis to hepatocellular carcinoma (4 ⇨ 6)		0.035	(0.0024; 0.046)	Hutchinson et al. (2006)[22]
Decompensated cirrhosis to hepatocellular carcinoma (5 ⇨ 6)		0.068	(0.041; 0.099)	Sweeting et al. (2007),[15] citing Planas et al. (2005)[23] (also used by Saab et al., 2010[24])
Decompensated cirrhosis to liver-related death (5 ⇨ 9)		0.168	(0.137; 0.25)	Hutchinson et al. (2006)[22]
Hepatocellular carcinoma to HCC death (6 ⇨ 10)		0.605	(0.545; 0.676)	Hutchinson et al. (2006)[22]
Mortality unrelated to HCV (1, 2, 3, 4, 5, 6 ⇨ 8)		Ratio excess mortality to general mortality		Sweeting et al. (2007)[15]
	0–9	1		
	1–19	3.26		
	20–29	4.29		
	30–39	5.55		
	40–49	2.81		
	50–59	1		
	60–69	1		
	70–79	1		
	80+	1		

NOTE: *where estimates for 95 per cent Confidence Interval are lacking, we assumed 50 per cent of point estimate as lower bound and 200 per cent as upper bound.[24]

2.1.1 Incidence of hepatitis C infection

Existing studies

Estimates for the incidence of hepatitis C in England vary widely. For example, a seroepidemiological study by Balogun et al. (2009) estimated that 106,000 persons aged 16 or older acquired HCV between 1986 and 2000 (an average of 7,571 persons per year; incidence not disaggregated by age).[4] Its findings should, however, be interpreted with a degree of caution as it drew on non-random samples. It examined serum specimens submitted to laboratories for routine diagnostic testing. Although the authors considered this sample to approximate to the general population, it is possible that the population from which the samples were taken was sicker than the general population. Sweeting et al. (2007) provided estimates of incidence using back calculation applied to counts of deaths and hospital episodes related to HCV and liver cancer, using a Bayesian approach.[15] Similar to Balogun et al. (2009),[4] incidence was not disaggregated by age. The study estimated an annual number of new cases of HCV for the mid-1980s to the mid-1990s that stabilised around 14,000, with wide confidence intervals.[15] These estimates were subsequently adopted by the Health Protection Agency (HPA)[25] and formed the basis for predicting the future burden of hepatitis C infection in England through to 2020, as reported in the 2011 and 2012 HPA reports on hepatitis C in the UK.[5-6]

Sutton et al. (2006) modelled incidence from prevalence in recent initiatives on drug injecting.[26] They reported an incidence of 16 per cent; however, it is difficult to generalise this figure to the wider population because of the nature of the study population (injecting drug users). Aarons et al. (2004) used HCV RNA testing of drug users who tested anti-HCV negative, identifying those in a 'window' period (just infected).[27] On this basis they estimated the annual incidence of HCV infection at 14 per cent in this population. Brant et al. (2008) also made use of the 'window' period and estimated the annual incidence in a population of known injecting drug users at 13 per cent, and among those attending drug/alcohol services at four per cent.[28] Likewise, Balogun et al. (2009), using the 'window' period, estimated the annual incidence of HCV infection in a population attending sexual health clinics at three per cent.[8]

Assumptions used in the present study

This study used median estimates of annual population HCV incidence generated by Sweeting et al. (2007) (Figure 2.2) as the principal assumption to estimate the burden associated with HCV infection, applying a set of different scenarios (see below).[15]

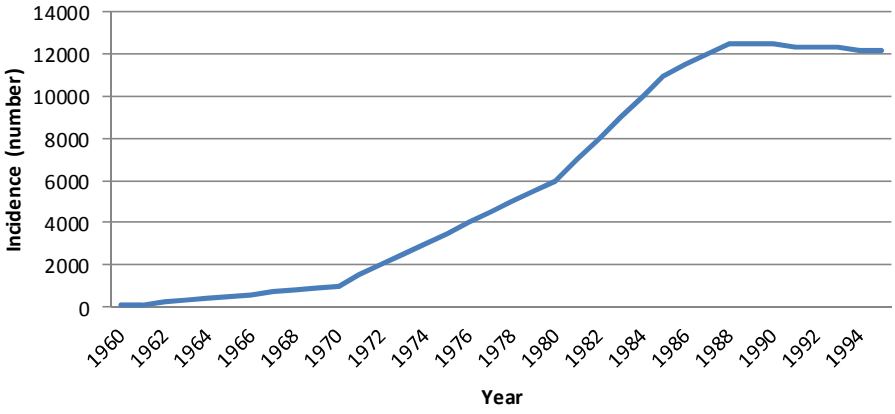

Figure 2.2 Annual incidence of hepatitis C virus infection in England, 1960–95

NOTE: figures represent point estimates

SOURCE: adapted from Sweeting et al. (2007)[15]

Given the uncertainties about estimates of incidence discussed above, we compared, in the baseline scenario, estimates generated using median incidence with those produced using low incidence. These were determined by the lower bound of the credible interval (2.5 per cent) of incidence estimates generated by Sweeting et al. (2007).[15]

As noted earlier, a limitation of existing evidence is the lack of age-specific estimates for incidence. Given the overlap between the population of individuals infected with HCV and injecting drug users, we used the age profile of the latter as an approximation. We generated two scenarios. First, we created a base scenario that draws on data from the hospital episode statistics, which provide detailed age profiles of persons admitted for drug-related mental and behavioural disorders and drug-related poisoning.[29] An examination of these profiles for the period 1998–2009 finds that persons aged 35 and under constitute the majority of those affected (75 per cent in the late 1990s and 60 per cent in the 2000s). We used principally the age distribution provided for the late 1990s as the nearest data point to the end point of the data on incidence used in our model (Figure 2.3). However, acknowledging that the profile of intravenous drug users has shifted towards younger ages since the 1990s, we also ran an alternative scenario with the age profile of the baseline scenario five years to the left (shown in the Appendices).

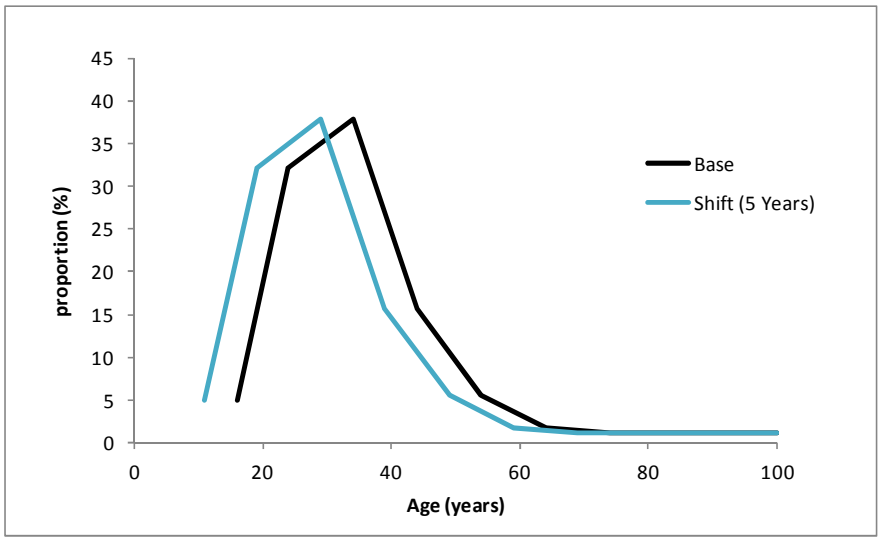

Figure 2.3 Age profile of persons hospitalised for drug-related mental and behavioural disorders and poisoning in England and Wales, 1998–99

NOTE: Base – data as derived from hospital episode statistics; Shift – shifted age profile of base scenario
SOURCE: NHS Information Centre for Health and Social Care (2009)[29]

2.1.2 Treatment module: Antiviral treatment

The model further allows for antiviral treatment (combination therapy with peginterferon alfa and ribavarin) to be applied at three progressive stages of the disease, mild HCV, moderate HCV and compensated cirrhosis (Figure 2.1). The treatment module is based on a number of assumptions set out in Table 2.2. We acknowledge that treatment response differs by HCV genotype. There are six HCV genotypes (1–6), with many subtypes and different strains.[30] For simplicity, we distinguished between HCV genotype 1 and all other genotypes only. This aimed to account for differences in response to antiviral treatment and duration of treatment required (genotype 1: 48 weeks; genotypes 2 and 3: 24 weeks). For genotypes 4, 5 and 6, duration of standard treatment is typically assumed to last 48 weeks; however, given the low frequency of this group (Table 2.2) we combined it with genotypes 2 and 3 to form one 'other' group (see also below).

We further assumed the proportion of infected persons who are diagnosed annually to be four per cent.[31] In line with assumptions by the Health Protection Agency, we assumed that 70 per cent of those diagnosed would be referred for further investigation.[32] Of these, 71 per cent would attend the clinic, of whom 88 per cent would meet criteria for treatment. Of these, 70 per cent would accept treatment. These figures translate in a cumulative treatment rate of 30.6 per cent, which we used in our model (Table 2.2). We applied this figure to the three progressive stages of the disease (mild, moderate, compensated cirrhosis).

The primary goal of antiviral treatment of chronic HCV is the attainment of a sustained viral response (SVR), defined as undetectable serum HCV-RNA levels six months after cessation of treatment.[30] Achievement of SVR is associated with improved histological and clinical outcomes, for example, lower rates of decompensation, hepatocellular carcinoma and mortality. We considered those in disease stages 2 (mild chronic HCV) and 3

(moderate chronic HCV) who achieve SVR following treatment to be clear of the virus and so re-enter the pool of uninfected (stage 0 in Figure 2.1). Those in disease stages 2 and 3 who do not respond to treatment (ie do not achieve SVR) were assumed to progress to the next stage of disease as outlined in Figure 2.1, according to disease progression probabilities shown in Table 2.1. Conversely, for those in disease stage 4 (compensated cirrhosis), we assumed a sustained risk to progress into the next disease stages even after treatment, but with a lower transition probability (Table 2.2).[24] A recent analysis by Saab et al. (2010) suggested that antiviral treatment of decompensated cirrhosis and post-transplant may be cost-effective compared to no treatment; however, we did not consider this in our model.

In line with Deuffic-Burban et al. (2009),[33] we assumed that effective antiviral treatment was available from 1991 onwards only and that treatment effectiveness (as measured by the per centage of SVR achieved) improved over time. We distinguished four time periods: before 1991, 1991–4, 1995–8, and 1999 onwards. For each period we assumed half of the effectiveness observed in the successive later period,[33] except for the period before 1991, for which we set treatment effectiveness at zero (ie not available) (see Table 2.2). Treatment response rates for the period 1999 onwards were taken from Manns et al. (2001).[34] These are likely to present a conservative assumption, as more recent work finds SVR for mild and moderate HCV to be slightly higher.[35]

We were unable to identify time-trend data on antiviral treatment of those with compensated cirrhosis; most studies that examined the effectiveness of antiviral treatment at this disease stage were published from the mid-2000s. We here distinguished two periods only: before 2005 (treatment effectiveness set at zero) and 2005+ (per centage SVR as in Table 2.2).

Finally, individuals were assumed to go through one line of treatment only ('naive' – not treated before). Kershenobich et al. (2011) noted that allowing for repeat treatment (second or third line) improves model fit only marginally.[36]

Table 2.2 Antiviral treatment module: model assumptions

Indicator	Proportion / rate	(95 per cent Confidence interval)	Reference
Genotype distribution			
Genotype 1	0.45		Health Protection Agency (2011)[6]
Other	0.55		*NB The 2011 HPA Commissioning template for estimating HCV prevalence gives the genotype distribution as follows: G1 45 per cent, G2 7.3 per cent, G3 43.8 per cent, G4 3.3 per cent, other 0.6 per cent*[32]
Diagnosed population *(of persons infected)*			
	0.0407		NICE (2010)[31]
Treated population			
Referred appropriately	0.7		Ramsey et al. (2011)[32]
Attend clinic	0.71		

Indicator		Proportion / rate	(95 per cent Confidence interval)	Reference
	Indicated for treatment	0.88		
	Per centage accepting treatment	0.7		
	Cumulative estimate	0.306	(0.153; 0.612)*	
Treatment response rates (1999+)				
	Genotype 1/disease stage 2	0.42	(0.38; 0.46)	Manns et al. (2001);[34] Salomon et al. (2003)[37]
	Genotype 1/disease stage 3	0.42	(0.38; 0.46)	*(assuming similar SVR for stages 2 and 3)*
(2005+)	Genotype 1/disease stage 4	0.33	(0.15; 0.6)	Bruno et al. (2010)[35]
	Other genotype/disease stage 2	0.79	(0.74; 0.84)	Manns et al. (2001);[34] Salomon et al. (2003)[37]
	Other genotype/disease stage 3	0.79	(0.74; 0.84)	*(assuming similar SVR for stages 2 and 3)*
(2005+)	Other genotype/disease stage 4	0.57	(0.285; 1.14)*	Bruno et al. (2010)[35]
Treatment response rates before 1999				
Stages 2 and 3 only	Genotype 1/1995-1998	0.2	(0.1; 0.4)*	Deuffic-Burban et al. (2009)[33]
	Genotype 1/1991–4	0.1	(0.05; 0.2)*	Deuffic-Burban et al. (2009)[33]
	Genotype 1/<1991	0		
	Other genotype/1995–8	0.4	(0.2; 0.8)*	*Estimated based on assumption by Deuffic-Burban et al. (2009)[33] for genotype 1, ie. half of SVR in 1999*
	Other genotype / 1991–4	0.2	(0.1; 0,4)*	*As above*
	Other genotype / <1991	0		
Stage 4	All genotypes / < 2005	0		
Disease progression probability for compensated cirrhosis following antiviral treatment				
		Annual probability	95 per cent Confidence interval	
	Compensated cirrhosis to decompensated cirrhosis	0.001	(0.00005; 0.002)	Saab et al. (2010)[24]
	Compensated cirrhosis to hepatocellular carcinoma	0.008	(0.004; 0.016)	Saab et al. (2010)[24]

NOTE: *where estimates for 95 per cent Confidence Interval are lacking we assumed 50 per cent of point estimate as lower bound and 200 per cent as upper bound.[24]

2.2 Output indicators

The model employed here to estimate the burden associated with HCV infection foresees two sets of output indicators: (i) HCV-related disease burden and (ii) economic burden. We describe these in more detail here.

2.2.1 HCV-related disease

The model provides estimates for:

- the prevalence of HCV infection
- the cumulative number of persons living with HCV infection at different stages of disease progression
- the total number of deaths attributable to HCV infection.

Prevalence describes the number of infected individuals in the overall population at a given point in time. It characterises the burden associated with acute and chronic HCV infection and HCV-related disease. In the model developed here, prevalence was treated as an endogenous variable, that is, it is generated by the model as a ratio of the total number of individuals infected with HCV across all cohorts in a given year. This allows us to examine the effects on current and future prevalence of interventions targeting individuals infected with HCV or at high risk of contracting it. For each cohort, we used population and mortality data for the UK. However, incidence data provided by Sweeting et al. (2007) cover England only.[15] Therefore, our final estimates are likely to underestimate prevalence for the UK as a whole. At the same time, the forecasts by cohort and year were only available up to 2010; after this date each year was assumed to have same mortality rates and similar population across cohorts. This means that the prevalence rates may be slightly overestimated post-2010.

To estimate the number of deaths attributable to HCV we used age-specific mortality rates derived from the World Health Organization (WHO) mortality database for the UK population. To estimate excess non-liver-related mortality in the HCV population, we used the excess-to-general mortality ratio described by Sweeting et al. (2007) (see Table 2.1).[15]

In line with the incidence figures that form the basis of the model, we use the year 1960 as the starting point for our estimates of HCV-related disease outputs. We project figures to year 2035.

2.2.2 Economic impact

We estimated four categories of economic impact associated with HCV infection in the UK: (i) cost of antiviral treatment; (ii) cost of treatment of HCV-related disease (decomposed cirrhosis, hepatocellular carcinoma); (iii) lifetime income loss; and (iv) productivity loss.

Cost of antiviral treatment

Most recent estimates from the Health Protection Agency (HPA) assume, based on estimates by the National Institute for Health and Clinical Excellence (NICE), that the cost of antiviral treatment of individuals with HCV varies between £6,246 for those requiring 24-week treatment (largely genotypes 2 and 3) and £12,741 for those requiring a standard treatment of 48 weeks (largely genotype 1).[32] We attempted to reconstruct these estimates by using costs of antiviral drugs as derived from the 2011 British National Formulary for peginterferon alfa-2a (Pegasys), peginterferon alfa-2b (ViraferonPeg) and ribavirin (Copegus, Rebetol),[38] and including costs of on-treatment monitoring taken from Hartwell et al. (2011)[39] and upgraded to 2010–11 prices using the 2011 Hospital and Community Health Services (HCHS) Pay and Prices Index,[40] by genotype. As this approach arrived at approximately the same costs as those used by the Health Protection Agency, we applied those used by the HPA. We further applied a discount rate of 3.5 per cent annually to future costs, as recommended by NICE.

Based on NICE figures, we assumed that of those receiving treatment, the majority of those with genotype 1 (72 per cent) receive peginterferon alfa-2a, while 28 per cent receive peginterferon alfa-2b (48 weeks). Of those with genotypes 2 and 3 (and all other), 64 per

cent receive peginterferon alfa-2a and 36 per cent peginterferon alfa-2b (types 2 and 3, 24 weeks; all other, 48 weeks) (Table 2.3).[41]

Table 2.3 Proportion of persons with HCV infection receiving antiviral treatment

Antiviral treatment	Proportion receiving treatment: genotype 1 (per cent)	Proportion receiving treatment: all other genotypes (per cent)
Peginterferon alfa 2a	72	64
Peginterferon alfa 2b	28	36

SOURCE: NICE (2010)[41]

Regarding duration of treatment, we assumed that for chronic (stage 2) and moderate chronic HCV (stage 3), 50 per cent of patients receiving treatment received short and 50 per cent standard treatment. In contrast, for compensated cirrhosis (stage 5) we assumed that duration of treatment was always of standard duration (depending on genotype). These assumptions were based on work undertaken by Grishchenko et al. (2009).[42]

Cost of treatment of HCV-related disease

The model as developed here did not permit disaggregating healthcare costs into 'investment', that is, the costs of antiviral treatment, and the costs related to treating the sequelae of (untreated) HCV infection. Instead, we calculated the latter, and present related figures, separately.

HCV infection-related treatment costs were derived from published economic evaluations of antiviral therapy of HCV infection,[43–4] which we adjusted to 2010–11 prices using the 2011 HCHS Pay and Prices Index.[40] We did not include cost of treatment of mild and moderate HCV. This was based on the assumption that such cases would receive antiviral treatment and related costs were already considered in the cost of antiviral treatment outlined above. We accept that by doing so we will miss cases where antiviral treatment is not successful and so will underestimate the 'true' cost associated with HCV-treatment. However, we believe these costs to be small, given the comparatively low proportion of persons with mild or moderate HCV infection who are currently being diagnosed and will subsequently receive treatment.

In the current model we did not include costs associated with the treatment of liver cirrhosis. As with mild and moderate HCV, part of the cost of treating persons with HCV-related cirrhosis is already captured in the cost element for antiviral treatment described above.

In contrast, we assumed that all persons with decompensated cirrhosis or with liver cancer will be known to the health service and receive treatment. We further assumed that every year two per cent of persons with HCV-related decomposed liver cirrhosis or with liver cancer will receive a liver transplant[39, 44], and we included the associated costs in our cost calculation. Table 2.4 provides an overview of the costs assumed here by disease stage.

Table 2.4 Cost of treatment of HCV-related disease

Disease stage	Mean 2003–4 values per annum *	Adjusted 2010–11 value per annum	Assumptions for cost calculation
Mild chronic HCV	138	170	Not included
Moderate chronic HCV	717	882	Not included
Compensated cirrhosis	1,138	1,400	Not included
Decompensated cirrhosis	9,120	11,218	98 per cent of all cases considered to receive treatment
Hepatocellular carcinoma (HCC)	8,127	9,996	98 per cent of all cases considered to receive treatment
Liver transplant	27,330	33,616	2 per cent of all cases of decompensated cirrhosis and HCC considered to receive transplant
Hospital costs year of transplant	9,458	11,633	
Post liver transplant	1,385	1,704	

NOTE: * Adapted from Martin et al. (2011)[44]

Loss of economic output

The loss of economic output was calculated as the income that individuals who die prematurely at a given age will lose over the period of remaining labour market participation (under or to age 65). For example, an individual dying at the age of 40 will forgo income equal to the sum of the yearly incomes that s/he would have received had s/he lived and worked to the age of 65. We here considered ages 16 to 64, and, to obtain a lower bound for the estimated loss, applied the minimum wage as applicable to year 2011.[45] In an alternative scenario, we obtained an upper bound for the estimated loss by applying the median wage as applicable to year 2011.

Hepatitis C has been found not only to affect labour market participation and productivity but also to affect these outcomes differently depending on disease stage.[46, 47] To account for this, we provided for differential patterns of labour participation and productivity by disease stage. For labour force participation, we selected a value of zero for those with cirrhosis and liver cancer; that is, those individuals were assumed not to participate in the labour force at all. For those with chronic HCV-infection we assumed workforce participation of 80 per cent. With regard to productivity, for those who do work, we assumed a figure of 92.5 per cent,[47] indicating that those with HCV infection are 7.5 per centage points less productive than those without. We calculated productivity loss as the product of the fraction of those who work, the fraction of productivity lost due to HCV infection and the yearly minimum wage.

CHAPTER 3 Results

This chapter provides a summary overview of the main findings of the cohort simulation model to estimate the burden associated with HCV infection in the UK. We begin by presenting the baseline scenario, which assumes that current treatment patterns prevail to the end of the observation period (2035). In this scenario, we compare estimates generated by using median incidence with those produced by using low incidence as determined by the lower bound of the credible interval of incidence estimates (2.5 per cent) generated by Sweeting et al. (2007).[15]

We then present two scenarios that differ from the baseline scenario with regard to (i) the proportion of persons with HCV infection receiving antiviral treatment and (ii) the application of median income as an upper bound for estimated productivity and lifetime income loss. In both scenarios, assumptions different from the baseline are applied from 2012 onwards. Table 3.1 provides an overview of the main assumptions used in each scenario.

Table 3.1 Overview of scenarios to estimate the burden associated with HCV infection in the UK

Scenario	Age profile	Mortality profile	HCV incidence	Proportion HCV infection receiving antiviral treatment	Income assumption
Baseline	Base age	General population	Median	30.6 per cent (cumulative estimate, see Table 2.2) (2010)	Minimum wage
For comparison			*Lower bound (2.5 per cent) of credible interval*		
Scenario 1	As baseline	As baseline	Median	Four times the baseline proportion[a]	Minimum wage
Scenario 2	As baseline	As baseline	Median	Four times the baseline proportion	Median income

We also ran sensitivity analyses on the baseline scenario by varying the assumption on the age profile, shifting the age distribution by five years towards younger ages. We applied this to both the median and low incidence baseline scenarios. In one further iteration of the baseline scenario (median incidence), we also modified the mortality profile to reflect

[a] We ran alternative scenarios by varying the proportion of those receiving antiviral treatment by factors two, three and four compared to baseline. Here we present only the findings from the latter (quadrupling the proportion); findings from the former (double, treble) are available from the authors on request.

the higher non-liver-related mortality levels of intravenous drug users who form the majority of persons contracting HCV, using the excess-to-general mortality ratio described by Sweeting et al. (2007) (see Table 2.1, page 6). The findings of these additional analyses are shown in the Appendices.

While we estimated figures for the entire period 1960–2035, we here focus on the period 1995–2035; we used 1995 as starting point in line with estimates provided by the Health Protection Agency.[6]

3.1 Baseline scenario: Comparing median and low incidence assumptions

Figure 3.1 shows the estimated prevalence of HCV infection, using median and low incidence assumptions, for the period 1995–2035. The precise figures are shown in Table 3.2 (page 19). Using the median incidence assumption, we estimate prevalence of HCV infection in the UK to increase from 0.27 per cent in 1995 to 0.61 per cent in 2035 (2010: 0.44 per cent). Conversely, the low incidence scenario generates estimates of 0.12 per cent in 1995 and 0.21 per cent in 2035 (2010: 0.17 per cent).

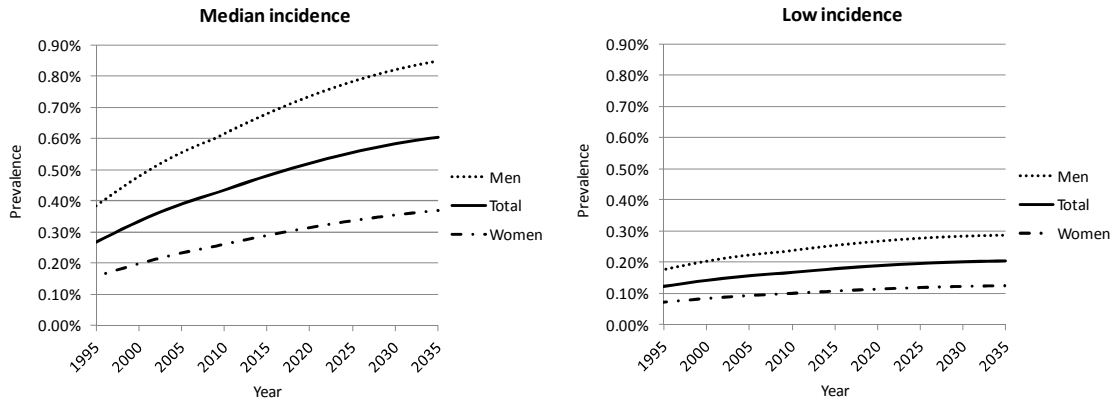

Figure 3.1 Baseline scenario: estimated HCV prevalence, 1995–2035

Translating prevalence figures into the estimated total number of persons living with HCV infection at different stages of disease progression, we find, for 1995, a two-fold difference between median and low incidence assumptions, of 152,712 and 70,466 persons, respectively (Figure 3.2; Table 3.2). This increases to a three-fold difference in 2035, of, respectively, 370,441 and 125,661 persons.

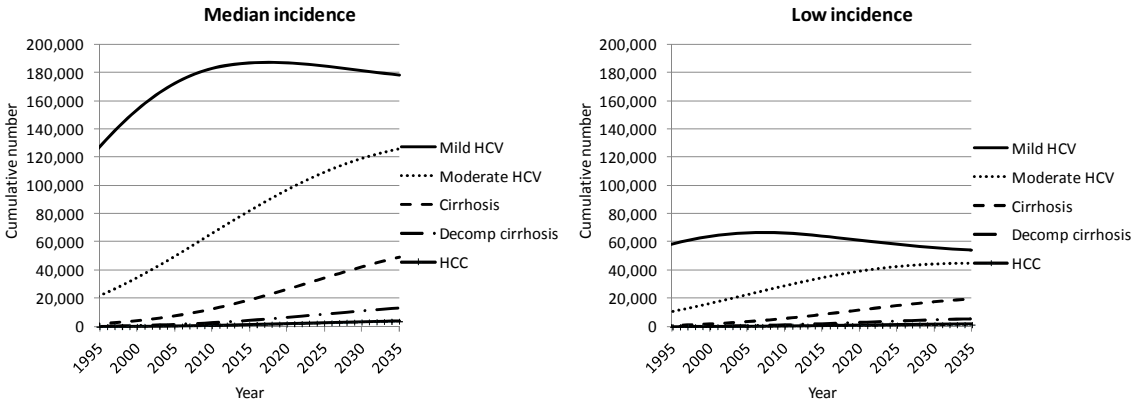

Figure 3.2 Baseline scenario: estimated cumulative number of persons living with HCV infection at different stages of disease progression, UK, 1995–2035

In both cases, we observe a flattening of the curve for the number of persons living with mild chronic HCV infection, from around 2010. This reflects the model assumption, insofar as the incidence figures we use suggest a flattening from the mid-1990s onwards (see Figure 2.2, page 8).

We further estimated the total number of deaths associated with HCV-related infection in the UK (Figure 3.3). As with the estimates for the disease burden, we find the cumulative number of deaths to differ by a factor of just over 2, with the total number of liver-related deaths estimated to rise from 142 in 1995 to 4,515 in 2035 under the median incidence assumption (Table 3.2). For the low incidence assumption, we estimate an increase from 65 liver-related deaths in 1995 to 1,847 in 2035.

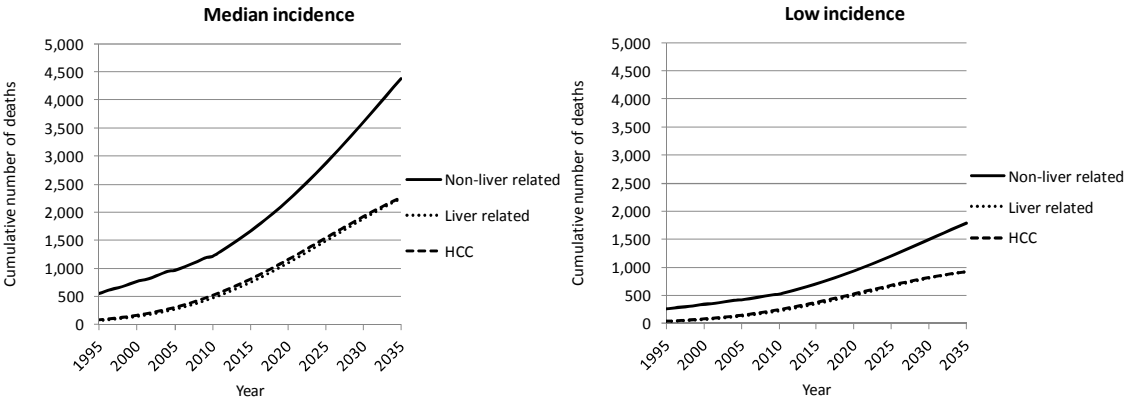

Figure 3.3 Baseline scenario: estimated cumulative number of deaths in the HCV cohort, UK, 1995–2035

Figure 3.4 provides estimates for the annual cost of antiviral treatment and of treatment of HCV infection, alongside the estimated lifetime income and productivity loss associated with HCV infection for the median and low incidence scenarios.

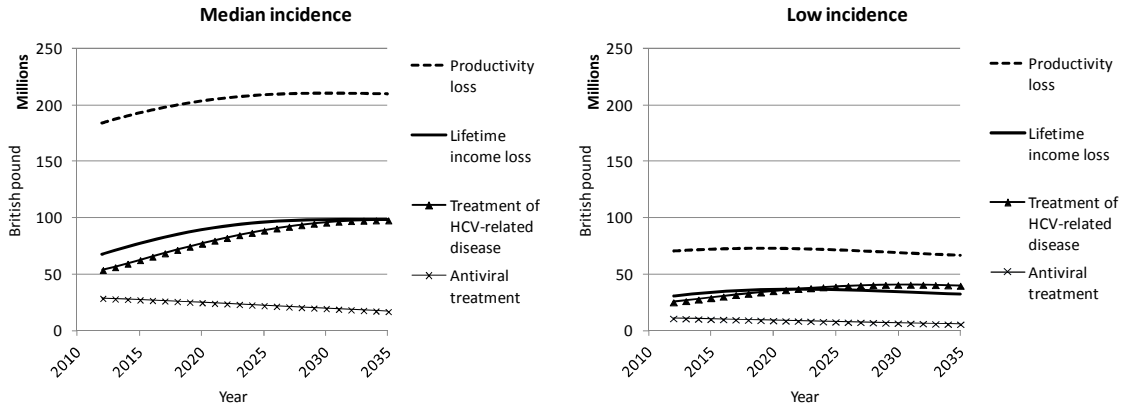

Figure 3.4 Baseline scenario: annual cost of antiviral treatment, treatment of HCV infection, lifetime income loss and productivity loss associated with HCV infection, UK, 2012–35

While the scale of the difference varies for the median and low incidence assumptions, we find that in both cases the losses associated with HCV infection in terms of lifetime income loss and productivity loss outweigh the costs that are required to finance antiviral treatment. Also, as the costs associated with providing antiviral treatment fall, reflecting the declining number of persons with mild HCV infection who progress into further disease stages, the costs of treating those with HCV-related disease increase steadily. It is worth reiterating that these estimates reflect a scenario in which current (ie 2010) treatment patterns of HCV infection remain stable during the foreseeable future.

As noted earlier, we also ran variations of the baseline scenario, by first using a younger age profile. The findings of these scenarios are presented in Appendix A for median incidence and Appendix B for low incidence. In brief we find that shifting the profile to younger ages yields a somewhat higher HCV prevalence, rising to 0.64 per cent in 2035 compared to 0.61 per cent in the baseline, median incidence scenario. Likewise, the number of persons living with HCV infection at different disease stages is estimated to be higher, in particular those with mild and moderate disease stages. In contrast, the cumulative number of liver-related deaths is estimated to be lower as is the associated healthcare cost although productivity, and in particular, lifetime income losses are estimated to be higher, reflecting the younger age profile (see Appendix A). Similar observations were made for the low incidence assumption, albeit at a lower level (Appendix B).

We also generated a variation of the baseline scenario applying an 'excess mortality' profile to reflect the higher non-liver-related mortality levels of intravenous drug users (Appendix C). Using the median incidence assumption, we project HCV prevalence to rise at a somewhat slower pace through to 2035, to 0.57 per cent. Similarly, the number of persons living with HCV infection at different disease stages is estimated to be lower, in particular those with mild and moderate disease stages, as is the estimated number of liver-related deaths. Finally, healthcare costs and productivity losses associated with HCV infection are estimated to be lower, compared to a scenario using the mortality profile of the general population.

Table 3.2 Baseline scenario: estimates of HCV-related disease progression, deaths, prevalence and costs, 1995–2035

	Disease progression (cumulative number)					Deaths (cumulative number)			Prevalence	Costs (annual, GBP)			
	Mild HCV	Moderate HCV	Cirrhosis	Decompensated cirrhosis	HCC	Non-liver-related deaths	Liver deaths	HCC deaths	Total (per cent)	Antiviral treatment	Treatment of HCV-related disease	Lifetime income loss	Productivity loss
Median incidence													
1995	127,676	22,241	2,227	416	152	544	65	77	0.27	1,103,589		14,486,063	101,759,227
2000	153,882	35,034	4,359	867	308	762	138	160	0.34	5,616,528		26,574,797	130,467,072
2005	172,358	50,076	7,762	1,637	567	958	265	300	0.39	15,727,097		42,595,291	156,122,142
2010	183,021	66,357	12,666	2,825	954	1,208	466	515	0.44	29,504,041		60,432,681	177,266,634
2015	186,814	82,319	19,031	4,450	1,467	1,655	745	804	0.48	27,386,212	62,636,067	76,917,716	192,793,016
2020	186,839	97,105	26,528	6,444	2,083	2,205	1,093	1,155	0.52	24,911,510	77,296,740	89,181,053	203,326,844
2025	184,566	109,665	34,562	8,667	2,752	2,861	1,485	1,542	0.56	22,274,028	88,888,237	96,049,970	208,763,415
2030	181,341	119,383	42,375	10,903	3,410	3,598	1,884	1,927	0.58	19,620,507	95,950,653	98,299,932	210,252,827
2035	178,148	126,155	49,235	12,915	3,988	4,371	2,247	2,268	0.61	17,060,018	97,939,202	98,329,224	209,674,631
Low incidence													
1995	58,344	10,815	1,044	192	71	253	30	36	0.12	509,280		6,978,250	47,187,049
2000	63,772	16,478	2,066	409	146	337	65	76	0.14	2,393,380		13,008,428	56,026,683
2005	66,363	22,674	3,665	776	268	416	126	142	0.16	6,338,848		20,457,239	63,425,372
2010	66,240	28,964	5,913	1,330	448	517	220	242	0.17	11,401,517		27,893,007	68,831,935
2015	64,035	34,623	8,730	2,065	678	703	347	373	0.18	10,227,910	29,042,266	33,629,796	71,789,107
2020	61,121	39,277	11,883	2,930	941	932	499	524	0.19	9,035,037	35,097,415	36,417,427	72,530,429
2025	58,194	42,556	15,015	3,834	1,207	1,201	660	680	0.20	7,869,522	39,240,306	36,238,997	71,229,101
2030	55,764	44,384	17,737	4,654	1,440	1,494	809	819	0.20	6,766,811	40,865,663	34,231,594	68,883,772
2035	54,053	44,970	19,744	5,282	1,612	1,785	925	923	0.21	5,752,710	39,950,569	32,226,032	66,627,412

3.2 Scenario 1: quadrupling the proportion of HCV-infected persons receiving antiviral treatment from 2012, minimum wage

In scenario 1 we quadrupled the estimated number of those receiving antiviral treatment from 2012. As shown in Figure 3.5, this is estimated to lead to a slow reversal in HCV prevalence from 2012, falling to 0.43 per cent in 2035 (Table 3.3, page 22) compared to 0.61 per cent in the baseline scenario (ie current treatment) (Table 3.2, page 19). In our model, a prevalence of 0.43 per cent was last observed for 2009 (Figure 3.5).

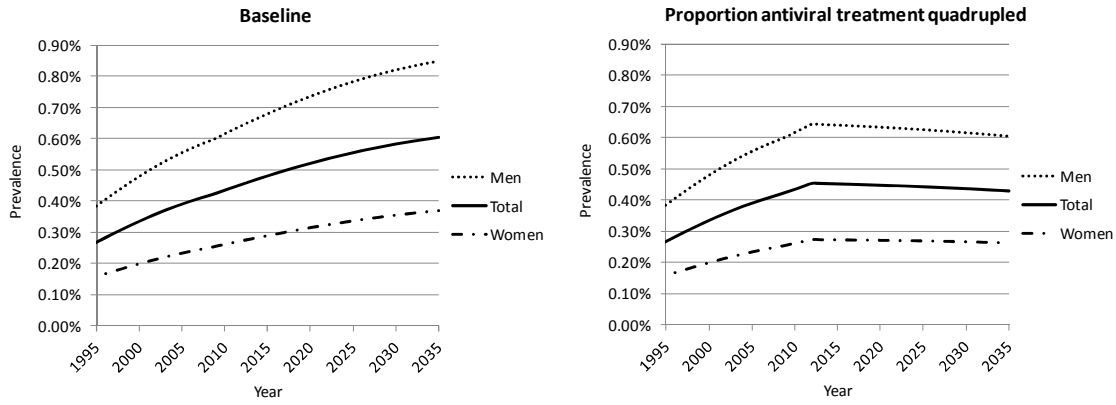

Figure 3.5 Scenario 1: estimated HCV prevalence, 1995–2035

Quadrupling antiviral treatment from 2012 is further estimated to lead to a small fall in the number of those with moderate HCV and a flatting of the curve of the estimated number of persons with cirrhosis (Figure 3.6). In 2035, the total number of those living with HCV infection at the various disease stages is estimated to be approximately 30 per cent lower compared to the baseline scenario.

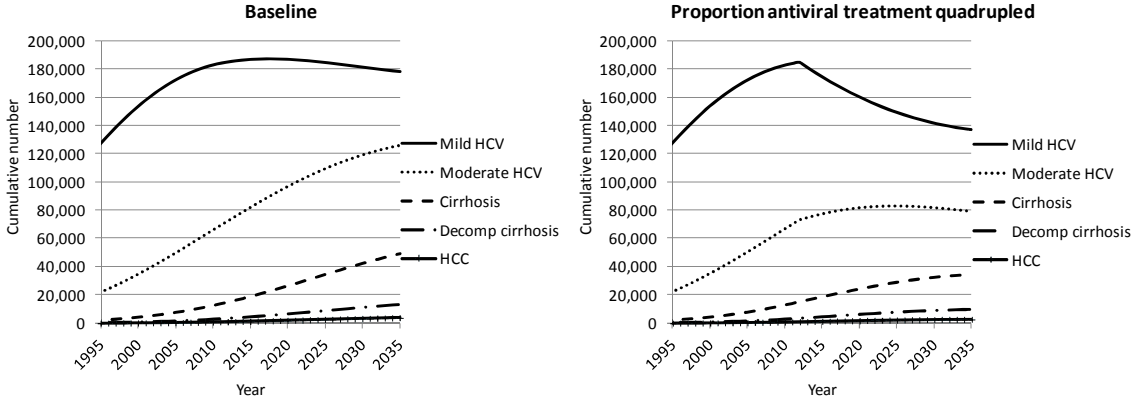

Figure 3.6 Scenario 1: estimated cumulative number of persons living with HCV infection at different stages of disease progression, UK, 1995–2035

Given the reduction in the number of those living with HCV-related disease, we estimate that quadrupling antiviral treatment from 2012 would lead to a 24 per cent reduction in the number of liver-related deaths by 2035, compared to the baseline scenario (Figure 3.7).

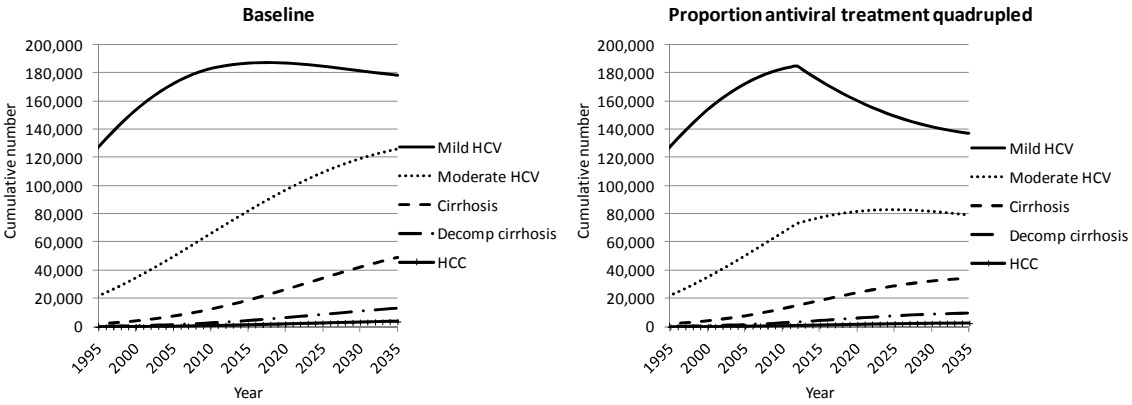

Figure 3.7 Scenario 1: estimated cumulative number of deaths in the HCV cohort, UK, 1995–2035

Turning to healthcare costs, quadrupling the proportion of HCV-infected persons receiving antiviral treatment is estimated to increase slightly the overall costs to the health service, compared to the baseline scenario. This is because of the higher investment required for antiviral treatment. However, cost of treatment of the sequelae of HCV infection without antiviral therapy is set to flatten from 2025 and eventually decline from 2030. Overall, we estimate the costs for the health service to rise to £119.8m, which is approximately four per cent (or £4.8m) higher than the baseline scenario (Figure 3.8; also Table 3.3, p. 22). However, this small increase has to be set against an associated fall in productivity loss, of 28 per cent (£59.3m), from £209.7m in the baseline scenario to £150.4m in scenario 1.

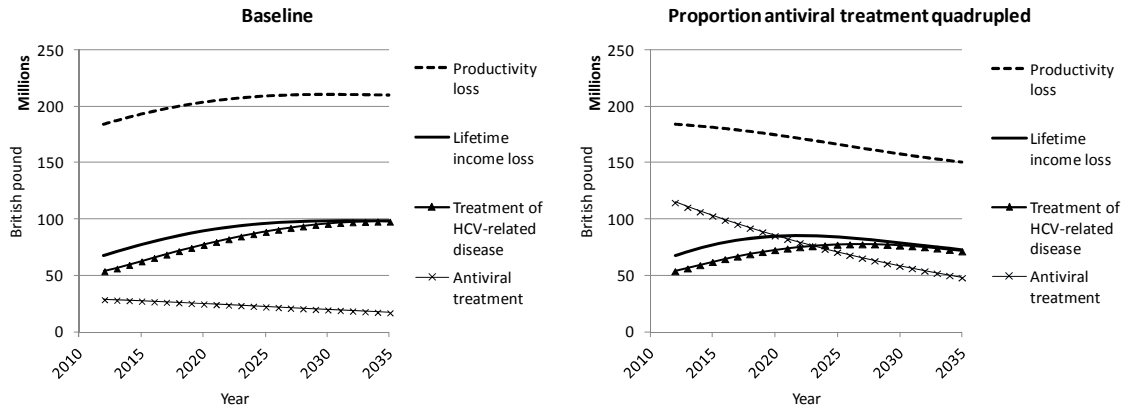

Figure 3.8 Scenario 1: annual cost of antiviral treatment, treatment of HCV infection, lifetime income loss and productivity loss associated with HCV infection, UK, 2012–35

Table 3.3 Quadrupling the proportion of HCV-infected persons receiving antiviral treatment from 2012: estimates of HCV-related disease progression, deaths, prevalence and costs, 1995–2035

	Disease progression (cumulative number)					Deaths (cumulative number)			Prevalence	Costs (Annual, GBP)			
	Mild HCV	Moderate HCV	Cirrhosis	Decompensated cirrhosis	HCC	Non-liver-related deaths	Liver deaths	HCC deaths	Total (per cent)	Antiviral treatment	Treatment of HCV-related disease	Lifetime income loss	Productivity loss
1995	127,676	22,241	2,227	416	152	544	65	77	0.27	1,103,589		14,486,063	101,759,227
2000	153,882	35,034	4,359	867	308	762	138	160	0.34	5,616,528		26,574,797	130,467,072
2005	172,358	50,076	7,762	1,637	567	958	265	300	0.39	15,727,097		42,595,291	156,122,142
2010	183,021	66,357	12,666	2,825	954	1,208	466	515	0.44	29,504,041		60,432,681	177,266,634
2015	175,004	77,052	18,406	4,416	1,448	1,593	743	801	0.45	102,844,019	62,085,495	76,658,179	181,260,294
2020	160,621	81,407	23,869	6,078	1,926	1,942	1,044	1,083	0.45	85,390,290	72,582,618	84,104,114	174,614,380
2025	149,595	82,671	28,595	7,593	2,350	2,317	1,322	1,339	0.44	70,730,851	77,427,356	83,600,482	166,210,474
2030	141,964	81,512	32,055	8,774	2,667	2,687	1,543	1,534	0.44	58,465,406	76,733,976	78,446,157	157,609,026
2035	137,313	78,814	33,979	9,496	2,846	3,013	1,682	1,648	0.43	48,251,207	71,550,770	72,418,666	150,363,450

3.3 Scenario 2: quadrupling the proportion of HCV-infected persons receiving antiviral treatment from 2012, median income

In scenario 2 we maintained the quadrupling of the estimated number of those receiving antiviral treatment from 2012, but applied median wage as an upper bound for the estimated productivity and lifetime income loss. This is in contrast to the baseline scenario and scenario 1, in which we applied minimum wage.

As we only modified the economic variables of the model, we present here the findings for economic output only, as shown in Figure 3.9. Under the baseline scenario, current (2010) treatment patterns of HCV infection remain stable during the foreseeable future; assuming median income as upper bound, we find that lifetime income loss and productivity loss steadily increase, from £28.6m in 1995 to £184.9m in 2035 or from £206.4m to £427m, respectively (Table 3.4). As in scenario 1, quadrupling the proportion of those receiving antiviral treatment is estimated to lead to a substantial decline in either output indicator, with productivity losses to fall to £304.7m by 2035.

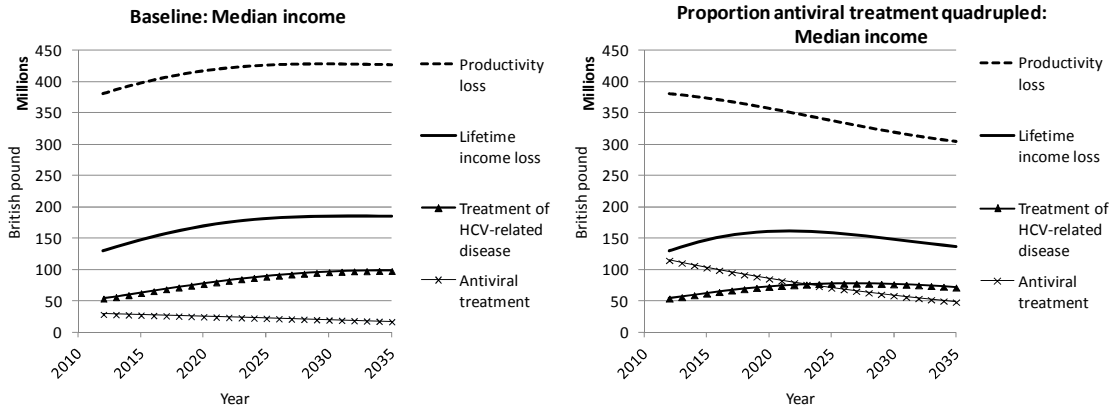

Figure 3.9 Scenario 2: annual cost of antiviral treatment, treatment of HCV infection, lifetime income loss and productivity loss associated with HCV infection, UK, 2012–2035

Table 3.4 Estimates of HCV-related costs, 1995–2035: median income

	Costs (annual, GBP)			
	Antiviral treatment	Treatment of HCV-related disease	Lifetime income loss	Productivity loss
Baseline scenario				
1995	1,103,589		28,603,570	206,355,410
2000	5,616,528		52,230,172	268,129,611
2005	15,727,097		83,191,696	322,808,598
2010	29,504,041		117,026,778	366,730,723
2015	27,386,212	62,636,067	147,462,684	397,482,797
2020	24,911,510	77,296,740	169,420,661	417,096,922
2025	22,274,028	88,888,237	181,274,377	426,385,421
2030	19,620,507	95,950,653	184,963,197	428,324,590
2035	17,060,018	97,939,202	184,942,999	426,988,562
Quadrupling the proportion of HCV-infected persons receiving antiviral treatment from 2012				
1995	1,103,589		28,603,570	206,355,410
2000	5,616,528		52,230,172	268,129,611
2005	15,727,097		83,191,696	322,808,598
2010	29,504,041		117,026,778	366,730,723
2015	102,844,019	62,085,495	146,965,769	373,419,765
2020	85,390,290	72,582,618	159,797,002	357,183,375
2025	70,730,851	77,427,356	157,877,512	337,926,046
2030	58,465,406	76,733,976	147,845,866	319,409,316
2035	48,251,207	71,550,770	136,642,733	304,684,321

CHAPTER 4 Discussion and conclusions

Analyses presented in this report sought to assess the healthcare and economic burden of HCV infection in the UK. We projected that, under current treatment patterns, the overall prevalence of HCV infection would increase from 0.44 per cent in 2010 to 0.61 per cent in 2035. This equates to an increase in the number of persons living with HCV infection from just under 266,000 in 2010 to 370,400 in 2035. We estimated that this rise in prevalence would be associated with an increase in annual healthcare costs, from £82.7m in 2012 to £115m in 2035. Productivity losses were estimated to rise from between £184m and £367m in 2010 to between £210m and £427m, depending on whether we assume minimum wage (lower estimate) or median income (upper estimate) for the productive population.

The figures estimated here crucially depend on the assumed incidence as one of the core components of the cohort simulation model applied in our analyses. We drew on incidence data derived from back calculation as applied to counts of deaths and hospitalisations related to HCV and liver cancer, and the above estimates reflect median incidence as calculated by Sweeting et al. (2007).[15] However, incidence data as provided by Sweeting et al. (2007) are characterised by considerable uncertainty and to illustrate the effect of this uncertainty on our model, we also presented estimates for the lower bound of the credible interval for incidence. This more than halved our estimates for prevalence, for the number of persons living with HCV infection, for the number of deaths attributable to HCV infection and for healthcare and economic costs.

Prevalence estimates for the median incidence assumption shown here compare reasonably well with figures presented by the Health Protection Agency (HPA). The HPA (2011) estimated that, in 2005, the prevalence of HCV antibodies in the adult population (aged 15 years and older) was 0.54 per cent (95 per cent Credible Interval, CrI 0.40, 0.75), or 218,000 individuals (95 per cent CrI 163,000, 305,000).[6] For England, an estimated HCV antibody prevalence of 203,000 (153,000, 286,000) translates into an estimated 150,000 individuals aged 15–59 in 2005 with chronic HCV infection[11] (using a chronicity rate of 74 per cent, which we also use in the present report)[20] or just over 160,000 adults aged 15 and over (0.4 per cent of the adult population).[6] Our model suggests the total number of persons with chronic HCV infection is higher, at around 232,000 (2005); however, our estimate relates to the UK as a whole. Indeed, adding estimates for Scotland, Northern Ireland and Wales to HPA figures for England results in an overall estimate of 216,000 individuals to be chronically infected with HCV in the UK.[5] Our estimated

prevalence for 2005 is similar to that given by the HPA, at 0.39 per cent; however, our estimate applies to the entire population.

Conversely, our estimates for the number of persons with compensated liver cirrhosis, decompensated cirrhosis and liver cancer are higher than those estimated and projected by the HPA. For example, for 2010, the HPA projected the number of individuals with HCV-related compensated liver cirrhosis in England to be 7,240 (95% CrI 5,600, 9,160), and the combined number of those with HCV-related decompensated cirrhosis or liver cancer 2,430 (95% CrI 2,310, 2,550).[5-6] Projections were not extended to include the devolved countries of the UK, so these figures are somewhat difficult to compare to those produced by our model.

Using the median incidence assumption, our model estimates the number of individuals in the UK with HCV-related compensated cirrhosis or liver cancer in 2010 to be considerably higher, at 12,666, with prevalence estimates for decompensated cirrhosis and liver cancer combined at 3,779 for the same period (Figure 4.1).

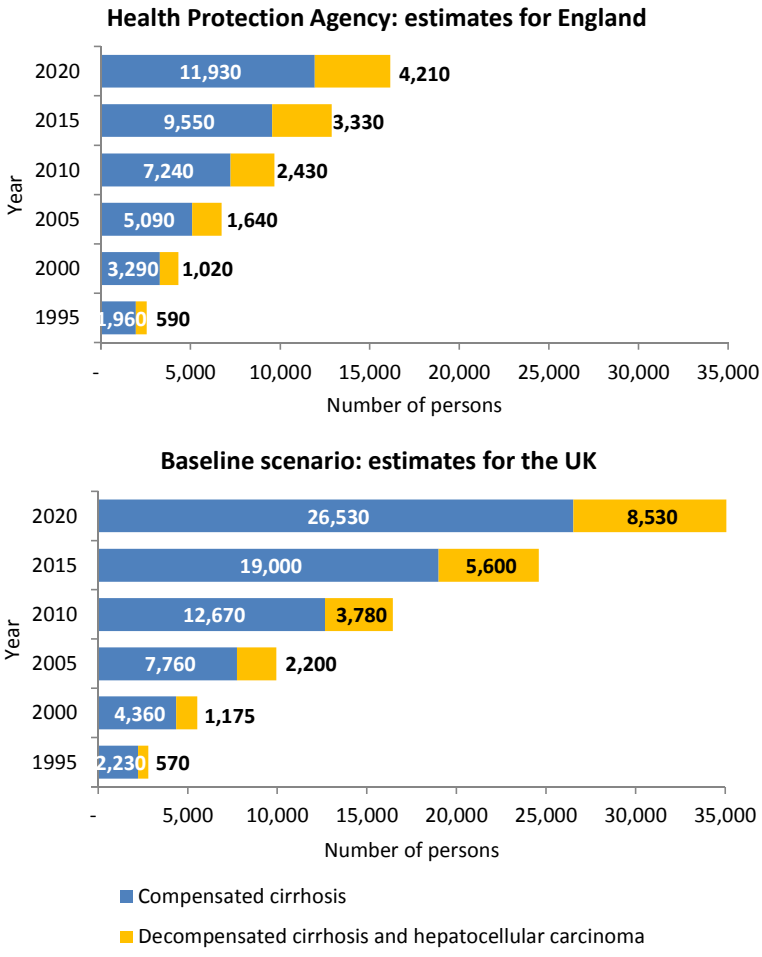

Figure 4.1 Estimated number of persons living with HCV-related cirrhosis or decompensated cirrhosis/hepatocelluar carcinoma in England (upper panel) or the UK (present study, baseline scenario, lower panel), 1995–2020

NOTE: data for upper panel taken from Health Protection Agency (2012);[5] figures in lower panel are rounded to the nearest decimal

One likely reason for this discrepancy is that the incidence figures used for our model provided estimates for the period 1960–94 only. For figures going forward we assumed a stabilisation of median incidence for the remainder of the projection period (to 2035). Conversely, if we use the lower bound of the incidence estimates provided by Sweeting et al. (2007)[15] we assume a steadily declining trend in the incidence of HCV infection in the UK, resulting in estimates that are substantially lower than those projected by the HPA. Thus, using the low incidence assumption we estimate, for 2010, the total number of individuals with HCV-related compensated cirrhosis to be 5,913 (compared to 7,240 as projected by the HPA[6], as mentioned above) and the combined number of those with HCV-related decompensated cirrhosis or liver cancer to be 1,778 (HPA 2,430).

At the same time, the forecasts by cohort and year used in the present analysis were only available up to year 2010, after which each year was assumed to have the same mortality rates and similar population across cohorts. This would mean that the prevalence rates are slightly over-estimated post-2010. Against this background and given the overall uncertainty about the 'true' prevalence of HCV infection in the UK, we assume that the projected figures for individuals living with HCV infection at different disease stages to lie somewhere between the HPA figures and the median incidence assumption proposed here. It will be important, in future, to gain a better understanding of more trend developments in HCV incidence to inform future projections.

In our further analysis of different scenarios we used the median incidence assumption. We explored different scenarios projecting the impact of providing antiviral treatment to a larger proportion of persons with HCV infection from 2012 onwards. Assuming that current treatment patterns prevail, we estimated the number of individuals with chronic HCV infection to increase from 265,000 in 2010 to approximately 370,000 in 2035. Quadrupling treatment rates would halt this rise, with the estimated number of chronically infected individuals falling to 262,000. While much of this reversal of trend would be among those with mild and moderate HCV infection, increasing treatment rates would also reduce the number of those with decompensated cirrhosis and hepatocellular carcinoma, from an estimated 17,000 under the current treatment assumption to 12,000 in the increased treatment assumption (2035).

This projected shift in the distribution of disease stages to milder disease is associated with a shift in projected healthcare costs. As noted above, our total estimate for annual healthcare costs associated with HCV in 2012 is £82.7m. Assuming current treatment patterns prevail, we estimated annual healthcare costs to increase to £115m by 2035. Increasing antiviral treatment would lead to an increase in healthcare costs overall, with the projected total increase amounting to four per centage points (or £4.8m) by 2035, compared to the baseline scenario. Much of the increase in healthcare costs was estimated to be attributable to the costs associated with antiviral treatment, which we found to be part compensated for by a fall in the costs of treatment of the long-term sequelae of (untreated) HCV at the early stages of disease progression. The average additional cost of antiviral treatment per annum between 2012 and 2035 is estimated at £43.8m.

We should add that our assumption on costs associated with antiviral treatment is probably more on the conservative side, using 2010 prices, which are likely to fall in future, although it is difficult to assess how new treatments that have become available

more recently will impact on the future costs of antiviral treatment. We also did not consider likely changes in the distribution of HCV genotypes as the population ages and potentially declining proportions of more difficult to treat genotypes. This could in turn lead to cost savings for providers as a higher proportion might achieve sustained virological response.[48]

We further calculated the productivity losses associated with HCV infection, which we estimated to range between £184m and £380m in 2012, set to increase to between £210m and £427m in 2035, based on our median incidence assumption. Increasing the proportion of antiviral treatment would lead to a reduction in HCV-related productivity losses of between £59m and £122m (28 per cent, quadrupling the proportion of those receiving antiviral treatment). The ranges given here represent a lower bound based on minimum wage for those who work and upper bound, assuming median income. The 'true' estimate is likely to lie somewhere between these two extremes.

Cumulatively, under the minimum wage assumption, the average gain in productivity per annum is estimated at £35.3m, which would be lower than the investment required to cover the additional cost of antiviral treatment if treatment rates are quadrupled, at £43.8m. However, these additional costs would be clearly outweighed under the median income assumption, which we estimate to result in an average productivity gain of £73.3m per annum.

In conclusion, our findings suggests that increasing treatment rates of those with HCV infection is associated with a gain in productivity because of a decline in the overall number of persons carrying the infection and, as a consequence, the number of those progressing to advanced disease stages. However, the impacts will be long-term. Immediate impacts, in terms of benefits to society as measured by productivity, are likely to be counterweighted by additional investments required to make antiviral treatment more widely available. At the same time, our estimates illustrate that the current pattern of treating only a very small proportion of HCV infected will have little impact on the future burden associated with HCV-related disease.

It is important to reiterate that the findings presented here are crucially influenced by the underlying assumptions and uncertainties around incidence in particular. This highlights the need for improved measures to enable better understanding of recent trends in the prevalence and incidence of HCV infection across the UK through, for example, improved surveillance and monitoring systems, alongside prevalence studies. Such systems will be important to inform the development and test the validity of existing models aimed at projecting the health and economic burden associated with HCV infection.

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APPENDICES

Appendix A: Baseline scenario, median incidence, age profile shifted to five years younger

This section presents the findings for a variation of the baseline scenario, which uses a younger age profile that is shifted five years to the left. We present findings for (a) HCV prevalence (Figure A.1); (b) the estimated number of persons with HCV at different disease stages (Figure A.2); (c) the estimated number of deaths in the HCV cohort (Figure A.3); and (d) the estimated annual healthcare and economic costs associated with HCV infection (Figure A.4).

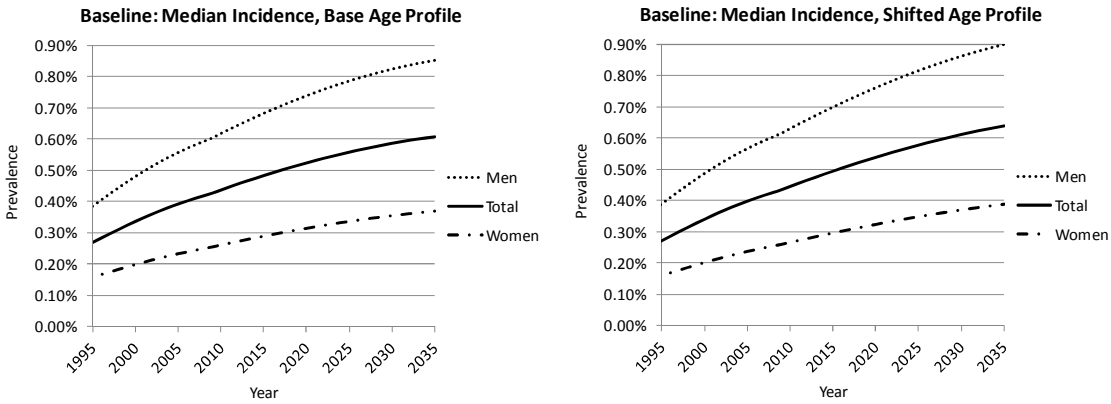

Figure A.1 Baseline scenario, shifted age profile: estimated HCV prevalence, 1995–2035

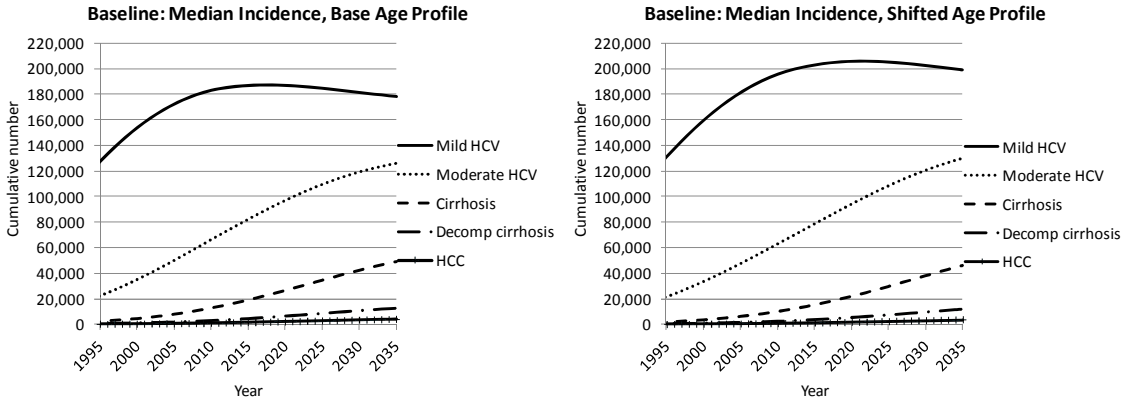

Figure A.2 Baseline scenario, shifted age profile: estimated cumulative number of persons living with HCV infection at different stages of disease progression, UK, 1995–2035

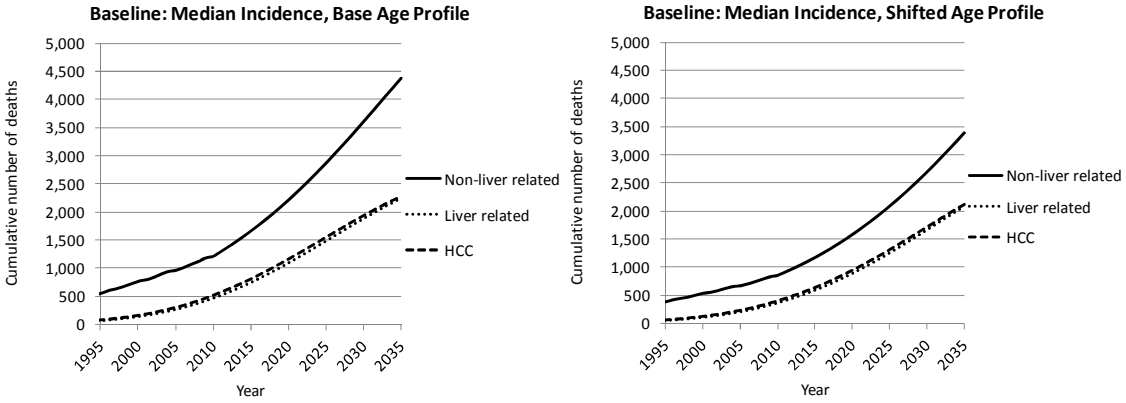

Figure A.3 Baseline scenario, shifted age profile: estimated cumulative number of deaths in the HCV cohort, UK, 1995–2035

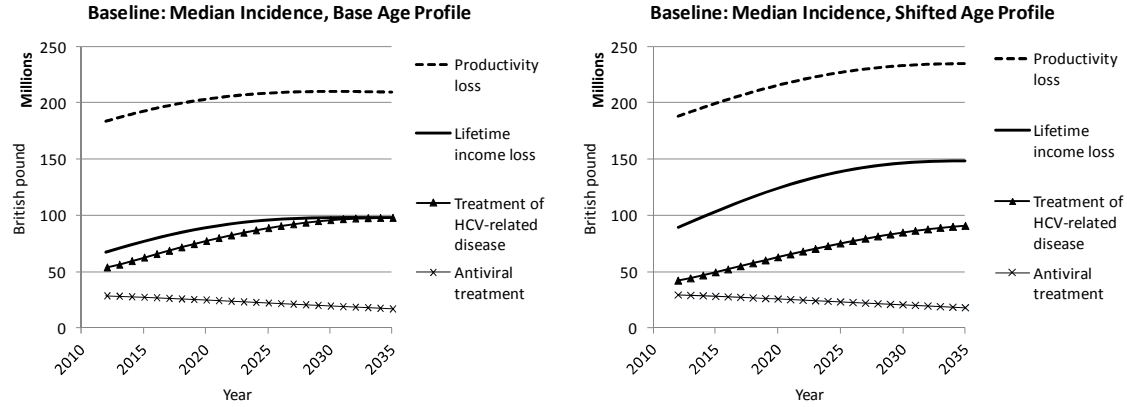

Figure A.4 Baseline scenario, shifted age profile: annual cost of antiviral treatment, treatment of HCV infection, lifetime income loss and productivity loss associated with HCV infection, UK, 2012–35

Appendix B: Baseline scenario, low incidence, age profile shifted to 5 years younger

This section presents the findings for a variation of the baseline scenario, which uses the lower bound of incidence and a younger age profile that is shifted five years to the left. We present findings for (a) HCV prevalence (Figure B.1); (b) the estimated number of persons with HCV at different disease stages (Figure B.2); (c) the estimated number of deaths in the HCV cohort (Figure B.3); and (d) the estimated annual healthcare and economic costs associated with HCV infection (Figure B.4).

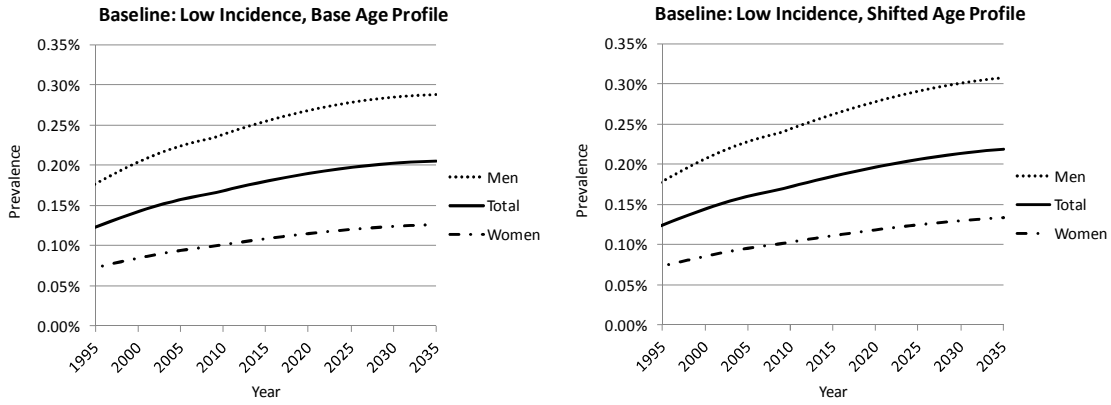

Figure B.1 Baseline scenario, low incidence, shifted age profile: estimated HCV prevalence, 1995–2035

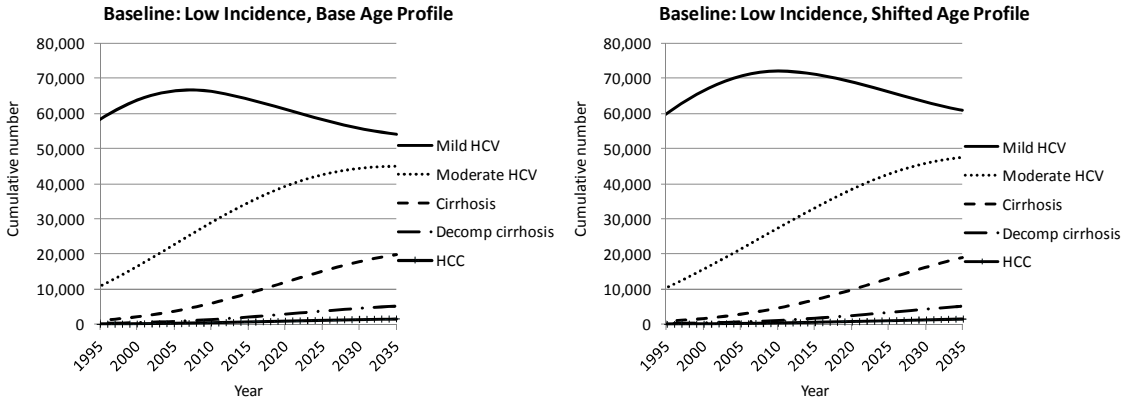

Figure B.2 Baseline scenario, low incidence, shifted age profile: estimated cumulative number of persons living with HCV infection at different stages of disease progression, UK, 1995–2035

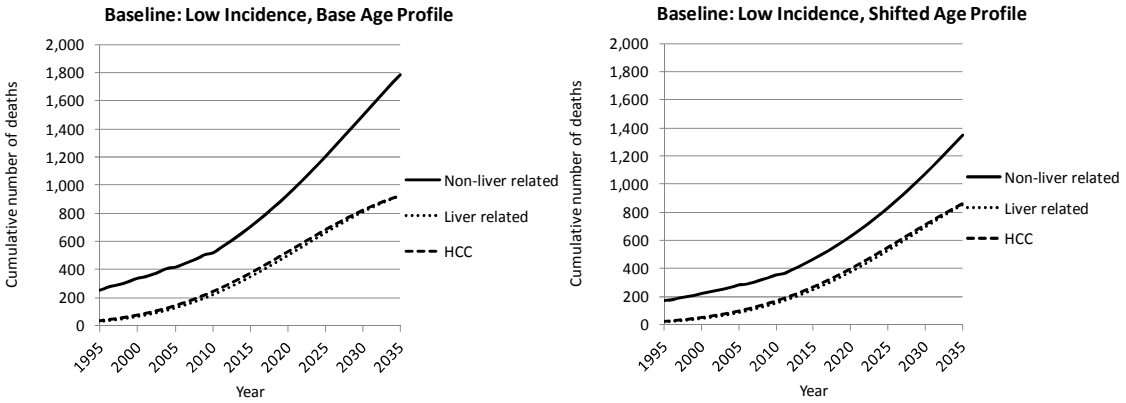

Figure B.3 Baseline scenario, low incidence, shifted age profile: estimated cumulative number of deaths in the HCV cohort, UK, 1995–2035

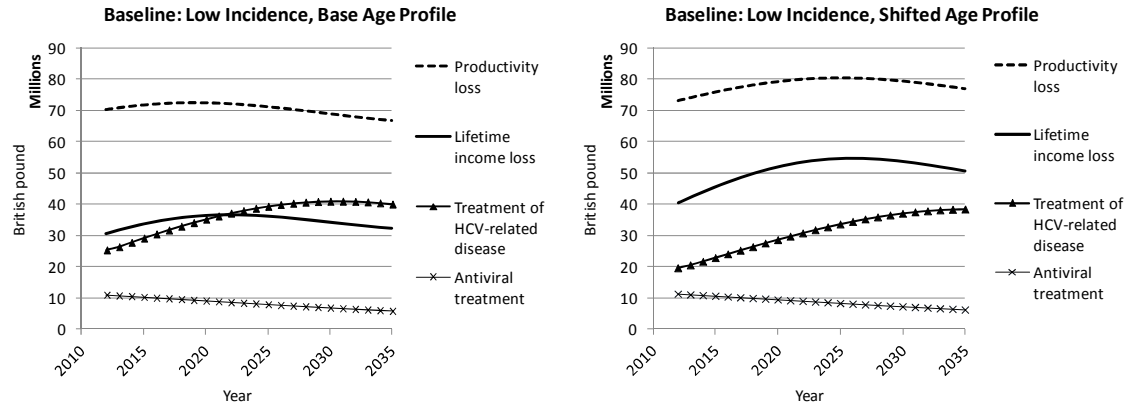

Figure B.4 Baseline scenario, low incidence, shifted age profile: annual cost of antiviral treatment, treatment of HCV infection, lifetime income loss and productivity loss associated with HCV infection, UK, 2012–35

Appendix C: Baseline scenario, median incidence, excess mortality

This section presents the findings for a variation of the baseline scenario, which uses median incidence and an 'excess mortality' profile to reflect the higher non-liver-related mortality levels of intravenous drug users. We present findings for (a) HCV prevalence (Figure C.1); (b) the estimated number of persons with HCV at different disease stages (Figure C.2); (c) the estimated number of deaths in the HCV cohort (Figure C.3); and (d) the estimated annual healthcare and economic costs associated with HCV infection (Figure C.4).

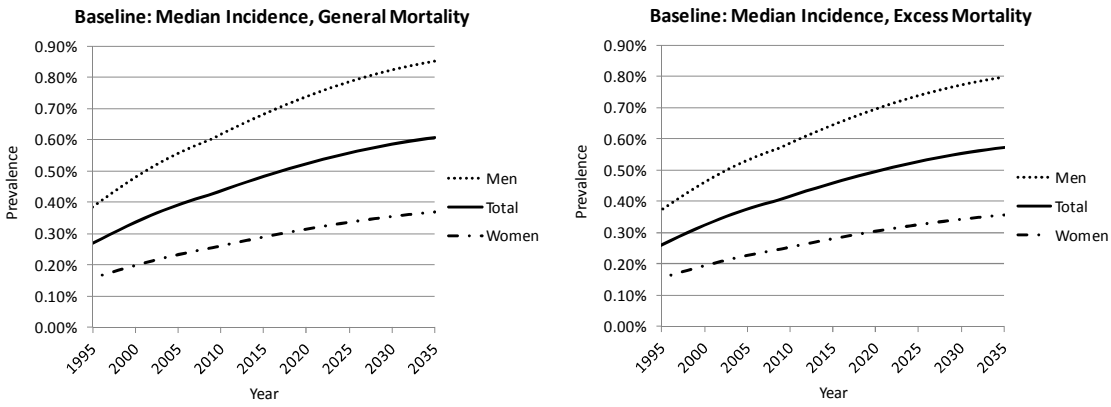

Figure C.1 Baseline scenario, excess mortality: estimated HCV prevalence, 1995–2035

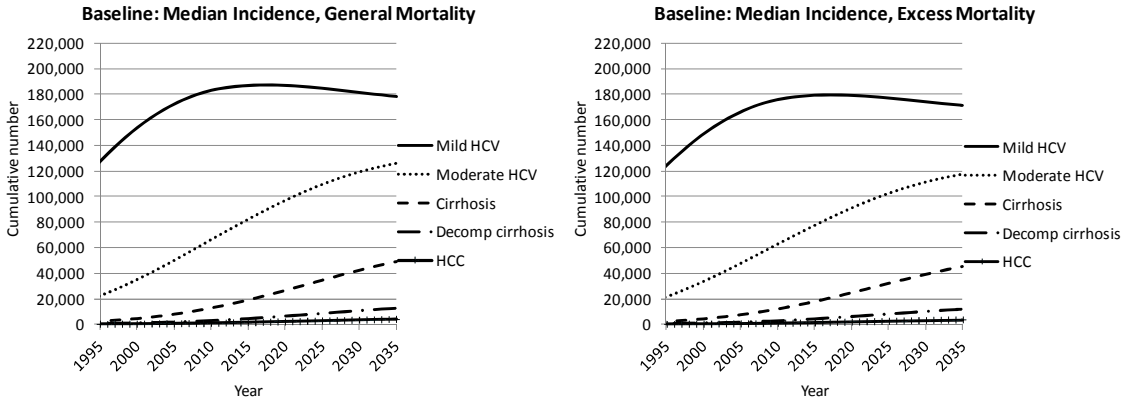

Figure C.2 Baseline scenario, excess mortality: estimated cumulative number of persons living with HCV infection at different stages of disease progression, UK, 1995–2035

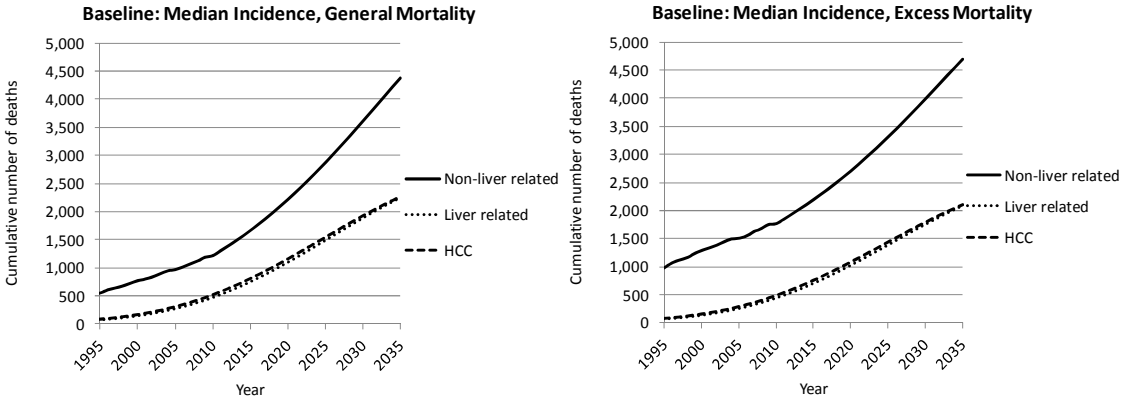

Figure C.3 Baseline scenario, excess mortality: estimated cumulative number of deaths in the HCV cohort, UK, 1995–2035

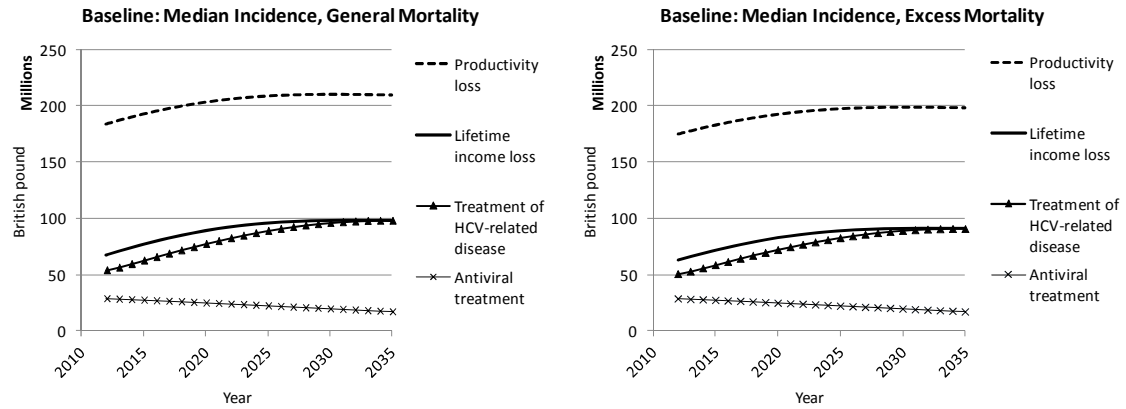

Figure C.4 Baseline scenario, excess mortality: annual cost of antiviral treatment, treatment of HCV infection, lifetime income loss and productivity loss associated with HCV infection, UK, 2012–35