



Public Health
England

Protecting and improving the nation's health

Hepatitis C in the UK

2018 report

Working to eliminate hepatitis C as a major public health threat

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Foreword



Duncan Selbie
Chief Executive

In the UK, around 200,000 people have chronic (long-term) infection with hepatitis C virus. The majority are from marginalised and under-served groups in society, such as people who inject drugs.

The recent UK fall in deaths from serious hepatitis C-related liver disease reported here, looks likely to be the result of increased treatment with new direct acting antiviral drugs, with increases in treatment of nearly 20% over the last year, and of 125% when compared to pre-2015 levels. Our ability to sustain current increases in treatment will ultimately be limited by our capacity to find and treat those who remain undiagnosed and to help those who are diagnosed but untreated to engage with accessible treatment services.

NHS England Operational Delivery Networks (ODNs) are in place to deliver treatment equitably across the country and the National Strategic Group on Viral Hepatitis, established by Public Health England, is bringing together partner organisations to help find the best ways to enact commitments at local, regional and national level to improve health services, minimise the number of new infections and reduce the health consequences of hepatitis infection for people in England.

To help with this, PHE have published a new [hepatitis C ODN profile tool](#) which provides local level estimates of hepatitis C prevalence, diagnoses, treatment and severe hepatitis C-related liver disease. This new tool will support prevention, testing and diagnosis, and treatment activities at local ODN level.

The findings of this report suggest that much good work has been done, but there is still much to do. If we are to eliminate hepatitis C as a major public health threat by 2030, it is essential that we continue to work cohesively together with stakeholders to pool our resource and maximise our impact.

This is the tenth Hepatitis C in the UK report and follows the WHO Global Health Sector Strategy on Viral Hepatitis 2016 to 2021 and the draft action plan for the health sector response to viral hepatitis in the WHO European region. Our report is structured to support UK monitoring of the Global Health Sector Strategy goals and summarises the impact of UK action plans to drive down mortality from HCV and reduce the number of new infections.

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Executive summary

On 28 May 2016, the World Health Assembly adopted a Global Health Sector Strategy (GHSS) on viral hepatitis for the period 2016-2021.^[1] This strategy introduced the first-ever global targets for viral hepatitis control.^[1] This report summarises the scale of the UK hepatitis C challenge in 2017, to help support focused action to eliminate hepatitis C as a major public health threat by 2030 at the latest.

Early estimates suggest that numbers of new cases of hepatitis C virus (HCV)-related end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC) in the UK remained relatively stable, at an average of 1,974 new cases per year between 2011 and 2015. However, mortality data suggest a fall in death registrations from these indications of 3% by 2016, with data suggesting a further fall of 11% in 2017. While 2017 data are still provisional, it seems likely that the fall observed since 2015 is the result of the increased treatment with new direct acting antiviral (DAA) drugs that has taken place over recent years (an increase of 19% in 2017/18, and of 125% when compared to pre-2015 levels). Interestingly, this fall is largely the result of a reduction in HCV-related ESLD; HCV-related HCC has continued to rise. As observed elsewhere,^{[2],[3],[4],[5]} this suggests that while DAA drugs may lead to a reduction in deaths from ESLD, the risk of HCC may persist after successful clearance of the virus. Overall, the World Health Organization (WHO) GHSS target of a reduction in HCV-related mortality of 10% by 2020^[1] looks likely to be achieved, and a reduction of at least 65% by 2030^[1] seems achievable.

Encouragingly, latest data from UK surveys of people who inject drugs (PWID)^{[6],[7]} suggest that around two thirds (66% in the Unlinked Anonymous Monitoring (UAM) survey in 2017; 64% in the Needle Exchange Surveillance Initiative (NESI) survey in 2015-16) of PWID are thought to be aware of their HCV antibody positive status (Note: comparison of 2017 UAM figure with previous years estimates should be made with care as the questionnaire has been revised). Although the WHO target of 50% of infected people in the WHO European region knowing their status by 2020^[8] is likely to have already been met in the UK, more needs to be done if we are to reach the 90% target by 2030.^[1]

Data from UK surveys of PWID^{[6],[7]} do not suggest any reduction in numbers of new HCV infections over recent years; prevalence of infection in recent initiates to drug use were similar in 2017 (22%) to those observed in 2008 (24%). In 2017, only an estimated 3 out of every 5 PWID in the UK reported having adequate needle/syringe provision for their needs. Taken together, these data suggest that the WHO GHSS call to reduce new cases of chronic HCV by 30% by 2020 and 80% by 2030,^[1] represents a significant challenge for UK HCV prevention and treatment services.

Overall, with the increasing availability of new DAA drugs, the UK is well-placed to meet WHO GHSS goals to reduce HCV-related morbidity and mortality, provided current improvements in numbers accessing treatment can be sustained in future years. Our ability to sustain the current increase in numbers accessing treatment will ultimately be limited by our capacity to find and treat those who remain undiagnosed, and to help those who are diagnosed but untreated to engage with local treatment services; only then will we be able to build on the current fall in avoidable HCV-related deaths. It will also be important to monitor equity of access to treatment and care services. At the other end of the spectrum, there is little evidence to support a fall in the number of new HCV infections; if GHSS goals to reduce these levels are to be reached, then a radical change in our response to tackling HCV in PWID is required.

We are interested in receiving your feedback on this report and would be grateful if you could take 2 minutes to complete a short survey:

<https://surveys.phe.org.uk/TakeSurvey.aspx?SurveyID=IIKI47I20>

Thank you!

Background

The World Health Organization (WHO) estimates that in 2015, viral hepatitis caused 1.34 million deaths, a toll similar to that of tuberculosis (1.37 million deaths) and higher than HIV (1.06 million deaths) or malaria (0.44 million deaths).^[9] Of these deaths, 96% were the result of complications of chronic hepatitis C and hepatitis B infection.^[9] However, unlike TB, HIV, and malaria, where scaled-up interventions have led to a decrease in mortality over recent years, deaths from viral hepatitis are continuing to rise.^[9]

In May 2016, the World Health Assembly adopted a Global Health Sector Strategy (GHSS) on viral hepatitis for the period 2016-2021,^[11] with its targets aligned with the 2030 Agenda for Sustainable Development and the relevant World Health Assembly resolutions. This strategy introduced the first-ever global targets for viral hepatitis, including a 30% reduction in new cases of hepatitis B and C by 2020 and a 10% reduction in mortality.^[11]

In 2015, an estimated 71 million people were living with chronic HCV infection (1% of the global population) and an estimated 1.75 million new infections occurred worldwide.^[9] However, there are major differences in the HCV epidemic both within and between WHO regions. In the WHO European Region it was estimated that more than 14 million people were living with chronic HCV infection in 2015, suggesting a relatively higher prevalence of 1.5% in this region, and an estimated 565,000 new infections in 2015.^[9] Recognising the differences in HCV epidemics between regions, a draft action plan for the health sector response to viral hepatitis in the WHO European region has been published, outlining relatively more ambitious proposals for targets and milestones to tackle the infection (see Appendix 1).^[8]

Closer to home in the UK, it is thought that around 210,000 people are living with chronic HCV.^{[10],[11],[12],[13]} Injecting drug use continues to be the most important risk factor for infection with around half of people who inject drugs (PWID) in England and Wales thought to have ever been infected, with levels being lower in Northern Ireland (23%)^[14] but higher in Scotland (58%).^[15] Prevalence of infection in the wider population varies around the UK, being concentrated in areas with high levels of current/past injecting drug use and high numbers of black and minority ethnic populations who have close links to countries with a high prevalence of HCV infection. HCV disproportionately affects populations who are marginalised and underserved and have poorer access to healthcare and health outcomes.

If we are to tackle HCV infection in the UK, and work towards elimination of HCV as a major public health threat by 2030 at the latest, it is critical that we continue to work with our partners to improve prevention, raise awareness, increase testing and get more diagnosed individuals into treatment and care.

Introduction

Hepatitis C is a bloodborne virus (HCV) that is often asymptomatic, and symptoms may not appear until the liver is severely damaged. As a consequence, many individuals with chronic HCV infection remain undiagnosed and fail to access treatment. These individuals can then present late with complications of HCV-related end-stage liver disease (ESLD) and cancer, which have poor survival rates.

HCV is a curable infection, and it is our aspiration to support the World Health Organization (WHO) in its goal to eliminate hepatitis C as a major public health threat by 2030 at the latest. This can be achieved via the collective action of all partner organisations involved in the prevention, diagnosis, treatment and care of those living with, or at risk of acquiring, HCV infection.

National action to tackle HCV is already underway, and being further developed across the UK.^[12, 16-18] In Wales, the NHS and its partners are working to a Liver Disease Delivery Plan to 2020.^[16] In Scotland, action is guided by the updated Sexual Health and Blood Borne Virus Framework, 2015 to 2020.^[17] In England, NHS England continues its approach to progressive roll-out of treatment to patients prioritised by Operational Delivery Networks (ODNs), and there is evidence that the system is addressing some of its challenges with innovative approaches to drug procurement and testing. PHE is capturing wider public health activities in their annual HCV report for England^[19] and their cross-agency National Strategic Group on Viral Hepatitis (NSGVH) continues to provide strategic direction and advice around viral hepatitis in England. In Northern Ireland, the Hepatitis B and C Managed Clinical Network publishes its annual report containing information on the epidemiology of hepatitis C, as well as public health and clinical activities related to hepatitis C disease prevention and control.^[20]

Informed by Global Health Sector Strategy (GHSS) goals and targets (see Appendix 1), countries are called upon to develop, as soon as practicable, ambitious national goals and targets for 2020 and beyond. These are intended to take into consideration the country context, including the country-specific nature and dynamics of viral hepatitis, the populations affected, the structure and capacity of the health care and community systems, as well as the resources that can be mobilised.^[1] Targets also need to be feasible and developed based on country realities, the best possible data, trends and responses, and should be monitored through a set of standard, measurable indicators.^[1]

This report summarises the scale of the UK problem in 2017, to help support focused action in UK countries to eliminate hepatitis C as a major public health threat by 2030, at the latest. To track our progress, the impact of key interventions in the following 2 **impact** areas are monitored:

- reducing transmission of HCV
- reducing morbidity and mortality due to HCV and its complications

To support this, it is also important to monitor the coverage of those interventions that are critical in driving down the levels of HCV infection and HCV-related mortality in the UK, namely:

- the adequacy of harm reduction in people who inject drugs (PWID)
- the proportion of infected people who are diagnosed
- the numbers, and ultimately the proportion, of infected people accessing treatment

The preliminary UK indicators (see Appendix 2), reported in the sections that follow, describe our progress so far and set out the scale of the challenge ahead.

Monitoring service coverage

A comprehensive response to hepatitis C requires the implementation of effective, high-impact interventions along the full continuum of hepatitis services, including interventions for prevention, testing, treatment and care. Mathematical modelling^{[21],[22]} suggests that HCV could be eliminated as a major public health threat by 2030 if the response reaches the service coverage targets set out in the GHSS on viral hepatitis^[1] (see Appendix 1).

In the UK, eliminating hepatitis C as a major public health threat by driving down HCV-related mortality and preventing new infections from occurring is potentially feasible with the tools currently available. Investment in 3 core intervention areas is needed: (i) ensuring adequate harm reduction for PWID, (ii) increasing the proportion of infected individuals who are diagnosed, and (iii) increasing the proportion of infected individuals who access and complete treatment, achieving a sustained virological response (SVR).

Adequate harm reduction

Harm reduction interventions for PWID, including access to sterile injecting equipment and effective drug dependence treatment, can prevent and control HCV among PWID.^{[23],[24],[25],[26],[27],[28]} Optimal access to clean injecting equipment and opioid substitution treatment (OST) is crucial in curbing the spread of HCV, particularly given that it also has the potential to prevent reinfection after treatment.

Globally, harm reduction for PWID falls short of the 2030 GHSS target of 300 sterile needles and syringes provided per PWID per year^[1] with, on average, only 27 syringe and needle sets distributed per PWID each year.^[9] However, these inevitably somewhat arbitrary figures, do not make any allowance for individual differences in need or secondary distribution. Therefore, in order to better reflect the adequacy of needle/syringe provision, data from UK surveys of PWID (Unlinked Anonymous Monitoring (UAM) Survey^[6] and Needle Exchange Surveillance Initiative (NESI) Survey^[7]) are presented here on self-reported adequacy of needle/syringe provision (Figure 1). In this metric, needle/syringe provision is considered 'adequate' when the reported number of needles received, met or exceeded the number of times the individual injected. In 2016 the UAM survey questionnaire was reviewed, resulting in a number of changes to data items from 2017 onwards.

Questions around Needle and Syringe Programme (NSP) access were updated to reflect changes in NSP provision that have been observed nationally and to incorporate information on secondary distribution of injecting equipment occurring among this population. Prior to 2017 participants in the UAM survey were asked how many needles they collected per month, and from 2017 onwards they were asked to report the

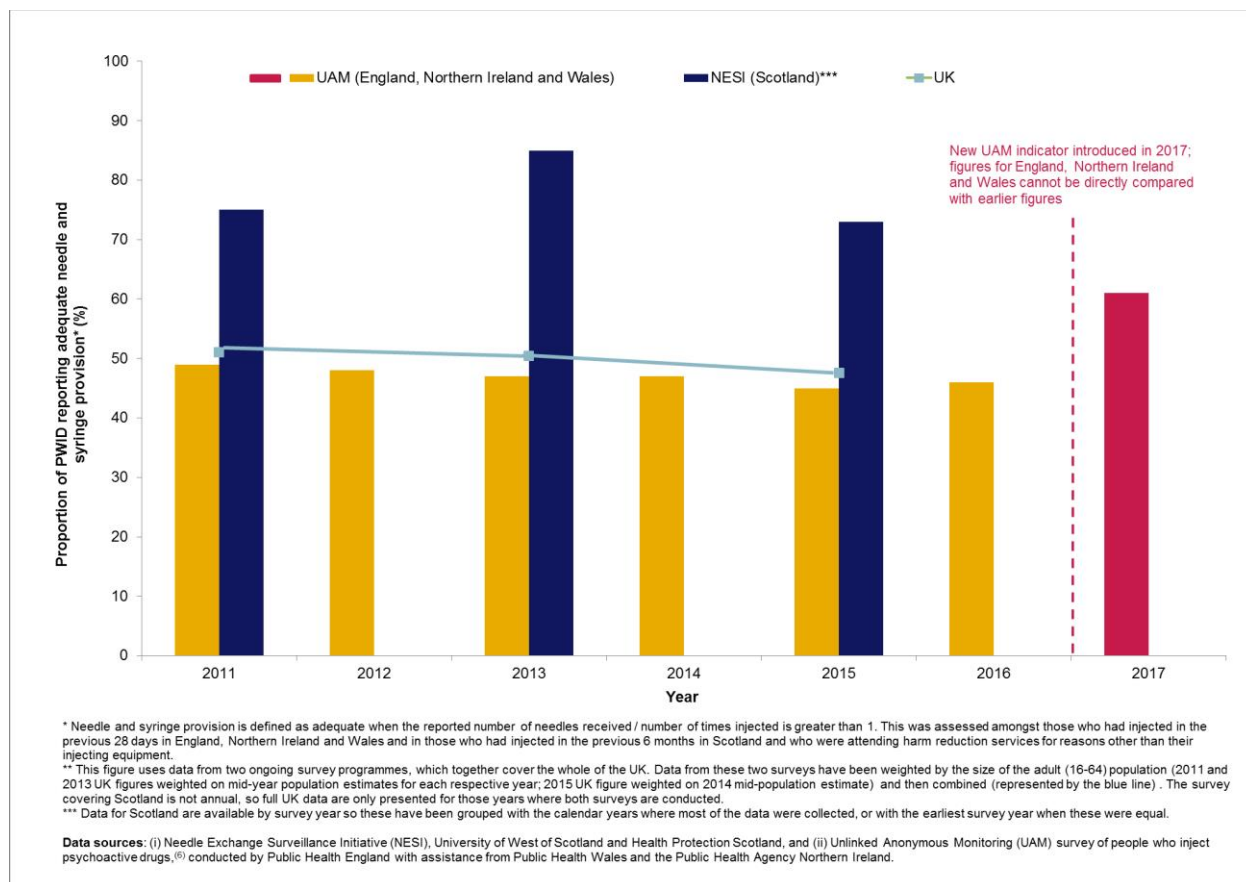
frequency of NSP visits per month and the number of needles collected per visit for themselves and for others. As a result the 2017 indicator is not comparable to previous years, but will hopefully be more representative from 2017 and provide trend data over the coming years. NESI participants are asked about the average number of times they inject drugs to obtain an average monthly injecting frequency. This is then used, along with information on the number of months participants injected within the last 6 months, to calculate the number of injecting events in the past 6 months. Participants are also asked about the number of new and unused needles and syringes, filters, spoons/cookers and water ampoules collected for themselves or others. Responses from these questions along with the total number of injecting events are then used to calculate the proportion of people who had enough needles for every injecting episode.

Figure 1 shows that in 2017, around 3 out of every 5 PWID in England, Northern Ireland and Wales (61%) reported having adequate needle/syringe provision for their needs. Whilst the 2017-18 survey for NESI is ongoing, data from the 2015-16 survey showed that around 7 in every 10 PWID in Scotland (73%) were assessed as having adequate needle/syringe provision for their needs, derived amongst those individuals who had recently injected and were attending harm reduction services for reasons other than for their injecting equipment (Figure 1).

In the 2017 UAM survey, 18% of people currently injecting psychoactive drugs reported direct sharing of needles and syringes, and this level has declined from 23% in 2007. When including the sharing of mixing containers or filters as well as needles and syringes, the proportion of those reporting sharing is higher at 36% but this figure for 2017 has declined from 45% reported in 2007. In NESI, levels of reported needle and syringe sharing in the past 6 months remained very low in 2015-16 (7%) and have now potentially reached a point of plateau. Similarly, reported sharing of other injecting equipment (spoons/cookers, filters, and/or water) in the past 6 months has more than halved from 48% in 2008 to 2009 to 21% in 2015 to 2016.

These findings indicate that, while the majority of PWID may be accessing NSPs, the amount of equipment provided needs to be increased and provision better targeted. NSPs can also be an important setting for delivering prevention information to PWID and an important route into drug treatment and recovery.

Figure 1. Estimated UK-wide proportion of PWID reporting adequate* needle and syringe provision, 2011 to 2017**



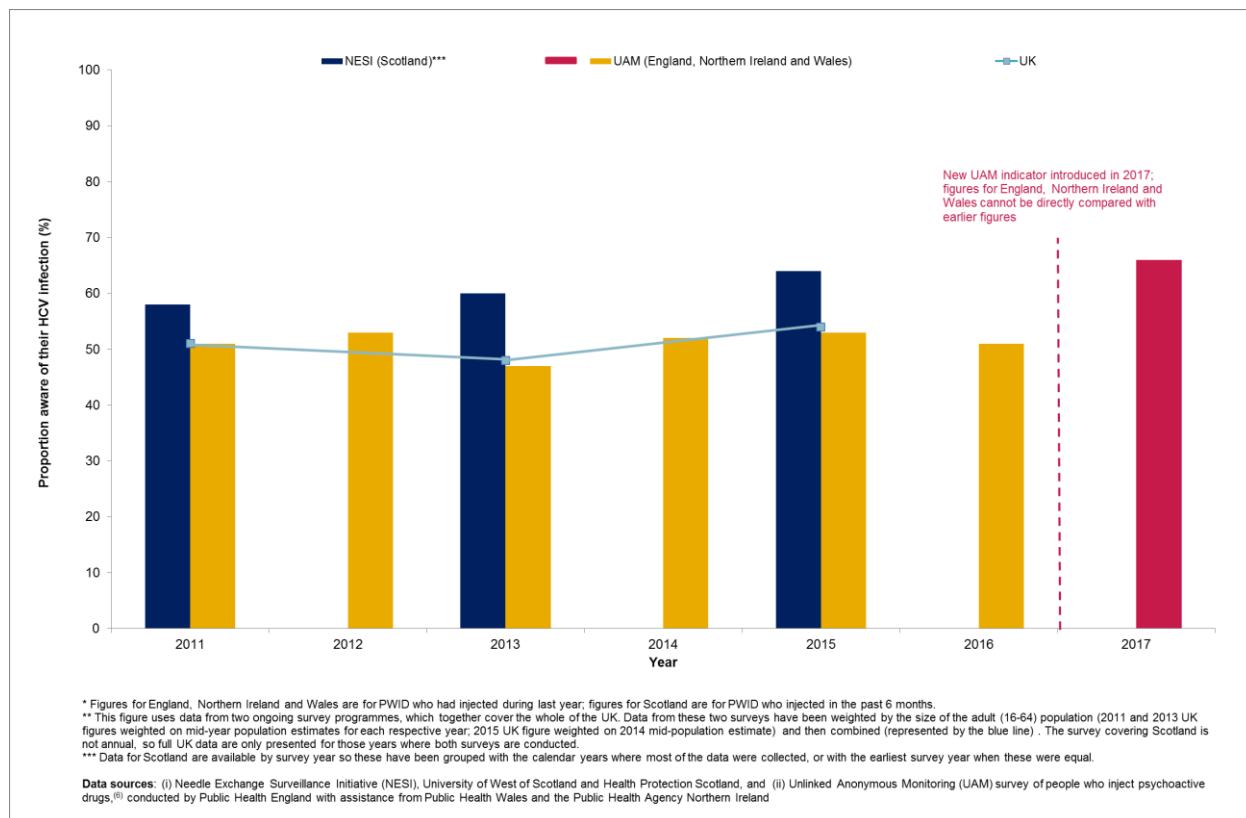
Increasing the proportion diagnosed

Early diagnosis of HCV infection is important for the most effective treatment and care, yet globally only 20% (14 million) of those infected have been tested and know their status.^[9] In the UK, levels of awareness of infection are well above the 20% global average, but are still suboptimal with positive results not always successfully linking individuals into treatment and care services.^[29]

While we work towards developing UK estimates of the proportion of individuals with chronic HCV infection who remain undiagnosed (currently these are unavailable for most UK countries), our best diagnosis monitoring data currently comes from national UK surveys of PWID (UAM and NESI^{[6],[7]}). Up until 2016, these surveys have suggested that only around one half of PWID sampled in the UK were aware of their HCV antibody positive status and this figure has remained relatively stable at this level over the last 6 years (Figure 2). However, data from the latest UAM survey suggest higher levels of awareness in 2017, with two thirds of PWID sampled in England, Wales and Northern Ireland (66%) aware of their HCV antibody positive status (Figure 2). This figure should be interpreted with caution as changes in the 2017 UAM survey,

introduced to differentiate between past and current HCV infection, have resulted in increased levels of non-response to this question. This is likely to account for some of the increase observed in this measure.

Figure 2. Estimated UK-wide proportion of PWID testing positive for HCV antibodies,* who are aware of their infection, 2011 to 2017**



The GHSS on viral hepatitis^[1] and the draft action plan for the health sector response to viral hepatitis in the WHO European region^[8] call for a major increase in the diagnosis of chronic HCV infection, with 50% of infected people in the WHO European region knowing their status by 2020 and 90% by 2030 (see Appendix 1). While the first target may have already been reached in the UK, more needs to be done if we are to reach the 90% target by 2030.

To reduce the levels of undiagnosed infection, it is necessary to roll out testing to more individuals at risk of infection, including priority populations like PWID, those in detained/secure settings, and to populations with close links to countries with a high prevalence of HCV infection.^[30] There are also those who may no longer be in contact with services because they acquired their infections many years earlier, for example following a period of injecting drug use or via blood transfusion before the introduction of screening of the blood supply in 1991. For the most part, HCV disproportionately affects populations who are marginalised and underserved and have poorer access to healthcare, so testing in alternative/community settings, using accessible technologies

like dried blood spot (DBS) testing^{[31],[29]} and point of care tests, as well as opt-out testing in prisons,^[32] will be key in reducing the levels of undiagnosed infection. If gains in testing are to be translated into cures, it is also important to ensure that we continue to work together to improve key linkages between testing and treatment services so that diagnosed individuals can access treatment and care.

Increasing the numbers accessing hepatitis C treatment

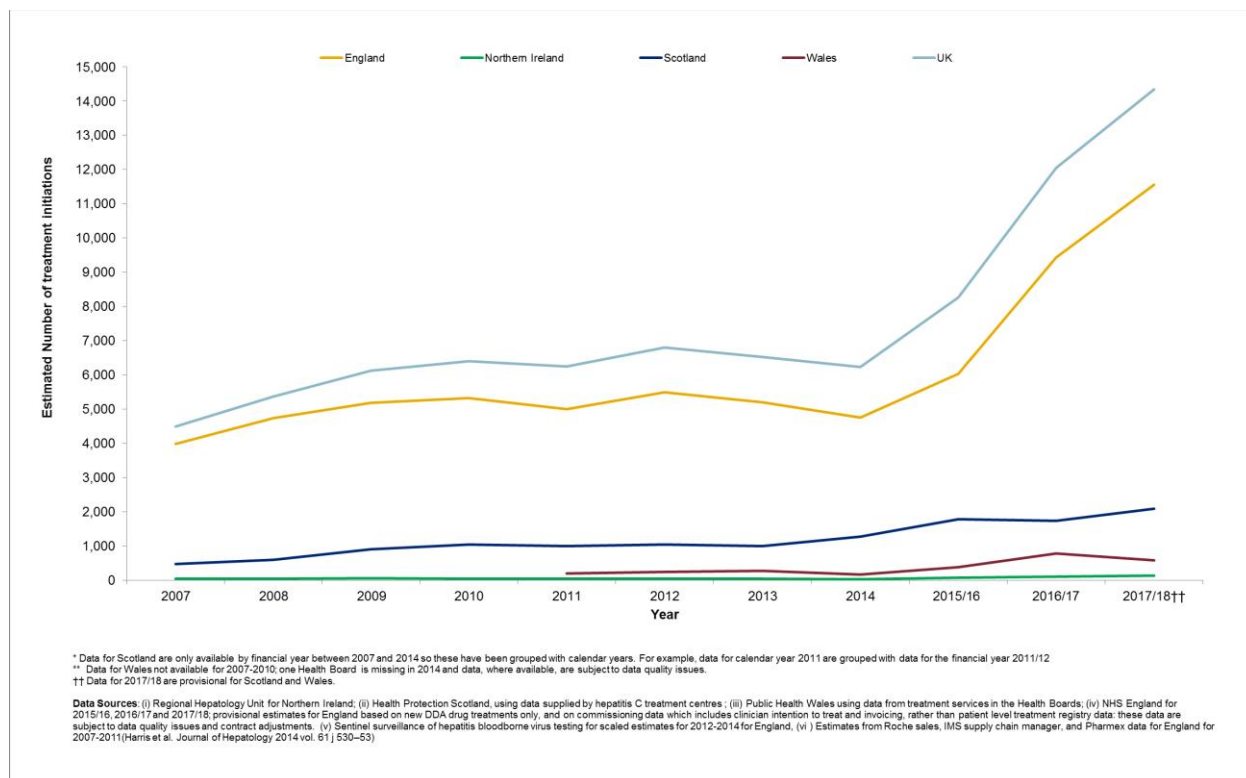
Among people diagnosed with chronic HCV infection globally, an estimated 7% started treatment in 2015 (1.1 million people).^[9] As of 2015, a cumulative total of 5.5 million people with chronic HCV had ever received treatment, although the majority of these treatments were older, less effective interferon-based regimens.^[9] The GHSS on viral hepatitis^[1] and the draft action plan for the health sector response to viral hepatitis in the WHO European region^[8] call for treatment coverage of people diagnosed with chronic HCV in the European region, and who are eligible for treatment, to reach 75% in 2020 and 80% by 2030. (see Appendix 1)

In the UK, new direct acting antiviral (DAA) drugs have the potential to transform the treatment landscape, offering a fast and effective cure to the vast majority who receive them, without many of the complications associated with previous treatments.^{[33],[34]} While prevention activity is key in reducing the rate of new infections, numbers already infected would remain high for many years without effective HCV treatment, which has the potential to dramatically reduce the number of deaths in the short and medium term.^{[33],[34]}

From the public health perspective, the new generation of DAA drugs offer a considerable advantage over previous HCV treatments because their all-oral, shorter treatment durations, and improved side-effect profiles make them easier to roll out in community/outreach settings where it is easiest to reach many of those infected. While the high price of these new drugs remains a major barrier to access in many countries worldwide, prices are falling and these medicines are being rolled out, in accordance with national recommendations,^{[35-40], [41], [42]} in all UK countries.

As we work towards producing UK estimates of the proportion of the chronically infected population who achieve a sustained virological response following treatment, Figure 3 summarises provisional estimates of the numbers initiating HCV treatment in the UK since 2007. Between 2009 and 2014, provisional estimates suggest that numbers initiating HCV treatment in the UK remained relatively stable at around 6400 initiations per year (6390; Range: 6130, 6808). Since 2014, numbers accessing treatment have increased dramatically, more than doubling pre-2015 levels to reach 14,348 treatment initiations by 2017 to 2018, with an increase of nearly 20% (19%) in 2017 to 2018 (Figure 3). This is the result of improved access to new DAA drugs that have been coming online since 2014 to 2015^{[38],[37],[35],[36], [39], [40], [41], [42]}

Figure 3. UK-wide estimates of numbers initiating HCV treatment, calendar years 2007 to 2014 and financial years 2015 to 2016 – 2017 to 2018*,**



In the 2017 UAM survey, among those participants testing positive for HCV antibodies who were aware of their infection, 72% reported ever having seen a Hepatologist. Of these, 42% reported ever being offered treatment and taking it, 34% reported being offered treatment but did not take it, and 23% reported that they were not offered treatment. In the 2015 to 2016 NESI survey, 28% of those who self-reported they were positive for HCV or had cleared infection following therapy, had ever received therapy for their HCV infection, 36% in the last year and 15% currently receiving treatment.

The measure, 'ever having seen a Hepatologist' will include consultations that took place in both DAA and interferon eras, so it will be interesting to see whether the numbers being offered and accepting treatment increase over the coming years as DAA rollout gains ground.

Monitoring impact

Reducing HCV-related morbidity and mortality

Up until 2014, mortality from HCV have been on the increase in the UK^[43] as people who acquired their infections decades earlier progress to advanced liver disease and access to suboptimal treatment has been inadequate.^{(9),(8),[44]} However, the new DAA drugs that are available^{[38],[37],[35],[36], [39], [40], [41]} offer the potential to significantly reduce the number of individuals progressing to serious HCV-related liver disease and to reduce the premature mortality that results.^[33] As new treatments are rolled-out to those who need them, it should be possible to achieve a rapid reduction in the severe morbidity and mortality that is currently observed^{[33],[34]} and has been predicted to continue in the future.^[29] Indeed, early evidence in the UK suggests that this fall in deaths has already begun.^[43]

Morbidity – Reducing the incidence of HCV-related ESLD/HCC

New cases of HCV-related ESLD/HCC are monitored using Hospital Episode Statistics (HES) in England, the Patient Episode Database in Wales (PEDW) and the Hospital Inpatient System (HIS) in Northern Ireland. New cases are identified by first linking all episodes of ESLD or HCC for an individual using their unique patient identifier and then linking these to hospital records with a diagnosis of HCV since 2004 (since 2000 for Northern Ireland). Once these are linked, a case of HCV-related ESLD or HCC is classified as 'new' if no previous episodes of ESLD or HCC for that individual are found in at least the previous 5 years (In England, less than 1% of ESLD/HCC episodes are estimated to have had a previous episode more than 5 years earlier). In Scotland, data on new (ie first time) ESLD/HCC hospitalisations are obtained via record-linkage of Scotland's National Hepatitis C Diagnoses Database to the national database on hospital admissions; thus, first-time ESLD/HCC hospitalisations for all individuals diagnosed with HCV (antibody positive) infection in Scotland are reported (including those with, but also those without, hepatitis C recorded on their hospital admission/discharge record).^{[45], [46], [47]}

Together these analyses have enabled us to produce UK-wide preliminary estimates of new cases (incidence) of HCV-related ESLD/HCC (Figures 4 and 5). However, it is important to recognise the limitations of these early estimates since different datasets were utilised in different UK countries, HCV may be unreported in HES, and patient episodes can only successfully be linked when identifiers exist in HES/PEDW/HIS to allow this. For example, in England (2010-2014) approximately 1.5% of individuals admitted had identifiers missing in HES and so were allocated a new HES identifier. Therefore, any previous episodes of ESLD for these individuals would not be linked.

As a result these early estimates of incidence remain preliminary but suggest that new cases of HCV-related ESLD/HCC in the UK remained relatively stable between 2011 and 2015, averaging 1,974 new cases per year (Range: 1,916 - 2,020; Figure 4). In 2016, preliminary UK figures suggest a potential rise in cases of HCV-related ESLD/HCC of 11%.

However, investigations revealed that nearly all of this increase occurred in a small number of specific geographic areas in England.^[48] This points strongly toward changes in identification or management practices; due to the long incubation time between infection and severe liver disease, genuine changes in ESLD/HCC incidence will tend to occur over the course of several years rather than abruptly in a single year. In much of England, the number of new cases of ESLD in those under 50 has remained stable or fallen in the past few years, although new cases have continued to rise in older age groups. In the absence of treatment interventions, modelling predicted a continued increase in ESLD and HCC.^[44] Further work is required to understand these new data, whether the rising burden in HCV-related disease will be less severe than anticipated, and the estimated impact of new treatment.

HES data for 2017 on admissions are not available for England due to incorrect classification by NHS Digital of some HCV codes as “restricted”. This resulted in identifiers which link admissions to a specific patient being stripped from HCV coded data sent by providers to NHS Digital. The error is a temporary issue which affected some data submitted between December 2017 and May 2018 and is now fixed. However, it means we were unable to de-duplicate individuals and identify multiple patient admissions in 2017. As we cannot identify when a patient was admitted for the **first time** with HCV-related ESLD/HCC as opposed to a repeat admission, the 2017 data show a dramatic increase in incidence of HCV-related ESLD/HCC that is **not real**. Investigations are ongoing with NHS Digital to see whether this error can be mitigated for subsequent HCV analysis. However, this error will have implications for estimating incidence of HCV-related ESLD/HCC from 2017 onwards, and adversely affect our ability to monitor the impact of new treatments, model estimates of future burden, and track progress towards achieving the WHO elimination of HCV as a major public health threat.

Figure 4. Preliminary estimates of incidence* of HCV-related ESLD/HCC in the UK***: 2010 to 2016**

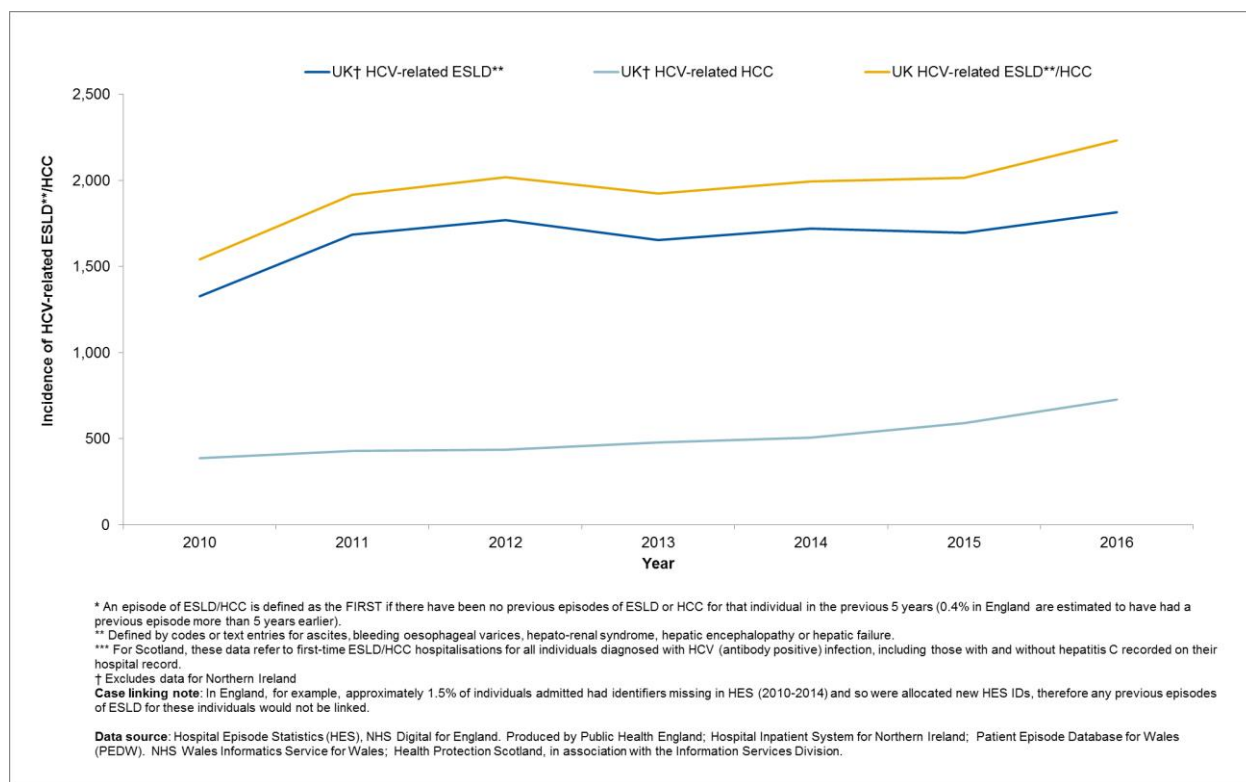
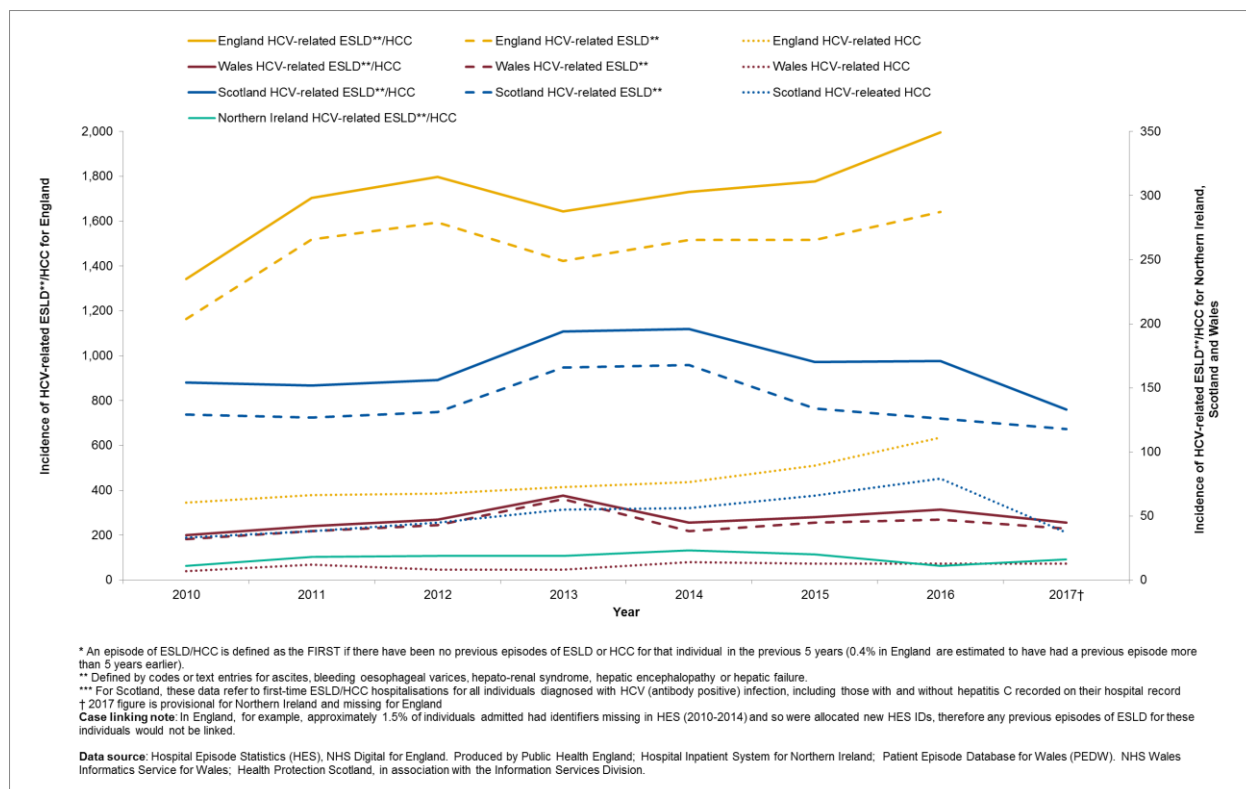


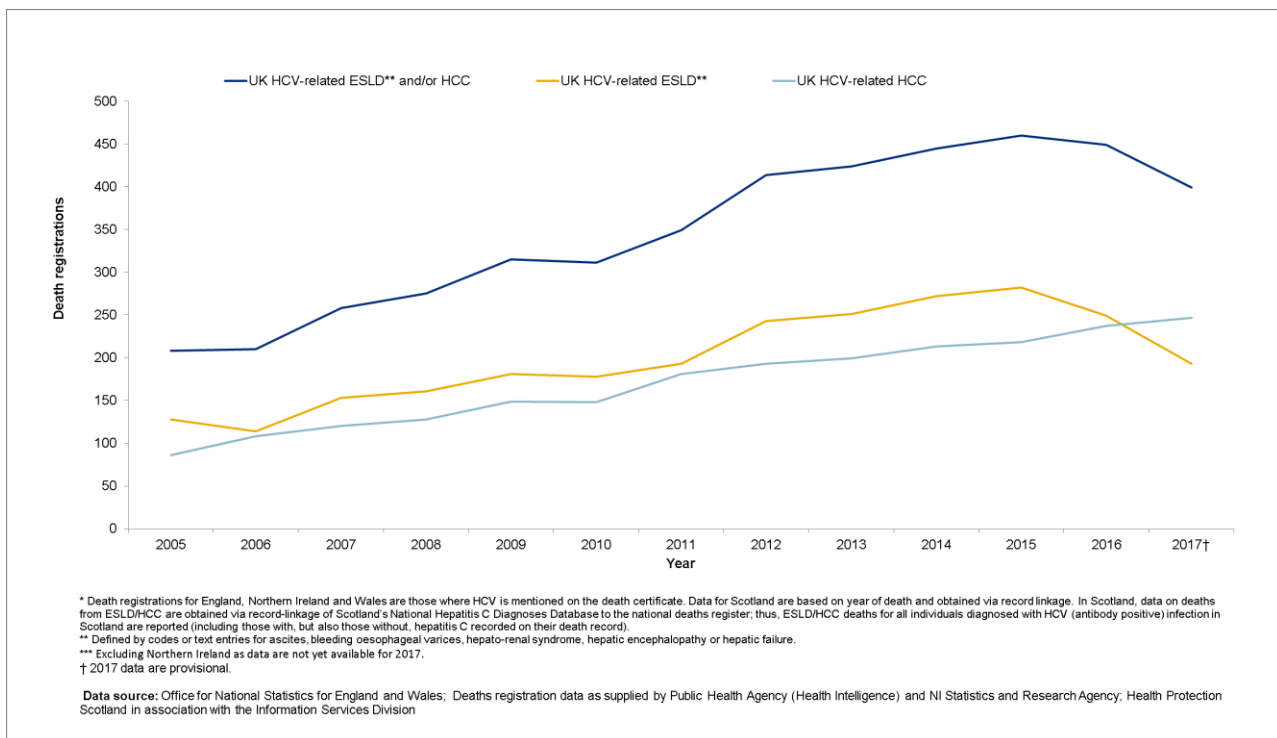
Figure 5. Preliminary estimates of incidence* of HCV-related ESLD/HCC in UK countries: 2010 to 2017*****



Mortality – Reducing deaths from HCV-related ESLD/HCC

Between 2005 and 2015, deaths registrations from HCV-related ESLD and HCC more than doubled in the UK, rising from 209 in 2005 to 468 in 2015. However, by 2016 a 3% fall in deaths had been observed, with provisional data suggesting a further fall of 11% by the end of 2017 (Figure 6). In 2018, reporting across all years was changed from monitoring by ‘date of death’ to monitoring according to the ‘date deaths were registered’ to reduce revisions that result from high numbers of late reports of HCV-related ESLD/HCC. However, as in previous years, provisional data should still be interpreted with caution. Nevertheless, it appears that the fall in deaths is likely to be the result of new DAA drugs that were introduced from 2014/2015 (Figure 3). Because HCV is not always reported on the death certificates of those who die with ESLD/HCC and are HCV infected,^[49] actual numbers of deaths will be higher.

Figure 6. Death registrations* for HCV-related ESLD and HCC in UK*** Countries: 2005 to 2017**

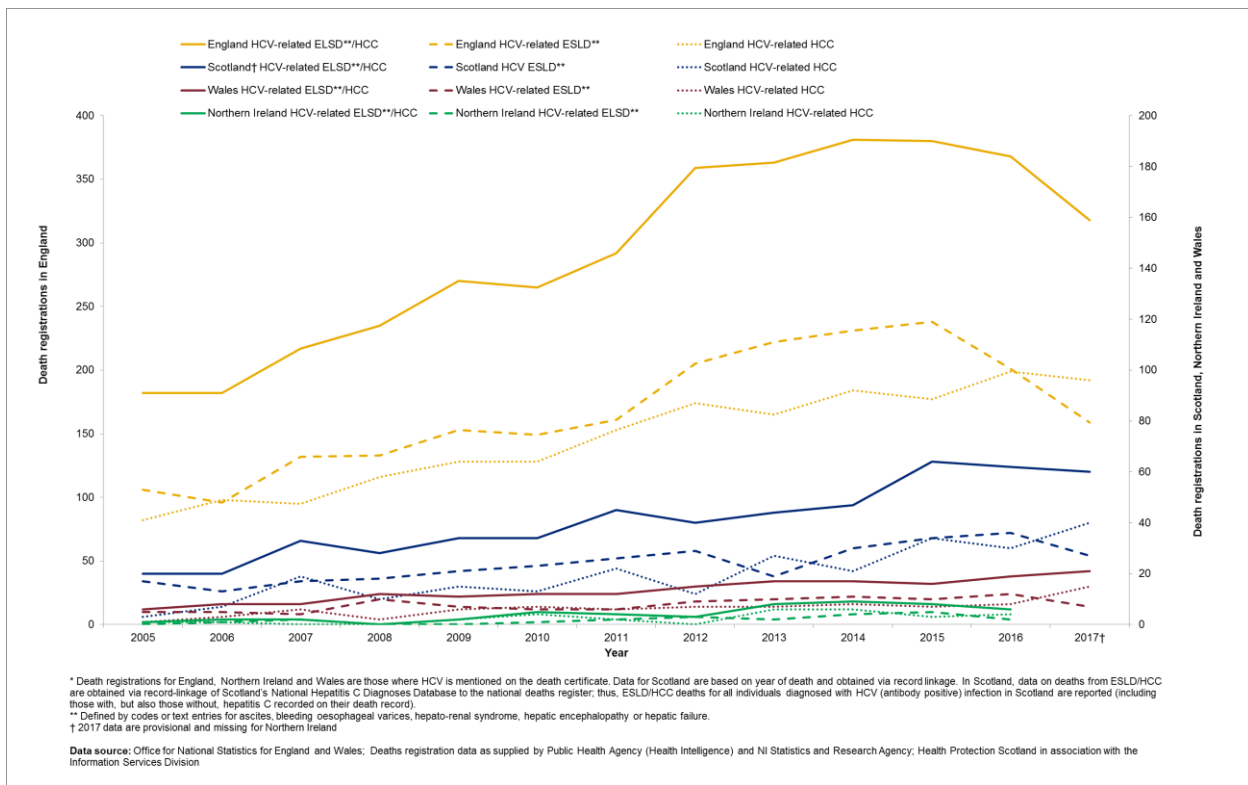


Interestingly, while death registrations for HCV-related ESLD/HCC in the UK have fallen overall in recent years, this is largely the result of falls in HCV-related ESLD; HCV-related HCC has continued to rise (Figures 6 and 7). As observed elsewhere, this suggests that while DAA drugs may lead to a reduction in deaths from ESLD, the risk of HCC may persist even after successful clearance of the virus, particularly amongst those with pre-existing co-factors for liver disease or whose liver disease is at an advanced stage when treated.^{[2], [3],[4], [5]} It is important to note that whilst HCC risk may persist post SVR, recent evidence does not support any increase in risk of HCC associated with interferon-free regimens when compared with interferon-based

regimens.^[50] The data presented here support the view that treatment outcomes are best when HCV infection is treated at an earlier stage, and underlines the importance of ongoing surveillance for HCC in those who clear the virus at more advanced stages of disease or who have co-factors for liver disease.^[51]

As more infected individuals access new therapies (Figure 3), the GHSS on viral hepatitis' call for a 10% reduction in HCV deaths by 2020 seems likely in the UK, and a reduction of 65% by 2030^[1] (see Appendix 1) within our reach, provided current improvements in numbers accessing treatment can be sustained.

Figure 7: Death registrations* for HCV-related ESLD and HCC in the UK: 2005 to 2017**



Reducing the number of new (incident) infections

Monitoring the impact of prevention measures on the incidence of infection remains a challenge as incident infection is difficult to measure directly. Ideally we would monitor the actual or estimated number of new chronic HCV infections that arise annually in PWID as well as any that result from net migration or other sources, and monitor this over time. However, the former is difficult to estimate because much of the acute infection is asymptomatic and undiagnosed and there is considerable uncertainty around the number of people in the UK who are injecting drugs.^[52-55] Added to this, it is also difficult to select a sentinel population of PWID for monitoring that is representative

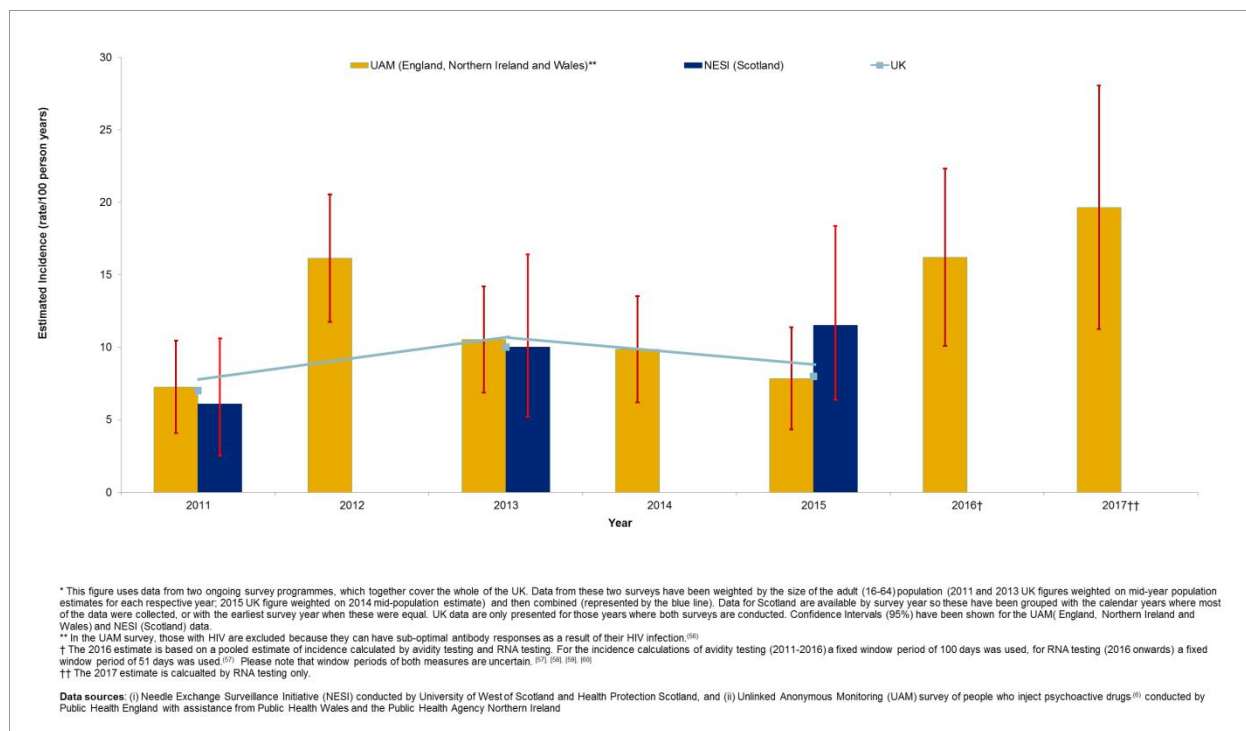
of PWID as a whole. As a result, a number of methods are used in the UK to generate information to provide insight into likely trends in incidence over time.^[29]

In England, Wales and Northern Ireland, recent transmission of HCV has been explored among the participants in the UAM Survey of PWID^[6] by looking for those who have recently developed antibodies to HCV. This has been undertaken in 2 ways. Prior to September 2016, antibody positive DBS were tested for avidity where DBS with overall weak avidity are likely to be from individuals who have recently been infected with the virus. From September 2016, instead of avidity all DBS have been tested for the presence of viral ribonucleic acid (RNA). Samples from recently-infected individuals will be positive for RNA but will not yet have developed antibodies against HCV. Avidity and RNA testing have been used to explore recent transmission among those survey participants who had injected during the preceding year.

In Scotland, recent transmission of HCV is also explored among participants in the NESI Survey of PWID^[7] by looking for those who test positive for HCV RNA, but are negative for HCV antibody. For those years where incidence estimates are available from both surveys, data are combined after weighting them by the sizes of the adult (16 to 64) populations for the countries they cover (blue line, Figure 8).

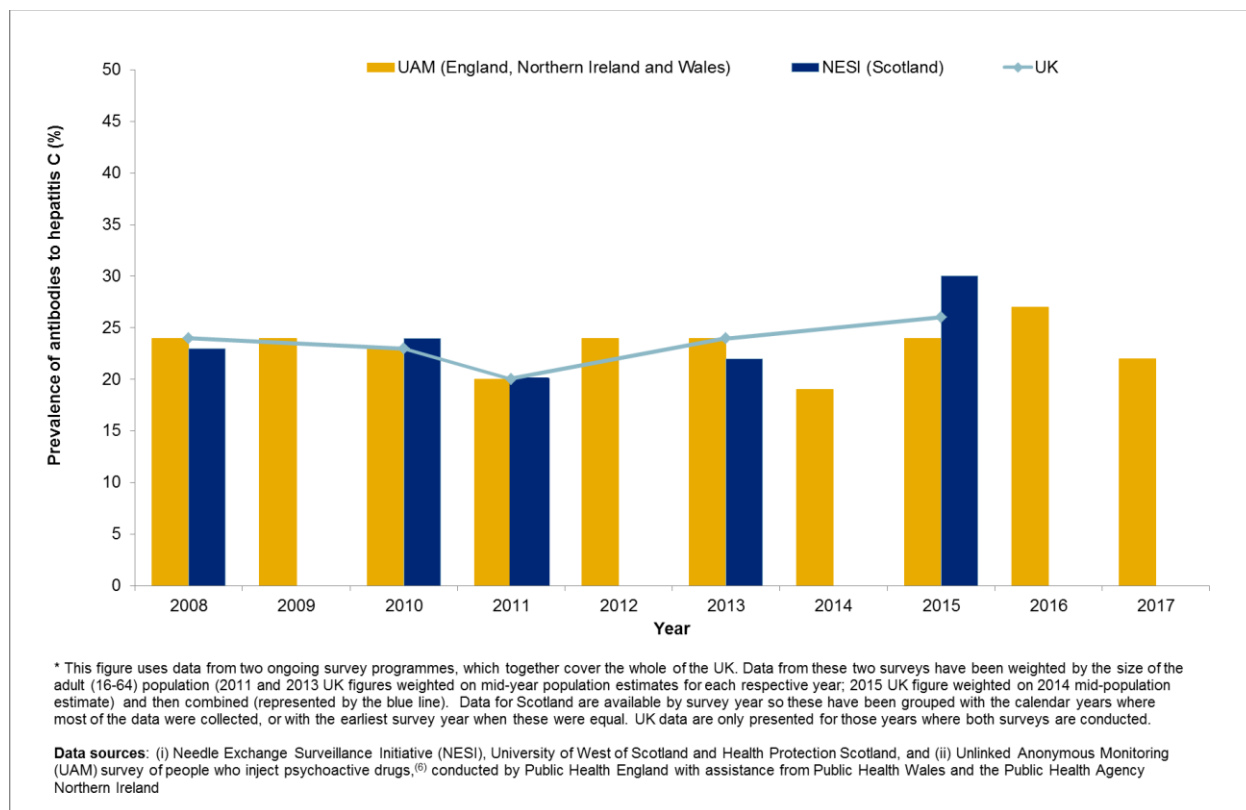
These data suggest that incidence of infection is higher in 2017 (19.6, 95% CI 11.2, 28.0) than in 2011 (7.3, 95% CI 4.1, 10.4) but has varied over the intervening years (Figure 8). However, it is possible that differences in the tests used have contributed to variation in estimated rates over time, although there is also substantial statistical uncertainty.

Figure 8. Estimated UK-wide incidence of HCV among PWID, 2011-2017*,**



Because most new infections are acquired via injecting drug use, the prevalence of infection among recent initiates to injecting drug use can be used as a proxy measure of incidence. When taken together, data from UK surveys of PWID in contact with services (UAM^[6] & NESI^[7]) suggest that incidence of infection has remained relatively stable over recent years, with levels of infection in 2017 (22%) being similar to those observed in 2008 (24%; Figure 9). However, these figures should be interpreted with caution as the proportion of survey participants who first injected in the last 3 years, has declined over time and so it is possible to observe a reduction in numbers despite a stable or increasing incidence rate.

Figure 9. Estimated UK-wide prevalence of antibodies to hepatitis C among people who began injecting drugs in the previous 3 years, 2008-2017.*



UK estimates of HCV incidence suggest that the call to reduce new cases of chronic HCV by 30% by 2020, and 80% by 2030^[1] (see Appendix 1), represent a significant challenge for UK HCV prevention and treatment services. If these goals are to be achieved, a radical change in the response to HCV among PWID is required.

Data sources

- Health Protection Scotland: www.hps.scot.nhs.uk/
- Hospital Episode Statistics, NHS Digital: www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=53
- Hospital Inpatient System, Northern Ireland: <https://www.health-ni.gov.uk/topics/dhssps-statistics-and-research/hospital-activity-statistics>
- MSD: www.msd-uk.com
- Needle Exchange Surveillance Initiative in Scotland (Health Protection Scotland, University of West of Scotland, Glasgow Caledonian University and West of Scotland Specialist Virology Centre): <http://www.hps.scot.nhs.uk/resourcedocument.aspx?id=5863>
- NHS National Services Scotland (Health Protection Scotland and Information Services Division): <https://nhsnss.org/>
- NHS England Specialised Commissioning: www.england.nhs.uk/commissioning/spec-services/
- Northern Ireland Hepatitis B and C Managed Clinical Network: <http://www.hepbandcni.net/>
- Northern Ireland Statistics and Research Agency: www.nisra.gov.uk
- Office for National Statistics mortality data: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths>
- Patient Episode Database for Wales, NHS Wales Informatics Service: <http://www.wales.nhs.uk/nwis/page/52490>
- Pharmex: <https://www.gov.uk/government/collections/commercial-medicines-unit-cmu>
- PHE Operational Delivery Network profile tool: <https://www.gov.uk/government/publications/hepatitis-c-commissioning-template-for-estimating-disease-prevalence>

- PHE Sentinel Surveillance of Hepatitis C Testing:
<https://www.gov.uk/government/publications/sentinel-surveillance-of-blood-borne-virus-testing-in-england-2015>
- Public Health Agency: www.publichealth.hscni.net
- Public Health Wales: www.publichealthwales.wales.nhs.uk/
- Roche: www.roche.co.uk/
- Unlinked Anonymous Monitoring survey of PWID in contact with specialist drug services. <https://www.gov.uk/government/statistics/people-who-inject-drugs-hiv-and-viral-hepatitis-monitoring>

Glossary of abbreviations

DAA	Direct acting antiviral
DBS	Dried blood spot
ESLD	End-stage liver disease
GHSS	Global Health Sector Strategy
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HES	Hospital Episode Statistics
HIS	Hospital Inpatient System
NSP	Needle and syringe programme
NESI	Needle Exchange Surveillance Initiative
NSGVH	National Strategic Group on Viral Hepatitis
NWIS	NHS Wales Informatics Service
ODN	Operational Delivery Network
ONS	Office for National Statistics
OST	Opioid substitution treatment
PEDW	Patient Episode Database in Wales
PHE	Public Health England
PWID	People who inject drugs
RNA	Ribonucleic acid
SVR	Sustained virological response
UAM	Unlinked Anonymous Monitoring Survey
WHO	World Health Organization

Appendices

Appendix 1.* WHO GHSS targets^[1] for viral hepatitis, relevant to HCV in the UK context, with 2020 targets updated to reflect the draft action plan for the health sector response to viral hepatitis in the WHO European Region.^[8]

TARGET AREA	2020 TARGETS ^[8]	2030 TARGETS ^[1]
Impact targets		
Incidence: New cases of chronic viral hepatitis C infection	30% reduction	80% reduction
Mortality: Viral hepatitis C deaths	10% reduction	65% reduction
Service coverage targets		
Blood safety:**Proportion of donations screened in a quality-assured manner	100%	100%
Safe injections:*** Percentage of injections administered with safety engineered devices in and out of health facilities	50%	90%
Harm reduction: A comprehensive package of harm reduction services to all PWID ^[61] including:	At least 200 sterile needles and syringes provided per person who injects drugs per year At least 40% of opioid dependent PWID receive OST 90% of PWID receiving targeted HCV information, education and communication	At least 300 sterile needles and syringes provided per person who injects drugs per year
Proportion of people with chronic HCV diagnosed and aware of their infection	50% [75% of estimated number of patients at late stage of viral hepatitis-related liver disease (cirrhosis or HCC) diagnosed]	90%
Treatment coverage of people diagnosed with chronic HCV who are eligible for treatment	75% (>90% cured) [90% of diagnosed patients with chronic HCV are linked to care and adequately monitored]	80%

* Abstracted from the WHO Global Health Sector Strategy for Viral Hepatitis^[1] and modified to reflect the draft action plan for the health sector response to viral hepatitis in the WHO European Region^[8]

** In England, 2020 and 2030 targets are already met.^[62]

***In England, 2020 and 2030 targets are already met in the health care setting as the UK follows the EU Directive for the prevention of sharps injuries in the health care setting,^[63] by using safety engineered devices.

Appendix 2. Preliminary UK indicators to monitor the impact of key interventions to tackle hepatitis C virus

Impact and Service Coverage Monitoring Areas • Preliminary UK Indicator	
Impact	<p>1. Reducing HCV-related morbidity and mortality</p> <ul style="list-style-type: none"> • Estimated incidence of HCV-related ESLD/HCC • Deaths from HCV-related ESLD/HCC
	<p>2. Reducing the number of new (incident) infections</p> <ul style="list-style-type: none"> • Estimated incidence of HCV among PWID • Estimated prevalence of anti-HCV among recent initiates to drug use
Service coverage	<p>1. Adequate harm reduction</p> <ul style="list-style-type: none"> • Estimated proportion of PWID reporting adequate needle/syringe provision
	<p>2. Increasing the proportion diagnosed</p> <ul style="list-style-type: none"> • Estimated proportion of PWID testing positive for anti-HCV, who are aware of their infection
	<p>3. Increasing numbers accessing treatment</p> <ul style="list-style-type: none"> • Estimated number initiating HCV treatment

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