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An evaluation of the 2007 Department of Health policy on hepatitis C virus clearance for healthcare workers performing exposure prone procedures

United Kingdom Advisory Panel for Healthcare Workers Infected with Bloodborne Viruses (UKAP)

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Health Protection Scotland

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Contents

Executive summary

In 2014, the Chief Medical Officers (CMOs) of the 4 countries in the United Kingdom (UK) raised concerns over the cohort of exposure prone procedure (EPP) performing health care workers (HCWs), who were employed before 2007 (preceding the Department of Health's 2007 guidance: 'Health clearance for tuberculosis, hepatitis B, hepatitis C (HCV) and HIV: New healthcare workers'), and who were not subject to additional bloodborne virus (BBV) clearance and may have stayed in the same EPP post with the same employer since this time. The United Kingdom Advisory Panel for Healthcare Workers Infected with Bloodborne Viruses (UKAP) was asked to investigate this issue and consider the HCV risk that this group of HCWs posed to their patients.

This report is prepared as a record of the supporting evidence for the recommendations of UKAP to the 4 UK CMOs, which were published as part of the 2019 UKAP health clearance guidance update. It presents findings of a risk assessment conducted in 2015 on the possible number of patient infections per year that would be expected to arise from this cohort of pre-2007 EPP performing HCWs, and the cost effectiveness of introducing a planned screening intervention. In summary:

In the UK, 24 of the 25 documented probable HCV transmissions from 13 HCWs have been associated with pre-2007 category 3[1] EPP performing HCWs specialising in obstetrics and gynaecology and other higher risk surgical specialities (that is, general, cardiothoracic and vascular surgery).

There was no evidence, at that point in time, that HCV infections attributed to HCW to patient transmission have occurred since 2007, though given the asymptomatic nature of infection and the long latency period we cannot rule out the possibility of an undetected transmission event(s) having occurred.

Since the introduction of the health clearance guidance, employment screening has diagnosed 38 HCWs living with HCV, of which 36 were first employed within the NHS before 2007. This indicates that many employers are going beyond policy and testing existing HCWs who undertake EPPs.

The number of undiagnosed HCWs performing EPPs who were employed pre-2007 is therefore considered likely to be low. Despite some evidence of HCV screening among pre-2007 employed HCWs, it remains unclear as to how many of this cohort remain untested

[1] Procedures where the fingertips are out of sight for a significant part of the procedure, or during certain critical stages, and in which there is a distinct risk of injury to the worker's gloved hands from sharp instruments and/or tissues. In such circumstances, it is possible that exposure of the patient's open tissues to the HCW's blood may go unnoticed or would not be noticed immediately.

(either through screening or due to voluntary presentation following exposure to the risk of HCV).

It is anticipated that any small risk from the pre-2007 cohort of HCWs living with HCV and undiagnosed will be reduced, as HCWs who started performing EPPs prior to 2007 leave the NHS, move jobs and are tested, or are diagnosed for medical reasons. There will, however, remain a small risk if occupational exposures continue to occur and/or those that occur are not reported and appropriately followed up to identify and manage any HCV seroconversions. The risk of a HCW being exposed occupationally is considered the same for those employed pre- and post-2007.

The risk of transmission modelled from UKAP data suggest an average risk of 0.1% per category 3 EPP performed by HCW living with HCV in the ‘higher risk’ specialities. This would result in 0.7 patient infections per year in total, equivalent to approximately a 1 in 580,000 chance of infection for individuals undergoing a category 3 EPP. The risk for individuals undergoing category 1 or 2 EPPs is likely to be negligible.

Assuming a background screening rate of HCWs of 25%, over a 10 year period, following a planned intervention (which achieves 80% screening), targeted at HCWs specialising in obstetrics and gynaecology and other higher risk surgical specialities (that is, general, cardiothoracic and vascular surgery), 5 chronic infections in patients will be prevented. With the quality-adjusted life year (QALY) loss for each patient living with HCV estimated at 1.7 QALYs, the intervention would result in a total QALY gain of 11.7 (including that gained by HCWs identified and treated) and a cost per QALY gain of £43,136 (£504,700/11.7). This figure for the screening intervention is above National Institure for Health and Care Excellence (NICE) thresholds for affordability, although there are significant uncertainties.

In conclusion, the risk of HCV transmission from HCWs specialising in ‘high risk’ surgical specialities to patients is minimal, and has almost certainly been in decline since the guidance on testing HCWs was introduced in 2007. Even though a proportion of these infections could be prevented by screening, a one-off screening intervention targeted at these HCWs was not deemed to be cost effective.

UKAP therefore recommends that the 2007 health clearance guidance should not be amended to include the pre-2007 cohort. Instead, UKAP recommends investing in educating HCWs on the significant positive impact of the new antiviral drugs for those individuals living with HCV and therefore benefits a HCW by knowing their status for both their health and their career prospects. New direct activing antiviral treatments are now available in the UK that will successfully clear HCV virus in the majority of patients (Kohli et al, 2014). These new NHS approved interferon-free regimens offer improved rates of virological cure, with few if any major side effects, and are administered orally for a few weeks. Thus, any negative impact of a positive diagnosis of HCV on the career of the HCW is much reduced. Also, given the likelihood of a gain in personal health after successful treatment, HCWs should be encouraged

to come forward for HCV testing if they have reason to believe that they may have been exposed (either through a specific occupational incident or outside their work environment), in line with the duty of care to patients, their professional responsibilities and legislative requirements.

1. Background

In 2013, a UKAP case which resulted in a major lookback revealed that a health car worker (HCW) in Obstetrics and Gynaecology had infected 4 patients with Hepatitis C (HCV) through exposure prone procedures (EPPs). Transmission was confirmed through phylogenetic analysis. At the point of the lookback exercise, the HCW had retired.

In 2014 the Chief Medical Officers (CMOs) of the 4 countries in the United Kingdom (UK) raised concerns over the cohort of EPP performing HCWs, who were employed before 2007 (preceding the Department of Health's 2007 guidance: 'Health clearance for tuberculosis, hepatitis B, hepatitis C and HIV: New healthcare workers'), and who were not subject to additional bloodborne virus (BBV) clearance and may have stayed in the same EPP post with the same employer since this time. The United Kingdom Advisory Panel for Healthcare Workers Infected with Bloodborne Viruses (UKAP) was asked to investigate this issue and consider the HCV risk that this group of HCWs posed to their patients.

This investigation was undertaken prior to the advent of World Health Organization, NHS and public health HCV elimination agendas. This investigation focused solely on managing the risk of transmission of HCV from HCWs to patients, not the contributions any such efforts would have to the wider goals of national and global hepatitis elimination. It presents the work that was undertaken to inform the updated guidance for health clearance of HCWs published in July 2019, which has since undergone minor updates in August 2020[2].

[2] Public Health England 'Integrated guidance on health clearance of healthcare workers and the management of healthcare workers living with bloodborne viruses (hepatitis B, hepatitis C and HIV)' August 2020 available at: https://www.gov.uk/government/publications/bbvs-in-healthcare-workers-health-clearance-and-management

2. Current guidance and legislation in the UK

In August 2002, Department of Health (DH) guidance recommended BBV testing for those HCWs who thought they may be at risk of BBV infections. Those HCWs found to be HCV RNA positive should cease EPP work. Resumption of EPPs was permitted provided the HCW responded effectively to treatment, defined as a negative RNA test 6 months after cessation of treatment, and further RNA negative test in a further test 6 months subsequent to the previous test[3] (Department of Health, 2002).

The 2002 guidance for managing HCWs living with HCV was also the first to recommend testing of HCWs who were about to start careers or training that would rely on the performance of EPPs. This principle of screening HCWs for BBVs was further developed and expanded to include HIV and HBV in the guidance on health clearance for HCWs new to the NHS published in 2007 (Department of Health, 2007). This guidance aimed to identify, and consequently restrict, all HCWs living with BBV new to the NHS from working in clinical areas where their infection may pose a risk to patients in their care, that is, the performance of EPPs, and working in renal dialysis units. The guidance did not apply to HCWs already employed in the NHS, with the exception of those moving to a post requiring the performance of EPPs for the first time in their career. Further, all HCWs are under an ongoing obligation to seek professional advice about the need to be tested if they have been exposed to a serious communicable disease (General Medical Council, 2013). Only if an HCW is determined to be HCV RNA positive after an exposure will they be restricted from performing EPPs to prevent HCW to patient transmission. No practice restrictions are recommended between the time of the potential exposure and the determination of the HCW's HCV status, which now is within 4 to 6 weeks post exposure.

2.1 Implementation of health clearance guidance

Anecdotal information suggests that variation in the interpretation of the health clearance guidance has given rise to inconsistencies between NHS employers across the UK in relation to which 'new' HCWs require additional clearance before appointment. A survey of UK Occupational Health (OH) services (recruited primarily through NHS Health at Work), undertaken by UKAP in 2014 suggested that many NHS employers go beyond the 2007 guidance recommending additional health clearance for new HCWs, and undertake BBV testing of existing EPP performing HCWs. It was not, however, clear how representative the 71 respondents were of all OH services, as at the time of the survey, the official number of OH

[3] The 2020 update to the integrated guidance on health clearance of HCWs and the management of HCVs living with bloodborne viruses (hepatitis B, hepatitis C and HIV) made a slight change for those HCWs who had returned to performing EPPs following successful treatment. The final check that they remain RNA negative following resumption of EPPs, has now been reduced from 6 months to 3 months.

services in the UK was unknown[4]. A summary of the main findings of the survey are provided in below.

From the OH Services responding to the survey, it was concluded that:

- most OH services correctly adhere to the recommendations of the Health Clearance Guidelines and provide standard or additional BBV clearance for non-EPP and EPP HCWs employed after 2007
- 49 respondents reported that they go beyond policy recommendations and test all new HCWs for HCV regardless of whether they are employed before or after 2007
- 13 respondents reported that most or all of their existing EPP HCWs have been tested to assess their fitness to perform EPP
- most OH services identified the exclusion of the pre-2007 cohort of EPP workers from additional clearance as a risk gap and would like to see periodic testing implemented

[4] In 2012, 'there were 436 trusts in England and 172 OH service providers. Trusts either have an in-house OH service or contract their service from another provider (or, for a small number, more than one provider, usually a different (local) NHS Trust). Some OH providers serve multiple NHS trust' (Dr Sian Williams, Health and Work Department, personal communication). NHS Scotland has 18 OH providers, one for each local NHS Board (n=14) and Special Board (n=4).

3. Published cases of HCW to patient transmission of HCV

Between 1991 and the UKAP investigation in 2015, there were more than 200 cases of HCW to patient transmission of HCV reported in scientific publications (Pozzetto et al, 2014). Excluding those associated with the diversion of opioids by HCWs addicted to morphine (which have resulted in the transmission of HCV to large numbers of patients) (Bosch, 1998; Ross et al, 2000; Cody et al, 2002; Schaefer et al, 2014; Warner et al, 2015), transmissions have been associated most with cardiothoracic, general, gynaecological, and orthopaedic surgical procedures (Duckworth et al, 1999; Esteban et al, 1996; Ross et al, 2002a; Ross et al, 2002b), disciplines generally regarded as ‘high risk’ areas for transmission from HCWs living with BBVs. A small number of documented cases have also been reported associated with non-EPPs (Mawdsley, et al 2005; Muir et al, 2014).

4. Review of UKAP referrals between 2002 and 2015

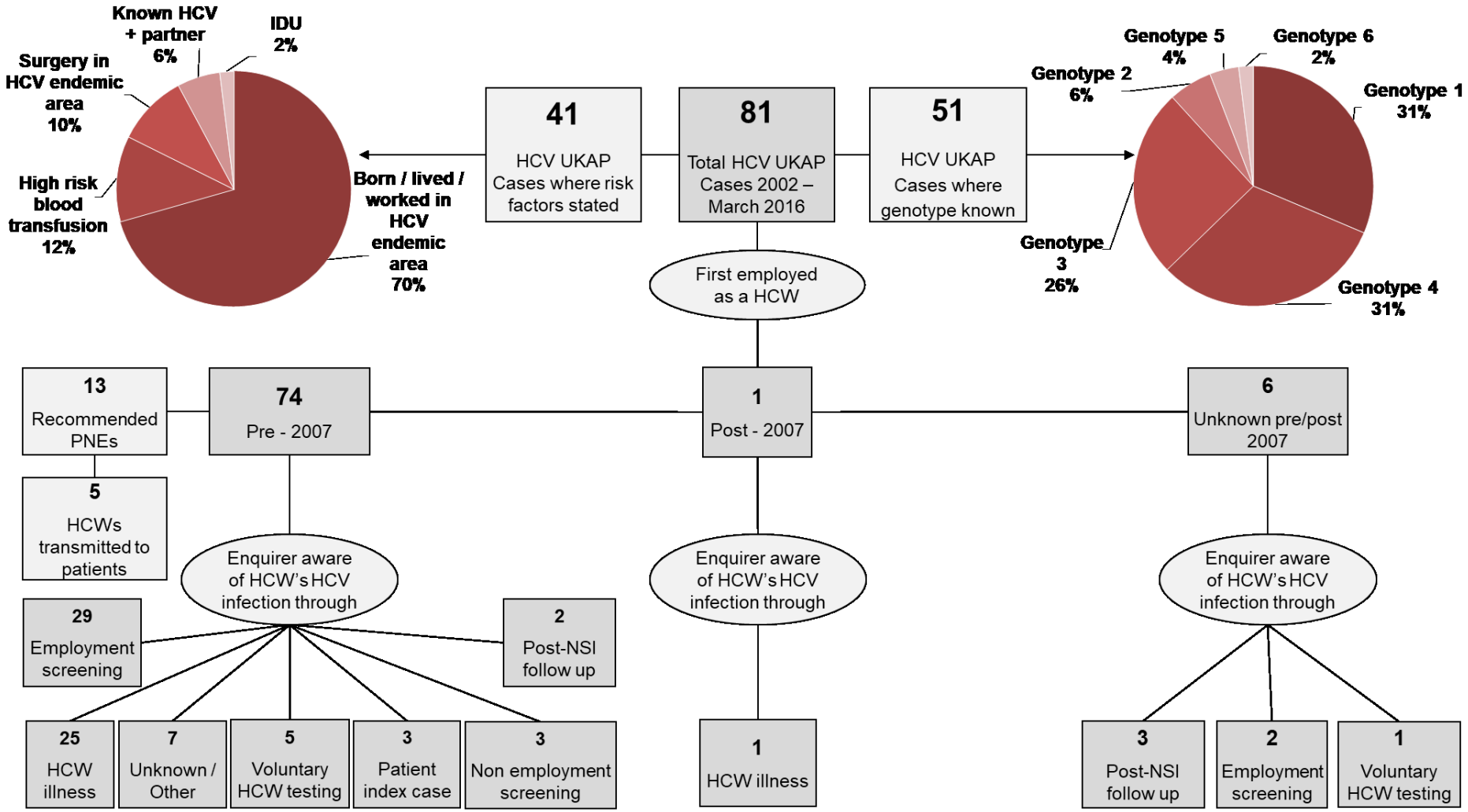
A review of UKAP data on HCWs living with HCV reported to UKAP between 2002 and 2015 found 81 incidents involving this cohort (Figure 1). The majority of these cases (n=74, 91%) were employed in the NHS before 2007. Thirty-nine per cent (n=29) of this pre-2007 cohort were diagnosed through employment screening and 34% (n=25) through HCW illness. The remainder were identified through pathways unrelated to their employment, for example partner notification.

Of the 81 HCWs living with HCV referred, 5[5] HCWs transmitted HCV infection to a patient(s); all were employed, and performing EPPs before 2007. Three were diagnosed following the identification of a positive patient who had undergone a procedure performed by the HCW. One HCW was diagnosed as a consequence of their illness and was later shown to have probably transmitted infection and another HCW was diagnosed on pre-employment screening for a new post.

Of those HCWs who are not known to have transmitted infection to a patient (n=76), information on employment history was available for 69 (92%); 68 were employed pre-2007, and of these, 29 were diagnosed through employment screening and 25 as a consequence of illness. Only 1 HCW with a pre-existing infection, diagnosed as a consequence of their infection, was identified post 2007.

[5] The results of the patient notification exercises associated with 4 of the 5 HCWs are included in the further analysis. The PNE associated with the remaining HCW was not included as was ongoing at the point of analysis.

Figure 1. HCWs living with HCV reported to UKAP, 2002 to 2015



5. Healthcare worker-to-patient transmission of HCV: result from retrospective investigations carried out in the UK between 1995 and 2013

5.1 Number of patient notification exercises undertaken

The policy on the management of patients of HCWs living with BBVs has evolved over time, guided by emerging evidence on the risk of HCWs transmitting BBVs to their patients. UKAP does not routinely recommend a PNE when transmission of HCV from a HCW living with HCV to patient (termed ‘index case’) has not been detected. Between 1995 and 2013, there were a total of 17 patient notification exercises (PNE) in the UK involving HCWs living with HCV, 12 of which followed detection of an index case(s). Results of the PNEs are available for all except one, and are summarised in Table 1.

Table 1. Summary of hepatitis C patient notification exercises: UK, 1995 to 2013

Year	Genotype	Occupation	Exposed	Tested	Index case(s)	Probable cases[1]	Possible cases[2]
1995	4a	Cardiovascular junior surgeon	295	270	1	0	0
1999	4	Gynaecologist	4,500	3,628	1	6	7
2000	2b	General surgeon	723	627	1	1	0
2000	1b	General Surgeon	1,670	1,151	2	2	3
2001	4	Obstetrician	211	198	1	0	0
2002	4a	Obstetrics & Gynaecology	2013	1315	1	1	7
2003	3b	Orthopaedic surgeon	650	373	0	0	1
2003	4	Transplant surgeon	15	7	0	0	0
2003	3b	Obstetrics & Gynaecology	357	276	0	0	1
2003	4	Obstetrics & Gynaecology	781	622	0	0	0
2003	1a	Trainee surgeon	9	5	0	0	0
2004	4a	Obstetrics & Gynaecology	2,186	1377	1	2	5
2005	3a	Dentist[3]	6,139	2,665	0	0	11
2008	1b	Dentist[3]	12,500	No PNE results available			
2008	3a	Acupuncturist[3]	5	5	0	0	0
2011	1b	Midwife[3]	72	36	1	0	0
2013	4	Obstetrics & Gynaecology	4,737	3,485	3	1	2
Total patients			36,863	16,040	12	13	37
Category 3 EPP patients only			18,147	13,334	11	13	37

[1] These were patients found to be HCV-positive and who on genotype determination and phylogenetic analysis were found to be carrying a virus indistinguishable from that of the HCW.
[2] These were patients found to be HCV antibody-positive but HCV RNA negative precluding the determination of the genotype and phylogenetic analysis.
[3] HCWs did not perform Category 3 EPPs.

5.2 Results by speciality

Fifteen PNEs involved HCWs who perform EPPs as part of their clinical duties. Of which, 5 worked in obstetrics and gynaecology (33%, 5/15), with a further 4 (27%) in general surgery or cardiothoracic surgery, 2 (13%) in dentistry, and 1 in each of orthopaedic surgery and transplant surgery (13%, 2/15). The remaining 2 PNEs were associated with a HCW who did not perform EPPs (Acupuncturist) and another who performed a mixture of EPPs and non-EPPs (Midwife).

All but one HCW to patient HCV transmission was associated with category 3[6] EPP performed by HCWs specialising in either obstetrics and gynaecology, general surgery, cardiothoracic surgery or vascular surgery (hereafter 'the higher risk specialities')

5.3 Estimates of transmission rates

As all but one HCW to patient HCV transmission was associated with category 3 EPP, the following analysis estimate risk associated with category 3 EPPs only.

5.3.1 Estimates of transmission rates from UK PNEs

In total, 18,147 patients were identified as being at risk following a category 3 EPP performed by an HCW living with HCV (n=13). Of these, 13,334 (73%) patients were tested. In addition to the eleven index cases, a further 13 patients were HCV RNA positive and were found to be carrying a virus indistinguishable from that of the HCW. A further 37 possible cases were identified however, there was no circulating virus for genotyping and phylogenetic analysis. These cases may be incidental cases who have spontaneously cleared the virus, remaining HCV Ab positive. Likewise, some of these cases may be actually true HCW to patients transmissions who cleared infection. If we assume that 15% spontaneously clear infection, there might have been 28 transmissions in total following a category 3 EPP performed by a HCW living with HCV.

Using the information derived from the PNEs, the rate of transmission associated with category 3 EPPs resulting in chronic infection, was the proportion of those found to be HCV RNA positive from the tested at risk population (that is, the index and probable cases) expressed as a percentage.

$$\text{HCV transmission rate (\%)} = \frac{\text{Number of HCW related HCV RNA positive cases found}}{\text{Number of category 3 EPP patients tested}}$$

[6] Procedures where the fingertips are out of sight for a significant part of the procedure, or during certain critical stages, and in which there is a distinct risk of injury to the worker's gloved hands from sharp instruments and/or tissues. In such circumstances, it is possible that exposure of the patient's open tissues to the HCW's blood may go unnoticed or would not be noticed immediately.

This gives a rate of transmission resulting in chronic infections in tested patients of 0.18% (CI 0.12 to 0.27%, random effects estimate). If we adjust for those cases of HCW to patient transmissions who cleared infection, the rate of transmission in tested patients would be slightly higher (0.21%, CI 0.14 to 0.32%, random effects estimate).

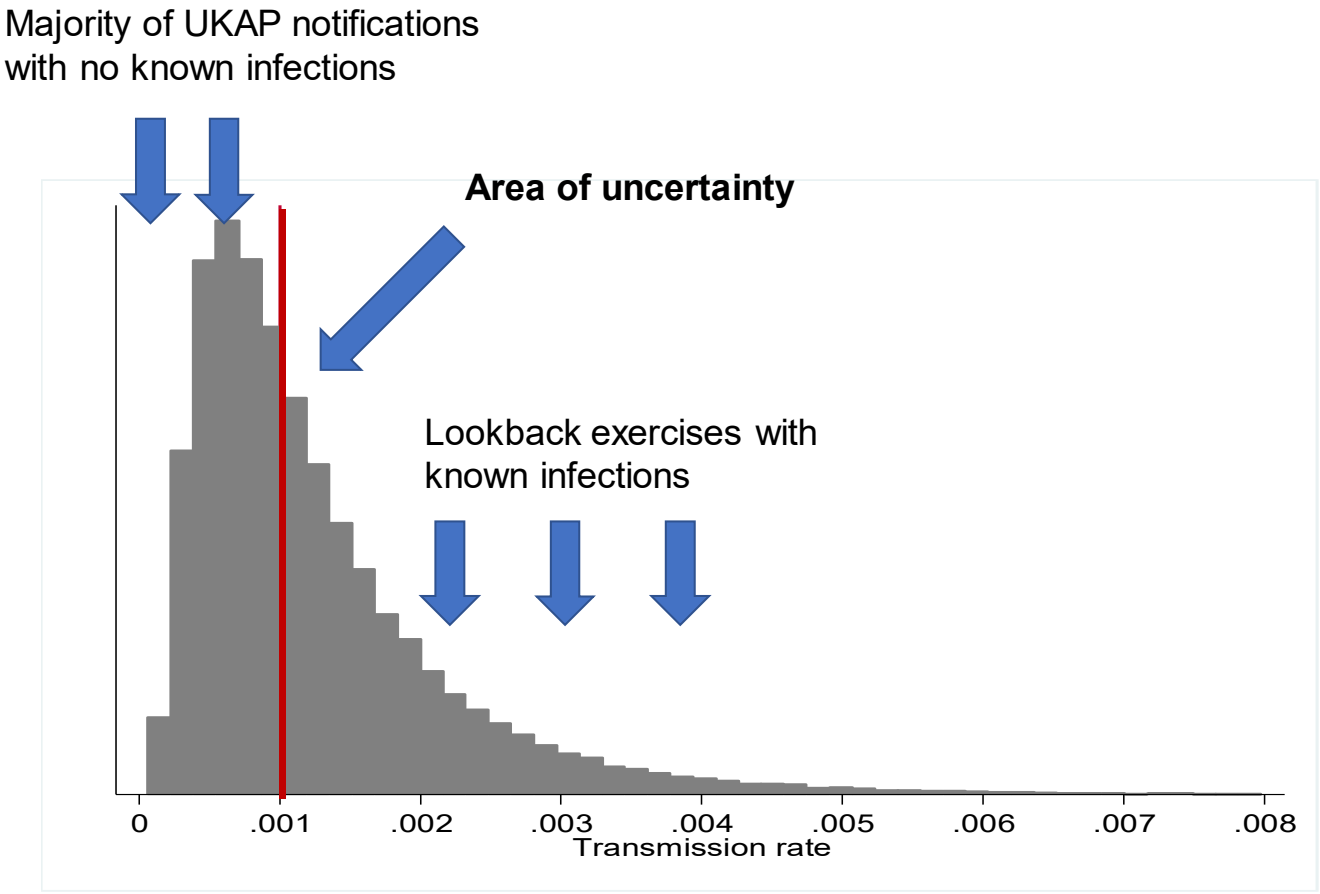
5.3.2 Estimates of transmission rates from a modelling exercise

In 8 incidents, the HCW was known to have transmitted infection to at least one patient prior to the notification exercise; a further 13 probable transmissions were ascertained through notifying and testing in the notification exercises. Those undertaken following the identification of a HCW living with HCV, without evidence of transmission to a patient having already occurred (that is, no index case identified), did not trace any cases. This leads to the notion of heterogeneity in risk of transmission: some 'higher risk' HCW appear to pose a greater risk to patients, with a number of transmission events, while the majority of 'lower risk' HCW have no known transmissions (henceforth zero case HCWs). As the PNEs in general are only conducted where transmission of HCV from HCW to patient has occurred, transmission rates using these data alone are biased upwards, as they are conditional on at least one transmission occurring.

The transmission risk from HCWs living with HCV can be estimated by combining data on the PNEs with known index case(s) and UKAP data for HCWs found to have been infected and who performed category 3 EPPs, but determined to have been at no (or very low) risk for patients; these cases therefore provide the 'missing zeros'. As noted above, there is marked variation in the rate of transmissions, with the majority of HCWs living with HCV having no known transmissions, but several cases occurring in some PNEs. The model therefore aims to estimate the extent of heterogeneity in transmission risk. Furthermore, all but one HCW to patient transmissions to date were associated with category 3 procedures performed by HCWs specialising in the higher risk specialities. The transmission risk model therefore estimates risk associated with category 3 EPPs in these specialities. The methodology and assumptions of the model can be found in Appendix 1.

The transmission risk model predicts an average transmission risk of 0.10% per category 3 EPP performed (95% Credible Interval, CrI 0.01% to 0.32%) in the high risk specialities. This means approximately 1 infection per 1000 category 3 EPPs. The confidence interval, however, is extremely wide, given the flexibility of the random effects model. The estimated standard deviation for the log rate of transmissions was 0.74, confirming there is marked heterogeneity in the rate of transmissions for individual HCWs (Figure 2). To quantify this, if the 'riskiness' of HCWs is divided into percentiles, the 75th percentile (higher than average risk) of HCWs living with HCV has nearly 3 times the risk of transmitting to a patient compared to the 25th percentile (lower than average risk). This explains the phenomenon that, if an index case is not found, subsequent cases are unlikely; these HCW are part of the lower-risk end of the scale, whereas lookback exercises with several cases (index and probable) are towards the higher end of the risk distribution.

Figure 2. Heterogeneity in risk of transmission from HCWs living with HCV in high risk specialities



6. Prevalence of HCV in health care workers

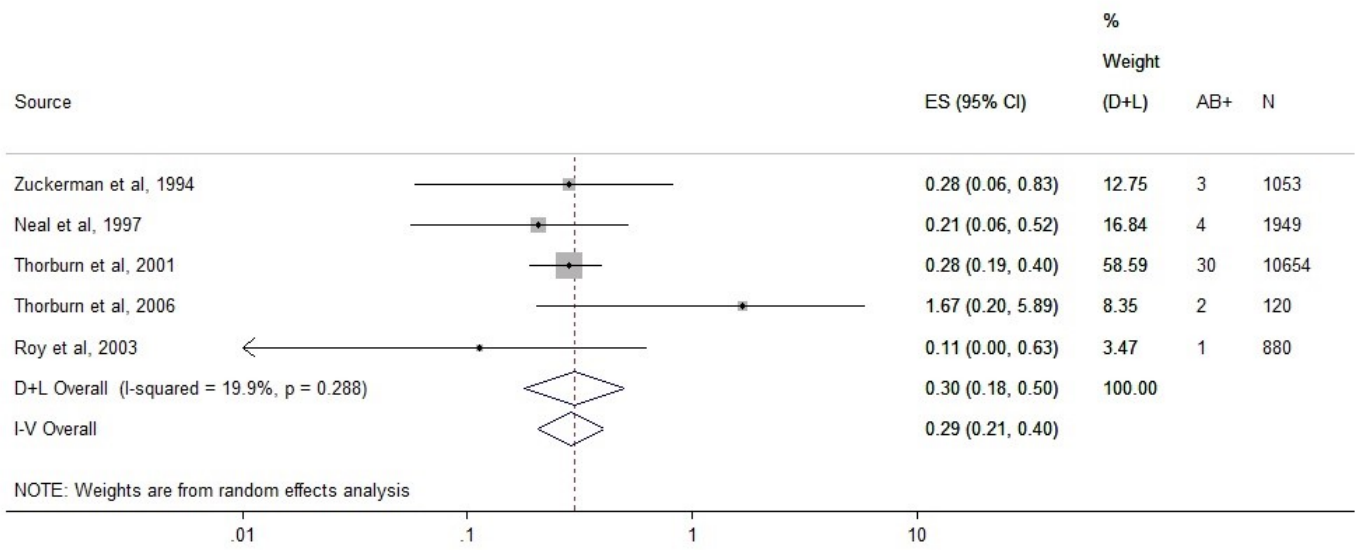
It is neither known how many HCWs generally in the UK, nor those conducting EPPs in the high risk specialities specifically, are living with HCV. Relatively few studies on the prevalence of HCV in healthcare workers (HCWs) in the UK have been conducted (Table 2). Estimates from these studies can be summarised via a random effects meta-analysis (see Figure 3), giving a pooled antibody (Ab+ve) prevalence of 0.30% (95% CI 0.21% to 0.50%).

Table 2. Summary of published HCV seroprevalence studies undertaken in the UK

Source	Description	Number tested	Ab Positive (n)	Ab Prevalence (%)	Chronic Infection[1] (%)
Zuckerman et al 1994	Anonymised stored blood samples from HCWs immunised against HBV since 1991	1,053	3	0.28	0.22
Neal et al, 1997	Nottingham, among hospital staff with blood samples taken for measuring anti-HBs levels from January 1994 to October 1995, HCV positive in both ELISAs	1,949	4	0.21	0.16
Thorburn et al, 2001	HCWs in Glasgow presenting for HBV immunisation between October 1994 and October 1997	10,654	30	0.28	0.21
Thorburn et al, 2006	Liver transplant surgeons attending the 9th Congress of the International Liver Transplantation Society	120[2]	2	1.7	0.8
Roy et al, 2003	Primary care dental workers in the West of Scotland	880	1	0.11	0.08

[1] % chronic infection based on 76%, except Thorburn et al, 2006 which gave exact prevalence
[2] denominator not given, estimated from rounded %.

Figure 3. Random effects meta-analysis



Estimates of HCV infection among HCWs may, however, be obtained from other sources. For instance, the overall prevalence of chronic infection in England in 2005 was estimated to be 150,000 (113,000 to 226,000) in the population of 30.3 million 15 to 59 year olds, giving a prevalence of 0.49% (95% CrI 0.37% to 0.75%). This estimate, however, included a large proportion of current or former people who inject drugs who are less likely to appear in the HCW workforce. An estimate of the prevalence in the 'never injecting population' gave a chronic prevalence of 0.064%. The prevalence of HCV infection among HCWs is, however, likely higher than that in the general population. A systematic review and meta-analysis of studies undertaken at the time of this UKAP investigation estimated the prevalence of HCV infection among HCWs compared to the general population, and reported a significantly increased odds ratio (OR) for HCV infection in HCWs, with an overall odds ratio vs controls of 2.7 for HCWs in high-risk settings vs. the general population in low prevalence countries. (Westermann et al 2015). Multiplying the estimate of chronic HCV prevalence in never-injectors by the odds ratio of 2.7 for HCWs in high risk gave an estimate of 0.17%.

This estimate is highly uncertain however, as prevalence varies substantially by ethnicity and the ethnic breakdown of the HCW population may be markedly different to that of the general population. Further, factors such as education and financial income are likely to be important factors that differ in consultant level HCWs.

In the absence of evidence of the prevalence of chronic HCV infection among HCWs currently performing EPPs, we use the pooled estimate of HCV seroprevalence in HCWs (Figure 3) as the baseline for this analysis, which after adjusting by 76% chronicity among those seropositive gives 0.23% (95% CI 0.14% to 0.38%). This is around 3.6 times higher than the estimate of chronic infection in the never injected population, but is broadly in line with estimates in the systematic review by Westerman, given the uncertainties surrounding the proportion of people who inject drugs in the different populations.

It should, however, be noted, that this estimate is based on data from studies undertaken between 1994 and 2006, and it is likely that HCV screening introduced in 2007, the introduction of personal protective equipment and safer sharps, and the greater availability of DAA treatment, will have resulted in an overall reduction in the prevalence of HCV infection amongst HCWs currently performing EPPs. We therefore explore the impact of using the lower prevalence estimate of 0.17% chronic prevalence, and other values within a plausible range.

7. Number of HCV transmissions to patients from a category 3 EPP performing HCW living with HCV

In general, 3 conditions are necessary for HCWs to pose a risk for HCV transmission to patients:

- the HCW must have the virus circulating in their bloodstream
- the HCW must be injured or have a condition that provides some other source of direct exposure to infected blood or body fluids
- the injury mechanism or condition must present an opportunity for the HCW's blood or body fluids to come into direct contact with the patient's mucous membranes, wound or traumatized tissue (recontact)

The risk of transmission in the presence of these conditions is, however, influenced by a number of factors including viral load and the nature of the exposure.

7.1 Number of NHS staff potentially engaged in EPPs

As of September 2015, approximately 1,353,649 people were working for the NHS in the UK. The vast majority of HCWs pose no risk to patients because they do not perform procedures in which they risk sustaining penetrating injuries, or where their injury would occur unnoticed. Indeed, and as noted before, all but 1 HCW to patient transmissions in the UK to date were associated with category 3 EPPs performed by HCWs specialising in either Obstetrics and Gynaecology, General Surgery, Cardiothoracic surgery or Vascular Surgery. The number of HCWs operating in these 'higher risk' specialities in 2015 is given in Table 3. Numbers are based on full time equivalents (FTE) and indicate a total of 16,755 medical staff of Consultant, associate specialist, speciality doctor, staff grade, or registrar level were potentially engaged in EPPs.

Given that surgeons on speciality training schemes from 2007 onwards will have been screened by the current health clearance policy before commencing employment, they are likely to pose little risk to patients (depending on how likely they are to become infected post screening). The risk of transmission, therefore, is likely greatest from consultant grade surgeons, from which the majority of, and all recent, transmissions have arisen.

Table 3. Regional number of health care workers (HCWs) breakdown* by 'higher risk' speciality and grade

Region	Total NHS Staff[1]	Total Obstetrics, Gynaecology and Surgery[1,2]	Total Obstetrics, Gynaecology and Surgery- Consultant Grades only[1,3]
England as of Oct 2015	1,089,370	13,621	4,891
Scotland as at Sept. 2015	137,728	1,591	554
Wales, data for 2014	72,464	811	283
N.Ireland, as of Mar. 2015	54,087	732	333
Total	1,353,649[4]	16,755	6,061

[1] Based on full time equivalents (FTE) and whole time equivalents (WTE)
[2] includes general surgery, cardiothoracic surgery and vascular surgery
[3] includes Associate Specialist and Staff Grade. *breakdown of surgical specialities not the same for all countries.
[4] Overall number of HCWs relate to NHS staff in England, Scotland, Northern Ireland and Wales as presented by the Monthly NHS HCHS Workforce statistics in England from the NHS Information Centre for Health and Social Care, the quarterly information on staff employed in NHS Scotland from Public Health and Intelligence, National Services Scotland, the March 2015, information on directly employed health & social care (HSC) staff from Northern Ireland's Department of Health, Social Services and Public Safety (2014), and total employed NHS staff numbers from Stats Wales (General Medical and Dental Practitioners are excluded as they are independent NHS contractors).

7.2 Estimates of the number of infections from consultant grade surgeons

The expected number of patients living with HCV per year can be calculated by multiplying the number of HCWs performing 'high risk' surgery (S), the average number of category 3 EPPs performed per year by this group (n), 1 minus the screening rate to give the unscreened proportion (1-α), the baseline prevalence in this group (π0), and the rate of infections occurring from a HCW living with HCV and performing EPP (λ) using the following formula:

$$\text{Annual number of infections} = S\ n\ (1-\alpha)\ \pi 0\ \lambda$$

Where:

- S = 6,061, the number of consultant grade HCWs in the 'high risk' specialities (defined above)
- n= 70, the average number of category 3 EPPs carried out per year by an average surgeon[7]
- α = 0%, assuming the worst-case scenario in which no HCW at consultant grade
- have been screened and all HCW living with HCV pose a risk to patients
- π0 = 0.23%, the baseline prevalence of HCV infection in this grou
- λ = 0.1%, the transmission rate of infections occurring from an HCW living with HCV performing category 3 EPPs

[7] Based on the opinion of the expert members of UKAP members, it was assumed around 70 category 3 EPPs are conducted per year by an average surgeon.

Table 4. Expected number of category 3 exposure prone procedures (EPPs) per year by Consultant grade Health care workers (HCWs) in 'high risk' speciality and resulting infections

	England	Scotland	Ireland	Wales	Total
Total Consultant grade HCWs	4,891	554	333	283	6,061
Total category 3 EPPs performed per year[1]	342,370	38,780	23,310	19,810	424,270
Performed by HCW living with HCV (0.23%)[2]	787	89	54	46	976
Resulting in transmission (0.1%)	0.8	0.09	0.05	0.05	1.0

[1] assumes an average surgeon performs 70 category 3 EPPs per year
[2] assuming the worst-case scenario in which no HCW at consultant grade have been screened and all HCW living with HCV pose a risk to patients.

8. Data and modelling limitations

The following limitations should, however, be borne in mind when interpreting the risk of transmission generated from the UK data.

The date of acquisition of HCV by HCWs reported to UKAP was unknown. In the absence of this information, PNEs may extend over the entire career of the HCW, and many of the patients tested may have been treated by a HCW who had not yet acquired their HCV infection; this would underestimate the risk of transmission.

Many patients potentially exposed to HCV were not tested, either because they were not contactable or because the patients declined testing. We have assumed these patients to be no different from those patients who did take up the test offer. This could overestimate the risk of transmission. In reality, our understanding of the risk of transmission is not yet fully understood and likely influenced by type and duration of procedure as well as technique within the procedure, experience of the surgeon, viral load of the surgeon, and possibly fatigue. This information was generally not available for those people tested in the PNEs.

The modelling of transmission rates makes a number of assumptions that cannot be tested. These include that:

- the number of cases identified through PNEs is broadly the same as the number of index cases
- variability in HCW risk of transmission has a normal distribution in log rates (opposed to other shapes or a dichotomous low/high risk pattern)
- conditional on the assumed variability in risk, the HCWs living with HCV notified to UKAP without evidence of transmission to a patient having already occurred are comparable to the HCWs who were known to have transmitted infection and for which PNEs were undertaken

Prevalence of HCV in consultant-grade HCWs in the high risk specialities who perform category 3 EPPs is unknown, with sparse data from more general surveys that do specifically examine this risk group.

9. Cost effectiveness of screening

The cost-effectiveness of screening the pre-2007 cohort of consultant grade HCWs specialising in high risk specialities was also assessed, given the modelling assumptions and estimates above. The calculation rests on the expected number of patients living with HCV identified with and without screening and the resulting total quality-adjusted life year (QALY) loss incurred by patients living with HCVs. Patients living with HCV also incur monetary costs for HCV treatments if diagnosed, or if reaching severe liver disease (due to late diagnosis or treatment failure), incur costs for healthcare and ultimately may require liver transplantation. The details of the analysis can be found in Appendix 2. Briefly, the following assumptions or estimates from the literature were used[8]:

Fifty per cent of patients undergoing surgery are aged 50 to 80, with the peak in 66 to 70 year olds, and the remainder evenly distributed across ages. (see appendix 1)

Clinical diagnosis is unlikely at mild stage disease (12% probability within 5 years), slightly more likely at moderate stage (22% probability within 5 years) but more likely once cirrhosis develops (92% probability within 5 years).

Upon diagnosis, treatment begins immediately and has an 80 to 95% success rate, depending on disease stage. Drug costs for the course of treatment are commercially sensitive and were previously estimated to be £20,000 for mild and moderate stage, and £40,000 for end stage liver disease (ESLD) or hepatocellular carcinoma (HCC). For the analysis, this was reduced to £10,000 for all stages, on the basis of anticipated treatment costs, in light of NHS England procurement activities. Costs and QALYs for health states are based on those outlined in Shepherd et al (Shepherd et al, 2007).

Age-specific disease progression rates are based on estimates of population-level disease progression from a back-calculation model, which combines information on progression rates from the literature with HES data on ESLD/HCC and HCV prevalence estimates (Harris et al, 2014).

Background voluntary HCV testing is assumed to reduce HCW prevalence by 25% from the baseline estimate of 0.23% chronic infection to 0.17%; a ‘planned’ screening intervention is assumed to reduce this by 80%, to 0.046% and therefore the resultant risk to patients over a period of 10 years, the time frame considered for the duration of the effectiveness of the intervention.

[8] The analysis presented in this report, and the assumptions underpinning the analysis were based on information available to the UKAP working group at the point of the analysis, taking in to account what was known at the time on anticipated future changes in HCV treatment.

The model uses a lifetime horizon for patient costs and QALYs, without discounting, as in the case of immediate interventions that prevent the long-term harms of HCV infection, discounting will generally increase the cost per QALY gained. Thus the cost per QALY presented (without discounting) is a minimum.

The cost of screening is assumed to be £150 per HCW, and includes costs associated with:

- identifying HCWs who should be screened and specifically those who have not been screened voluntarily since the introduction of the additional health clearance requirements in 2007
- inviting those to be tested to an OH appointment
- the testing process itself (including laboratory costs)
- updating HR files with the clearance status of all those tested

With the assumed background screening, there will be approximately 8 transmissions over a 10 year period. Introducing the 'planned' screening intervention will result in prevention of approximately 6 transmissions over the same period. The screening intervention would cost £500,000, minus £29,700 incurred in healthcare costs for 5 prevented infections in patients, plus £34,300 additional costs of treating healthcare workers for HCV infection, resulting in a net cost of £504,700. The QALY loss for each patient living with HCV was estimated at 1.7 QALYs, with a total QALY gain of 11.7 for the intervention and a cost per QALY gain of £43,300 (£504,700/11.7 – note that all figures have some rounding). This figure is outside National Institure for Health and Care Excellence (NICE) thresholds for affordability (£20,000 to £30,000).

There is significant uncertainty in many parameters, which was assessed via sensitivity analysis. The most important drivers were prevalence of HCV in the HCW population and transmission rate, which have a direct impact on the expected number of infections prevented and therefore the preventative impact of screening. Costs of screening are important; if the cost of screening were halved (£75) then screening could be within cost effective thresholds (cost per QALY £21,800). If prevalence or transmission rates are lower than that modelled here, costs per QALY increase far beyond NICE thresholds. Costs of treatment are commercially sensitive, and NHS England procurement efforts has led to significant drops in cost to below £10,000 per patient, however this saving would still not reduce the cost per QALY to below NICE thresholds. If 95% sustained viral response (SVR) rates are achieved for all stages of disease, this again would have minimal impact to the cost per QALY. If prevalence among HCWs or transmission rates are at the upper 95% uncertainty bounds, a screening intervention could be within costs-effectiveness levels. The resulting risk to patients would, however, need to be 50% higher for the cost per QALY to be less than £30,000 and on the basis of the information derived from PNEs undertaken to date, this scenario would be unlikely.

10. Conclusions on the risk of transmission

In summary in the UK, 24 of the 25 documented probable HCV transmissions from 13 HCWs have been associated with pre-2007 category 3 EPP performing HCWs specialising in obstetrics and gynaecology and other higher risk surgical specialities (that is, general, cardiothoracic and vascular surgery).

There is no evidence, at this point in time, that HCV infections attributed to HCW-patient transmission have occurred since 2007, though given the asymptomatic nature of infection and the long latency period we cannot rule out the possibility of an undetected transmission event(s) having occurred.

Since the introduction of the health clearance guidance, employment screening has diagnosed 38 HCWs, of which 36 were first employed within the NHS before 2007. This indicates that many employers are going beyond policy and testing existing HCWs who undertake EPPs.

The number of undiagnosed HCWs living with HCV and performing EPPs who were employed pre-2007 is considered likely to be low. Despite some evidence of HCV screening among pre-2007 employed HCWs, it remains unclear as to how many of this cohort remain untested (either through screening or due to voluntary presentation following exposure to the risk of HCV).

It is anticipated that any small risk from the pre-2007 cohort of HCWs living with HCV and undiagnosed HCWs will be reduced, as HCWs who started performing EPPs prior to 2007 leave the NHS, move jobs and are tested, or are diagnosed for medical reasons. There will, however, remain a small risk if occupational exposures continue to occur and/or those that occur are not reported and appropriately followed-up to identify and manage any HCV seroconversions. The risk of a HCW being exposed occupationally is the same for those employed pre- and post-2007.

The risk of transmission modelled from UKAP data suggest an average risk of 0.1% per category 3 EPP performed by a HCW living with HCV in the ‘high risk’ specialities. This would result in 1.0 patient infection per year in total, assuming the worst case scenario in which no HCW at consultant grade is screened and all HCWs living with HCV pose a risk to patients.

The risk of hepatitis C transmission to a patient from a category 3 EPPs performed by HCWs living with HCV is minimal, and likely to be negligible for category 1 and 2 EPPs. This risk has likely been in decline since the guidance on testing HCWs was introduced in 2007. A proportion of these transmissions could be prevented by screening, but this does not meet NICE cost effectiveness thresholds.

11. Potential options for reducing the residual risk of HCV transmission associated with the current UK Health Clearance Policy

The 2007 guidance on health clearance for new HCWs who will perform EPPs was based on a report published in December 2002 on Health Clearance for Serious Communicable Diseases, produced by an ad hoc Risk Assessment Expert Group set up by the CMO and Ministers in England. Consideration of existing HCWs employed prior to this guidance was excluded from the terms of reference of this group. Since this point, the UK has continued to identify HCV transmission from HCWs living with HCV, all of whom were employed in the NHS pre-2007 and have not been required to demonstrate that they are non-infectious for HCV (as well as HIV and hepatitis B).

UKAP were asked to consider the following options for addressing the risk of transmission from those HCWs who fall outside the criteria for Health Clearance screening:

- no change to the extant policy
- request that health care providers, via occupational health departments, individually risk assess all existing HCWs who perform EPPs to determine if they may have been exposed, and test to demonstrate non-infectiousness as appropriate
- test all existing health care workers employed prior to 2007 who undertake EPPs to demonstrate a baseline non-infectiousness as this group has never before had to demonstrate BBV non-infectiousness before undertaking EPPs
- introduce a system of re-testing of new and existing HCW who perform EPPs to demonstrate continuing non-infectiousness

12. UKAP recommendation for reducing the residual risk of HCV transmission associated with the current UK Health Clearance Policy

In light of the knowledge that all but 1 HCV transmission from a HCW to patient has been associated with category 3 EPPs performed by HCWs in the higher risk specialities, UKAP could not recommend screening all existing HCWs employed pre-2007 (one-off or repeated) (options 3 and 4), as the risk of transmission from the majority of EPP HCWs is likely negligible. However, restricting an intervention to existing category 3 EPP HCWs specialising in the higher risk specialities, where the risk of transmission is estimated to be minimal, was not considered cost effective. Furthermore, and pragmatically, restricting an intervention by category of EPP would be hard to implement prospectively since in surgical specialities, many EPPs fall between categories 2 and 3, depending on the technique employed by the HCW, and it is possible for a category 1 or 2 EPP to become a category 3 EPP as a result of some unforeseen event during the course of an operation. In this scenario, if the HCW was not cleared to perform category 3 EPPs, they would need to seek help from a colleague to continue the operation in the category 3 phase of the procedure.

Given the lack of cost effectiveness for a one-off intervention to screen all category 3 EPP HCWs specialising in the higher risk specialities, neither could UKAP endorse a system of re-testing new and existing HCWs (option 4).

For the same reason as given above, UKAP did not endorse an approach that required occupational health departments to identify and individually risk assess all existing HCWs who perform EPPs to determine if they may have been exposed, and test to demonstrate non-infectiousness as appropriate (option 2). On reflection, neither would restricting this approach to category 3 EPP HCWs in the high risk specialities be feasible, as implementing a consistent approach to assessing the practice of individual HCWs would have been complex given that categorisation of procedures are affected by variations in technique and technical developments.

UKAP therefore recommends that the 2007 health clearance guidance should not be amended to include the pre-2007 cohort (option 1). Instead, UKAP recommends investing in educating HCWs on the significant positive impact of the new antiviral drugs for treating HCV infection and therefore the benefits of a HCW knowing their status for both their health and their career prospects. Antiviral treatments are now available in the UK that will successfully clear hepatitis C virus in the majority of patients (Kohli et al, 2014) and new drugs being made available will offer virological cure for the majority of treated patients, with oral once-daily regimens that are interferon-free. Side effects with these new agents are minor. Thus any negative impact of a

positive diagnosis of hepatitis C on the career and livelihood of the HCW is much reduced. Also, given the likelihood of a gain in personal health after successful treatment, HCWs should be encouraged to come forward for HCV testing, if they have reason to believe that they may have been exposed (either through a specific occupational incident or outside their work environment), in line with the duty of care to patients, their professional responsibilities and legislative requirements. This is to an extent, a similar approach to option 2, albeit the onus is on the HCW to self-identify their risk of exposure rather than a proactive approach by their employers' occupational health service.

UKAP will keep under review the literature on occupational transmission of HCV and revise guidelines as necessary.

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Appendix 1: Transmission risk from HCW living with HCV

In this model, 2 sources of data are used: data on patient notification exercises (PNE) with known index case(s) and UKAP data on local risk assessments for HCW (who perform category 3 EPPs), found to have been living with HCV, but determined to have been at no (or very low) risk for patients.

Fortune et al (unpublished manuscript) previously considered PNEs for which there was a known index case or not, finding that those with no index cases did not trace any further cases when the PNE was conducted. This led them to categorise HCW into 2 groups: 'high-risk' HCW with known index cases, that may have transmitted HCV infection to a number of further cases identified by the PNE; and 'low-risk' HCW with no index case (henceforth zero-case HCWs), which may be considered as being virtually no risk of transmissions having occurred.

Of course, such a distinction occurs due to underlying heterogeneity in risk of transmission in the HCW population, which will not dichotomise exactly to 'low' and 'high' risk. This leads us to consider distributional forms for heterogeneity in the underlying risk, expressed statistically as random effects. Therefore the PNEs (and low-risk local assessments) resulting in no cases fall toward the lower tail of this distribution, where the risk to the patient is non-zero, but small enough that no patients were living with HCV; while the PNEs that found one or more cases as being towards the upper tail of the distribution.

In order to make further progress we make the following modelling assumptions. Firstly, underlying risk of transmission to patients in HCWs living with HCV is assigned a random effect, such that the log rate of transmission has a normal distribution, with standard deviation σ. Secondly, index cases and subsequent cases are assumed to be related by a scaling factor λ such that the number of subsequent cases is proportional to the index cases (thought of another way, the proportion detected by local risk assessment). This is also given a random effect as they are not of course exactly related, with SD= $\sigma\lambda$. Therefore:

$$\text{Log(index cases)} \sim b_0 + \text{Log}(n) + N(0,\sigma^2)$$
$$\text{Log(subsequent cases)} \sim \text{Log(index cases)} + \text{Log}(\lambda) + N(0,\sigma_\lambda^2)$$
$$\text{Log}(n) \sim b_n + N(0,\sigma_n^2)$$

In the above, n is the denominator, or number of patients at risk tested in lookback PNEs, which is also assumed to vary between HCW according to a random effects distribution. Within this framework, PNE data have a rate of index cases and subsequent cases, given the number tested. The number of patients at risk, n, is not known for the zero case HCWs; this is therefore assumed to have the same distribution as the PNE data. The number of index cases is by definition zero for the zero case HCWs, but subsequent cases can have a small, but non-zero,

risk of occurring. This setup is required as only the ‘initial’ proportion of index cases is known when a PNE is not conducted, and it cannot be reasonably assumed that these HCW transmitted zero cases.

The model makes various parametric assumptions about the distribution of levels of risk, both in terms of index cases and subsequent cases. The Normal distribution is convenient and frequently used for random effects in the log risk of events, but other possibilities – including a more dichotomous structure in risk, bimodal, or other shapes – are, of course, possible. The number of undetected cases is therefore highly sensitive to these assumptions, requiring also the extrapolation of the risk distribution to unobserved data. Further, the ratio between ‘initial’ (index) cases and subsequent probable cases is assumed to be broadly proportional – it is not of course known whether this ratio can be extended in the way here to the HCW that did not result in any index cases (henceforth ‘zero-case HCW’). In the extreme case, where zero-case HCW genuinely have a zero probability of transmitting to patients (that is, would all have yielded no further cases if PNEs were conducted) then the estimate here would be lower.

Further significant uncertainties are associated with the zero-case HCWs: the number at risk is not known, and extrapolated from the distribution of at-risk patients in PNEs. Secondly, the analysis necessarily assumes that the probability of detecting HCV in a HCW is the same, regardless of whether they transmitted to patients; if this is not the case, and detections are more likely where the HCW has transmitted, then the proportion of zero-case HCW would be under-estimated, leading to over-estimates of transmission risk. Nevertheless, the model accounts at least in part for both random variability in risk and the potential for unobserved cases, which can only be considered in this manner. Given the sparsity of data and the flexibility of the model, with random effects at each level, the estimate of unobserved cases is highly uncertain.

Appendix 2: Cost effectiveness analysis of screening Consultant grade surgeons in 'higher risk' specialities

The following sets out the cost-effectiveness arguments for undertaking screening for consultant-grade surgeons working in the higher risk surgery or Obstetrics and Gynaecology specialities[9].

1. Cost effectiveness analysis

1.1 Costs of intervention vs. treatment

The cost of the intervention is calculated as the screening cost per HCW (including staff time, administration, overheads and treatment costs of HCWs living with HCV diagnosed) multiplied by the number of HCW to be screened. This is offset by the extra healthcare and treatment costs of patients living with HCV (once diagnosed) that occur without screening, and the healthcare costs (and later treatment) of HCWs that remain living with HCV. Therefore, the net cost of the intervention is calculated by subtracting the potential healthcare savings from the cost of screening.

1.2 Measuring benefits: QALYs

A patient living with HCV may potentially experience progression to severe liver disease, ultimately leading to loss of life years. In addition, the years that a patient lives with severe disease may be of a lower quality of life, which leads to the notion of QALYs. So if a particular health state has a QALY of 0.9, then 10 years lived in this health state will be considered of equivalent value to the patient as living 9 years at full health. In this way the full loss to a patient is expressed – both in life years lost (death of course has a QALY value of zero) and a lower quality of life due to infection.

1.3 Treatment

If patients are treated and the treatment is successful, a SVR is considered to be a permanent cure if the patient is of mild or moderate stage disease, and greatly reduced disease progression for cirrhosis and more advanced disease stage. Timing of diagnosis is therefore important, as the probability of SVR is also reduced at more advanced disease stages.

[9] HCWs specialising in either obstetrics and gynaecology, general surgery, cardiothoracic surgery or vascular surgery.

1.4 Cost effectiveness

Cost effectiveness is calculated via the cost per QALY gained, that is, the net cost of the intervention divided by the gain in QALYs that the intervention provides. This is a function of the expected number of infections with and without the screening intervention over a period of time.

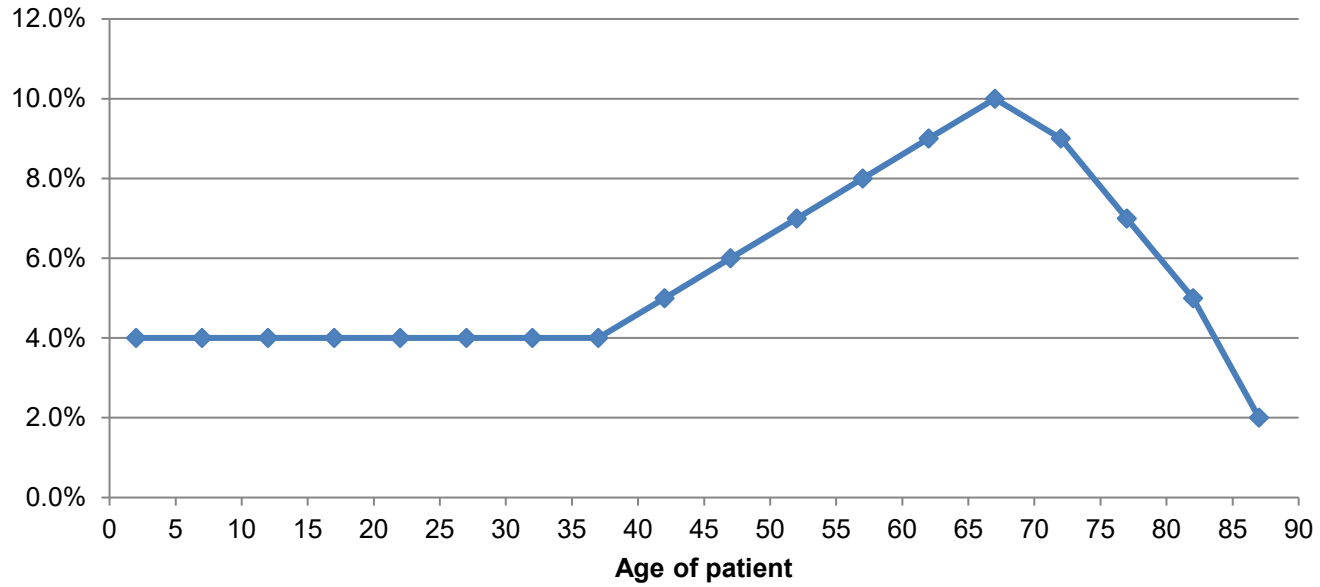
Note that NICE typically considers treatments and interventions to be cost effective if they provide a cost per QALY gained of under £20,000 to £30,000. Of further note is that costs and QALYs are typically discounted over time in CE analysis; ie, future costs are not given as much weight as immediate costs, and future benefits are worth less than immediate ones. In the case of immediate interventions that prevent the long-term harms of HCV infection, this will generally increase the (discounted) cost per QALY gained.

2. Modelling assumptions[10]

2.1 Age distribution of patients

Firstly, an age distribution of those undergoing EPPs is assigned. This assumes the majority of EPPs occur in those in their 60s.

Figure 1. Modelled age distribution of those undergoing surgical procedures



The age at infection will, of course, affect the remaining life years and QALYs that a patient has.

[10] The analysis presented in this report, and the assumptions underpinning the analysis were based on information available to the UKAP working group at the point of analysis, taking into account anticipated future changes in HCV treatment.

2.2 Disease progression rates

Disease progression rates are based on the posterior summaries of progression rates from Harris et al, which uses estimates from the literature combined with observed HES data and estimates of population prevalence (Harris et al, 2014).

2.3 Diagnosis and treatment

The baseline scenario is for a low probability of diagnosis at mild stage disease (2.5% per year), increasing for moderate stage (5% per year), and very likely diagnosis at cirrhosis (50% per year). These probabilities result in 12%, 22% and 92% probabilities of diagnosis within 5 years for mild, moderate and cirrhosis stage. If the patient reaches ESLD/HCC prior to diagnosis, diagnosis occurs almost immediately, provided the patient does not die beforehand.

Table 1. Disease stage by annual, 5 and 15 year probability of diagnosis[1]

Disease stage (Metavir score)	Annual probability of diagnosis Pr(detect)	5-year probability of diagnosis Pr(detect)	15-year probability of diagnosis Pr(detect)
Mild (F0/F1)	2.5%	11.8%	31.3%
Moderate (F2/F3)	5.0%	22.1%	52.8%
Cirrhosis (F4)	50.0%	91.8%	99.9%

[1] Diagnosis guaranteed at ESLD/HCC stage (although may die before treatment starts)

It is assumed that upon diagnosis, treatment is immediately initiated, using direct acting antiviral (DAA) therapy. SVR rates are 95% at mild stage and 90% at moderate stage, at which point the patient is considered cured and has no QALY loss or further progression. SVR rates are 85% for those with cirrhosis and 80% for ESLD/HCC, if SVR is achieved then disease progression may still occur, but at a much lower rate. The actual annual rates of diagnosis in England are not known, therefore rates are estimated based on the estimated number of chronic infections and the known number of individuals testing as antibody positive for the first time each year. It is unknown whether rates in HCWs living with HCV via EPP would be lower than those assumed.

Table 2. Treatment outcomes, costs and post-treatment QALYs and costs

Stage	SVR rate1	Cost2	Post-SVR QALY loss	Post-SVR cost
Mild stage (F0/F1)	95.0%	£10,000	0.0%	£259
Moderate (F2/F3)	90.0%	£10,000	0.0%	£259
Cirrhosis (F4)	85.0%	£10,000	5.0%	£518
ESLD/HCC	80.0%	£10,000	20.0%	£1,036

[1] assumed that DAAs received immediately upon diagnosis
[2] likely future costs of treatment

2.4 Costs and QALYs

Patients living with HCV are assumed to incur no costs while undiagnosed, but if diagnosed and having failed treatment have ongoing healthcare costs, which rise according to disease stage. Post-SVR, patients also have small follow up costs, which also rise for more advanced disease stages. These costs are based on a selected Health Technology Assessment (HTA) report (Shepherd et al, 2007).

Table 3. QALY loss/cost[1] by stage of illness

Stage	QALY loss	Cost (diagnosed)
Mild stage (F0/F1)	0.0%	£138
Moderate (F2/F3)	0.0%	£717
Cirrhosis (F4)	22.0%	£1,138
ESLD/HCC	32.0%	£9,000
Liver transplant	32.0%	£36,800
Post-transplant	32.0%	£1,385

[1] assume very little or none while undiagnosed pre-cirrhosis

The cost of treatment itself is assumed to be £10,000 for all disease stages, reflecting the fall in costs with NHS England procurement negotiations.

QALYs are adapted from the Health Technology Assessment report of Shepherd et al (2007). They assumed reduced QALYs in mild disease stage due to injecting drug use and its associated harms for many of those living with HCV. However, undiagnosed mild or moderate disease stage in the patient population is assumed here to result in no QALY loss. QALY loss for cirrhosis stage and beyond is therefore defined as the difference between mild and advanced stages in Shepherd et al. Post-SVR QALYs are defined similarly, assuming a small loss in QALYs post-SVR for those in advanced disease stages.

2.5 Impact and costs of screening

Given the assumed size, HCV prevalence and transmission rate of the target population and resulting numbers of patient transmission and QALY loss or costs, the impact and cost of screening is considered. At the baseline, the cost of screening per HCW is assumed to be £150, resulting in a total cost of £485,000 for the intervention. The proportion screened under the programme is assumed to be 80%. In addition, a proportion of those HCWs living with HCV are assumed to already have been screened voluntarily; this is fixed at 25%.

Table 4. Baseline prevalence of HCV among HCWs performing EPPs

Healthcare worker population	
Number of surgery, obstetrics and gynaecology consultants	6,061
HCV prevalence surgery	0.23%
Transmission rate	0.10%
Cost of screening per HCW	£150
Proportion screened under programme	80%
Proportional already voluntarily screened	25%
EPPs per HCW per year	70
Total EPPs per year	**424,270**

Finally, the time span for the assessment of the intervention is set to 10 years; that is, we consider the patients that may or may not be living with HCV during this period (although the healthcare costs and QALY calculations are based on a lifetime horizon).

3. Results

Given the age distribution at infection, progression rates, diagnosis and treatment assumptions and resulting QALY loss, the average remaining QALYs for uninfected patients is estimated to be 26.7 and for patients living with HCV 25.0, a loss of 1.7 QALYs for those living with HCV. In addition, the average healthcare and treatment costs for those living with HCV (based on treatment costs in 2015/16), is £5,530.

Next, the expected number of infections within the 10-year time frame with and without screening is calculated. Under the assumptions here, 7.3 infections are expected without screening and 1.95 infections with the screening intervention. Thus around 5 additional infections are expected without screening, with an additional healthcare cost of £29,658 and 9.1 QALYs lost.

Table 5. Expected number of infections, costs and QALYs lost within 10-year time frame with and without screening

Infections, costs and QALYs lost over 10 year time frame		
No screening	Infections	7.3
	QALY Loss	12.4
	Cost	£40,443
Screening	Infections	1.95
	QALY Loss	3.3
	Cost	£10,785
Difference (screening benefit)	Infections Prevented	5.4
	QALY Gained	9.1
	Cost Saved	£29,658

In addition to the differences in numbers of infections and healthcare costs for patients, the cost of treating HCWs living with HCV and their subsequent QALY gains were also incorporated. HCWs were assumed to have higher diagnosis rates than patients, and therefore incur a lower average QALY loss as treatment is started sooner. The average gain was estimated as 0.33 QALYs for immediate diagnosis (and treatment) via screening, vs. later diagnosis. For 10 HCWs living with HCV with an 80% screening rate, this results in a QALY gain of 2.6 and a cost saving of £34,302, as those identified earlier are less likely to reach advanced disease stages and hence have lower healthcare costs.

Table 6. Additional impact of early versus late detection of HCV infection on QALYS lost

HCW costs and QALYs		
	QALY loss for late vs. early diagnosis	0.33
No screening	Undiagnosed Infections	10
	QALY Loss	3.5
	Cost	£57,776
Screening	Undiagnosed Infections	3
	QALY Loss	0.9
	Cost	£15,407
Difference (screening benefit)	Infections Treated Early	8
	QALY Gained	2.6
	Cost	-£34,302

Finally, the net cost (intervention cost minus healthcare costs saved for both patients and HCWs) is calculated, and the cost per QALY gained. The net cost is £504,676 with 11.7 QALYs gained, so the cost per QALY is £504,676/11.7 = £43,135. This is outside NICE thresholds for cost-effective interventions.

Table 7. Total net cost per QALY gained of screening intervention

Total QALY gain	
	11.7
Cost effectiveness of intervention	
Total cost of intervention	£500,033
Net cost (intervention minus costs averted)	£504,676
Cost Per QALY Gained	**£43,135**

4. Sensitivity analyses

It is worth assessing different scenarios to assess the resulting change in cost per QALY gained. A brief summary is given below:

Table 8. Sensitivity analysis summary table

Parameter /assumption	Change	Impact on cost per QALY gained	Explanation
Age distribution	Lower, all patients age 16 to 20	£24,500↓	Patients progress more slowly at younger ages and are therefore more likely to be diagnosed and treated before advanced disease.
	Higher, all patients age 66 to 70	£66,540↑	Converse of above.
Diagnosis rates	20% per year at mild stage, 50% moderate	£58.200 ↑	Patients diagnosed more quickly and treated at earlier disease stage; more treatment costs
	0% mild/moderate, 20% cirrhosis	£27,900 ↓	Fewer patients treated overall so lower cost, although there is greater QALY loss.
Prevalence of HCV in HCW population	0.14% (lower 95% CI of estimate)	£70,900 ↑	Far fewer patients living with HCVs prevented and therefore small difference in QALY loss vs. expense.
	0.38% (upper 95% CI of estimate)	£26,400 ↓	Converse of above.
Transmission rate	0.03% (3 in 10,000); lower 95% CI	£99,300 ↑	Similar arguments to above, but more extreme as wider 95% CI for transmission rate.
	0.32% (3 in 1,000); upper 95% CI	£13,900↓	Converse of above; with higher risk of infection, screening would be highly cost effective.

Parameter /assumption	Change	Impact on cost per QALY gained	Explanation
Cost of screening per HCW	£75	£21,800↓	Cost of screening intervention greatly reduced, decreasing cost per QALY to within NICE thresholds.
	£250	£71,900 ↑	Converse of above
HCW costs/QALYs not included	All HCW costs/QALYs at zero	£51,700↑	The total intervention costs includes the treatment of HCWs living with HCVs but the total QALY gain includes HCWs too.
Time frame for patient infections	5 years	£73,000 ↑	Number of patients living with HCV within 5 years would not warrant screening.
	15 years	£30,200 ↓	Number of patients living with HCV within 15 years is greater; more impact of screening for same cost
SVR rates	95% at all disease stages	£47,300 ↑	Rates are high for most patients already so change in QALY gain is minimal; although the increased post-SVR costs for those with cirrhosis/ESLD makes this more expensive.

The age distribution and diagnosis rates have some impact on results, but of far greater importance is the prevalence and risk of transmission of HCV in the HCW population. Cost of screening has a direct impact by definition.

Whether the costs of treating HCWs who screen positive for HCV should be included in the intervention cost is debatable; however, if the costs of treatment is not considered as part of the intervention, then neither should the healthcare costs averted or QALY gain. From a purely patient-based perspective in which only patient costs or QALYs and the screening intervention cost are considered, the intervention is actually less cost effective: the QALY gains in HCWs who are successfully treated are fairly small, but still a reasonable proportion of the total gain.

Finally the time frame is important – the number of patients living with HCV over 5 years would not be sufficient to justify the costs, but if the impact of the intervention is sustained over a longer period the cost effectiveness improves. This is of relevance if the screening must be repeated every 5 or 10 years in order to maintain its effectiveness.

5. Conclusions

In summary, a screening intervention will not fall within NICE thresholds under the baseline, most likely estimated rates of transmission resulting in infection, and assumptions used in this model. However, higher HCW prevalence or transmission rates could result in the intervention being within NICE thresholds. Conversely, if HCW prevalence or transmission are lower than expected, screening becomes even less cost-effective.

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