


Meta-analysis: risk of hepatitis C virus infection associated with hospital-based invasive procedures

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Summary

Background: Healthcare settings, where invasive procedures are frequently performed, may play an important role in the transmission dynamics of blood-borne pathogens when compliance with infection control precautions is suboptimal.

Aims: To understand and quantify the role of hospital-based invasive procedures on hepatitis C virus (HCV) transmission.

Methods: We conducted a systematic review and meta-analysis to identify recent studies reporting association measures of HCV infection risk that are linked to iatrogenic procedures. Based on expert opinion, invasive procedures were categorised into 10 groups for which pooled measures were calculated. Finally, the relationship between pooled measures and the country-level HCV prevalence or the Healthcare Access and Quality (HAQ) index was assessed by meta-regression.

Results: We included 71 studies in the analysis. The most frequently evaluated procedures were blood transfusion (66 measures) and surgery (43 measures). The pooled odds ratio (OR) of HCV infection varied widely, ranging from 1.46 (95% confidence interval: 1.14–1.88) for dental procedures to 3.22 (1.7–6.11) for transplantation. The OR for blood transfusion was higher for transfusions performed before 1998 (3.77, 2.42–5.88) than for those without a specified/recent date (2.20, 1.77–2.75). In procedure-specific analyses, the HCV infection risk was significantly negatively associated with the HAQ for endoscopy and positively associated with HCV prevalence for endoscopy and surgery.

Conclusions: Various invasive procedures were significantly associated with HCV infection. Our results provide a ranking of procedures in terms of HCV risk that may be used for prioritisation of infection control interventions, especially in high HCV prevalence settings.

As part of AP&T's peer review process, a technical check of this meta-analysis was performed by Dr. Y. Yuan. The Handling Editor for this article was Professor Grace Wong, and it was accepted for publication after full peer-review.

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INTRODUCTION

Hepatitis C virus (HCV) is mainly a blood-borne virus associated with an estimated global sero-prevalence of 2.5%.¹ However, wide between-country discrepancies are observed, with Egypt and Pakistan having high anti-HCV prevalence in the general population.¹ Chronic HCV infection, which is most of the time asymptomatic, may lead to serious complications like cirrhosis or hepatocellular carcinoma (HCC), with about 20% developing HCC.² Highly effective and well-tolerated direct-acting antiviral treatments (DAAs) are now available, but these treatments remain costly. An estimated 79% of people chronically infected with HCV worldwide still did not know their status in 2019,³ limiting the population impact of DAAs. In addition, the residual risk of HCC is suspected to remain relatively high among patients who cured chronic HCV infection.⁴ Moreover, HCV treatment should not be the only way of fighting new infections, as accumulating evidence suggests that even after the DAA therapy-induced sustained virological response reinfection can occur, especially in people who inject drugs.⁵ Therefore, prevention interventions to limit the risk of HCV contamination remain key in the global response against HCV.⁶

Although injection drug use has been established to be the most important risk factor for acquiring a new HCV infection globally,⁷ healthcare settings may play an important role in HCV transmission dynamics, due to the high frequency of invasive procedures and over-representation of HCV-infected individuals among hospitalised patients. Medical procedures have been linked to multiple HCV outbreaks worldwide, for instance in Egypt,⁸ India⁹ or the United States.¹⁰ In healthcare settings where compliance with infection control interventions is suboptimal, patients may still become infected following blood transfusion or haemodialysis.^{11,12} Previous hospitalisation has been identified as a major risk factor for HCV infection in many countries.¹³ In the countries where HCV prevalence is high, infection control interventions may not be systematically implemented, and data are scarce regarding HCV infection risks.

In this context, a better control of hospital-acquired infections would significantly help in the fight against HCV epidemics. This requires a clear understanding of the role played by different high-risk procedures within healthcare settings. We conducted a systematic review and meta-analysis to synthesise the strength of association between different hospital-based invasive procedures and HCV infection risk, in order to rank these procedures according to the risk of iatrogenic HCV transmission.

MATERIAL AND METHODS

Search strategy and selection criteria

We searched PubMed, Web of Science and Scopus for studies published between January 2000 and December 2020 using the following concepts: hepatitis AND risk factor AND hospital

AND procedure (Table S1). This systematic review was registered in PROSPERO (ID: CRD42021224886) and reported according to PRISMA guidelines.

Studies were eligible if: (i) exposure group was composed of adults, who were hospitalised or who had outpatient visit; and (ii) they reported measures of association (odds ratios, ORs; risk ratios, RRs; or prevalence ratios, PRs) by comparing the proportion of people positive for HCV RNA or anti-HCV antibody between a group who underwent a specific healthcare procedure and another group not exposed to the procedure. There was no restriction in terms of the study design and non-exposure group.

Studies were excluded if: (i) they exclusively included paediatric patients, drug users or blood donors; (ii) patient recruitment started before 2000; (iii) they were not written in French or English; or (iv) they did not present original results.

Article titles and abstracts were screened by two independent investigators (M.C. and P.H.) using the Covidence review tool.¹⁴ Full-text articles were then retrieved and assessed for their eligibility by the same two authors. Any conflict in articles screening or full-text assessment were resolved by a third senior researcher (K.J. or L.T.). For each study, the following data were extracted by P.H.: total number of patients; patient type; study design; and measures of association and sample size of the exposed/non-exposed groups. Any doubt concerning data extraction was resolved by a senior researcher (K.J. or L.T.).

Data analysis

The procedures were categorised into 10 groups and validated by medical experts (L.B.L.N. and Y.S.) (Table 1; Table S10, Text S2). Risk of blood-borne infection was supposed to be the same within these groups. Measures associated with the same procedure but reported across different populations (e.g. by gender) were considered independently in the meta-analysis.

We performed random-effect meta-analyses to pool ORs for an association between each procedure group and the risk of HCV infection using the R 'meta' package.¹⁵ When two or more distinct procedures were classified in the same procedure group within the same study population, a three-level model¹⁶ was used to account for the dependence between the measures of association. I^2 statistics were used to assess the heterogeneity across the studies. Procedure-specific forest plots were visually inspected for potential outliers. Measures that were not ORs (RRs and PRs) were considered to be equivalent to ORs and included in the same analyses. When both adjusted ORs (AORs) and crude ORs were available in the same study, the AORs were preferred. In a same study, if risk estimates were available for old-dated and undated (without specified date) blood transfusion, estimates associated with undated blood transfusion were preferred.

In a second step, pooled ORs for low HCV prevalence (<5%) and high HCV prevalence (>5%) countries were computed following the previously described method and compared through subgroup

Group	Procedures within group (as found in selected studies)
Surgery	Surgery, operation, bloody operation, splenectomy, laparoscopy, organ biopsy, caesarean section
Transplantation	Transplantation, renal transplantation
Blood transfusion	dated blood transfusion/non-dated blood transfusion
Intravenous (IV)/Catheter	Cholangiography, IV pyelography, IV injection, IV-line, sclerotherapy, catheter, central venous catheter, cannula, phlebotomy
Haemodialysis	Haemodialysis
Wound care	Wound suture, wound care
Injection	IM injection, percutaneous injection, subcutaneous injection, injection/vaccination, injection
Other procedures	Electromyography, haemorrhoids treatment, tapping ascites, abscess drainage, abortion, biopsy, ligation of oesophageal varices, urinary catheter
Endoscopy	Endoscopy, colonoscopy, gastroscopy
Dental care	Tooth extraction, dental anaesthesia, dental procedure, dental care, tooth filling

Note: Procedure names are reported as mentioned in each of the articles.
Abbreviation: IM, intramuscular.

analyses for each procedure group. Prevalence data for each country were collected from the MapCrowd online global data on hepatitis C (Table S9).¹⁷ Procedure-specific pooled ORs were stratified by country for the two most represented procedure groups. In addition, subgroup analyses were performed to compare estimates between cohort and non-cohort studies.

Third, the pooled OR for blood transfusion based on transfusions performed with either recent dated or an unspecified date of realisation was compared to the one based on transfusions performed before 1998, which is the latest cut-off date used within selected articles. Indeed, we assumed cut-off dates found in the studies selected to reflect local implementation of mandatory HCV screening in blood donors.

Finally, meta-regressions were performed to investigate the potential effect modifier of: (i) the HCV prevalence level (as a continuous variable), and (ii) the Healthcare Access and Quality (HAQ) index, a 0–100 score quantifying the strength of healthcare quality and access based on amenable mortality data in each country (Table S9).¹⁸ The HAQ index was retrieved for 2000, 2005, 2010 and 2015 and was associated with each study based on their publication year.

The risk of bias was assessed by P.H. on the articles included. Nine bias assessment criteria were adapted from Lam et al.,¹⁹ and publication bias was assessed by testing for asymmetry in the overall and procedure-specific (for procedures with more than 10 measures of association) funnel plots.²⁰

RESULTS

Among the 1961 initially identified studies, 71 were included in the review and meta-analysis,^{21–91} as described in the flow diagram

TABLE 1 Aggregation of procedures found within selected articles

(Figure 1). The total number of participants across all selected studies was 120,568.

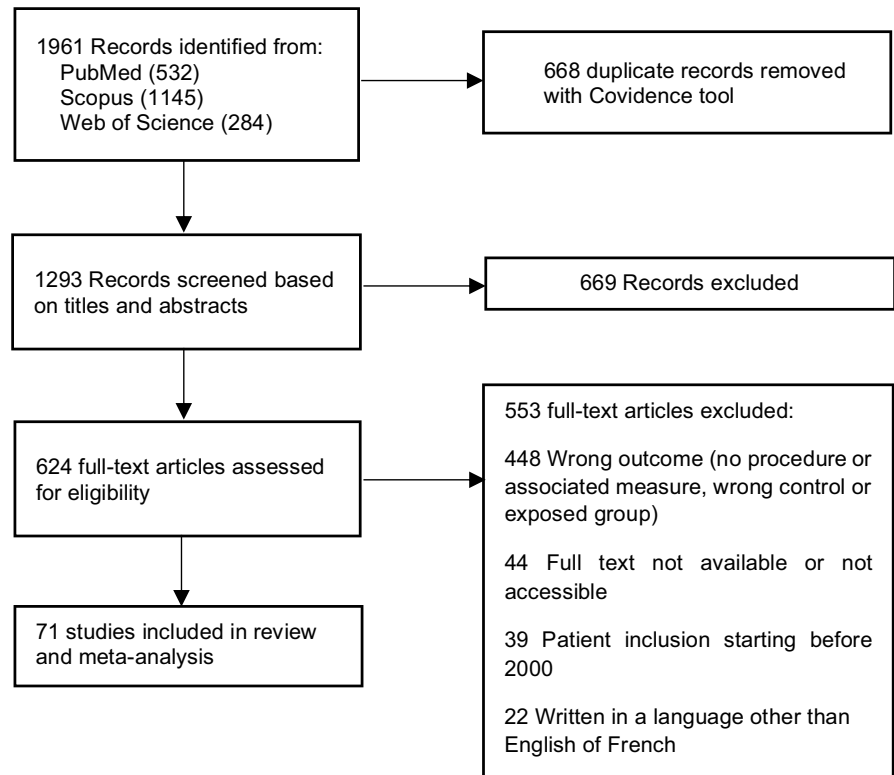
Figure 2A shows an increase in publications related to HCV risk assessment within hospitals between 2000 and 2015, while the number of publications remained stable between 2015 and 2020. Together, Pakistan (14 studies) and Egypt (9 studies) represented one-third of all included studies (Figure 2C). Over a fifth of studies were focused on haemodialysis patients (22.5%) (Figure 2B). Most studies were cross-sectional (55%) or case-control (22.5%) studies (Figure 2D).

Forty-five different procedures were assessed (Table 1). The number of outcome measures by each of the 10 procedure groups ranged from 5 to 66, with surgery and transfusion as the largest groups (43 and 66 respectively) (Figure 3; Table S8). Visual inspection of procedure-specific forest plots (Figures S6–S15) led to the exclusion of a single outlier for haemodialysis (Figure S6).

All pooled ORs were significantly superior to one, except for endoscopy and haemodialysis (Figure 3).

The risk of HCV infection differed according to procedure groups with pooled OR estimates ranging from 1.46 (95% confidence interval [CI, 1.14–1.88]) for dental procedure up to 3.22 (95% CI [1.7–6.11]) for transplantation. The wound care and transplantation groups had OR estimates of 2.83 (95% CI [1.85–4.32]) and 3.22 (95% CI [1.7–6.11]), representing the higher risk groups. The haemodialysis, surgery, other procedure, intravenous (IV)/Catheter and transfusion groups had high/moderate pooled ORs, with estimates of 2.02 (95% CI [0.98–4.17]), 2.28 (95% CI [1.43–3.64]), 2.30 (95% CI [1.77–3.00]), 2.42 (95% CI [1.68–3.51]) and 2.6 (95% CI [2.1–3.22]) respectively. Injection was associated with a low/moderate risk of HCV infection with an estimate of 1.67 (95% CI [1.17–2.38]). Finally, the dental procedure and endoscopy groups presented the lowest

FIGURE 1 Study selection.



risks of getting HCV infected (1.46 95% CI [1.14–1.88] and 1.48 95% CI [0.95–2.30] respectively).

Country-stratified analyses were performed for transfusion and surgery (Figure 4). For these two procedure groups, estimated ORs varied widely between countries. The highest strength of association between blood transfusion and risk of HCV infection was reported in Germany (OR = 5.39 95% CI [2.67–10.89]) but this estimate corresponds to only one study and is associated with transfusions performed before 1991. Pooled ORs for the association between blood transfusion and risk of HCV infection were also high in Egypt (OR = 5.16 95% CI [1.86–14.28]), Iran (5.11 [1.04–24.99]), Turkey (4.50 [1.71–11.86]) and Malaysia (4.00 [2.18–7.35]), although the confidence intervals were quite wide. There were less high-risk countries concerning surgery, for which Egypt and India had high pooled ORs (5.20 [2.50–11.00] and 4.62 [0.82–26.02] respectively).

Overall, procedure- and prevalence-specific pooled ORs tended to be higher in high prevalence countries (Figure 5; Tables S3 and S6) although this difference was not significant ($p = 0.33$, Figure 5). Nevertheless, a significant difference was observed for endoscopy ($p = 0.0044$, Table S3) and surgery ($p = 0.013$, Table S3). These results were supported by procedure-specific meta-regressions (Table S4) showing prevalence (as a continuous variable) to have a significant positive effect on the OR level of the endoscopy ($p = 0.004$) and surgery ($p = 0.01$) groups. However, prevalence (as a continuous variable) was not found to have a significant positive effect on the risk of iatrogenic HCV

infection as a whole ($p = 0.20$, Table S6). In addition, no overall association was found between HAQ level and risk of iatrogenic infection ($p = 0.93$, Table S6), while in procedure-specific analyses a negative significant impact of the HAQ level was observed for endoscopy only ($p = 0.017$, Table S5).

For blood transfusions performed before 1998, 17 studies were selected for the pooled OR calculation, whereas there were 49 studies available for undated/most recent blood transfusions (Figures S1 and S2). The estimated pooled OR of HCV infection associated with blood transfusions performed before 1998 (OR = 3.77 95% CI [2.42–5.88]) was significantly higher than the pooled OR associated with undated/most recent blood transfusions (2.20 [1.77–2.75], $p = 0.012$).

Across all studies, bias was low for most criteria, but several studies presented a potentially high risk of bias for criteria related to exposure assessment (almost 90% of all studies) and to potential confounding (almost 60%, Figure S3; Table S2). No study had at least potentially high bias risk for more than two criteria (out of nine). Nevertheless, the overall funnel plot showed asymmetry and the associated Egger test was highly significant, suggesting potential publication bias (Figure S4).

Average ORs in non-cohort studies were found to be higher than in cohort studies (2.26 95% CI [1.94–2.63] vs. 1.96 [1.41–2.72]) but this difference was not significant ($p = 0.44$). Per-procedure comparisons between cohort and non-cohort studies showed no significant differences, but the difference for the transplantation group was at the edge of statistical significance ($p = 0.054$).

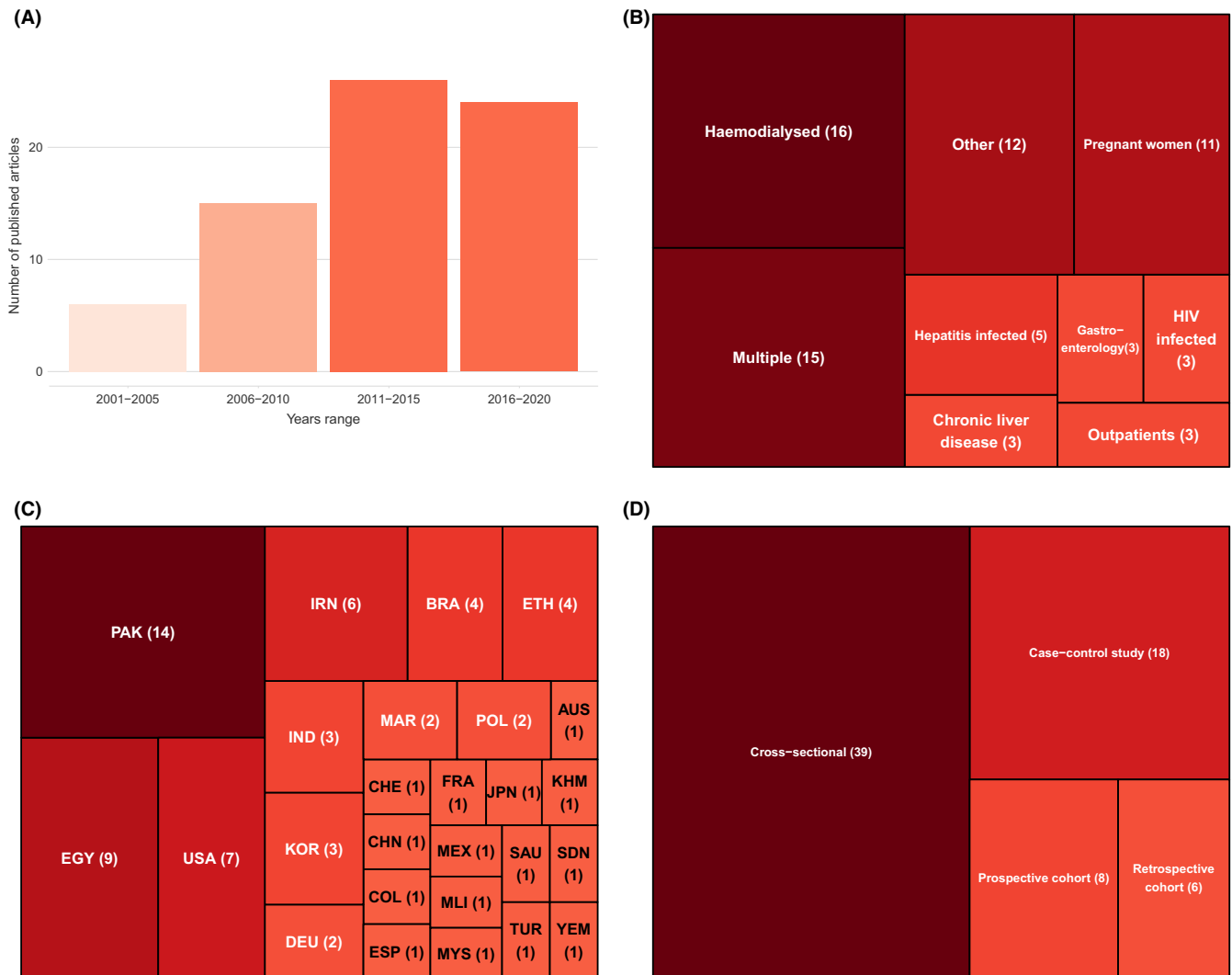


FIGURE 2 Study characteristics. Number of included studies by: (A) year of publication; (B) type of patients; (C) country; (D) Study designs. Total number of studies, 71.

DISCUSSION

In this systematic review and meta-analysis, we identified 71 studies assessing the association between hospital-based invasive procedures and the risk of HCV infection, representing a total of 120,568 participants. The overall strength of evidence remained of limited confidence as the bias analysis found a lack of high-quality studies. Nevertheless, we estimated pooled ORs of HCV infection that were significantly associated with most invasive procedures performed in hospitals. Our results suggest a prioritisation of iatrogenic procedures: transplantation and wound care were associated with the highest risk of HCV infection whereas dental procedures and endoscopy were associated with the lowest risk. We also underlined a large between-procedure and between-country variability, and showed that the per-procedure risk tended to be higher in countries with high HCV prevalence, while the level of healthcare quality and access in the country (as measured by the HAQ) only appeared to play a minor role.

The geographical coverage of selected studies was in line with global observed prevalence levels, with a third of these studies coming from the two countries with the highest HCV prevalence worldwide (Egypt and Pakistan). In addition, the most represented population was composed of haemodialysed patients, for which the risk of HCV infection is historically substantial.⁹² Regrettably, only few studies used cohort data.

The estimated per-procedure risks seemed to be mostly in line with the available literature concerning HCV. Generally, the risk was higher for procedures with frequent blood contact.

We found the highest risk of infection to be associated with transplantation. This risk is quite high considering that most of countries now require HCV testing in donors.⁹³ This might result from reverse causality; those infected with HCV have higher chance of undergoing these invasive procedures because of liver-related complications. Surprisingly, we found a high risk of infection to be associated with wound care. This might be related with the fact that four of five studies assessing this procedure were conducted in Egypt, the

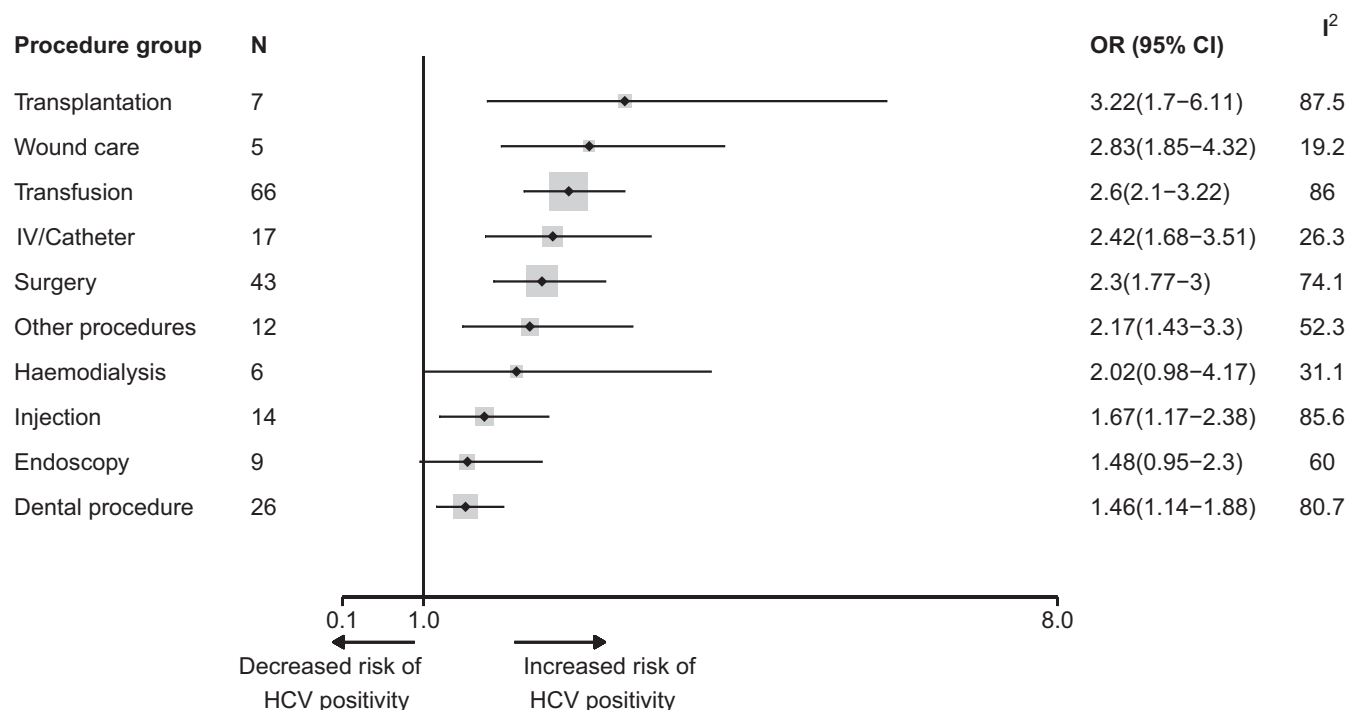


FIGURE 3 Forest plot reporting pooled OR estimates for HCV infection risk associated with different groups of iatrogenic procedures. Points correspond to average estimates and error bars correspond to 95% CI of these estimates. The solid line represents the limit for which OR = 1 and the dotted line the value of the overall estimate. The total number of observations used for each pooled OR calculation is specified in the column *N* and represented as the size of the grey area around each point estimate; the heterogeneity for each estimation is depicted in the column *I*². A given study could be used in the OR estimation of multiple procedures groups. Procedures are sorted based on the value of their associated mean estimate, from the highest to the lowest. CI, confidence interval; HCV, hepatitis C virus; OR, odds ratio.

country with high HCV prevalence. The estimate of the HCV infection risk through sutures found in the only previous meta-analysis by El-Ghitany et al. was lower than our estimate, but increased in the most recent studies.¹³

The intermediate risk we found for blood transfusion could be explained by the fact that there is still high discrepancy in systematic screening of blood products between countries (only 80% of donations are screened in low-income countries).⁹³ Haemodialysis was also associated with an intermediate risk of HCV infection. Our estimate was within the same order of magnitude than the one reported in the previous meta-analysis.¹³

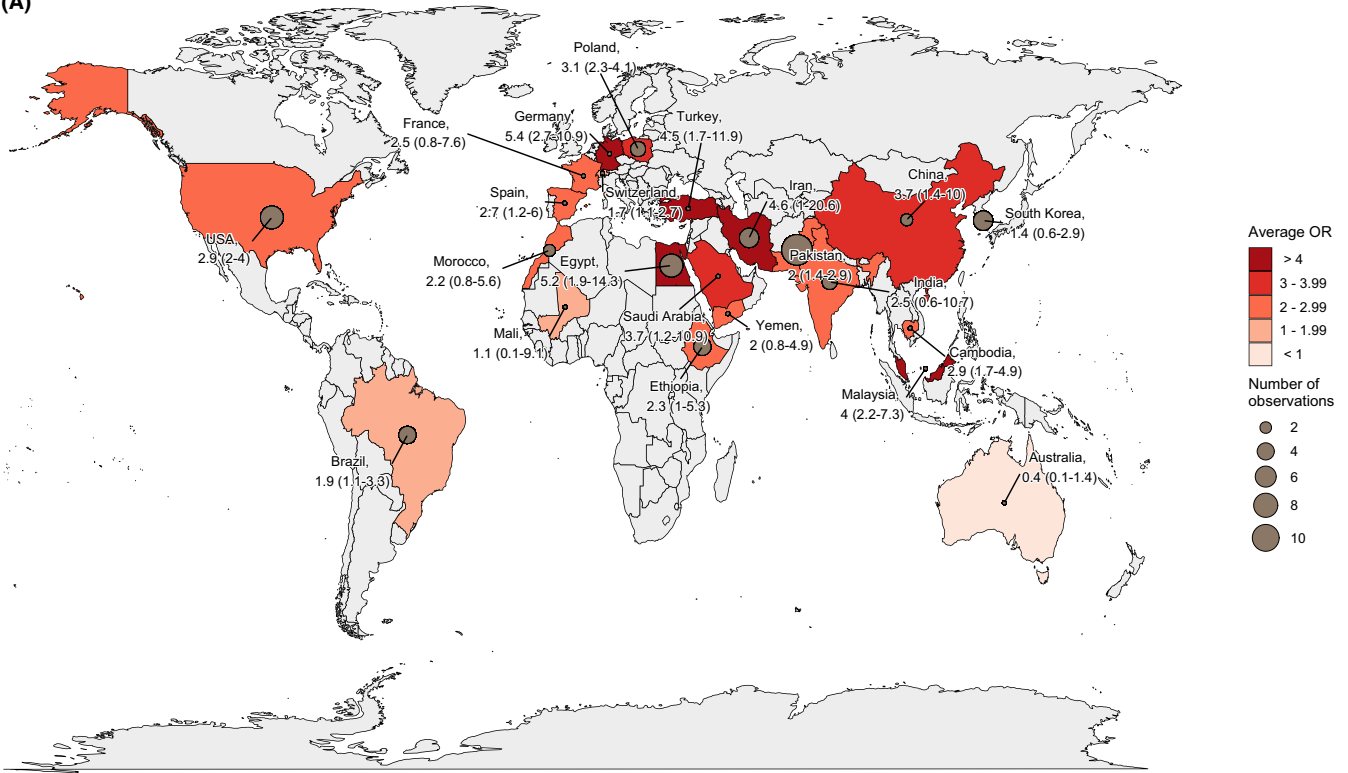
We found injection to be one of the lowest at-risk procedures. Injection was described in the past to be at high risk of HCV infection, in particular because of the reuse of contaminated syringes,⁸ but this risk might have dropped over the last decade, in particular after the publication of multiple World Health Organization (WHO) and Centers for disease control and prevention (CDC) guidelines for safe injections.⁹⁴ The injection is one of the most frequently performed procedures and most adults have universally received it. There may be more chance of recall errors compared to other procedures as this is often given during childhood (e.g. vaccination).

Finally, dental procedures and endoscopy were found to be the lowest risk groups, in line with current literature findings. Indeed, only a few cases of HCV contamination after endoscopy have been

described and dental practices are often at low risk of contamination.^{92,95} This result is also consistent with previous estimations showing low risk associated with these two procedures.¹³

Country-level prevalence was overall found to be related to a higher risk of HCV contamination, although it was only significantly associated with endoscopy and surgery risks when looking at specific procedures. The lack of significance for other procedures may be explained in several ways. First, many countries were represented by less than three studies, leading to a lack of power for some procedures and countries and less accurate OR estimates. Second, these non-significant associations may also indicate the presence of other causes of heterogeneity. In particular, there may be high differences in terms of prevalence between hospital settings within the same country. Procedure ranking differed between low and high prevalence countries. In particular, haemodialysis and endoscopy were found to be to most at-risk procedures in high prevalence countries. However, considering that this was based, for these countries, on only one study (for haemodialysis) or two studies (for endoscopy), the associated confidence intervals were very wide and this ranking should not be over-interpreted. Observed between-country variations may also result from different infection control practices; we explored this assumption using the HAQ index, which is internationally validated and available for all countries in our analysis. However, we found no significant relationship between the risk of getting HCV

(A)



(B)

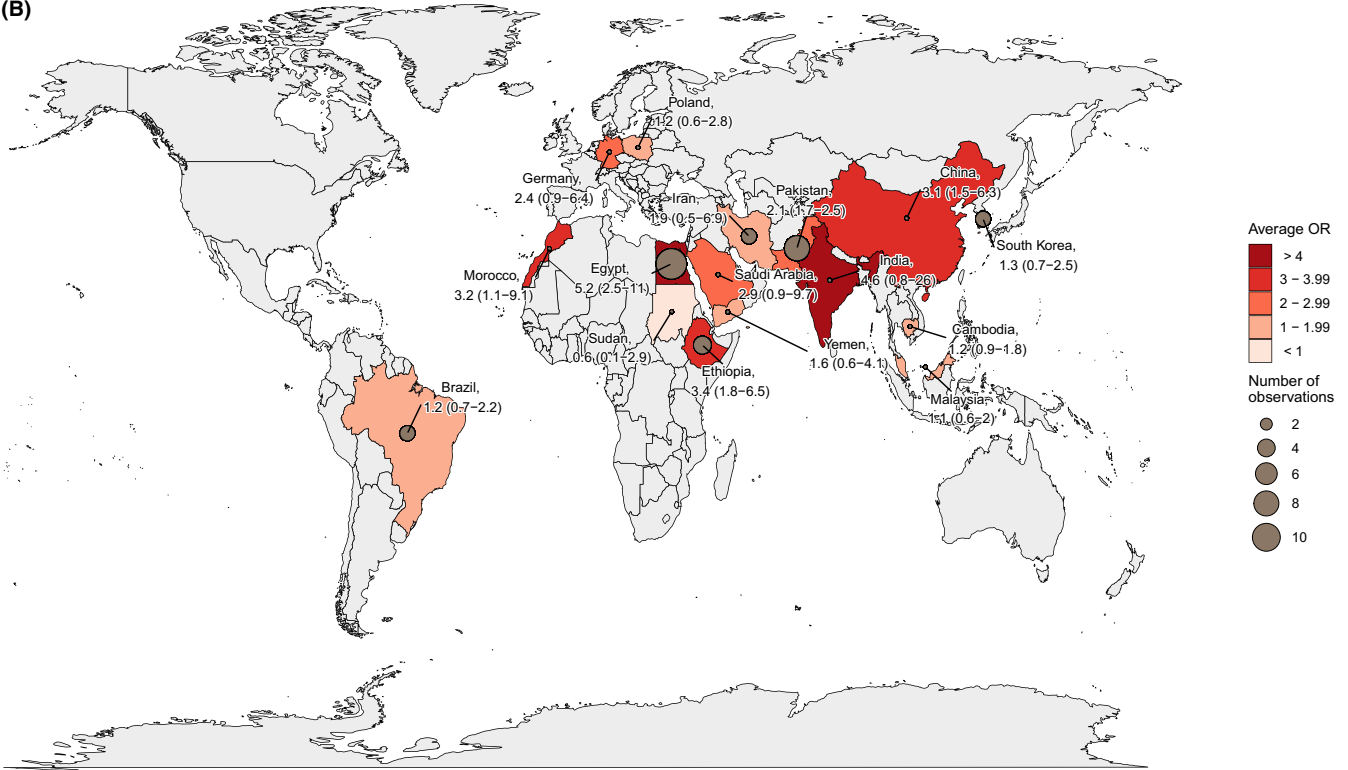


FIGURE 4 Maps of risks of HCV infection for: (A) Blood transfusion (B) Surgery in various countries. Brown points correspond to the number of observations (outcome measures) used to compute a given pooled OR. Each country is coloured based on the value of the estimated OR following a light red to dark red colour gradient. Values of average estimates are reported as well as their 95% CI. CI, confidence interval; HCV, hepatitis C virus; OR, odds ratio.

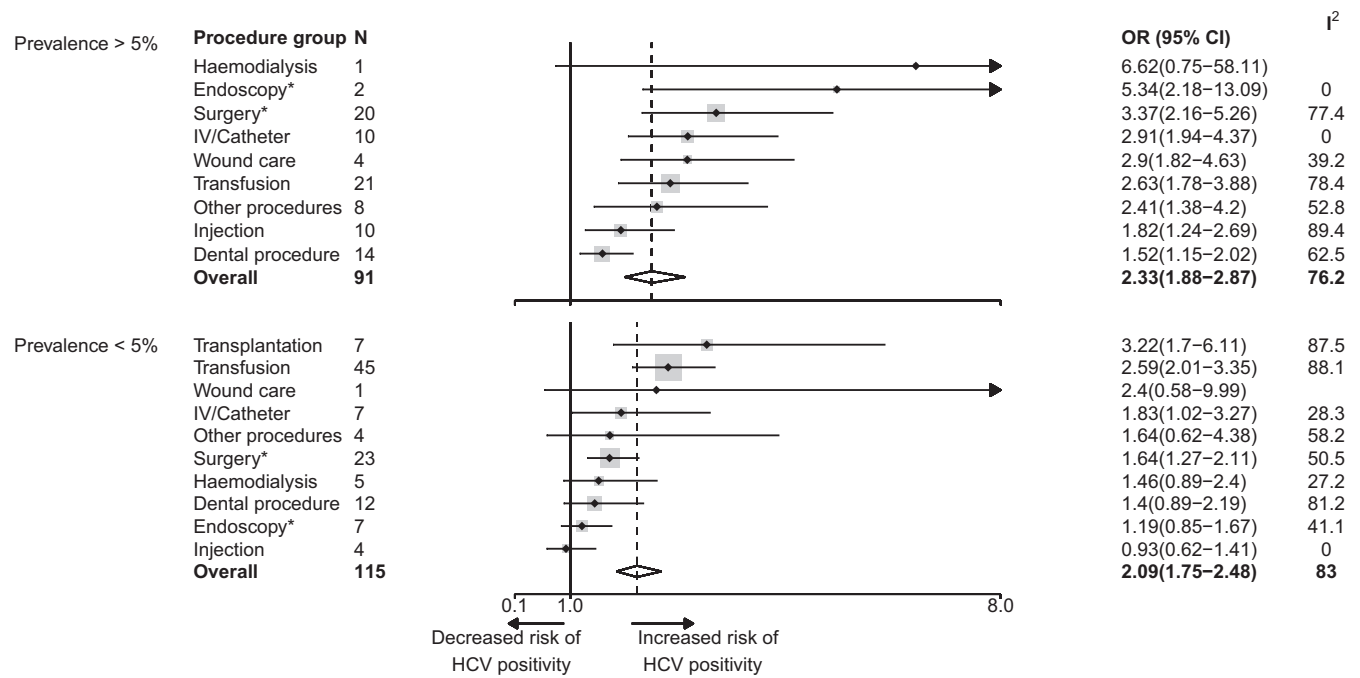


FIGURE 5 Forest plot reporting pooled OR estimates for HCV infection risk associated with different groups of iatrogenic procedures for high HCV prevalence countries (>5%) versus low HCV prevalence countries (<5%). The high prevalence group includes Egypt, Pakistan and Mali. Points correspond to average estimates and error bars correspond to 95% CI of these estimates. The solid line represents the limit for which OR = 1 and the dotted line the average value of the overall estimate. The total number of observations used for each pooled OR calculation is specified in the column N and the heterogeneity for each estimation is depicted in the column I². A given study could be used in the OR estimation of multiple procedures groups. Procedures are sorted based on the value of their associated mean estimate, from the highest to the lowest. There was no measure reported for transplantation in high HCV prevalence countries. *: procedures for which a significant difference was found between high and low prevalence countries; Blanks within the I² column correspond to the absence of heterogeneity because of procedure group counting only one observation. Overall difference between high and low prevalence countries: *p*-value = 0.33. CI, confidence interval; HCV, hepatitis C virus; OR, odds ratio.

contaminated and this index, except for the risk linked to endoscopy. The HAQ index may not be the right indicator to accurately reflect compliance with infection control intervention within hospitals. Second, there could be a high heterogeneity in this compliance between settings within the same country, that this index is unable to capture.

Our study carries several methodological as well as more study-related limitations.

First, no grey literature or papers in languages other than French or English were included in this review, resulting in a potential information loss. Some other methodological simplifications could have influenced our final results. In fact, pooling adjusted and non-adjusted measures could have led to overestimation of risks associated with some procedures. Our results also highly depend on the initial procedures classification we proposed, which may contribute to the high between-study heterogeneity we observed for many procedure groups. However, this classification was necessary due to the overall high number of unique procedures identified in the review. In particular, we could not take into account the different type of surgeries because we did not have this information in approximately 75% of the studies concerned by this procedure. Moreover, the high heterogeneity could also result from other sources (e.g. prevalence or infection control).

This study highlighted several caveats in the existing literature, notably through the risk of bias tool that we adapted from another review¹⁹; in particular, modifying the wording of criteria such as the outcome assessment method or confounders incorporation to better fit the specificities of our study. Overall, this bias analysis showed a lack of high-quality studies. On the one hand, 90% of studies presented at least a probably high bias concerning the assessment of exposure to hospital-based procedures, mostly using questionnaires to collect risk factors for HCV infection. This is consistent with the distribution of studies design, since almost 80% of studies were either cross-sectional or case-control studies. This over-representation of non-longitudinal designs may in particular have led to overestimated ORs of HCV infection associated with invasive iatrogenic procedures, due to differential recall bias between HCV-infected cases and controls. We investigated this through a separate assessment of pooled ORs in non-cohort and cohort studies, lower ORs were found in cohorts although differences were not significant. However, ORs for all other procedures, as well as overall ORs, did not differ significantly between cohorts and non-cohorts, supporting our choice to consider all study designs together. On the other hand, more than 50% of studies included a potential risk of bias due to incomplete or missing use of adjustment variables when estimating measures of association between HCV infection and iatrogenic procedures.

Overall, heterogeneity in measures associated with iatrogenic procedures was shown and may reveal potential publication bias. In particular, non-significant risk measures might have been voluntarily neglected resulting, again, in an overestimation of the risk associated with these two groups of procedures.

For some procedure groups, only few data were available, which led to important uncertainty in the associated OR estimates. Although there might not be a clear minimum number of studies to include within a meta-analysis,⁹⁶ it is recommended to have at least 10.⁹⁷ Almost half of procedure groups had less than 10 risk measures (and six of them were based on less than 10 studies), wound care being the procedure for which this number was the lowest with only five measures (and five studies). This lack of data could have interfered with the results of meta-regressions and having more studies could have given us more accurate results. Also, some procedures like surgery might have described operations during which multiple systematic procedures were performed and not taken into account (pre-surgical anaesthesia). More generally, we rarely had access to measures of risks associated with a unique realisation of each procedure. Patients might have undergone the same procedure multiple times but this information was not taken into account. In particular, the risk of getting HCV infected during haemodialysis is highly related to the duration of haemodialysis and the risk related to blood transfusion is somehow positively proportional to the number of received transfusions.⁹⁸ These limitations may have caused overestimation of the risk associated with hospital-based procedures.

In addition, the date of realisation of a procedure was not always available, and some measures might have been based on procedures performed a long time ago, thus leading again to an overestimation of the risk for some of them, as standard operating procedures have evolved. Indeed, we found the pooled OR of blood transfusions performed before 1998 to be higher than the pooled OR of undated/most recent blood transfusions, strongly suggesting that the risk was higher for older procedures—all the more so that the undated procedures could also have included old procedures.

In conclusion, despite the uncertainty in our estimates and the probable decrease in the general risk of HCV infection through hospital-based procedures over the last 20 years, this work shows that healthcare settings remain an important gateway of HCV infection and underline the importance of implementing efficient infection control.

Our results suggest a risk-based ranking for iatrogenic procedures, transplantation and wound care being the most at-risk procedures. In addition, they confirm the important role of blood screening in decreasing the risk of HCV infection during blood transfusion. We also show that the strength of association between HCV infection and iatrogenic procedures tend to be higher in high prevalence countries. This could partly be explained by the high global heterogeneity in infection and prevention control knowledge in healthcare workers, especially concerning blood-borne pathogens.⁹⁹

Two main tracks appear to be key to control HCV iatrogenic infections. First, knowledge of existing infection control interventions

should be improved in order to make them fully effective. Second, prevention efforts should be specifically targeted at high-risk procedures, such as transplantation, wound care or procedures involving IV injection, and in high HCV prevalence settings. In this regard, our work provides support to identify the procedures on which these efforts should be focused and is therefore of high value to assist decision makers in setting priorities. Our results may also prove useful for future modelling studies assessing the effectiveness and cost-effectiveness of control interventions to limit HCV transmission in healthcare settings.

In 2016, the WHO set targets for global HCV elimination as a public health problem by 2030—an 80% reduction in incidence and a 65% reduction in mortality from 2015 levels.¹⁰⁰ However, taking into account delays in implementation of the WHO recommendations and publication delays, studies published between 2016 and 2020 would probably not reflect the impact of these targets.

In order to reach WHO targets, high prevalence countries such as Egypt and Pakistan have engaged in elimination programmes based on large-scale test-and-treat campaigns.¹⁰¹ By helping efficiently scale up prevention interventions, our work has the potential to improve the cost-effectiveness of these campaigns, reaching the WHO targets faster and more easily.

AUTHORSHIP

All authors approved the final version of the manuscript.

Guarantor of article: Paul Henriot

AUTHOR CONTRIBUTIONS

Paul Henriot: Conceptualization (equal); formal analysis (lead); funding acquisition (lead); methodology (equal); visualization (lead); writing – original draft (lead); writing – review and editing (equal). **Mathieu Castry:** Writing – review and editing (equal). **Liem Binh Luong Nguyen:** Writing – review and editing (equal). **Yusuke Shimakawa:** Writing – review and editing (equal). **Kevin Jean:** Conceptualization (equal); formal analysis (equal); methodology (equal); supervision (equal); writing – review and editing (equal). **Laura Temime:** Conceptualization (equal); formal analysis (equal); methodology (equal); supervision (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST

We declare no competing interests.

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SUPPORTING INFORMATION

Additional supporting information will be found online in the Supporting Information section.

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